Nutrition and Health

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Nutrition and Health is a major resource of relevant, clinically based nutrition volumes for the professional that serve as a reliable source of data-driven reviews and practice guidelines.

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Mark L. Dreher

Dietary Fiber in Health and Disease

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Preface

Although dietary fiber (fiber)-rich diets have been crucial throughout human evolution for overall health, a comprehensive focus on fiber research did not begin until the 1970s with several articles in leading nutrition and medical journals regarding the *dietary fiber hypothesis*, which postulated that the global transition from fiber-rich traditional diets to low-fiber Western diets was a major cause of the rapid rise in rates of chronic diseases. Since the fiber hypothesis, there has been a continuously increasing level of research every year, making fiber and its effects on health among the most studied of any food component. Adequate fiber intake is being increasingly recognized for its "essential" role in human health in promoting a healthy colonic microbiota, energy metabolism, lowering blood lipids, maintaining immune and inflammatory homeostasis, digestive health, body weight regulation, cardiometabolic disease prevention, healthy aging, and reducing premature mortality. However, fiber is a major shortfall "nutrient" in global populations with high adherence to the Western dietary pattern, as only approximately 5–10% of these populations consume daily adequate fiber, which is a serious public health concern.

This book provides a comprehensive review of the latest research on the benefits of consuming adequate fiber for optimal human health and disease prevention. The book will go beyond fiber's traditional role in promoting intestinal motility and stool bulk to explain the relatively new research showing the important role of fiber in establishing and maintaining a healthy colonic microbiota, which is essentially a symbiotic human organ, associated with the regulation of immune and inflammatory homeostasis through its fermentation of fiber to bioactive short-chain fatty acids and health-promoting bacteria. There are extensive summaries and assessments of the major prospective cohort studies and randomized controlled trials (RCTs) and their meta-analyses on the role of dietary fiber in general health and cardiometabolic-related diseases. For general health, this book focuses on fiber's effects on the colonic microbiota, body weight regulation, digestive health, and aging. For chronic disease risk, the book focuses on digestive tract diseases or syndromes—irritable bowel syndrome, inflammatory bowel disease, and diverticular disease—and cardiometabolic-related diseases such as coronary heart disease, hypertension, chronic kidney disease, stroke, and type 2 diabetes. Figures are extensively used to highlight important findings.

Tables summarize fiber-rich food composition and findings from cohort studies and RCTs and their meta-analyses to help highlight the importance of fiber in health and disease prevention.

This book will serve as a very useful, comprehensive resource for dietitians, physicians, nurses, nutritionist, pharmacists, food industry scientists, academic researchers and educators, naturopathic doctors, health professionals, graduate and medical students, policy makers, and others interested in the role of fiber in health and disease.

Wimberley, TX, USA Mark L. Dreher, Ph.D.

Series Editor Page

The great success of the *Nutrition and Health* series is the result of the consistent overriding mission of providing health professionals with texts that are essential because each includes (1) a synthesis of the state of the science; (2) timely, in-depth reviews by the leading researchers and clinicians in their respective fields; (3) extensive, up-to-date fully annotated reference lists; (4) a detailed index; (5) relevant tables and figures; (6) identification of paradigm shifts and the consequences; (7) virtually no overlap of information between chapters but targeted, interchapter referrals; (8) suggestions of areas for future research; and (9) balanced, data-driven answers to patients' as well as health professionals' questions which are based upon the totality of evidence rather than the findings of any single study.

The series volumes are not the outcome of a symposium. Rather, each editor has the potential to examine a chosen area with a broad perspective, both in subject matter and in the choice of chapter authors. The international perspective, especially with regard to public health initiatives, is emphasized where appropriate. The editor(s), whose trainings are both research and practice oriented, have the opportunity to develop a primary objective for their book, define the scope and focus, and then invite the leading authorities from around the world to be part of their initiative. The authors are encouraged to provide an overview of the field, discuss their own research, and relate the research findings to potential human health consequences. Because each book is developed de novo, the chapters are coordinated so that the resulting volume imparts greater knowledge than the sum of the information contained in the individual chapters.

Dietary Fiber in Health and Disease, **edited as well as written by Mark L. Dreher, Ph.D.**, is a very welcome addition to the *Nutrition and Health* series and fully exemplifies the series' goals. This volume represents a critical, in-depth review of recent developments in the fields of fiber research and plant-based clinical studies and includes a timely analysis of the new data concerning the human microbiome. The volume is designed as an important resource for physicians in many clinical fields who see patients of all ages, nutritionists and dietitians, research and public health scientists, and related health professionals who interact with clients, patients, and/or family members. The volume provides objective and relevant information for professors and lecturers, advanced undergraduates and graduates, and researchers and clinical investigators who require extensive, up-to-date literature reviews, instructive tables and figures, and excellent references on all aspects of the role of fiber in human health and disease. This volume is especially relevant

as the number of research papers and meta-analyses in the clinical nutrition arena increases every year and clients and patients are very much interested in dietary components, such as fiber, for disease prevention. Certainly, the obesity epidemic remains a major concern especially as the comorbidities, such as the metabolic syndrome, type 2 diabetes, hypertension, and hyperlipidemia, are seen more frequently in individuals whose diets contain lower than recommended levels of fiber-rich foods.

Dr. Dreher, who has written every chapter in this volume, has made every effort to provide health professionals with the most up-to-date and comprehensive volume that highlights the key, well-accepted nutrition information available to date on the importance of fiber intake especially from plant-based diets, for many aspects of health and wellness. Clear definitions and distinctions are made concerning commonly asked patient questions such as what are the differences between the various types of dietary and supplemental fibers and their negative and positive health aspects. Explanations are also provided for the numerous types of vegetable-based diets that are often questioned by clients and patients and discussed by health professionals even among themselves as there are many findings in this field of nutrition research that are complex.

This volume includes review chapters that address the *essential* role of fiber in human health and its value in promoting a healthy colonic microbiota, modulating energy metabolism, lowering blood lipids, maintaining immune and inflammatory homeostasis, enhancing digestive health, body weight regulation, cardiometabolic disease prevention, increasing the potential for healthy aging, and reducing premature mortality. All chapters contain key points and keywords as well as targeted references, useful tables and figures, and a listing of recommended readings. In addition, the volume contains an extensive index and helpful appendices. The volume chapters are organized in a logical progression so that the reader can identify areas most relevant for their needs. All chapters and the entire volume are available online and are downloadable.

The author of the volume, Dr. Mark L. Dreher, Ph.D., is an internationally recognized expert in the field of dietary fiber research. Currently, he serves as president and chief science officer of Nutrition Science Solutions, LLC. He received his education in biochemistry and agricultural biochemistry and nutrition at UCLA and the University of Arizona. Dr. Dreher started his career as a research scientist in medical food product development at McGaw Laboratories in Irvine, California. Later, he served as assistant professor in food and nutrition at North Dakota State University, leading research on sunflower seeds, dry edible beans, and emerging grains. During his subsequent 30-plus-year career in the food, agricultural, and pharmaceutical industries, he held key roles in over 150 new healthy product development projects and food-based clinical research trials. He has authored or coauthored over 50 research journal articles and book chapters. Dr. Dreher has authored the *Handbook of Dietary Fiber* in 1987 and was an editor and contributor to the 2nd edition of the *Handbook of Dietary Fiber* and the *Complex Carbohydrates in Foods* book. He served as the chair of the International Life Sciences Institute—North American Food, Nutrition and Safety, and Carbohydrate Committees—and vice chair of the Functional Foods for Health Committee. Dr. Dreher was a member of the 1997 Joint FAO/WHO Expert Consultation

on Carbohydrate and Human Nutrition. He was a fellow in the National Center for Food and Agricultural Policy and Resources Leadership Program for the Future in Washington, DC. Dr. Dreher is an active member of the American Society for Nutrition, American Heart Association, Academy of Nutrition and Dietetics, and Institute of Food Technologists. Dr. Dreher is actively engaged in projects and research related to the role of healthy diets, whole foods, and phytochemicals in health, chronic disease prevention, and optimal aging.

Dr. Dreher provides extensive summaries and assessments of the major prospective cohort studies, randomized controlled trials, and relevant meta-analyses on the role of dietary fiber in general health and cardiometabolic-related diseases. The book focuses on fiber's effects on the colonic microbiota, body weight regulation, digestive health, and aging. Diseases and syndromes reviewed include those of the digestive tract including irritable bowel syndrome, inflammatory bowel disease, and diverticular disease. The interactions between metabolic diseases, such as type 2 diabetes, and the effects on the cardiovascular system are examined with emphasis on coronary heart disease, hypertension, chronic kidney disease, and stroke.

Part One: Overview

The four introductory chapters in the first part provide readers with the basics of dietary fiber including its sources. Fiber comes naturally from whole or minimally processed plant foods including whole grains, fruits, vegetables, legumes, and nuts or seeds eaten as part of a healthy diet, isolated from natural sources, such as β-glucan or psyllium, or from synthetic forms including polydextrose and methyl cellulose that can be consumed alone, added to processed foods, or consumed as part of dietary supplements. The evolution of humans from hunter/gatherers to agricultural societies to the development of cities in Greece and Rome through the Middle Ages, the Renaissance, the preindustrial and Industrial Revolution, and wars and, finally, the description of the Western-type diet versus the Mediterranean diet and other relevant historic developments are reviewed with an emphasis on fiber intakes during each period. The ten tables and figures and 90 references provide a broad background to help keep readers up-to-date on fiber basics. The second chapter reviews the benefits of dietary fiber. Fiber's role in digestive health that is linked to its promotion of laxation, fermentation to bioactive short-chain fatty acids, and maintenance of a healthy colonic microbiota ecosystem is discussed in Chap. 2. There is a review of the studies showing that high-fiber diets are associated with lowered risk of obesity and overweight, cardiovascular disease, hypertension as well as type 2 diabetes, and certain cancers and healthier aging. This chapter includes 8 important figures and 1 table, over 120 references, and an appendix that includes a list of 50 high-fiber foods. Chap. 3 delves into the role of fiber in maintaining the gut's microbiome. Dietary fiber is the primary energy source for maintaining the intestine's bacterial community, and fibers are the source of bioactive fermentation metabolites such as short-chain fatty acids including butyrate which are important in maintaining normal colonic and systemic bioactive balance. The three

detailed tables and nine figures summarize the data from observational studies and intervention trials concerning the effects of dietary fiber intakes on the microbiota and its health effects. Chap. 4 concentrates on the importance of the microbiota throughout the life span. Fiber-rich healthy dietary patterns promote the development of the neonate's immune function that helps to protect the colon from infections such as *C. difficile*. We learn that human milk contains >1,000 distinct fiber oligosaccharides. As the child and adolescent mature, adequate fiber intake is associated with reduced risk of inflammatory bowel disease and colorectal cancer as well as decreased risk of weight gain, obesity, type 2 diabetes and the metabolic syndrome, and breast cancer and is also seen to delay the aging process, including frailty and premature death. The chapter includes over 150 relevant references and 11 figures and a detailed table of relevant clinical studies.

Part Two: Fiber and the Gastrointestinal Tract

Part Two contains four chapters that examine the critical issues of constipation, irritable bowel syndrome, inflammatory bowel disease, and diverticular disease. Chap. 5 reviews the key role of fiber in preventing and alleviating constipation. The consumption of adequate fiber (>25 g/day), recommended fluid intake, and regular physical activity are each discussed. Fiber mechanisms associated with improved laxation and reduced constipation include increasing stool weight and bulk volume through the increase in volume contributed by fiber and the microbiota, reducing gas volume trapped in the stool, and increasing bowel movement frequency and quality. Adequate intake of fiber from whole cereal; fruits, including dried fruits; vegetables; and common fiber-rich food ingredients including polydextrose, psyllium, konjac glucomannan, guar gum, and inulin is discussed with regard to providing constipation relief. The three comprehensive tables and five figures provide valuable data for the reader. The next three chapters provide updates on the role of fiber in helping those with serious digestive diseases. Irritable bowel syndrome (IBS), examined in Chap. 6, is the most common gastrointestinal disorder occurring in people younger than 45 years. IBS is a chronic and relapsing functional colonic disorder characterized by abdominal pain, bloating, distension, and other changes in bowel habits that lack visible structural or anatomic abnormalities. Emerging research, reviewed in the seven tables and figures in the chapter, shows that the colon of the IBS patient contains colonic microscopic and molecular abnormalities including low-grade inflammation and neuronal hyperexcitability. Often, there is also microbiota dysbiosis associated with reduced bacteria diversity including lower levels of butyrate-producing bacteria and increased levels of pathogenic bacteria. Celiac disease (gluten sensitivity) and bile acid malabsorption may also be seen in IBS patients. Certain foods can be triggers for IBS symptoms. Avoidance of certain food components, called FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols), may reduce acute IBS symptoms. Chap. 7 describes inflammatory bowel disease (IBD), an intestinal inflammatory condition with two major phenotypes, ulcerative colitis and Crohn's disease. IBD is characterized by chronic relapsing

gastrointestinal tract inflammation including irritation and/or swelling that primarily affects the colon. Dietary patterns associated with low-fiber Western diets, high intake of animal protein, fatty foods, and sugar, may increase the risk of IBD onset. IBD develops as a result of interactions of genetic, epigenetic, environmental, and immunological factors. Individuals with IBD often have a genetic predisposition or epigenetic gene expression that can disrupt encoded proteins targeted to preserve the colonic mucosal barrier and lead to chronic colonic inflamed tissues. Clinical studies are tabulated and dietary recommendations for IBD patients are provided. Chap. 8 examines the influence of diet on diverticular disease. Diverticulae or colonic submucosal herniated pouches and/or diverticulosis' incidence increases with age affecting 5–10% of adults under 40 years, 30% by the age of 50 years, and 70% by the age of 85 years. Up to 80% of individuals with colonic diverticulae are asymptomatic and have few complications over their lifetime. The chapter summarizes the data from the 11 intervention trials that looked at the effects of fiber-rich diets, foods and/or supplements with wheat bran, bran crisps, psyllium, and methylcellulose, on the symptoms of diverticular disease. All six randomized controlled studies showed beneficial effects on symptoms and/or bowel function. The five open-label trials also showed beneficial effects that have been tabulated.

Part Three: Fiber's Role in Weight Management and Related Metabolic Consequences

The three chapters included in the third part review the potential for increased dietary fiber to reduce the risk of becoming overweight or obese and increase the potential for weight loss in overweight and/or obese individuals. We learn, in Chap. 9, that obesity is a complex multifactorial disease resulting from chronic increased energy intake and insufficient energy expenditure that is caused by many factors including but not limited to genetic, environmental, lifestyle, and emotional factors as well as age and sex of the individual. The chapter includes details of the major healthy diets including the Mediterranean diet, the DASH diet, and other healthy eating diets and summary tables of studies utilizing these diets and others in which obese and overweight individuals consumed higher than their normal levels of fiber. The chapter contains over 120 references, 6 in-depth tables, 15 descriptive figures, and two appendices. Chap. 10 concentrates on diets containing whole plant foods and their role in weight control. Whole plant foods are generally associated with lower energy density, reduced obesity, and decreased chronic disease risk than highly processed plant foods. However, these foods, including grains, fresh and dried fruits, vegetables, nuts, and pulses, vary widely in nutrient composition, energy density, and physical properties; the chapter includes over 100 references, 3 tables that review the relevant observational and intervention studies, 10 figures, and an informative appendix that describes these aspects of the food categories. Chap. 11 looks at the data that link high-fiber diets with beneficial effects in individuals with type 2 diabetes. The chapter reviews the prospective cohort studies that consistently show that increased intake of total fiber and cereal fiber and lower glycemic index and lower

glycemic load diets are effective in reducing diabetes risk. The meta-analyses of randomized controlled trials including people with prediabetes and diabetes are also tabulated as these show that increased fiber intake significantly lowers fasting blood glucose and glycosylated hemoglobin levels that are higher in diabetics and associated with many adverse cardiovascular effects. The chapter prioritizes three effects of increased fiber intake for the diabetic patient: reduction in the risk of obesity and visceral fat accumulation, promotion of a healthy microbiota ecosystem, and improved control of postprandial and fasting glycemic response. There are 135 references, 2 tables, 8 figures, and an additional appendix that help the reader understand the importance of higher fiber intakes for patients with type 2 diabetes.

Part Four: Fiber's Role in Aging with Emphasis on Cardiovascular and Cerebrovascular Outcomes

The five chapters in Part Four review the effects of aging on the gastrointestinal tract and the potential for increased fiber intake to reduce the risk of coronary heart disease, hypertension, chronic kidney disease, and stroke, all of which are major killers of seniors. Chap. 12, containing over 150 relevant references, reviews the data showing that adequate fiber intake (14 g/1000 kcal) is associated with healthy aging through its effects on lowering the risk of cardiovascular disease, stroke, weight gain, metabolic syndrome, type 2 diabetes, certain cancers, colonic microbiota dysfunction, frailty, and periodontitis. The chapter examines the dose-response meta-analyses that estimate the associations between increasing total fiber intake by 10 g/day and significant reduction in all-cause mortality by 10–11%, coronary heart disease by 11–20%, cardiovascular disease by 9%, and cancer, especially colorectal cancer, by 6–9%. Chap. 13 emphasizes the importance of fiber-rich diets to reduce the risk of coronary heart disease (CHD). CHD is still a leading cause of death globally, and its prevalence is expected to increase as the global population ages. CHD most often is seen after the fifth decade of life in men and the sixth decade of life in women. The major causative agent of CHD is higher than recommended levels of cholesterol in the blood that has been implicated in the development of atherosclerotic plaques in coronary vessels. Lifestyle changes recommended for those with high cholesterol levels include adopting a diet low in saturated and *trans* fatty acids; incorporating fiber, antioxidants, plant sterols, and stanols into the diet; exercising regularly; not smoking; and maintaining a healthy weight. The chapter, with nine important tables and figures, examines the scientific evidence from controlled intervention and prospective studies that link fiber-rich diets from whole plant foods; viscous, soluble fiber supplements; and/or food ingredients such as β-glucan or psyllium with lowering elevated blood lipids and reducing CHD risk. Related to Chaps. 13 and 14 reviews the association between fiber intake levels and risk of high blood pressure. There is a strong link between hypertension and subsequent CHD that may be the result of high cholesterol levels seen in both conditions. Moreover, both conditions are also found in patients with excess body weight. Overweight and obesity are associated with increased activity of the renin-angiotensin-aldosterone system, insulin

resistance, and reduced kidney function associated with salt-sensitive hypertension. Rates of hypertension are twice as likely to occur in obese (40%) vs. normal weight (20%) individuals. Thus, as has been reviewed in earlier chapters, higher fiber intakes are associated with reduced risk of obesity and other risk factors for hypertension that are outlined in the tables within the chapter. Hypertension and obesity are also major risk factors for chronic kidney disease (CKD) that is discussed in Chap. 15. The chapter concentrates on patients with CKD and its stages and reviews the literature concerning the specific needs of CKD patients for low phosphorus intakes and other dietary considerations linked to fiber. The final chapter in this part, Chap. 16, examines the factors associated with increasing the risk of stroke as well as the factors associated with reducing its risk. Stroke risk is linked to poor diet, low physical activity, and smoking, high systolic blood pressure, high body mass index (BMI) used to define obesity, high fasting plasma glucose, and above-normal total cholesterol. In addition to several other dietary factors, prospective studies consistently show that fiber intake is inversely associated with a 12% lower stroke risk per 10 g/day total fiber intake. Cereal fiber appears to be the most effective fiber source.

Part Five: Fiber's Role in Cancer Prevention and Survival

Chapters 17 and 18 provide objective, up-to-date reviews of the associations between fiber intakes and colorectal and breast cancers. As with the preceding chapters, there is an examination of the known or suspected dietary-related risk factors. The dietary risk factors for colorectal cancer reviewed in Chap. 17 include higher intakes of alcohol, total dietary fat and red meat intake, and lower intakes of dietary fiber, calcium, and folate. With regard to fiber, the mechanisms by which it can lower colorectal cancer risk are reviewed including the ability of fermentable fiber to lower colonic pH and inhibit pathogenic bacteria, increase butyrogenic bacteria to promote healthy colonic mucosal cells, reduce colon inflammation, and inhibit cancer cell proliferation and facilitate apoptosis. Insoluble fiber reduces exposure to carcinogens by bulking stools and binding carcinogens to reduce their colon and rectum exposure. The chapter, containing 100 important references, tabulates the convincing evidence that higher intake of fiber-rich foods reduces colorectal cancer risk and that low-fiber intake is associated with an increased risk of colorectal cancer. Data are organized in three informative tables and five figures. Chapter 18 looks at all of the studies linking fiber intake with breast cancer risk, both positive and negative studies, and tabulates these in six relevant tables and seven figures. The chapter, with more than 120 references, examines the types of breast cancer and the genetics behind these differences and clinical studies on breast cancer primary prevention as well as secondary prevention of recurrence. The mechanisms by which high dietary fiber may reduce breast cancer risk and improve survival include the reduction in the risk of excess weight and/or abdominal fat gain, lowering of elevated C-reactive protein associated with increased inflammation, and reduction in insulin resistance and circulating estrogen levels.

Conclusions

Of importance to physicians and other health professionals who provide advice concerning diet, foods, nutrition, and clinical management of nutritionally related conditions and/or diseases is the identification of reputable sources of nutrition information. *Dietary Fiber in Health and Disease* provides chapters that review and integrate these relevant resources. The volume examines the national food guides that review the components of a healthy diet. These recommendations may differ somewhat across nations due to the availability of local plants and mixtures of plant- and animal-derived food sources; however, virtually all recommendations include higher than currently consumed concentrations of fiber. The volume provides clear definitions of the types of fibers including soluble, insoluble, and fermentable and the clinical data linking these types to relevant diseases. This comprehensive volume examines patient-related topics including chapters on the gastrointestinal tract including laxation and constipation and diseases of the colon; obesity and weight control; diabetes; heart, kidney, cognitive, and immune functions; and relevant cancers including breast and colon and provides appendices, tables, and figures that give physicians tools that can help to alter patient dietary habits as well as reviews of the many types of dietary fiber supplements. Patients and consumers are concerned about many claims that are made for common fibers found in foods, such as juice drinks, soy products, and novel fruits, and genetic modification of foods. This volume examines these and other provocative areas of diet information. There are more than a dozen chapters that provide clinically relevant information on risk reduction as well as the use of fiber for the reduction of treatment-related adverse effects on gut function. The 18 chapters within this valuable volume provide a wealth of timely information for health providers, medical students, graduate students, nurses, dietitians, and other related health professionals.

Dr. Mark Dreher is an internationally recognized leader in the field of human nutrition with more than 30 years of research in the importance of adequate fiber intake for the reduction in the risk of obesity and critical clinical outcomes reviewed in this comprehensive volume. Dr. Dreher is a proven excellent communicator and has worked tirelessly to develop this volume that is destined to be the benchmark in the field of clinical nutrition because of its extensive covering of the most important aspects of the complex interactions between diet, health, and disease. Hallmarks of all of the chapters include complete definitions of terms with the abbreviations fully defined for the reader and consistent use of terms between chapters. Key features of this comprehensive volume include the informative key points and keywords that are at the beginning of each chapter and relevant references at the end of each chapter. The editor has added two useful appendices including a detailed table of major fiber sources that detail the amount of fiber per portion, calories, and energy density and a second table that includes the important aspects of the six most common diet patterns including vegan diets and the Mediterranean diet. The volume also contains more than 180 detailed tables and figures; an extensive, detailed index; and more than 1700 up-to-date references that provide the reader with excellent sources of worthwhile information about the role of fiber as part of overall nutrition and food intake, fiber's

value beyond the standard definition of the nutritional value of foods, human physiology, and pathophysiology of the diet-related morbidities and comorbidities that have been linked to low-fiber diets.

In conclusion, *Dietary Fiber in Health and Disease*, **edited as well as written by Mark L. Dreher, Ph.D.**, provides health professionals in many areas of research and practice with the most up-to-date, organized volume on well-accepted, data-driven nutrition research associated with the importance of fiber intake in major chronic disease reduction that is often discussed by patients with their healthcare provider. This volume serves the reader as the benchmark in this complex area of interrelationships between fiber and the microbiome and fiber-rich foods and body weight, type 2 diabetes, cardiovascular and cerebrovascular health, diseases of the gastrointestinal tract, kidney and brain function, and reduction in the risk of colorectal and breast cancers. Moreover, the interactions between obesity, genetic factors, and the numerous comorbidities are clearly delineated so that practitioners as well as patients and clients can better understand the complexities of these interactions. Dr. Dreher is applauded for his efforts to develop this volume with the firm conviction that nutrition research serves as an essential source of important data for all health professionals. This excellent text is a very welcome addition to the *Nutrition and Health* series.

Morristown, NJ, USA Adrianne Bendich, Ph.D., F.A.C.N., F.A.S.N.

About the Series Editors

Adrianne Bendich, Ph.D., F.A.S.N., F.A.C.N., has served as the **"Nutrition and Health" Series Editor** for more than 20 years and has provided leadership and guidance to more than 200 editors that have developed the 80+ well-respected and highly recommended volumes in the series.

In addition to **"Dietary Patterns and Whole Plant Foods in Aging and Disease," edited as well as written by Mark L. Dreher, Ph.D.,** major new editions published in 2012–2017 include the following:

1. **Dietary Fiber in Health and Disease,** edited as well as written by Mark L. Dreher, Ph.D., 2017
2. **Clinical Aspects of Natural and Added Phosphorus in Foods**, edited by Orlando M. Gutierrez, Kamyar Kalantar-Zadeh, and Rajnish Mehrotra, 2017
3. **Nutrition and Fetal Programming**, edited by Rajendram Rajkumar, Victor R. Preedy, and Vinood B. Patel, 2017
4. **Nutrition and Diet in Maternal Diabetes**, edited by Rajendram Rajkumar, Victor R. Preedy, and Vinood B. Patel, 2017
5. **Nitrite and Nitrate in Human Health and Disease, Second Edition**, edited by Nathan S. Bryan and Joseph Loscalzo, 2017
6. **Nutrition in Lifestyle Medicine**, edited by James M. Rippe, 2017
7. **Nutrition Guide for Physicians and Related Healthcare Professionals, Second Edition**, edited by Norman J. Temple, Ted Wilson, and George A. Bray, 2016
8. **Clinical Aspects of Natural and Added Phosphorus in Foods**, edited by Orlando M. Gutiérrez, Kamyar Kalantar-Zadeh, and Rajnish Mehrotra, 2016
9. **L-Arginine in Clinical Nutrition**, edited by Vinood B. Patel, Victor R. Preedy, and Rajkumar Rajendram, 2016

10. **Mediterranean Diet: Impact on Health and Disease**, edited by Donato F. Romagnolo, Ph.D. and Ornella Selmin, Ph.D., 2016
11. **Nutrition Support for the Critically Ill**, edited by David S. Seres, MD, and Charles W. Van Way, III, MD, 2016
12. **Nutrition in Cystic Fibrosis: A Guide for Clinicians,** edited by Elizabeth H. Yen, M.D., and Amanda R. Leonard, MPH, RD, CDE, 2016
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38. **Chocolate in Health and Nutrition**, edited by Dr. Ronald Ross Watson, Dr. Victor R. Preedy, and Dr. Sherma Zibadi, 2012
39. **Iron Physiology and Pathophysiology in Humans**, edited by Dr. Gregory J. Anderson and Dr. Gordon D. McLaren, 2012

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Chapter 1
Introduction to Dietary Fiber

Keywords Dietary fiber • Whole plant foods • Fiber-rich diets • Fiber supplements • Fiber history • Health benefits • Functional properties • Biological mechanisms • Adverse effects

Key Points

- Over millions of years of human evolution, dietary fiber (fiber) has played an important role in maintaining healthy colonic microbiota and laxation, energy and cardiometabolic processes, and immune and inflammatory signaling required for human health and chronic disease prevention.
- It is estimated that approximately 95% of populations consuming Western diets eat an inadequate daily fiber level. This fiber gap can adversely affect human health via increased risk of weight gain and dysfunctional colonic microbiota, contributing to global obesity and chronic disease pandemics.
- Fiber comes from whole or minimally processed plant foods including whole grains, fruits, vegetables, legumes, nuts, and seeds eaten as part of a healthy diet; isolated from natural sources (e.g., β-glucan, psyllium); or from synthetic forms (e.g., polydextrose, methylcellulose) added to processed foods or consumed as dietary supplements. Fiber food functionality or health effects depend on the specific fiber's composition, physical properties, and degree and rate of fermentation in the colon.
- The effects of increased fiber intake and its fermentation metabolites can result in reduced risk of obesity, cardiometabolic chronic diseases and related premature mortality, and improved odds for healthy aging.
- No tolerable upper limit has been set for fiber intake in healthy individuals, but excessive intake of some highly fermentable fibers may increase risk of flatulence and gastrointestinal distress in sensitive individuals. When increasing fiber intake, it is recommended to do so gradually along with increasing fluid intake to help allow the gastrointestinal tract to adapt and to take medication at least 1 h before or 2 h after fiber-rich foods or supplements are consumed to avoid possible fiber-drug interactions.

Introduction

Although dietary fiber (fiber) has played an important role in human diets, food processing, and health since the earliest humans [1–12], today it is one of the most critical shortfall "nutrients" in Western diets [1–7]. Over millions of years, humans evolved with high-fiber diets, which helped maintain healthy colonic microbiota and laxation, balance energy and cardiometabolic processes, and promote optimized immune and inflammatory signaling required for human health and weight control [6–11].

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Intake of fiber, which is the main source of microbiota-accessible carbohydrates in the diet of adult humans, is now inadequate in the Western diet when compared with both the diets consumed in non-industrialized populations and that of our ancestors [6]. This fiber intake gap, especially since the 1970s, provides insufficient fiber nutrients for the colonic microbiota, leading to a less diverse and healthy microbiota but also to a reduction in the production of fermentation metabolites important for maintaining healthy physiological and immunological functions. Consequently, the lower fiber Western diet has been a major trigger in increasing the risk of microbiota dysbiosis and excess energy intake, which has contributed to the rise of global obesity and chronic disease pandemics. The objective of this chapter is to provide an overview of fiber's history, definition, components, intake, sources, functional properties, health mechanisms, and potential adverse effects.

Fiber Background

Preagricultural Diets

The preagricultural or Paleolithic period, characterized by the hunting and gathering of foods, lasted around 2.5 million years and ended about 10,000 years ago with the emergence of agriculture [8–11]. These preagricultural diets primarily consisted of meat, fish, and high-fiber plant foods, primarily from uncultivated fruit and vegetables that contained markedly higher-fiber content (average >13 g fiber/100 g) than today's commercial varieties (average <4 g fiber/100 g) and also occasionally included wild cereal grains, nuts, and seeds when available. These high-fiber diets are believed to have played an important role in maintaining a healthy colonic microbiota and laxation, energy and cardiometabolic processes, and immune and inflammatory signaling required for human health and noncommunicable disease prevention [1–12]. The Western diet, which is now consumed by a majority of the populations in developed countries, represents a major change in diet composition from the preagricultural diet (Table 1.1). The low-fiber Western diet and lifestyle has been labeled a "disease of

Table 1.1 Daily nutritional intake of preagricultural vs. current Western dietary pattern [8–11]

Nutritional components	Preagricultural diet	Current Western diet
Diet energy density (kcal/g)	Low	High
Dietary bulk (satiating)	More	Less
Sugar and sweeteners (% energy)	Limited amount of honey	17%
Glycemic load	Low	High
Grain products	Low	High
Fruit, vegetables, and nuts (% energy)	65%	8%
Fiber intake (g/day)	50–100	<15–17
Protein intake (% energy)	37% from lean game, eggs, fish, shellfish, or nuts	15% from meat, poultry, dairy, fish, eggs, legumes or nuts
Fat intake (% energy)	22	32
n-6:n-3 fatty acids	1:1	9.8:1
Sodium (mg)	800	>3000
Potassium (mg)	10,000	2500
Vitamin C	600	100
Vitamin E (mg)	33	9
Vitamin A (mg retinol eq)	3000	1000
Calcium (mg)	1900	900
Physical activity (kcal/d)	>1000	Sedentary (<150–490)

civilization" because of its association with the rapid increase in obesity and noncommunicable disease rates, especially since the 1970s [12].

Early Pioneers and Events in the Evolution of Fiber and Health

Fiber has been recognized as an important component in human health and food supply since the early Greek and Persian physicians (350 BC–600 AD) who were among the earliest to recognize the benefits of roughage (fiber) [13, 14]. Hippocrates in 371 BC first mentioned coarse bran (fiber) and observed that the human body worked better with bread made from course bran than fine flour [6, 7]. Subsequently, a number of Greek and Persian physicians further advised in the medical literature of the day that bread with bran was good for the bowels (e.g., promoting regularity and healthier stool properties). Fiber-rich grain products were the primary source of baked goods until 1874 when the invention of the steel roller milling system provided an economical process to convert whole grain to white flour at an affordable price [15]. This resulted in a major shift to today's lower fiber bakery products, which promote mindless eating behavior as, without fiber, they are less satiating. With the expansion of the availability of refined, low-fiber grain products, physicians and health advocates in the late nineteenth and early twentieth centuries began to educate the public and develop products to encourage increased whole grain and bran consumption. In the 1880s, the British doctor. Thomas Allinson championed the health benefits of whole grain and bran through books, including one titled *Wholemeal Bread* [16]. John Harvey Kellogg became a leading advocate of bran's health benefits, and in 1915 Kellogg introduced Bran Flakes, the first high-fiber cereal, promptly followed by the introduction of All Bran™ 1 year later [17]. In 1936, Dr. Ted Dimmock published research on the effects of wheat bran for the relief of constipation and hemorrhoids [13–15]. During World War II, Dr. Thomas Cleave successfully treated constipated British sailors with bran and proposed the hypothesis that Western diets, rich in refined carbohydrates and low in fiber, were the root cause of rapidly emerging noncommunicable diseases [13–15]. In 1953, dietary fiber was first used as a collective term for the nondigestible constituents that make up plant cell walls by Dr. Hipsley in a study on pregnant women showing that higher dietary fiber was associated with lower toxemia incidence [18]. From 1945 through the1960s, Dr. Alexander Walker published numerous articles on his medical research in important medical journals on the effects of diet changes in populations moving from rural to urban areas in South Africa [19]. He observed that increased sugar and meat consumption and decreased fiber intake by the new urban populations were directly related to noncommunicable diseases. In the 1960s and 1970s, Drs. Trowell, Burkitt, Walker, and Painter first developed the *dietary fiber hypothesis* [13, 14]. They postulated that fiber intake was inversely associated with colon cancer, heart diseases, diabetes, and other Western diseases. Their dietary fiber hypothesis stimulated increased fiber research projects in health and disease, nutrition, analytical methods, and food technology, and now fiber is one of the most widely studied and published food components.

Fiber Definition, Components, and Methodology

Early methods measuring crude fiber were developed in the mid-1800s to get a rough check of the indigestible content of animal feeds, but this methodology only quantified a fraction of the fiber content as it is now defined [18]. The 1970s dietary fiber hypothesis stimulated the development of better dietary fiber definitions and methodology more appropriate for humans [20]. In 1981, all the international analytical associations and interested groups began a 28-year long process of developing an international consensus on definition of and methodology for dietary fiber, which led to the 2009 CODEX Alimentarius Commission establishment of international dietary fiber definition standards

[18, 20–22]. The Association of Official Agricultural Chemists (AOAC) Official Method of Analysis enzymatic-gravimetric method is the de facto working analytical measure of total dietary fiber until further method update based on the CODEX Alimentarius Commission definition is established [22]. Dietary fiber is defined basically as carbohydrates with three or more monomeric units, which are not hydrolyzed by the endogenous enzymes of the human small intestine, including naturally occurring non-starch polysaccharides and oligosaccharides found in food (e.g., cellulose, hemicellulose, gums, and mucilages), isolated from food raw material (e.g., resistant oligosaccharides, dextrins, maltodextrins and starch, inulin, pectins, beta-glucan, psyllium, and oligofructans), and synthetic forms (e.g., polydextrose, methyl cellulose) [21, 22]. As fiber is not absorbed by the small intestine by definition, there is no validated direct blood biochemical assay that reflects fiber dietary intake and health status [1].

Fiber Adequate Intake

Adequate fiber intake levels were established by a number of international health authorities in the first decade of the twenty-first century based especially on fiber's heart health and laxation benefits. In 2002, the US National Academy of Sciences Institute of Medicine set the adequate intake for fiber at 14 g/1000 kcal, which translates to 38 g/day for men and 25 g/day for women, based on the intake level observed to protect against coronary heart disease (CHD) [1]. Adequate daily total fiber intake by age and gender is summarized in Fig. 1.1. The adequate fiber intake for children is similar to adult recommended intakes [1]. A 2003 World Health Organization report recommended a population goal for the intake of fiber of at least 25 g/day from fiber-rich foods (e.g., fruit, vegetables, and whole grains) [2]. This population goal is based on evidence associating adequate intake of fiber with improved health compared to low-fiber Western diets for decreased risk of weight gain (convincing), diabetes type 2 (probable), and cardiovascular diseases (probable) [2]. In 2010, the European Food Safety Authority (EFSA) panel recommended adult fiber intake for (1) bowel function, with 25 g/day deemed to be adequate for normal laxation in adults, and (2) health benefit to reduce risk of coronary

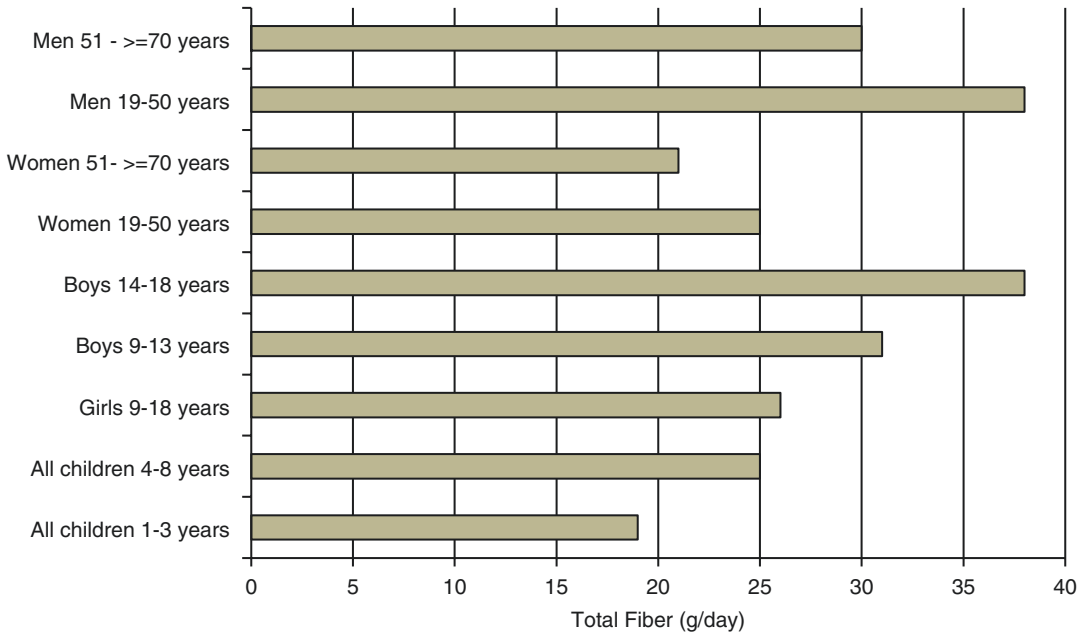

Fig. 1.1 Adequate daily total fiber intake by age and gender [1]

heart disease, type 2 diabetes, and weight gain with the consumption of diets containing fiber-rich foods at fiber intakes of ≥25 g/day [3]. Recommended adult intake of fiber for most developed countries ranges from 30–35 g/day for men and 25–32 g/day for woman [7]. For children, recommendations vary from country to country with a general range of the recommended grams of fiber equaling the child's age plus 5 g of additional fiber. For adolescents recommendations are 20–26 g/day for girls and 24–38 g/day for bodys.

Fiber Regulatory

Based on the recognized health benefits of fiber, a number of international fiber-related regulations were enacted. For health claims, two examples include the following: (1) In 1997, the US FDA finalized health claims for soluble fiber from certain foods and reduced risk of coronary heart disease, based on a significant scientific agreement, which was subsequently affirmed by the EFSA and other international authorities [23, 24]. For caloric value, Health Canada published labeling and advertising policy establishing 2 kcal/g (8 kJ/g) for fiber in 2012 [25]. EFSA, US, and Australian/New Zealand health claims associated with fiber are related to promoting bowel fecal bulk or regularity, maintaining or lowering blood cholesterol and post prandial glycemic response, and reducing CHD risk [7]. A claim that a food is high in fiber can be typically made on products that contain at least 6 g fiber/100 g or at least 3 g fiber/100 kcals (418 kJ). A "source of fiber" requires at least one half the amounts required for a high fiber claim [7].

Current Fiber Intake Levels

In developed countries, Germany, Hungary, and Finland have the highest average fiber intake ranging from 24–25 g/day for men and 21–23 g/day for women [7]. Other countries are far behind with average intakes of ≤ 20 g/day for men and ≤ 15 g/day for women. The typical US fiber intake is consistently reported in an ongoing national survey to be about half the recommended level of fiber intake and ranges from 15 to 17 g/day. Only approximately 5% of the population meet the adequate intake of 25 g/day for women and 38 g day/day for men (Fig. 1.2) [5, 26, 27]. Although males tend to consume higher fiber intakes than females, because of their higher energy intakes, females have higher fiber dietary density than their male counterparts. Fiber dietary density also tends to increase in adults over 60 years of age compared to younger adults [27]. Globally grain products are the largest source of fiber followed by vegetables, potatoes, and fruits [7].

Fiber Sources

Whole Plant Foods

Adequate fiber intakes can be achieved by substituting at least one whole or minimally processed plant food (e.g., whole grains, legumes, vegetables, fruits, and nuts and seeds) for a highly processed or high glycemic, lower fiber food or food high in added sugar and fat at each meal or snack [5]. Grocery stores offering samples of fresh fruits and vegetables to shoppers entering the store had 25% higher sales of those foods compared to stores with no sampling promotions [28]. The fiber and energy density of the top 50 higher fiber whole or minimally processed plant foods are listed in Table 1.2 [5, 29–31]. Higher fiber whole or minimally processed foods tend also to be rich sources

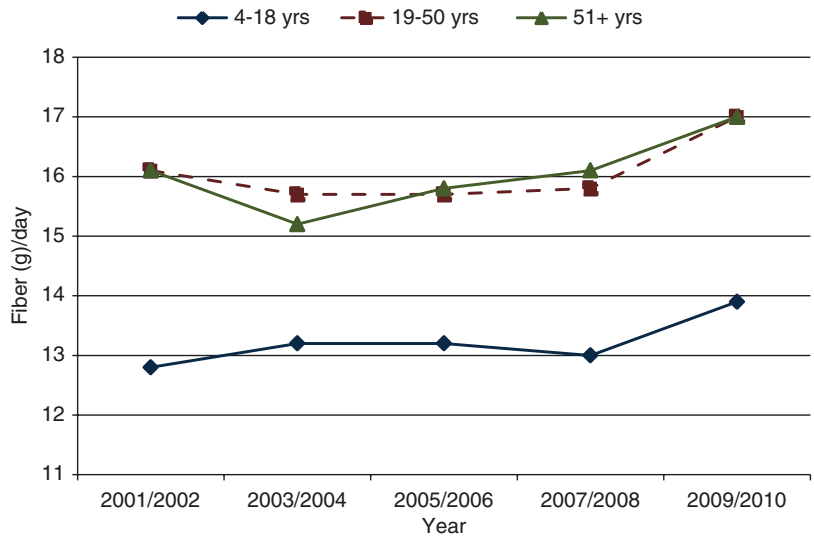

Fig. 1.2 Ten-year trend in mean fiber intake by age group in the USA [26]

Table 1.2 Fifty high-fiber whole or minimally processed plant foods ranked by amount of fiber per standard food portion [5, 29–31]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds, whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5

Table 1.2 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

of bioactive nutrients and phytochemicals, which may work synergistically with fiber to promote health (Table 1.3) [31–40]. Highly processed plant foods tend to be less potent at promoting health. Whole apples are more effective at lowering total cholesterol than apple juice because of the loss of pectin during the juicing process (Fig. 1.3) [41]. Compared with whole fruits, 100% fruit juices are very low in fiber with similar levels of sugar and total calories (energy) (Table 1.4) [42].

Table 1.3 Estimated range of energy, fiber, nutrients, and phytochemicals composition of whole or minimally processed foods/100 g edible portion [31–40]

Components	Whole grains	Fresh fruit	Dried fruit	Vegetables	Legumes	Nuts/seeds
Nutrients and phytochemicals	Wheat, oats, barley, brown rice, whole grain bread, cereal, pasta, rolls, and crackers	Apples, pears, bananas, grapes, oranges, blueberries, strawberries, and avocados	Dates, dried figs, apricots, cranberries, raisins, and prunes	Potatoes, spinach, carrots, peppers, lettuce, green beans, cabbage, onions, cucumber, cauliflower, mushrooms, and broccoli	Lentils, chickpeas, split peas, black beans, pinto beans, and soy beans	Almonds, Brazil nuts, cashews, hazelnuts, macadamias, pecans, walnuts, peanuts, sunflower seeds, and flaxseed
Energy (kcal)	110–350	30–170	240–310	10–115	85–170	520–700
Protein (g)	2.5–16	0.5–2.0	0.1–3.4	0.2–5.0	5.0–17	7.8–24
Available carbohydrate (g)	23–77	1.0–25	64–82	0.2–25	10–27	12–33
Fiber (g)	3.5–18	2.0–7.0	5.7–10	1.2–9.5	5.0–11	3.0–27
Total fat (g)	0.9–6.5	0.0–15	0.4–1.4	0.2–1.5	0.2–9.0	46–76
SFA[a] (g)	0.2–1.0	0.0–2.1	0.0	0.0–0.1	0.1–1.3	4.0–12
MUFA[a] (g)	0.2–2.0	0.0–9.8	0.0–0.2	0.1–1.0	0.1–2.0	9.0–60
PUFA[a] (g)	0.3–2.5	0.0–1.8	0.0–0.7	0.0–0.4	0.1–5.0	1.5–47
Folate (μg)	4.0–44	<5.0–61	2–20	8.0–160	50–210	10–230
Tocopherols (mg)	0.1–3.0	0.1–1.0	0.1–4.5	0.0–1.7	0.0–1.0	1.0–35
Potassium (mg)	40–720	60–500	40–1160	100–680	200–520	360–1050
Calcium (mg)	7.0–50	3.0–25	10–160	5.0–200	20–100	20–265
Magnesium (mg)	40–160	3.0–30	5.0–70	3.0–80	40–90	120–400
Phytosterols (mg)	30–90	1.0–83	N/A	1.0–54	110–120	70–215
Polyphenols (mg)	70–100	50–800	N/A	24–1250	120–6500	130–1820
Carotenoids (μg)	N/A	25–6600	0.6–2160	10–20,000	50–600	0.0–1200

[a]SFA (saturated fat), MUFA (monounsaturated fat), and PUFA (polyunsaturated fat)

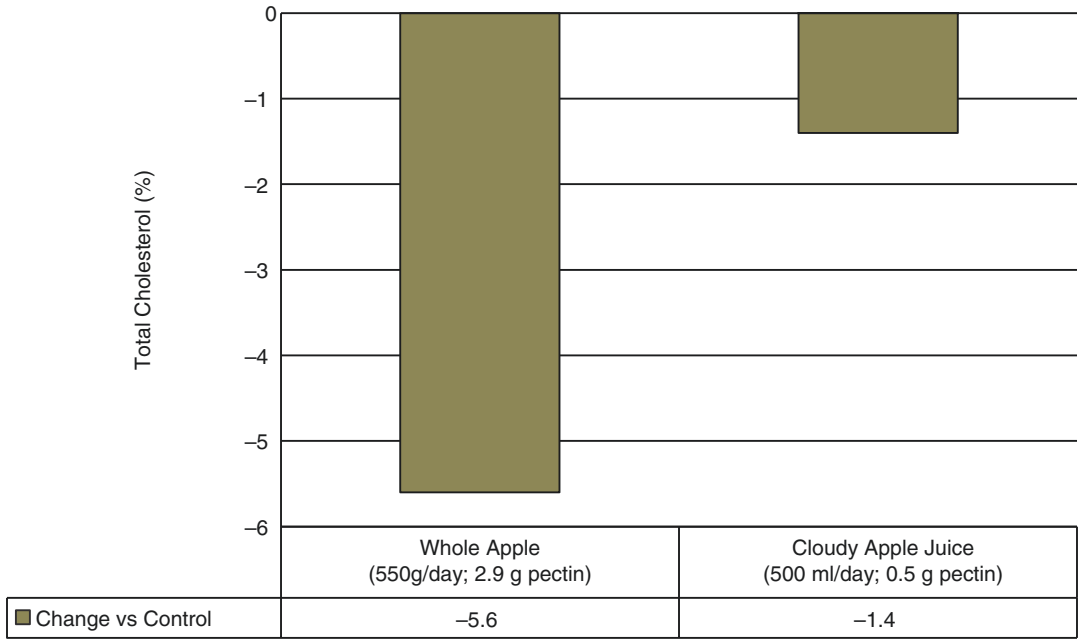

Fig. 1.3 Effect of whole apple vs. cloudy juice intake on lowering total cholesterol % after 4 weeks ($p = 0.064$) [41]

Table 1.4 Whole fruits compared to 100% fruit juices [42]

Fruit	Apple		Orange		Grape		Cranberry	
Type	Fruit	Juice	Fruit	Juice	Fruit	Juice	Fruit	Juice
Dietary fiber (g/100 g)	2.4	0.2	2.4	0.2	0.9	0.2	3.6	0.1
Total sugar (g/100 g)	10.4	11.9	9.4	10.4	16.3	14.2	4.3	12.1
Energy (kcal/100 g)	52	57	47	56	67	60	46	46

Healthy Dietary Patterns

High adherence to healthy dietary patterns, including those based on the US Dietary Guidelines, the Dietary Approaches to Stop Hypertension (DASH), Mediterranean diet (MedDiet), lacto-ovo vegetarian, or healthy vegan diets, is based on the same core idea of increasing intake of whole or minimally processed plant foods with, for example, fruits and vegetables covering at least half the plate (Table 1.5) [4, 31, 32, 43]. All of these dietary patterns meet or exceed the US adequate intake of fiber and double the usual intake of fiber in the Western diet (Fig. 1.4).

Fiber Ingredients and Supplements

The health effects of fiber ingredients and supplements cannot be assumed to be equivalent to those of fiber-rich whole or minimally processed plant foods unless directly confirmed by randomized controlled trials (RCTs) [1, 44, 45]. This is especially true for many supplements because they are added to the diet rather than used as replacements for low-fiber, high glycemic refined foods [44, 45]. Excessive processing in the preparation of fiber ingredients and supplements may change the three-dimensional (3-D) fiber plant cell wall matrixes to adversely affect fiber functionality and health benefits including changes in solubility, viscosity, gel formation, particle size (for insoluble fiber), and degree/rate of fermentation, which can reduce health clinical efficacy depending on the degree of processing [44–46]. However, many isolated soluble, viscous fiber ingredients and supplements have similar health effects as whole or minimally processed fiber-rich foods, including β-glucan, psyllium, and pectin, which significantly reduce total cholesterol and low-density lipoprotein (LDL) cholesterol to reduce CHD risk or psyllium and methyl cellulose fiber which promote laxation as long as the processing is not too extreme (e.g., extreme hydrolysis, baking, heat/pressure extrusion) [46]. The delivery vehicle for the fiber ingredient may influence the potential health effects. One study suggests that the effectiveness of β-glucan in lowering serum LDL cholesterol may be somewhat less when baked into bread and cookies than when added to orange juice because of food matrix effects [47]. A number of common fiber ingredients or supplements characterized by their physical properties and health benefits are shown in Table 1.6 [1, 44–73]. Clinical studies show that most isolated fiber supplements do not provide health benefits similar to fiber-rich diets or whole foods [46]. Most supplement fiber beneficial effects are proportional to their viscosity or gelling properties, low fermentable fibers that increase water binding or fermentable fibers associated with microbiota health.

Table 1.5 Comparison of common dietary patterns per 2000 kcal (approximated values) [4, 31, 32, 43]

Components	Western dietary pattern (US)	USDA base pattern	DASH diet pattern	Healthy Mediterranean pattern	Healthy vegetarian pattern (lacto-ovo based)	Vegan pattern
Emphasizes	Refined grains, low-fiber foods, red meats, sweets, and solid fats	Vegetables, fruit, whole grain, and low-fat milk	Potassium-rich vegetables, fruits, and low- fat milk products	Whole grains, vegetables, fruit, dairy products, olive oil, and moderate wine	Vegetables, fruit, whole grains, legumes, nuts, seeds, milk products, and soy foods	Plant foods: vegetables, fruits, whole grains, nuts, seeds, and soy foods
Includes	Processed meats, juices and sugar-sweetened beverages, and fast foods	Enriched grains, lean meat, fish, nuts, seeds, and vegetable oils	Whole grain, poultry, fish, nuts, and seeds	Fish, nuts, seeds, and pulses	Eggs, nondairy milk alternatives, and vegetable oils	Nondairy milk alternatives
Limits	Fruits and vegetables, whole grains	Solid fats and added sugars	Red meats, sweets, and sugar-sweetened beverages	Red meats, refined grains, and sweets	No red or white meats, or fish; limited sweets	No animal products
Estimated nutrients/components						
Carbohydrates (% total kcal)	51	51	55	50	54	57
Protein (% total kcal)	16	17	18	16	14	13
Total fat (% total kcal)	33	32	27	34	32	30
Saturated fat (% total kcal)	11	8	6	8	8	7
Unsat. fat (% total kcal)	22	25	21	24	26	25
Fiber (g)	16	31	29+	31	35+	40+
Potassium (mg)	2800	3350	4400	3350	3300	3650
Vegetable oils (g)	19	27	25	27	19–27	18–27
Solid fats (g)	31	18	–	17	21	16
Sodium (mg)	3600	1790	1100	1690	1400	1225
Added sugar (g)	79 (20 tsp)	32 (8 tsp)	12 (3 tsp)	32 (8 tsp)	32 (8 tsp)	32 (8 tsp)
Plant food groups						
Fruit (cup)	≤1.0	2.0	2.5	2.5	2.0	2.0
Vegetables (cup)	≤1.5	2.5	2.1	2.5	2.5	2.5
Whole grains (oz.)	0.6	3.0	4.0	3.0	3.0	3.0
Legumes (oz.)	–	1.5	0.5	1.5	3.0	3.0+
Nuts/seeds (oz.)	0.5	0.6	1.0	0.6	1.0	2.0
Soy products (oz.)	0.0	0.5	–	–	1.1	1.5

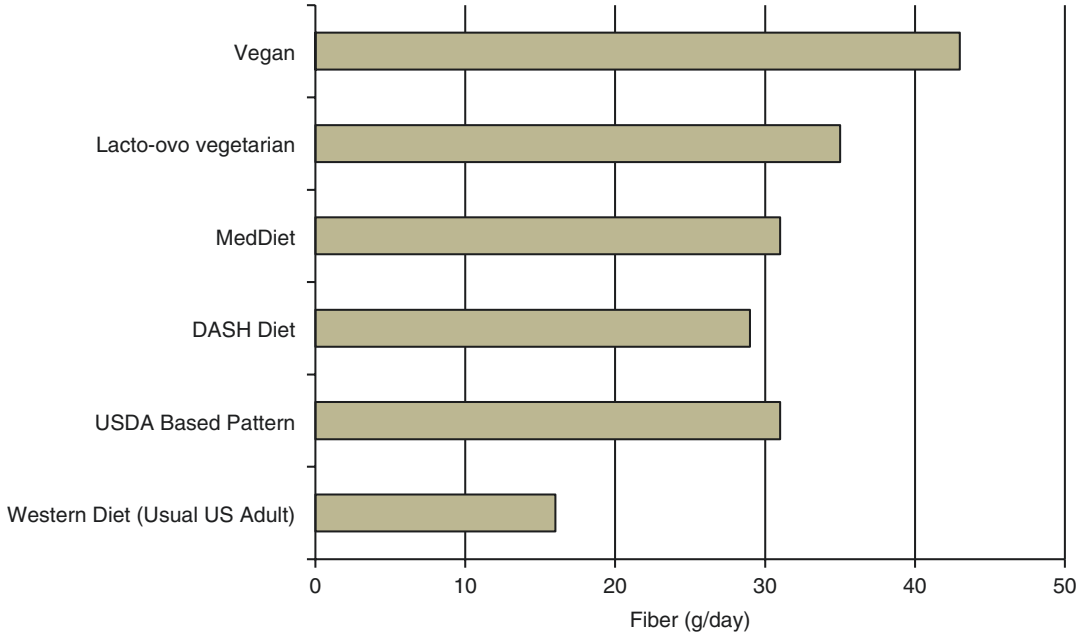

Fig. 1.4 Fiber content per 2000 kcal/day for various dietary patterns [4, 31, 32, 43]

Table 1.6 Overview of the health effects of common fiber supplements and ingredients[a] [1, 44–73]

	Insoluble	Soluble non-viscous		Soluble low viscosity		Soluble higher viscosity		
Health benefits	Wheat bran	Resistant dextrins	Partially hydrolyzed guar gum	Inulin/ Chicory root	Polydextrose	Psyllium	β-Glucan/ Whole oats	Poly Glycoplex
Improve glycemic control	–	–	–	–	–	+	+	+
LDL cholesterol lowering	–	–	–	–	–	+	+	+
Hypertensive blood pressure lowering	–	–	–	–	–	+/–	+	–
Weight control/ loss	+/–	+/–	–	–	+/–	+/–	+/–	+/–
Laxation/Stool softener	+	+/–	+/–	–	+/–	+	+/–	–
Fermentability	Variable depending on particle size	+/–	+/–	+	+/–	+/–	+/–	+/–

[a]+ positive effect, +/– modestly positive effect, – no significant effect

Fiber Health Mechanisms

Potential mechanisms associated with adequate fiber intake may lower the risk of weight gain and obesity, chronic diseases, and premature mortality and improve odds for healthy aging compared to low-fiber Western diets. These health benefit mechanisms are summarized in Fig. 1.5 [1, 5, 7, 30, 33, 44–77]. Adequate fiber intake is a major factor in helping to promote improved hunger control, energy metabolic processes, and cardiometabolic health and maintaining a healthy colonic microbiota and laxation and immune and inflammatory signaling required for human health and chronic disease

Adequate Fiber Intake

Food Intake
Slows eating rate/reduces hunger
Reduces food energy density (2 kcal/g vs 4 kcal/g refined carbohydrates)
Increases food volume/bulk/viscosity

Stomach
Delays emptying rate (w/ bulking/viscosity)
Increases satiety/satiation

Small Intestine
Decreases postprandial absorption rate
Increases release of satiety peptides

Pancreas
Lowers insulin response and β-cell activity

Colon
Promotes colonic health (e.g., lower pH, better laxation, fermentation to SCFAs, calcium absorption, healthy microbiota)
Stimulates release of glucagon-like peptide-1 neuropeptide
Reduces endotoxin leakage into circulation
Lowers risk of diverticula and colorectal polyps

Fecal Excretion
Increases fecal macronutrient and bile acid excretion
Lower net metabolizable energy

Circulatory System
Lowers postprandial lipid, glucose, insulin and inflammatory markers
Attenuates fasting glucose/insulin, systemic inflammation, LDL-cholesterol
Promotes insulin sensitivity and adiponectin levels

Body Weight and Composition
Reduces risk of weight gain/obesity
Lowers risk of abdominal or visceral body fat

Liver
Increases lipoprotein uptake and bile acid synthesis/secretion
Decreases lipogenesis and inflammation

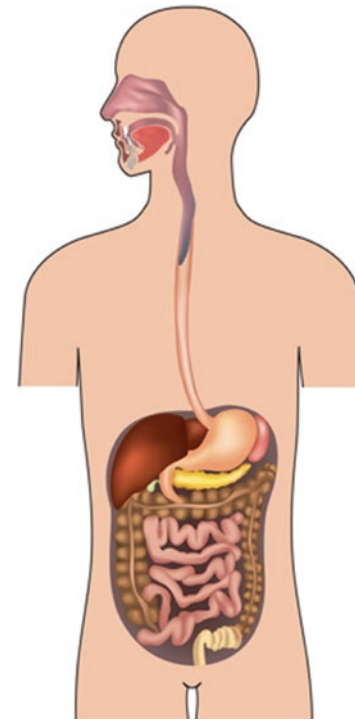

Fig. 1.5 Potential fiber-related mechanisms associated with health benefits [1, 5, 7, 30, 33, 44–77]

prevention. Fiber mechanisms depend on the specific fiber composition, physical properties, and degree of colonic fermentation [44, 45]. A potential plasma marker of fiber intake is an odd-chain fatty acid (heptadecanoic acid) synthesized in the liver from propionic acid (a metabolite of colonic fiber fermentation) [74]. Heptadecanoic acid has also been shown to be inversely associated with diabetes and CHD risk. Also, the effect of fiber intake compared to whole plant foods, fish, and red meat on CHD risk based on RCTs measuring systolic blood pressure and LDL-cholesterol outcomes are summarized in Fig. 1.6 [75].

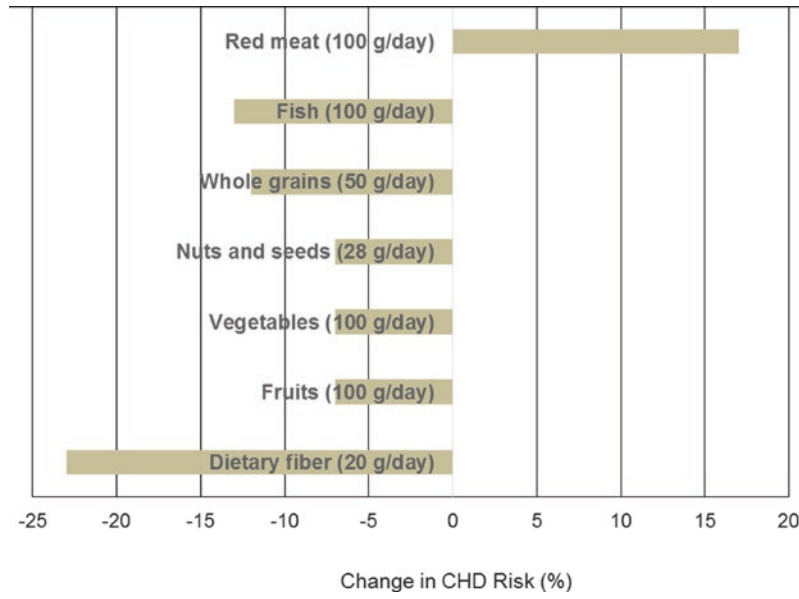

Fig. 1.6 Coronary heart disease(CHD)risk projections from the intake of common foods based onpopulation demographics and dietary habits from National Health and Nutrition Examination Surveys estimated associations of diet and disease and from meta-analyses of prospective studies and clinical trials [75]

Potential Fiber Adverse Effects

Upper Tolerable Intake

No tolerable upper limit has been set for fiber as no specific intake level has been shown to cause significant adverse effects on mineral balances or gastrointestinal function in healthy individuals [1, 5, 30]. Vegetarian diets which may provide >50 g fiber/day have not generally caused adverse health effects in adults [5, 30]. Although very high intakes of certain isolated and synthetic fibers may contribute to excessive flatulence, bloating, and diarrhea, the consumption of a variety of fiber sources by healthy individuals is generally tolerated without significant adverse effects.

Mineral Bioavailability

Although fiber's potential interference with mineral absorption may be a concern, consuming fiber at recommended levels does not significantly adversely affect mineral absorption when consumed with a diverse, healthy, balanced diet [1, 5, 30]. Despite in vitro studies showing that fiber has mineral binding properties, both animal and human studies have failed to show negative effects of fiber on mineral bioavailability, and some studies report that fiber increases mineral absorption in the colon as a result of microbiota fermentation which releases bound minerals [78]. Most studies investigating the effects of cereal, vegetable, and fruit fibers on the absorption of calcium, a critical short-fall mineral, report no adverse effect on calcium absorption or balance [1]. Although cereal brans contain phytates, which can bind calcium, major bran foods such as breakfast bran cereal and 100% whole-grain breads are typically fortified with calcium. Additionally, it has been demonstrated that some fibers and prebiotics can increase calcium bioavailability over lower fiber diets [78–80]. Excessive consumption of oxalates in some vegetables, such as spinach and Swiss chard, can reduce calcium absorption [81, 82].

As vegetarians are generally the highest fiber consumers, they have been the focus of a more detailed assessment of fiber-rich foods and mineral bioavailability [81, 82]. Well-planned vegetarian fiber-rich diets can provide mineral balance at all stages of the life cycle, including pregnancy and lactation. Adult vegetarians appear to have the ability to adapt to vegetarian diets with increasing absorption of minerals. Vegetarian children, pregnant women, and premenopausal women should consume good sources of non-heme iron, such as iron-fortified breads and cereals, beans and lentils, raisins, and blackstrap molasses along with good sources of vitamin C, such as tomatoes and citrus fruits for optimal iron absorption. Cooking in cast iron pans can increase the amount of iron in their diets. Zinc-rich fiber food sources include legumes, whole grains, and nuts. Food preparation techniques, such as leavening bread, can increase zinc bioavailability. Vegetarians who do not consume sources of iodine, such as iodized salt or seaweed, may be at risk for iodine deficiency, because plant-based diets are typically low in iodine. Vegans should plan to include calcium-fortified foods or dietary supplements. Dieting plans should consider low-oxalate greens (e.g., bok choy, broccoli, Chinese cabbage, collards, and kale) and fruit juices fortified with calcium, calcium-set tofu, soy and rice-milk fortified with calcium, and fortified breakfast cereals, which can contribute significant amounts of dietary calcium for the vegan.

Gastrointestinal Tolerance

The primary potential negative side effects of excessive fiber intake in the colon include excess gas from colon fermentation (flatulence), distention, and abdominal discomfort [83, 84]. To help reduce or avoid any potential side effects, fiber should be increased gradually over time to help allow the colon to adapt and fluid intake should also be increased as fiber can bind water. Generally, healthy adults without food intolerances or irritable bowel syndrome (IBS) can handle 50–70 g fiber/day (about 2× the AI) without excessive abdominal fullness and increased flatulence sensations [1]. Some foods or ingredients may contain levels of highly fermentable fiber, sugar alcohols, or other components, which may cause gastrointestinal distress, if they are consumed above a trigger threshold [5, 30]. These types of foods may include: chicory root fiber, artichokes, leeks, onions, bananas, rhubarb, figs, and prunes.

Highly fermentable fiber supplements or fiber-enriched processed foods may cause excessive gastrointestinal distention or flatulence in sensitive individuals at the recommended fiber intake levels [1, 5, 30]. Excessive fiber intake may promote fast transit time that does not allow for intestinal cells to fully absorb the excess water, and this may promote very soft wet stools or mild diarrhea, because water follows undigested and unabsorbed carbohydrates and is eliminated in the feces [84]. Also, people may experience abdominal cramping, bloating, or gas when they abruptly increase their fiber intakes or excessive intake of guar gum, inulin (chicory root fiber), oligofructose, or fructooligosaccharides [5, 30, 49, 84]. However, a gradually increased intake of fiber-rich foods over a period of time or trying fiber sources individually to determine tolerance can minimize or help avoid these symptoms [5, 30, 84]. It is important for those individuals with a sensitive gastrointestinal tract to carefully read the ingredient label of any new fiber-rich processed foods as highly fermentable fibers such as chicory root fiber or similar fructo- or galacto-oligosaccharide sources are being increasingly added to lower calories in Greek yogurts, snack cereals, and nut bars. Extremely rare reports indicate that large bolus intakes of oat bran, wheat bran, or highly viscous, soluble fiber supplements, usually in people with impaired intestinal motility or with difficulty chewing, can lead to esophageal or intestinal obstruction [85, 86].

Drug Interaction

When high-fiber meals or fiber supplements are consumed simultaneously with oral drugs, a fiber-drug interaction may occur with the gastrointestinal processes of drug absorption, plasma clearance, and colon transit rate [87]. Thus, clinicians and pharmacists should generally advise patients to take medication at least 1 h before or 2 h after fiber-rich foods or supplements are consumed to avoid a fiber-drug interaction [87, 88]. Currently, there are only a limited number of human studies on isolated fibers and drug interactions, primarily in the hypoglycemic and lipid-lowering drug areas, which show mixed effects [87]. Some fiber-drug interactions, when taken within 0–2 h, of potential concern include the following: (1) pectin may decrease the absorption of lovastatin (Mevacor) [88]; (2) psyllium may reduce the absorption of lithium, carbamazepine (Tegretol), and digoxin (Lanoxin) and increase the efficacy of colestipol (bile acid sequestrant) [89, 90]; and (3) guar gum may slow the absorption of digoxin and acetaminophen, decrease the absorption of metformin, and increase the lipid-lowering effect of gemfibrozil [87, 90].

Conclusions

Despite the evidence that adequate fiber intake is important in reducing the risk of weight gain, promoting cardiometabolic health, maintaining a healthy colonic microbiota and laxation and immune and inflammatory signaling required for human health and disease prevention, fiber is the leading shortfall "macronutrient" in the developed countries. It is estimated that approximately 95% of populations consuming Western diets eat an inadequate daily fiber level. This fiber gap can adversely affect human health via increased risk of weight gain and dysfunctional colonic microbiota, which is a contributor to growing global obesity and chronic disease pandemics. Fiber comes from whole or minimally processed plant foods including whole grains, fruits, vegetables, legumes, and nuts and seeds eaten as part of a healthy diet, or isolated from natural sources (e.g., β-glucan, psyllium), or from synthetic forms (e.g., polydextrose, methyl cellulose) added to processed foods or consumed as dietary supplements. Fiber food functionality or health effects depend on the specific fiber's composition, physical properties, and degree and rate of fermentation in the colon. The effects of increased fiber intake and its fermentation metabolites can result in reduced risk of obesity, cardiometabolic chronic diseases and related premature mortality, and improved odds for healthy aging. No tolerable upper limit has been set for fiber intake in healthy individuals, but excessive intake of some highly fermentable fibers may increase risk of flatulence and gastrointestinal distress in sensitive individuals. When increasing fiber intake, it is recommended to do so gradually along with increasing fluid intake to help allow the gastrointestinal tract to adapt and to take medication at least 1 h before or 2 h after fiber-rich foods or supplements are consumed to avoid possible fiber-drug interactions.

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Chapter 2
Overview of the Health Benefits of Adequate Fiber Intake

Keywords Dietary fiber • Microbiota • Energy density • Body weight • Coronary heart disease • Blood pressure • Diabetes • Colorectal cancer • Healthy aging • Blood lipids • Systemic inflammation

Key Points

- Low fiber intake is a major public health concern. Inadequate fiber intake is associated with increased risk of weight gain and obesity, chronic disease, and premature aging and mortality.
- Health effects associated with adequate fiber intake include slowing the eating process and reducing food metabolizable energy for better body weight regulation, stimulating laxation and healthy colonic microbiota including, attenuating elevated blood lipids and blood pressure for cardiometabolic health, and increasing insulin sensitivity and lowering systemic inflammation to reduce diabetes, colorectal cancer and premature aging risk (inflammaging).
- Fiber-rich whole (or minimally processed) plant foods and healthy dietary patterns are generally lower in energy density, saturated and trans-fatty acids, sodium, and sugar and higher in essential nutrients and phytochemicals necessary to support optimal health and weight control compared to the usual low fiber Western diets.
- High-viscosity, gel-forming fibers consumed in fiber-rich whole plant foods or supplements tend to have similar effects on attenuating blood lipids and postprandial glycemic response and promoting laxation. However, fiber supplements tend to be less effective than fiber-rich foods at supporting weight loss since they typically do not directly displace higher energy-dense foods.
- Increased fiber intake is consistently associated with better health, reduced chronic disease risk, and healthy aging even when initiated in mid-life (ages 45–65 years).

Introduction

Dietary fiber (fiber) is a major shortfall "nutrient" in the USA and in global populations with high adherence to the Western dietary pattern, as only approximately 5% of these populations consume adequate fiber [1–5]. Low-fiber intake is a major public health concern as the scientific literature has found strong links with it to adverse health outcomes and increased risk of weight

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gain and obesity [1–7]. In contrast, adequate fiber intake, depending on the fiber's composition and physical properties, produces secondary fermentation metabolite-enabled cross-talk signaling capability which can influence many healthy human phenotype processes such as colonic microbiota diversity and health, body weight regulation, reduced cardiovascular disease, colorectal cancer risk, and improved healthy aging and longevity compared to lower fiber intake [1–18]. An overview of potential fiber health-related mechanisms is summarized in Table 2.1 [5, 6, 13–45]. For example, an analysis of the 1999–2010 US National Health and Nutrition Examination Survey (NHANES) observed, after multivariate adjustments, that risk of elevated C-reactive protein (CRP), obesity, and metabolic syndrome are reduced with increasing fiber intake (Fig. 2.1) [41]. Fiber-rich whole or minimally processed foods have the additional benefits of being generally lower in energy density, saturated and trans-fatty acids, sodium, and added sugars and richer in essential nutrients and phytochemicals and represent the majority of foods in all healthy dietary patterns (Appendices 1 and 2). The objective of this chapter is to provide an overview of the health effects of adequate fiber intake.

Table 2.1 Potential fiber-related biological mechanisms associated with better gastrointestinal, and cardio- and energy metabolic health and reduced risk for major chronic diseases [5, 6, 13–45]

Target	Increase	Decrease
Food intake	Eating time	Diet energy density
		Hunger
Stomach	Food volume/bulk/viscosity	Gastric emptying rate
	Satiety/satiation signals	
Small intestine	Food volume/bulk/viscosity	Lipid emulsification
	Release of satiety peptides	Mucosal uptake and re-secretion
		Postprandial macronutrient absorption rates
Pancreas	Digestive enzyme secretion	Insulin response
		β-cell activity
Colon	Laxation	pH
	Fermentation to short chain fatty acids (e.g., butyrate)	Bowel transit time
		Pathogenic bacteria
	Healthy microbiota	Inflammatory activity
	Release of incretins (e.g., GLP-1)	Carcinogen concentrations
		Endotoxin leakage into circulation
		Diverticula and colorectal polyps
Fecal excretion	Bile acids	Metabolizable energy
	Unabsorbed dietary fat and other macronutrients	
Circulatory system	Satiety hormones	Postprandial lipids, glucose, and insulin
	Insulin sensitivity	Fasting total cholesterol and LDL-C
	Adiponectin	Blood pressure in hypertensive individuals
	Leukocyte telomere chain length	C-reactive protein/inflammaging
		Fasting glucose and insulin
Body weight and composition	Weight control	Energy intake
	Energy metabolism	Weight gain/obesity
		Abdominal/visceral body fat
Liver	Lipoprotein uptake	Lipogenesis
	Bile acid synthesis and secretion	Inflammation
	Detoxification processes	

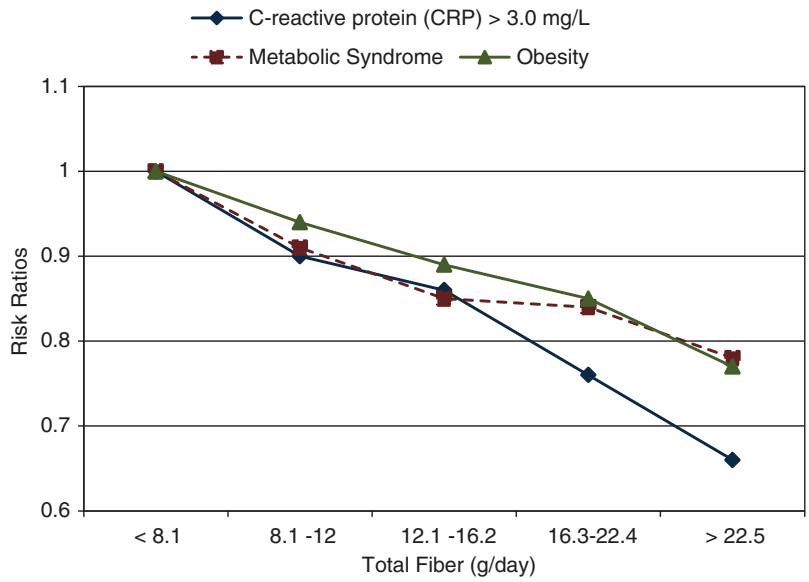

Fig. 2.1 Effect of increasing fiber intake on cardiometabolic risk factors from the 1999–2010 US National Health and Nutrition Examination Survey (CRP *p*-trend <0.001; multivariable adjusted [41]

Digestive Health

The association between coarse bran (fiber) and digestive health was first recognized by Hippocrates who observed in 371 BC that the human body works better with bread made of course rather than finely ground flour [3, 46, 47]. Good digestive health is associated with appropriate nutrient absorption, intestinal motility and immune function, and a balanced colonic microbiota [48]. Fiber is the most important dietary component for good digestive health because of its promotion of laxation, fermentation to bioactive short-chain fatty acids (SCFAs), and maintenance of a healthy colonic microbiota ecosystem [3, 7, 29].

Laxation

Fiber affects laxation by increasing fecal bulk, stool softening, reducing transit time, and improving stool regularity as mediated by fiber water-binding capacity and fermentation, which alters osmotic balance and increases fecal biomass (e.g., fiber, bacteria and gas) [49]. Fiber sources that combine low fermentability and high water-binding capacity such as wheat bran, psyllium fiber, and methylcellulose from supplements, food ingredients, or fiber-rich diets are particularly effective in promoting laxation [29, 50]. In randomized controlled trials (RCTs), both wheat bran and psyllium fiber were shown to decrease transit time and increase daily stool regularity as well as promote healthier stool weights and structure, compared to low fiber controls. Wheat bran was more effective at reducing transit time, and psyllium was more effective at increasing stool water content (softer stools) and weight [45]. Individuals with low-fiber intake are five times more likely to have hard stools compared to those with higher-fiber diets, especially diets supplemented with wheat bran or psyllium [45]. Although coarse wheat bran increases stool volume 2 1/2 times more than fine bran when consumed at the same dose, the fine wheat bran is more fermentable resulting in increased prebiotics and SCFAs

associated with colon health [51, 52]. A systematic review of 65 intervention studies found that wheat bran improved bowel function by significantly increasing total stool weight by 3.7 g/gram intact wheat fiber and reducing transit time by 45 min/g when baseline transit time was greater than 48 hours [53]. Highly fermentable fiber may cause excessive gastrointestinal distention or flatulence in sensitive individuals at the recommended fiber intake levels [54]. Excessive fiber intake may promote diarrhea because water follows the undigested and unabsorbed carbohydrates into the large intestine. If transit time is too fast for intestinal cells to absorb the excess water, it will be eliminated in the feces [55]. People may experience abdominal cramping, bloating, or gas when they abruptly increase their fiber intakes or excessive intake of guar gum, inulin (chicory root fiber), oligofructose, fructooligosaccharides, polydextrose, or resistant starch [56]. However, a gradually increased intake of fiber-rich foods over a period of time or trying fiber sources individually to determine tolerance can minimize or help avoid these symptoms. An analysis of the US constipation medical costs estimated that if fiber intake was increased by 9 g/day from bran (equivalent to one serving of high-fiber breakfast cereal/day), there could be approximately a billion dollars in annual health-care savings [57]. Studying laxation is a relatively complex process with a wide range of variability in individuals as the rate of bowel laxation can be influenced independently of diet with fast transit times related to stress, extraverted personality, exercise, and slower rates associated with relaxation, introverted personalities, and sedentary lifestyles [58].

Colonic Microbiota

Over the last decade, the colonic microbiota has become recognized as a "symbiotic human organ" which provides a number of important human biological functions (e.g., nutrients absorption, synthesis of vitamins, food fermentation to SCFAs, bile acid transformations, barrier effects against pathogens), immune system function (e.g., inflammatory response, immunoglobulin A, T-cell homeostasis), and metabolic health (e.g., insulin sensitivity, satiety hormones, and cardiometabolic risk factors) [59–63]. The health-promoting effects of the microbiota are significant as its complement of genes are at least 150 times more than that of the whole human genome. The colonic microbiota produces a large number of bioactive compounds that can influence health including beneficial metabolites such as SCFAs, secondary bile acids, choline or potentially toxic metabolites such as ammonia, sulfur-containing compounds, indoles, and phenols. The composition and activity of the microbiota is affected by diet, heredity, lifestyle, disease, and antibiotic use [64].

This symbiotic relationship between the microbiota and human health evolved over millions of years with humans consuming a high-fiber diet [59, 65]. Fiber-rich dietary patterns compared to low-fiber Western dietary patterns promote both healthy colonic microbiota and human health (Fig. 2.2) [61, 62]. Increased fiber is important in reducing colonic pH to increase symbiotic bacteria diversity and decrease pathogenic bacteria, increasing fecal butyrate concentration to promote colonocyte health as a barrier to lipopolysaccharide (LPS) absorption and inhibit colorectal cancer initiation and progression, and attenuating colonic inflammation, secondary bile acid formation, cardiometabolic dysfunction, insulin resistance, and unhealthy aging, especially frailty [59–68]. A crossover RCT (19 healthy normal weight adults; 53% females; age 19–25 years; basal diet supplemented with 40 or 10 g fiber/ day for 5 days; 15-day washout) found higher-fiber diets overall were shown to increase microbiota diversity and stability compared to lower-fiber diets within 5 days [66]. Additionally, the higher-fiber diet promoted a higher *Prevotella*/*Bacteroides* ratio, increased fecal SCFAs, and modulated the expression of microbiota metabolic pathways such as glycan metabolism, with genes encoding carbohydrate-active enzymes active for fiber, compared to the low-fiber diets. The equilibrium between fiber intake, gut microbiota SCFAs, and colonic pH being maintained in the acidic range provides an

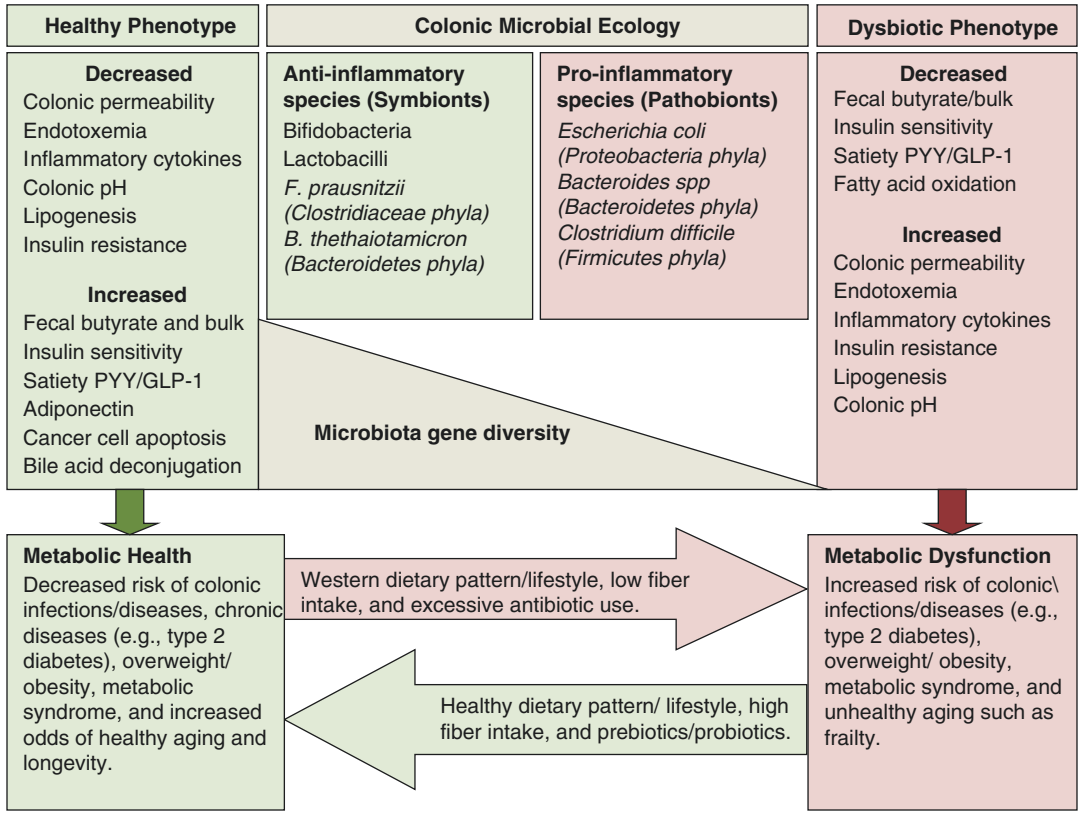

Fig. 2.2 Effect of healthy fiber-rich dietary patterns vs. Western low-fiber dietary patterns on colonic microbiota, cardiometabolic health, and aging [61, 62]

important protective barrier against the expansion of pathogenic bacteria in the colon [60]. With an adequate fiber intake, there are generally higher levels of butyrate-producing bacteria, which maintain an acidic colon at 5.5 pH as butyrate tends to maintain a presence in the colon. Butyrate is also an important energy source for colonocytes and involved in the regulation of cell proliferation, differentiation to reinforcement of the colonic barrier, and colonic anti-inflammatory support. However, when fiber becomes limiting, the colon pH increases to 6.5, which coincides with reduced fermentation and SCFAs, which increases levels of *Proteobacteria*, including a wide variety of pathobionts and increased endotoxemia risk.

The symbiotic relationship between fiber, colonic microbiota, and optimal human health exists throughout the lifecycle [59–63]. These fiber and microbiota interactions begin at birth where active cross-talk signaling between the microbes and human immunity and metabolism begins to take shape [63]. Populations consuming low-fiber Western diets compared with populations consuming a more traditional or healthy fiber-rich diet have more dysfunctional microbiota, which predisposes individuals to a variety of chronic diseases [59, 60, 65, 67]. In contrast, higher-fiber diets are important in maintaining a diverse, healthy microbiota, which may lower the risk of most noncommunicable diseases, including type 2 diabetes, metabolic syndrome, colorectal cancer, and obesity [60–62, 64, 65, 67]. In the elderly, those in longer-term care facilities consuming standardized, low-fiber diets had significantly higher levels of frailty, less diverse and less healthy microbiota, and higher systemic inflammation than those living in their community residences and consuming more diverse, higher-fiber diets [68].

Body Weight Regulation

Adults

The European Food Safety Authority (EFSA) has recommended that adults should consume >25 g fiber/day from whole grains, fruits, and vegetables to improve weight maintenance and sustain weight reduction in overweight and obese individuals [5]. A systematic review of 43 prospective cohort, case-control, and randomized trials found probable evidence that increased fiber intake was predictive of less weight gain, whereas higher-energy diets rich in refined grains, sweets, and desserts were predictive of elevated weight gain and waist size [12]. Observational studies consistently show that populations consuming fiber-rich diets tend to be leaner than those with low-fiber diets [10–14, 69–71]. The 2012 International Study of Macro−/Micronutrients and Blood Pressure (INTERMAP) cross-sectional study (1,794 free living Americans; mean baseline age 49 years; four 24-h dietary recalls and two timed 24-h urine collections) found that normal-weight US adults consumed healthy dietary patterns lower in total energy and higher in nutrient dense foods (e.g., fresh fruit, whole grains bread, cereals and pasta, and brown rice) compared with overweight individuals [69]. Lean participants had lower intakes of meats, fats, sugar-sweetened beverages, carbonated drinks, and nonalcoholic beverages. Their diets were consequently higher in many macro- and micronutrients (vegetable protein, fiber, vitamin A and C, magnesium, and nonheme iron) and lower in animal protein, fats, dietary cholesterol, and sodium. The Nurses' Health Study (74,091 US women; mean baseline age 50 years; mean BMI 25; 12-year follow-up) found that women with the greatest increased intake of total fiber gained an average of 1.5 kg less than those with the smallest increase in intake of fiber (p trend <0.0001) independent of body weight at baseline, age, and changes in covariate status [70]. Women in the highest quintile of fiber intake had a significant 49% lower risk of major weight gain than women in the lowest quintile. In a US prospective study (252 women; mean baseline age 40 years, mean BMI 24; 20-month follow-up), each 1 g increase in fiber consumed significantly reduced weight by 0.25 kg and body fat by 0.25% [71]. Three long-term clinical trials (1–4 years) showed that consuming high-fiber diets >30 g fiber/day can effectively promote weight loss similar to reduced energy diet regimens [42, 72, 73]. Also, in a 12-week RCT, various combinations of fiber-rich diets with and without psyllium (>30 g/day) were significantly more effective in reducing body weight and improving body composition than lower-fiber diets (20 g/day) [74]. A systematic review of RCTs used for the 2015 US Dietary Guidelines Advisory Committee, found that after weight loss is achieved, healthy fiber-rich dietary patterns can slow weight regain to maintain a 4–10 kg weight loss after 1 year and 3–4 kg after 2 years [2]. Fiber supplements tend to be less effective in promoting satiety, reduced energy intake, or weight loss than healthy dietary patterns (≥30 g/fiber/day), in part because some physical property changes occur in processing and fiber supplements do not displace other high-energy-density foods [75].

Children and Adolescents

Several longitudinal studies consistently find that healthy dietary patterns or added fiber are associated with lower BMI and body fat in children and adolescents [76, 77]. A study of overweight Latino youth (85 adolescents; mean baseline age 14 years; 56% male; 2-year follow-up) found that adolescents who decreased total fiber intake (mean decrease of 3 g/1000 kcal) significantly increased visceral adipose tissue volume by 21% compared with those who had increased fiber intake (Fig. 2.3) [76]. A US longitudinal study (170 overweight/obese children; age 7–11 years; 16-week family-based behavioral weight loss study) found that decreased food away from home was associated with significantly improved diet quality (e.g., higher-fiber and lower-sugar and fat intake) and greater reductions in BMI

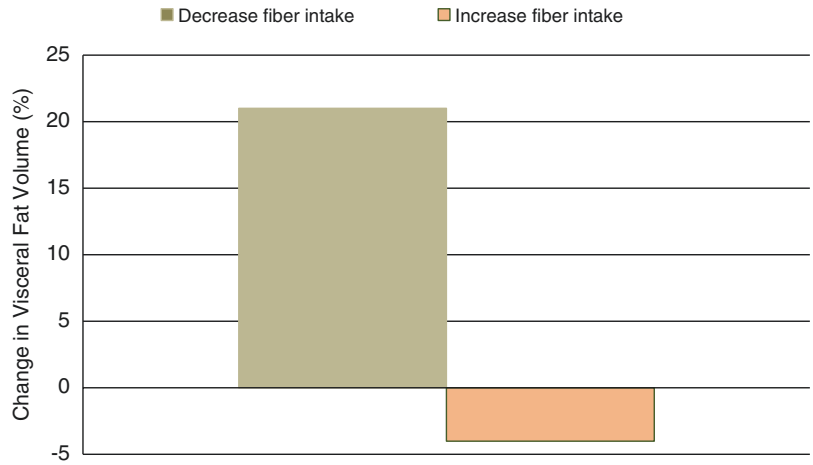

Fig. 2.3 Effect of change of fiber density by increasing or lowering fiber intake by 3 g/1000 kcal on visceral fat volume over 2 years in overweight Latino youth ($p = 0.02$) [76]

and percent body fat [77]. As fiber is a major shortfall "nutrient" in Western children and adolescent diets, these studies demonstrate the importance of healthy dietary patterns with adequate fiber in youth to prevent weight and abdominal fat gain or to promote weight loss in overweight or obese youth.

Chronic Disease Risk

Cardiovascular Disease (CVD)

A number of review articles conclude that adequate fiber intake significantly reduces the risk of CVD [3–9]. Several dose-response meta-analyses of prospective cohort studies suggest an inverse association between fiber intake and CVD risk with a 9–11% reduction per 7–10 g fiber increment/day [78, 79]. There is strong clinical evidence that healthy dietary patterns can significantly lower the CVD risk by 22–59% depending on the level of adherence [2]. In 2008, after thorough evaluation of the available data, the Academy of Nutrition and Dietetics Evidence Analysis Library Committee concluded that higher-fiber intakes may help to attenuate elevated serum lipid levels, blood pressure, and systemic inflammatory markers as key mechanisms to explain fiber's CVD protective properties [3]. The European Prospective Investigation of Cancer (EPIC) Norfolk cohort (22,915 participants; mean age 58 years; mean BMI 26) found fiber intake to be inversely associated with total cholesterol, LDL-C, and triglycerides and positively associated with HDL-C regardless of genetic profile such as APOE polymorphism [80].

Coronary Heart Disease (CHD)

The US Academy of Sciences, Institute of Medicine established the fiber adequate intake primarily based on fiber's effects on reducing coronary heart disease (CHD) risk [6]. Dose-response meta-analyses of prospective studies estimate that for each 10 g/day increment of fiber, there is decreased risk of all coronary events by 8–11% and CHD deaths by 24% [79, 81]. Numerous randomized trials have consistently demonstrated that intakes of ≥26–30 g total fiber/day from whole foods (including whole grains, especially oats and barley, fruit, vegetables, legumes, nuts) or ≥3–12 g isolated soluble,

viscous fiber supplements/day (including oat/barley beta-glucan, psyllium, guar, or pectin) can lower LDL-C by 4–8% [31–35]. The National Cholesterol Education Program (Adult Treatment Panel III) recommends early treatment of hypercholesterolemic patients with high-fiber diets and soluble, viscous fiber supplements [82]. A large randomized, double-blind, placebo trial in Finnish men (21,930 smokers; aged 50–69 years; 6.1-year follow-up; 1,399 first nonfatal myocardial infarction cases and 635 coronary heart disease deaths) reported a 31% reduction in CHD risk (35 g vs. 16 g fiber/day), with cereal fiber having a stronger effect than vegetable or fruit fibers and soluble fiber being more effective than insoluble fiber [37]. Additionally, the 2015 US Dietary Guideline Advisory Committee Scientific analysis showed that healthy dietary patterns can significantly lower the CHD risk with the MedDiet by 29–61%, the US Dietary Guidelines pattern by 24–31%, and DASH diets by 14–27% [2].

Blood Pressure

Adequate fiber intake is associated with modestly lower blood pressure, especially in individuals with hypertension. Three meta-analyses of randomized trials report that increased fiber intake by 6–11.5 g/day can modestly lower pooled mean systolic blood pressure by 0.9–1.2 mm Hg and diastolic blood pressure by 0.7–1.7 mm Hg [30, 83, 84]. However, after stratification of subjects, blood pressure reductions were significantly greater in older (>40 years) and in hypertensive populations with reduced systolic blood pressure by 6 mm Hg and diastolic blood pressure by 4.2 mm Hg. Beta-glucan was found to be among the most effective blood pressure lowering fibers with 4 g/day lowering systolic blood pressure by 2.9 mm Hg and diastolic blood pressure by 1.5 mm Hg [30]. The 2015 US Dietary Guidelines Advisory Committee Scientific analysis concluded that healthy dietary patterns, especially the DASH-style diets, can significantly lower systolic blood pressure by 6 mm Hg and diastolic blood pressure by 3 mm Hg compared to Western patterns mainly because of the increased fiber, potassium and carotenoids, and lower saturated fat and sodium content [2].

Stroke

Adequate intake of fiber is associated with lower total stroke risk. Several meta-analyses of prospective studies consistently found an inverse dose-response relationship between fiber intake and stroke risk [85–88]. One meta-analysis (6 prospective studies; 314,864 subjects; 8–18 years of follow-up; 8,920 stroke events) reported a 12% reduction in stroke risk for each 10 g fiber/day [85]. Another meta-analysis of dietary patterns (21 prospective studies; 1,023,131 participants; age 34–79 years; cohorts from the USA, Europe, and Asia) showed a 17% lower stroke risk for the highest- vs. lowest-fiber intakes [87]. The 2015 US Dietary Guidelines Advisory Committee Scientific analysis found that healthy dietary patterns such as the MedDiet and US Dietary Guidelines patterns can significantly lower stroke risk by13–60%, depending on the level of adherence [2].

Type 2 Diabetes (Diabetes)

Adequate intake of fiber, particularly with low-glycemic foods, is associated with a lower incidence of diabetes. A dose-response meta-analysis (17 prospective studies; 488,293 participants; 4–14 years of follow-up; 19,033 diabetes cases) found a significant nonlinear inverse association between total fiber intake and diabetes risk with intake below 25 g fiber/day and a linear reduction

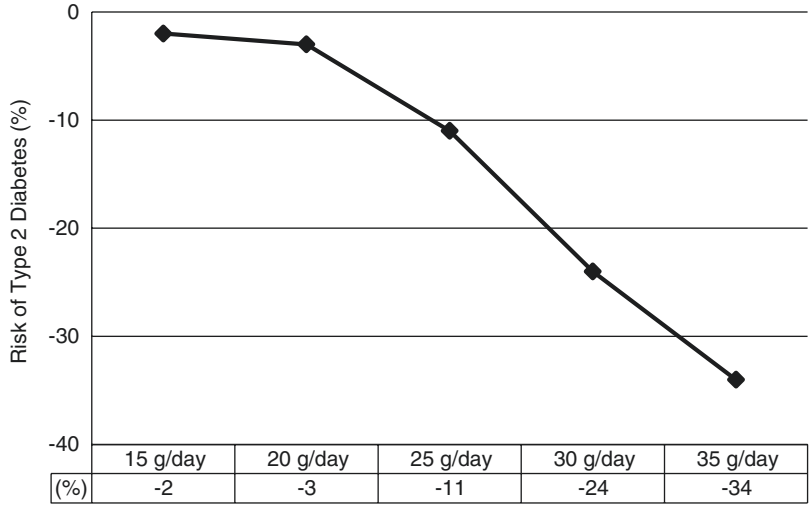

Fig. 2.4 Effect of increasing fiber intake on type 2 diabetes risk from a dose-response meta-analysis of 17 prospective cohort studies (p for nonlinearity <0.01) [15]

in risk above 25 g fiber/day (Fig. 2.4) [15]. This analysis also found that the risk of diabetes decreased with cereal fiber, fruit fiber, and insoluble fiber intake. The InterAct study meta-analysis (19 cohort studies; 617,968 participants; age 21–79 years; 4–16 years of follow-up; 41,066 diabetes cases) reported a diabetes risk reduction per 10 g fiber/day increase in total fiber by 9%, cereal fiber by 25%, fruit fiber by 5%, and vegetable fiber by 7%. The overall evidence indicates that the intake of total and cereal fiber is significantly inversely related to the risk of diabetes [89]. The EPIC-InterAct Study (26,088 participants; mean baseline age 52 years; 10.8 years of follow-up; 11,559 participants with diabetes) reported that fiber intake of 26.5 g/day was associated with a significant 18% lower risk of diabetes vs. 19 g fiber/day, after multivariate adjustments [89]. A Finnish Diabetes Prevention Trial (522 middle-aged, overweight subjects; 172 men and 350 women; mean age 55 years; mean BMI 31; 3 years) showed that a comprehensive lifestyle program with 15 g fiber/1000 kcal, exercise, and 5% weight loss significantly lowered diabetes risk by 58% over 3 years [90]. A pooled analysis of three large US cohort studies suggests that diets high in glycemic index or glycemic load foods and low in cereal fiber (refined carbohydrates) are associated with a significantly higher risk of diabetes [91]. The 2015 US Dietary Guidelines Advisory Committee Scientific Report analysis showed that healthy dietary patterns significantly lower the risk of developing diabetes by 21% compared to a 44% increased risk seen with a low-fiber Western-type diet [2]. The association between fiber and diabetes is partially explained by fiber's effect on reducing the risk of body weight gain and obesity [90].

Cancer

Fiber was hypothesized to reduce cancer risk, especially colorectal cancer, in the early1970s based on data showing lower rates of colorectal cancer among Africans who consumed a traditional diet high in fiber compared to those with an urban Western diet [92]. There are a number of postulated fiber anticancer mechanisms affecting the initiation and/or progression of cancer, such as the effects of SCFAs on colon pH, butyrate's control of cell division rates, and fiber effects on reducing obesity risk and associated metabolic and signaling changes related to cancer risk [3, 93–95].

Colorectal Cancer

Adequate fiber intake is associated with a reduced risk of colorectal cancer. In 2011, the World Cancer Research Fund (WCRF) and American Institute of Cancer Research (AICR) Continuous Update report concluded that there is convincing evidence that fiber-rich diets are protective against the risk of colorectal cancer [96]. A dose-response meta-analysis (16 prospective studies; 1,985,552 participants; 4.5–26 years of follow-up; 14,514 colorectal cancer cases) found a significantly lower colorectal cancer risk by 10% for each 10 g/day intake of total fiber and cereal fiber and a 17% reduction for each three servings (90 g/day) of whole grain daily with further reductions at higher intake [17]. The EPIC cohort study (477,312 EU participants; mean age 51 years; 30% men; women 43% postmenopausal; mean BMI for men 26 and for women 25; mean follow-up of 11 years, 4517 colorectal cancer cases) observed an inverse association between total fiber intake and colorectal risk with10 g/day increase in fiber reducing colorectal cancer by 13% (Fig. 2.5) [97]. Similar linear associations were observed for colon and rectal cancers. The US Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (57,774 adults; mean age 62 years; flexible sigmoidoscopy at baseline and 3 or 5 years) found that those consuming ≥12.8 g fiber/1000 kcal had a significantly lower risk of any incident distal colorectal adenoma or rectal adenoma by 24% compared to those consuming <9.9 g fiber/1000 kcal with cereal and fruit fiber sources being the most effective, after adjusting for potential confounders [98]. Although the association was not statistically significant for colorectal cancer overall (15% risk reduction; *p*-trend = 0.10), a reduced risk of distal colon cancer was observed with increased total fiber intake (38% risk reduction; *p*-trend = 0.03). A Cochrane systematic review of five RCTs lasting 2–4 years reported that total fiber had insignificant effects on colorectal adenoma

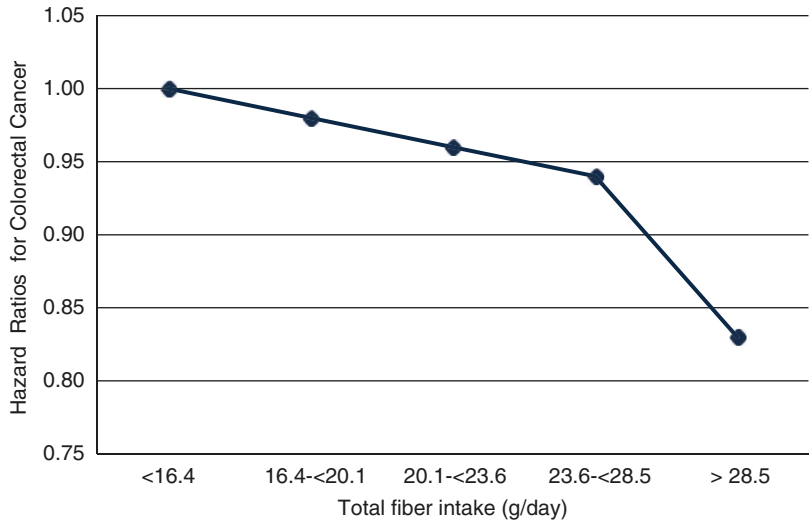

Fig. 2.5 Effect of increasing fiber intake on colorectal cancer risk in adults (mean age 52 years) followed for 11 years (*p*-trend ≤0.017, multivariate adjusted) [97]

recurrence [99], which is thought to be a result of short study duration and dietary compliance issues [100]. A large North American cohort trial (96,354 Seventh-Day Adventist adults) found that vegetarian diets reduced overall colorectal cancer risk by 22% compared to nonvegetarian diets [101].

Breast Cancer

The 2014 Continuous Update of the World Cancer Research Fund and American Institute for Cancer Research (WCRF and AICR) found a limited-suggestive consistent significant inverse association between consumption of foods rich in fiber by women before or ≥12 months after diagnosis for primary breast cancer and risk of all-cause mortality [102]. Although the 2017 WCRF and AICR Continuous Update Project Report found the relationship between fiber and breast cancer to be inconclusive [103], several subsequent meta-analyses of prospective studies show modest but significant reduction in breast cancer risk of 5–7% for each approximately 10 g/day increase in fiber intake [16, 104]. An EPIC prospective study (334,849 women; mean age 50 years; 11.5 years of median follow-up; 11,576 breast cancer cases) found significantly reduced breast cancer risk by 5% for intakes of total fiber and fiber from non-starchy vegetables by 10% but not with fiber from fruit, cereals, or legumes. For vegetable fiber, stronger significant associations were observed for estrogen receptor-negative and progesterone receptor-negative tumors by 26% than for estrogen receptor-positive and progesterone receptor-positive tumors with a reduced risk by 8% at higher vs. lower intake [105]. The Nurses' Health study II (90,534 premenopausal women; mean age 36 years; 20-year follow-up; 2,833 invasive breast cancer cases) suggests that adequate fiber intake during adolescence and early adulthood may be particularly protective against breast cancer risk with the risk of breast cancer reduced by 25% at higher vs. lower intake [106]. Fiber-rich, healthy dietary patterns are associated with moderate reduced risk of postmenopausal breast cancer, but the evidence for premenopausal breast cancer risk is more limited and inconclusive at this time [2]. Several proposed mechanisms for fiber's protective effect include the sequestration of estrogen in the digestive system and reduction of β-glucuronidase activity in the colon resulting in increased estrogen excretion in the feces [105].

Other Cancers

Two additional cancers that may be affected by adequate fiber intake are prostate and gastric cancer. The 2014 WCRF and AICR continuous update report concluded that there is no or limited evidence that increased fiber intake is directly protective against the risk of prostate cancer [107]. However, the Physicians' Health Study (926 men diagnosed with nonmetastatic prostate cancer; diet questionnaires for a median of 5.1 years after diagnosis; followed for 10 years) suggests that a low-fiber, Western dietary pattern was associated with higher prostate cancer-specific and all-cause mortality, and a high-fiber prudent dietary pattern was associated with lower all-cause mortality (Fig. 2.6) [108]. A meta-analysis (19 case-control and 2 cohort studies; 580,064 subjects) reported that fiber had a significant inverse dose-response effect on gastric cancer risk with a reduction of 44% for each 10 g increased fiber consumed daily [109].

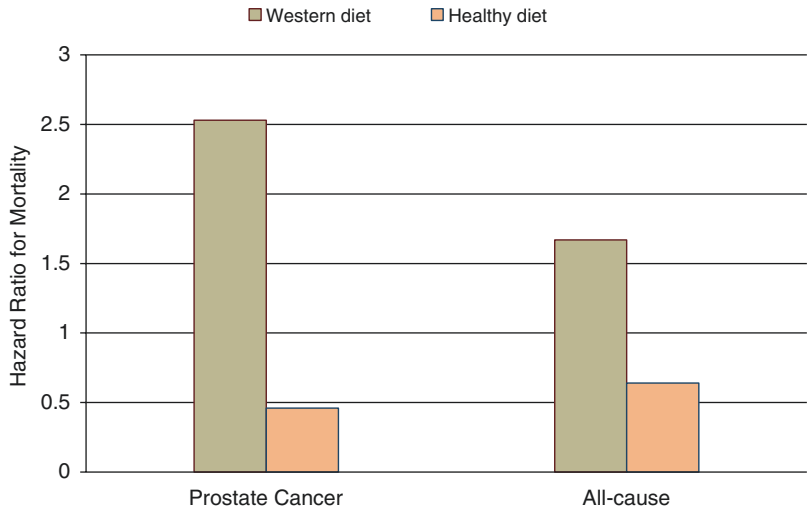

Fig. 2.6 Effect of a high prudent (healthy) vs. Western dietary pattern score on post-diagnosis prostate cancer specific and all-cause mortality risk over 10 years (p-trends ≤0.02; multivariate adjusted) [108]

Healthy Aging

The consumption of healthy dietary patterns in midlife (45–65 years) that provide adequate micronutrients, fiber, and antioxidants while controlling energy intake can promote healthy aging defined as (1) staying free of premature major chronic diseases, (2) maintaining good physical and cognitive function with no limitations in core activities of daily living, (3) experiencing no serious depressive symptoms, and (4) having good overall self-perceived health. A prospective study of French midlife adults (2,796 participants; mean age 52 years; 13 years of follow-up) observed that individuals consuming moderate energy healthy dietary patterns (≤2,500 kcal/day in men and ≤1,820 kcal/day in women) had significantly improved odds of healthy aging by 46%, and those consuming above this energy target had an insignificant 7% improved odds of healthy aging [110]. In an exploratory study, individuals with higher-fiber intake were significantly better at controlling caloric intake, which translated into lower BMI and more dietary satisfaction [111]. A number of intervention trials and cohort studies suggest that fiber-rich diets can significantly lower systemic inflammation, which is an important factor in the aging process (inflammaging) [38, 40, 41, 112]. Several longitudinal studies and an intervention trial have suggested that fiber-rich diets can significantly reduce periodontal disease markers [113–115]. In a cross-sectional analysis of the Nurses' Health Study (2,284 women; mean age 59 years; mean BMI 26; 87% postmenopausal), waist circumference was negatively associated and fiber was positively associated with leukocyte telomere length with a significant increase in telomere length by 0.19 units between the extremes of fiber intake, after multivariate adjustment [43]. Several review articles suggest that SCFAs from the fermentation of fibers by colonic microbiota can reduce the inflammaging processes by target signaling modifications in physiological functions, epigenetic changes involved in alterations in DNA methylation patterns, posttranslational modification of histones, and chromatin remodeling which represent important emerging avenues for healthy aging research [116, 117]. The Australian Blue Mountains Eye Study (1,609 adults; aged 49 years and older;

free of cancer, coronary artery disease, and stroke; followed for 10 years) observed that subjects with the highest vs. lowest intake of total fiber intake had a 79% increased odds of aging successfully, multivariate-adjusted [118]. These findings suggest that increasing intake of fiber-rich foods could be a successful strategy for reaching old age disease free and fully functional.

Longer Life Expectancy

Prospective studies suggest that healthy dietary patterns improve the odds of longer life expectancy [119]. A number of studies suggest that adequate fiber intake has an independent role in reducing risk of all-cause and disease-specific mortality. The Nurses' Health Study (72,113 women; mean age 50 years; mean BMI 25; 18 years of follow-up; 6,011 deaths occurred, including 1,154 cardiovascular deaths and 3,139 cancer deaths) observed that women with higher prudent diet scores and adequate fiber intake had significantly lower all-cause mortality risk by 17%, whereas women with higher Western diet scores and low-fiber intake had significantly higher all-cause mortality risk by 21%, after multivariate adjustments (Fig. 2.7) [120]. A meta-analysis (25 cohort studies; 1,752,848 midlife individuals; average 12.4 years of follow-up) suggests that fiber is inversely associated with mortality risk (Fig. 2.8) [121]. The large US National Institutes of Health (NIH)-AARP Diet and Health Study (567,169 men and women; mean age 62; mean BMI 27; 9 years of follow-up; 20,126 deaths in men and 11,330 deaths in women) found that increased fiber intake by 15 g/day significantly reduced all-cause mortality rates by 22% in both men and women and CVD mortality in men by 24% and women by 34% (multivariate adjusted) [122]. Also, an inverse association between fiber intake and cancer death was observed in men, but not in women. Similarly, an EPIC prospective study (452,717 men and women; mean age 51 years; mean BMI 25.5; mean 12.7 years of follow-up; 23,583 deaths) found an inverse association with total mortality and circulatory mortality risk with a 10% reduction in risk per 10 g fiber/day [123].

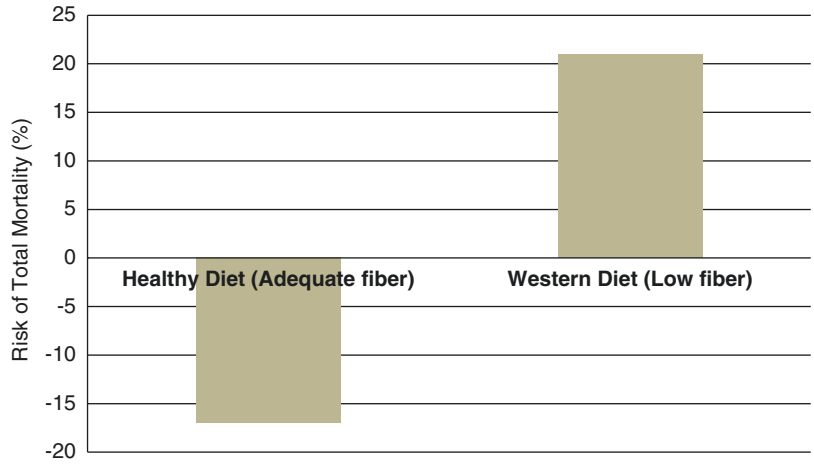

Fig. 2.7 Effect of a prudent (healthy) or Western dietary pattern type on total mortality of women in midlife (45–65 years) over an 18-year follow-up from the Nurses' Health Study (p-trend <0.001) [120]

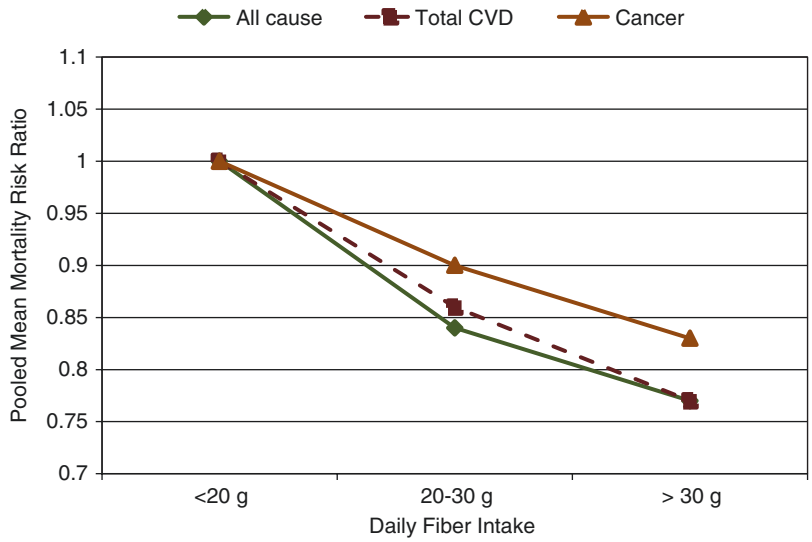

Fig. 2.8 Effect of daily fiber intake and all-cause, total cardiovascular disease (CVD), and cancer mortality risks from a meta-analysis of 25 prospective cohort studies [121]

Conclusions

Low fiber intake is a major public health concern as the scientific literature shows strong associations with increased risk of weight gain and obesity, chronic disease, and premature aging and mortality. Health effects associated with adequate fiber intake include slowing the eating process and reducing food metabolizable energy for better body weight regulation, stimulating laxation and healthy colonic microbiota (including lower colorectal cancer risk), attenuating elevated blood lipids and blood pressure for cardiometabolic health, and increasing insulin sensitivity and lowering systemic inflammation to reduce diabetes and premature aging risk (inflammaging). Fiber-rich foods are also typically lower in energy density, saturated and trans-fatty acids, sodium, and sugar, which supports better health and weight control, especially when displacing high energy-dense and low-nutrient-quality foods in Western diets. High-viscosity, gel-forming fibers consumed in either fiber-rich whole or minimally processed plant foods or as supplements tend to have similar effects on attenuating postprandial glycemic response, improving blood lipid profiles, and promoting laxation. However, fiber supplements tend to be less effective than fiber-rich foods at supporting weight loss since they typically do not directly displace higher energy-dense foods. Increased fiber intake is consistently associated with better health, reduced chronic disease risk, and healthy aging even when initiated in mid-life (ages 45–65 years).

Appendix 1. Fifty High-Fiber Whole or Minimally Processed Plant Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds, whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report. Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part D, Chapter 1: Food and nutrient intakes, and health: Current status and trends. 2015;97–8. Table D1.8

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Appendix 2. Estimated Range of Energy, Fiber, Nutrients, and Phytochemicals Composition of Whole or Minimally Processed Foods/100 g Edible Portion[a,b]

Components	Whole grains	Fresh fruit	Dried fruit	Vegetables	Legumes	Nuts/seeds
Nutrients and phytochemicals	Wheat, oats, barley, brown rice, whole grain bread, cereal, pasta, rolls, and crackers	Apples, pears, bananas, grapes, oranges, blueberries, strawberries, and avocados	Dates, dried figs, apricots, cranberries, raisins, and prunes	Potatoes, spinach, carrots, peppers, lettuce, green beans, cabbage, onions, cucumber, cauliflower, mushrooms, and broccoli	Lentils, chickpeas, split peas, black beans, pinto beans, and soy beans	Almonds, Brazil nuts, cashews, hazelnuts, macadamias, pecans, walnuts, peanuts, sunflower seeds, and flaxseed
Energy (kcal)	110–350	30–170	240–310	10–115	85–170	520–700
Protein (g)	2.5–16	0.5–2.0	0.1–3.4	0.2–5.0	5.0–17	7.8–24

Appendix 2 (continued)

Components	Whole grains	Fresh fruit	Dried fruit	Vegetables	Legumes	Nuts/seeds
Available carbohydrate (g)	23–77	1.0–25	64–82	0.2–25	10–27	12–33
Fiber (g)	3.5–18	2.0–7.0	5.7–10	1.2–9.5	5.0–11	3.0–27
Total fat (g)	0.9–6.5	0.0–15	0.4–1.4	0.2–1.5	0.2–9.0	46–76
SFA[a] (g)	0.2–1.0	0.0–2.1	0.0	0.0–0.1	0.1–1.3	4.0–12
MUFA[a] (g)	0.2–2.0	0.0–9.8	0.0–0.2	0.1–1.0	0.1–2.0	9.0–60
PUFA[a] (g)	0.3–2.5	0.0–1.8	0.0–0.7	0.0.0.4	0.1–5.0	1.5–47
Folate (ug)	4.0–44	<5.0–61	2–20	8.0–160	50–210	10–230
Tocopherols (mg)	0.1–3.0	0.1–1.0	0.1–4.5	0.0–1.7	0.0–1.0	1.0–35
Potassium (mg)	40–720	60–500	40–1160	100–680	200–520	360–1050
Calcium (mg)	7.0–50	3.0–25	10–160	5.0–200	20–100	20–265
Magnesium (mg)	40–160	3.0–30	5.0–70	3.0–80	40–90	120–400
Phytosterols (mg)	30–90	1.0–83	N/A	1.0–54	110–120	70–215
Polyphenols (mg)	70–100	50–800	N/A	24–1250	120–6500	130–1820
Carotenoids (ug)	N/A	25–6600	0.6–2160	10–20,000	50–600	0.0–1200

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[a]SFA (saturated fat), MUFA (monounsaturated fat), and PUFA (polyunsaturated fat)

[b]U.S. Department of Agriculture, Agriculture Research Service, Nutrient Data Laboratory. 2014. USDA National Nutrient Database for Standard Reference, Release 27. http://www.ars. usda.gov./nutrientdata. Accessed 17 February 2015

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Chapter 3
Insights on the Role of Fiber in Colonic Microbiota Health

Keywords Microbiota • Short-chain fatty acids • Prebiotics • *Bifidobacteria* • Dietary fiber • Dietary patterns • Fruit • Vegetables • Whole grains • Nuts • Supplements • Resistant starch • Inflammation

Key Points

- The diet has been estimated to contribute to as much as 60% of microbiota composition variation with fiber and animal products being the most influential food components.
- Fiber is the primary energy source for maintenance of a healthy bacterial community and source of bioactive fermentation metabolites such as short-chain fatty acids (SCFAs), especially butyrate, which is important for attenuating colonic and systemic inflammation for human health, including maintaining the colonic protective barrier against pathogenic bacteria.
- Changing from a low fiber, meat based diet to a high fiber, plant based diet can significantly improve microbiota health within 24 hrs, but it may take over 10 days for major changes in primary enterotype identity to occur.
- Western diets which contain approximately half of the recommended adequate intake levels of fiber, have led to a fiber which gap is a major factor responsible for microbiota dysbiosis, which predisposes individuals to increased colonic and systemic inflammation, insulin resistance associated with many chronic diseases, and increased frailty in older age.
- Numerous intervention trials show that the increased intake of fiber-rich whole foods, fiber ingredients, or supplements such as prebiotics support a healthier microbiota ecosystem

Introduction

The human microbiota consists of trillions of bacteria, fungi, and viruses that reside primarily in the colon and are an essential part of a complex ecosystem important for human health [1–7]. This microbiota is a bioactive biomass weighing approximately 2 kg, similar to that of a major human organ. It is estimated to contain at least 100 times as many genes as the whole human genome [4–6]. The traditional view was that microbiota effects were limited to colon health, but are now known to be important in maintaining overall physiological homeostasis by preventing increased plasma endotoxemia associated with systemic inflammation, insulin resistance, obesity, and adipose tissue inflammation associated with the risk of many noncommunicable diseases, unhealthy aging, and frailty [1–13].

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The composition of the colonic microbiota is not constant but differs between individuals and can fluctuate markedly within individuals depending on diet, health status, or antibiotic use [1–4]. Interindividual variation in bacterial diversity is a result of environmental factors, such as diet, antibiotic use, lifestyle, hygiene, obesity, and long-term senior residence care [7–14]. An unhealthy alteration in microbial composition, defined as dysbiosis, predisposes an individual to a higher risk of chronic diseases and obesity. The microbiota serves a number of functions including roles in nutrient absorption and food fermentation, stimulation of the host immune system, barrier effects against pathogens, and maintenance of endothelial colonocytes required for health and wellness throughout the life cycle [1–14]. Although each individual has a unique microbial composition, in a healthy human colon, the core bacterial composition is dominated by the phyla *Firmicutes* and *Bacteroidetes*, with only a minor proportion of the phylum *Proteobacteria*, which includes a wide variety of pathogens, such as *Escherichia*, *Salmonella*, *Vibrio*, *Helicobacter*, and *Yersinia*, and many other notable genera [1–4, 7, 8, 15].

Diet is estimated to be responsible for approximately 60% of the colonic microbiota composition variation [1–4, 10, 14]. The colonic microbiota evolved in conjunction with the consumption of diets containing high amounts of dietary fiber (fiber), which was a large part of our preagricultural and preindustrial ancestors' diets [16]. The current low-fiber Western diets (which contain an average of approximately half of the recommended adequate fiber levels) has caused a fiber gap that is increasingly being shown to be a factor responsible for microbiota dysbiosis, which predisposes individuals to a variety of chronic diseases [14], while high fiber intake has been associated with increased fecal *Bacteroides*, *Prevotella*, *Lactobacillales*, and *Bifidobacteria* groups which help to maintain a healthy microbiota. The colonic microbiota bacteria ferments fiber to yield energy, which is important in the growth and maintenance of the microbial community and also leads to the formation of short-chain fatty acids (SCFAs) acetate, propionate, and butyrate, which are beneficial in promoting healthy microbiota and colon and have an important role in maintaining human health inflammatory homeostasis [1, 4, 14]. SCFAs are either absorbed into the circulation or metabolized by the colon, giving rise to minimal loss in the feces, and are used by the human body for a variety of different purposes. These colonic SCFAs have an available energy density of 2 kcals/g compared to 4 kcals/g for refined carbohydrates. Butyrate is an important energy source for colonic epithelial cells, pH control, and anti-inflammatory and anti-obesity functions; acetate and propionate can be utilized by the liver for lipogenesis and gluconeogenesis, respectively [1–4]. Adequate fiber intake tends to support the butyrate-producing bacteria, which help to maintain colon pH at approximately 5.5, but when fiber becomes limiting, the luminal pH can increase to 6.5, which coincides with reduced butyrate-producing bacteria and increased acetate- and propionate-producing bacteria [4].

Over the last decade, the number of human studies on effects of fiber-rich diets and foods, food ingredients, and supplements on modifying the colonic microbiota composition has substantially increased [1–4]. This is because of the expanded use of molecular techniques, such as 16S rRNA sequencing and dedicated DNA chips, which have made it possible to rapidly detail the composition of the human colonic microbiome. The primary objective of this chapter is to assess the effects of fiber, whole plant foods, and dietary patterns on colonic microbiota ecosystem health.

Fiber Fermentation in Model Systems

The effects of fiber fermentation to SCFAs in model systems have been extensively evaluated. The production of specific SCFAs by a range of insoluble and soluble fine-powdered fiber sources is shown in Fig. 3.1 [17]. Resistant starch is regarded as the most butyrogenic fiber source. This

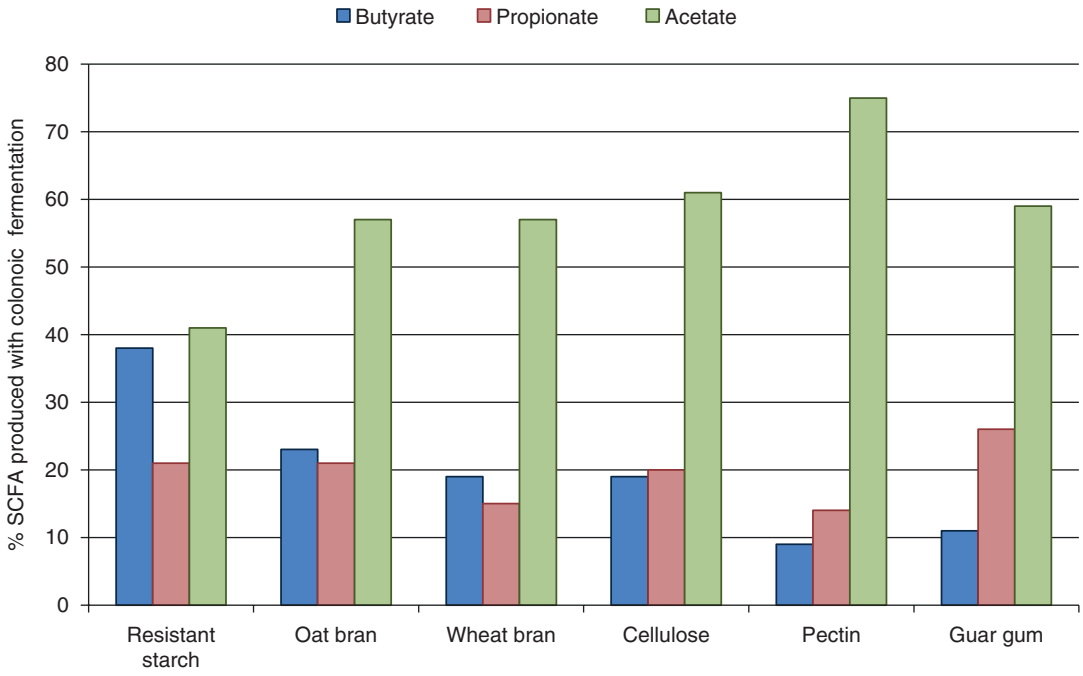

Fig. 3.1 Proportion of short-chain fatty acids (SFCAs) produced during model system fermentation from specific common fiber sources (fine powdered) [17]

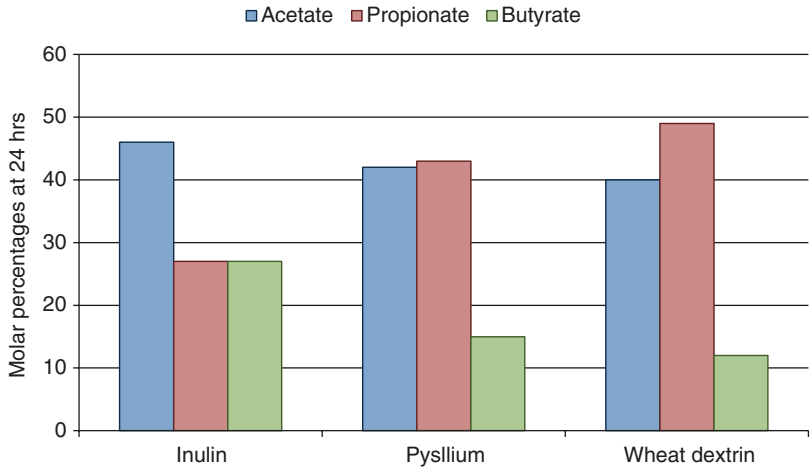

Fig. 3.2 Specific short-chain fatty acids (SCFAs) produced from common commercial soluble fiber supplements and ingredients [18]

analysis indicates that essentially all fiber sources are fermented in the colon, but the degree depends on the composition and physical properties such as solubility and particle size. The molar percentages at 24 h for specific SCFA production from common commercial soluble fibers including wheat dextrin, inulin, and psyllium are summarized in Fig. 3.2 [18]. This study found that at 24 h inulin SFCAs were significantly different from those of psyllium and wheat dextrin. Inulin fermentation resulted in a higher level of butyrate production and significantly higher gas volume at 8–24 h compared to psyllium and wheat dextrin (Fig. 3.3) [18]. Psyllium had a declining rate of

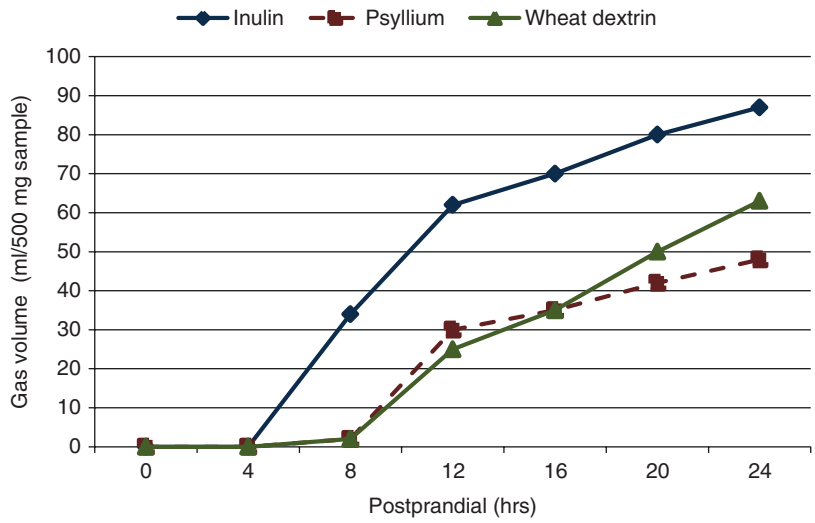

Fig. 3.3 Effect of common commercial soluble fibers on total bowel gas production (inulin gas volume $p < 0.0001$ after 8 h) [18]

SCFA production from 12 to 24 h, whereas wheat dextrin and inulin had a higher rate during that period, which suggests that psyllium may not provide as much SCFAs to the distal colon as wheat dextrin and inulin. An exploratory microbial analysis showed wheat dextrin had more colony-forming units (CFUs) for *Bifidobacteria* (6.12 log10 CFUs/μL) and *Lactobacillus* (7.15 log10 CFUs/μL) compared with the control (4.92 and 6.35 log10 CFUs/μL), or either partially hydrolyzed guar gum or inulin [19].

Human Studies on Fiber and Microbiota Health

Dietary Patterns/Geography and Lifestyle

The type of dietary pattern, especially diets higher in fiber density, generally have the most significant influence on promoting a more diverse, healthier microbiota ecosystem (Table 3.1) [20–32]. Other potential factors affecting core microbiota composition include sex, socioeconomic status, genetics, body mass index (BMI), sanitary, and other environmental conditions. More large and high-quality trials are needed to clarify some of the current complex or contradictory findings related to the specific effects of microbiota species, subspecies, or phyla related to human health [21, 27].

Table 3.1 Summary of observational studies and intervention trials on the effects of dietary patterns on the microbiota and metabolites

Objective	Study Details	Results
Cross-sectional/geographical studies		
Gutierrez-Diaz et al. Assess the association between the adherence to a Mediterranean dietary (MedDiet) pattern, and its components, with fecal microbiota in a cohort of adults (Spanish) [20]	**MedDiet**: 31 adults; 23 females/eight males; mean age of 42 years; higher MedDiet score ≥ 4 [14 g fiber/1000 kcals] vs. lower MedDiet score < 4 [11 g fiber/1000 kcals]; all diets contained 850 mg phenolic/1000 kcal; fecal microbiota quantified by ion torrent 16S rRNA gene-based analysis	Higher MedDiet fiber level was directly associated with higher fecal SCFA concentrations (Fig. 3.7); increased abundance of phylum *Bacteroidetes*, family *Prevotellaceae*, and genus *Prevotella*; and decreased levels of phylum *Firmicutes* and the genus *Ruminococcus*. Higher cereal intake was associated with higher levels of *Bifidobacterium* and *Faecalibacterium*
Wu et al. Compare measures of dietary intake, gut microbiota composition, and the plasma metabolome between healthy human vegans and omnivores (USA) [21]	**Vegans vs. omnivores**: 21 urban adults; 15 vegans/six omnivores; fiber intake for vegans (35 g/day) and omnivores (18 g/day); 3 × 24 h dietary recalls; fecal 16S rRNA-tagged sequencing; fasting plasma and urinary metabolites	The differences in colonic microbiota between omnivores and vegans sampled in an urban environment in the Northeastern USA were quite modest, but the vegan diet plasma metabolome differed markedly from omnivores because of the phytonutrients from the whole foods. Higher consumption of fiber by vegans was not associated with significantly higher levels of fecal SCFAs
De Filippis et al. Evaluate the effect of the MedDiet on the microbiota and its metabolites (Italian) [22]	**MedDiet**: 153 healthy adults; vegans, vegetarians, and omnivores had high MedDiet adherence; 7-day weighed food diary; fecal and urinary samples. Microbiota profiles were quantified by 16S rRNA gene sequences	This study shows the interconnection between MedDiet patterns, fiber, gut microbiota, and microbial metabolites. Increased consumption of fruit, vegetables, legumes, and fiber by subjects with satisfactory adherence to the MedDiet resulted in increased levels of fecal SCFAs, *Prevotella*, and some fiber-degrading *Firmicutes* compared to those with lower adherence to the MedDiet. Western omnivore diets with adequate fiber intake are not necessarily detrimental to microbiota. Low adherence to MedDiets was associated with higher urinary trimethylamine oxide levels
Matijasic et al. Examine differences in the human fecal microbiota composition driven by long-term omnivore vs. vegan/lacto-vegetarian dietary patterns (Slovenia) [23]	**Vegetarian vs. omnivore**: 60 adults; 31 vegetarians (11 lacto-vegetarians, 20 vegans); 29 omnivores; fecal bacteria quantified by DNA extraction and 16S rRNA	Vegetarian diets were associated with higher ratios of *Bacteroides/Prevotella*, *Bacteroides thetaiotaomicron*, *Clostridium clostridioforme*, and *Faecalibacterium prausnitzii*, but with lower ratio of *Clostridium* cluster XIVa compared to omnivore diets

(continued)

Table 3.1 (continued)

Objective	Study Details	Results
Ou et al. Examine if the influence of diet on colon cancer risk is mediated by the microbiota through their metabolites (African-American vs. Native African) [24]	**Urban African-American vs. rural native African diet/lifestyle**: 12 healthy African-Americans, urban Western diets; 12 native Africans, rural traditional diet; age- and sex-matched; mean age 58 years; fecal microbiota were analyzed with 16S ribosomal RNA gene pyrosequencing together with quantitative polymerase chain reaction of the major fermentative, butyrate-producing, and bile acid-deconjugating bacteria	African-Americans consumed twice the protein, three times the dietary fat, and less fiber than the native Africans. The African-American and native African adults had fundamentally different predominance core colonic microbiota: *Bacteroides* vs. *Prevotella*, respectively. The native Africans had significantly higher total bacteria and fecal SCFAs than the African-Americans. Stool butyrate concentrations were significantly correlated with the abundance of the butyrate producers *Clostridium* cluster IV and *Clostridium* cluster XIVa in the native Africans. Fecal secondary bile acid concentrations were higher in African-Americans
Lin et al. Assess the effects of diets in children from Bangladesh and the USA on microbiota composition (US vs. Bangladeshi) [25]	**Affluent US vs. urban Bangladeshi children**: six Bangladeshi children (ages 8–13 years) living in the urban slum of Dhaka, with diets mainly from rice, bread, and lentils, along with little meat; four US children (ages 10–14 years) in affluent regions of California and Oregon with more diverse diets rich in animal fat, protein, carbs, and vegetables; fecal specimens for microbiota profiles quantified by 16S rRNA monthly for 5 months	The distal colon of Bangladeshi children had significantly greater bacterial diversity than that of US children, including novel lineages from several bacterial phyla. Bangladeshi and US children had distinct fecal bacteria community membership and structure; the microbiota of Bangladeshi children was enriched in *Prevotella*, *Butyrivibrio*, and *Oscillospira* and depleted in *Bacteroides* relative to US children. Bangladeshi children had significantly less month-to-month microbiota stability than US children. These results suggest that differing environmental and genetic factors are important in shaping microbiota systems
Zimmer et al. Assess the effects of vegetarian vs. omnivorous diets on microbiota composition (German) [26]	**Vegetarian vs. omnivorous diets**: 249 vegetarians and vegans vs. 249 control omnivores; matched for age and gender; mean age approx. 52 years; fecal samples were evaluated by classical bacteriological isolation and plating identification	Total counts of *Bacteroides* spp., *Bifidobacterium* spp., *Escherichia coli*, and *Enterobacteriaceae* spp. were significantly lower in subjects on the vegan diet compared to those on the omnivorous diet. Subjects consuming the vegetarian diet ranked between vegans and omnivores. Also, subjects on a vegan or vegetarian diet showed significantly lower stool pH and counts of *E. coli* and *Enterobacteriaceae* than those on the omnivorous diet suggesting a healthy microbiota environment (Fig. 3.6)
Kabeerdoss et al. Compare effects of lacto-vegetarian and omnivorous diets on the fecal microbiota of young women (Southern India) [27]	**Lacto-vegetarian vs. omnivorous**: 32 lacto-vegetarian and 24 omnivorous women from a similar social and economic background; median age 19 years; median BMI 21; macronutrient intake and anthropometric data were collected; fecal microbiota of interest were quantified by real-time PCR with SYBR Green primers targeting 16S rRNA genes	Omnivores had an increased relative abundance of *Clostridium* cluster XIVa bacteria, specifically *Roseburia-E. rectale* and butyryl-CoA-transferase gene, associated with microbial butyrate production, compared with vegetarians. Both diets had the same median crude fiber intake. The relative proportions of other microbial communities were similar in both groups

Table 3.1 (continued)

Objective	Study Details	Results
Wu et al. Investigate the effects of diet on colonic microbiota (USA) [28]	**Western vs. traditional diet**: 98 healthy volunteers; collected diet information using two questionnaires that queried recent diet and habitual long-term diet (food frequency questionnaire); stool samples were collected, and DNA samples were analyzed by 454/Roche pyrosequencing of 16S rDNA gene segments and, for selected samples, shotgun metagenomics	The *Bacteroides* enterotype was highly associated with animal protein and saturated fats which suggest meat consumption (Western diet) The *Prevotella* enterotype was associated with higher-carbohydrate−/fiber-based diet more typical of agrarian societies (vegetarian diet)
De Filippo et al. Assessment of microbiota differences between urban European and rural African children [29]	**Urban European vs. rural African children**: 14 healthy rural African children, 10.0–14.2 g fiber/day; 15 healthy European children, living in the urban area of Italy, 5.6–8.4 g fiber/day; ages between 1 and 6 years. Microbiota major bacteria profiles quantified by 16S rDNA sequencing	The rural African children showed a significant enrichment in *Bacteroidetes* and depletion in *Firmicutes*, with a unique abundance of bacteria from the genus *Prevotella* and *Xylanibacter*, known to contain bacterial genes for cellulose and xylan hydrolysis, completely lacking in the European children. The African children had significantly higher fecal SCFAs (Fig. 3.4) and significantly lower *Enterobacteriaceae* (*Shigella* and *Escherichia*) than European children (Fig. 3.5)
Intervention trials		
Tap et al. Assess the short-term effects of increased fiber intake on the microbial composition (France) [30]	**Crossover RCT (high vs. low fiber)**: 19 healthy normal-weight adults; ten females/nine males; age 19–25 years; basal diet supplemented with 40 or 10 g fiber/day; 5 days; 15-day washout period; fecal samples analyzed by a 16S rRNA gene pyrosequencing, intestinal cell genotoxicity assay, metatranscriptomics sequencing approach and SCFAs	Higher-fiber diets increased microbiota diversity and stability and promoted a higher *Prevotella*/*Bacteroides* ratio, increased fecal SCFAs, and modulated the expression of microbiota metabolic pathways such as glycan metabolism, with genes encoding carbohydrate-active enzymes active for fiber, compared to the low-fiber diets, within 5 days. This was particularly true when subjects switched from their 10 g fiber diet to the 40 g fiber/day diet
David et al. Compare the effects of plant- vs. animal-based diets on microbiota (USA) [31]	**Crossover RCT (plant- vs. animal-based diets)**: ten US adults; six males/four female; ages 21–33 years; BMI range from 19 to 32; two diets: a plant-based diet (rich in whole grains, legumes, fruits, and vegetables; 26 g fiber/1000 kcals); and an animal-based diet (consisting of meats, eggs, and cheeses; 0 g fiber/day); 5 days; 6-day washout; fecal microbiota quantification by 16S rRNA gene/PCR amplified	Plant-based diets increased saccharolytic bacteria and SCFA fecal content, whereas animal-food-based diets increased the total count of bile-tolerant microorganisms, decreased the levels of *Firmicutes* able to ferment plant polysaccharides, and increased the levels of the products of amino acid fermentation and *Bilophila wadsworthia*, known to elevate the risk of inflammatory bowel disease. This study suggests that microbiota can rapidly respond to large changes in diet composition within 24 hrs

(continued)

Table 3.1 (continued)

Objective	Study Details	Results
Kim et al. Evaluate the effects of a strict vegetarian diet on blood biomarkers of glucose and lipid metabolisms, fecal microbiota, and SCFAs in obese subjects with diabetes or hypertension (Korea) [32]	**Open-label (strict vegetarian diets)**: six obese subjects with type 2 diabetes and/or hypertension were assigned to strict vegetarian diets for 1 month, and blood biomarkers of glucose and lipid metabolisms and fecal microbiota were determined by 16S rRNA gene sequencing	Strict vegetarian diets reduced the *Firmicutes*-to-*Bacteroidetes* ratio in the microbiota, and led to a decrease in pathogenic bacteria such as the *Enterobacteriaceae* and an increase in commensal microbes such as *Bacteroides fragilis* and *Clostridium* species belonging to clusters XIVa and IV. Additional benefits included reduction in body weight, blood triglycerides, total cholesterol, low-density lipoprotein cholesterol, and hemoglobin A1c and improved fasting glucose, postprandial glucose, and fecal lipocalin-2 levels
Wu et al. Investigate the association of diet and colonic microbiota over 10 days (USA) [28]	**Parallel RCT (low-fiber/high-fat vs. high-fiber/low-fat diets)**: ten omnivorous adults; controlled-feeding study; high-fat/low-fiber vs. low-fat/high-fiber diets; 10 days; stool samples were collected; DNA samples were analyzed by 454/Roche pyrosequencing of 16S rDNA gene segments and, for selected samples, shotgun metagenomics	Diets can change microbiota species composition within 24 h, but overall enterotype identity remained stable during the 10-day study. Transit time was faster with the high-fiber diet (2–4 days) than with the high-fat diet, as expected. The changes in microbiota species composition were faster than clearance of stool from the colon

Children

Two international cross-sectional studies with children suggest that traditional diets with higher fiber density support a more diverse, healthier core microbiota ecosystem than do Western lower-fiber diets [25, 29]. The first study (ten children; age 8–24 years; six Bangladeshi and four US children; Bangladeshi diet was of limited variety, mainly rice, bread, and lentils; US diet was diverse, rich in animal products, protein, refined carbohydrates, and some vegetables) observed distinct fecal bacteria community composition and structure with the microbiota of Bangladeshi children being more diverse and enriched in *Prevotella*, *Butyrivibrio*, and *Oscillospira* and depleted in *Bacteroides* relative to US children [25]. The second study (29 healthy children; age 1–6 years; 14 rural African children with 10–14 g fiber/day vs. 15 Italian children with 6–8 g fiber/day) observed that rural African children had a significant enrichment in *Bacteroidetes* and depletion in *Firmicutes*, with a unique abundance of bacteria from the genus *Prevotella* and *Xylanibacter*, known to contain bacterial genes for cellulose and xylan hydrolysis, completely lacking in the European children [29]. The African children had significantly higher fecal SCFAs (Fig. 3.4) and lower *Enterobacteriaceae* (*Shigella* and *Escherichia*) than European children (Fig. 3.5).

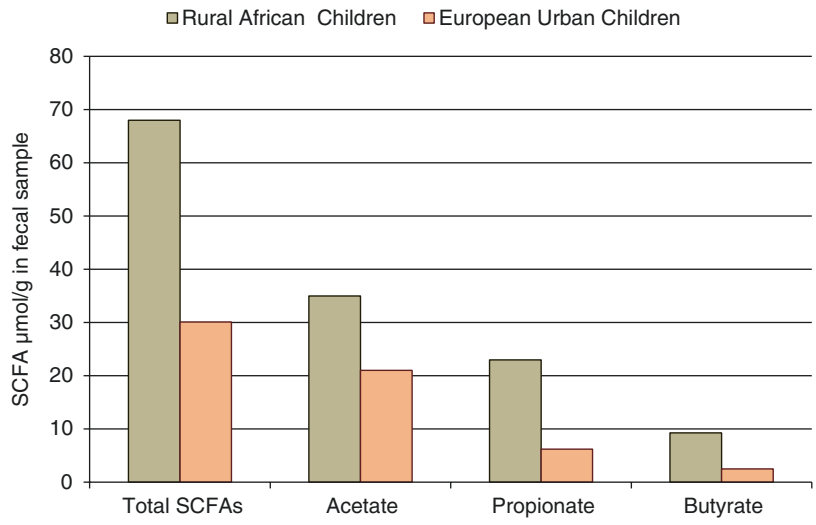

Fig. 3.4 Amounts of short-chain fatty acids (SCFAs) in fecal samples of African and European children between 1 and 6 years ($p < 0.001$) [29]

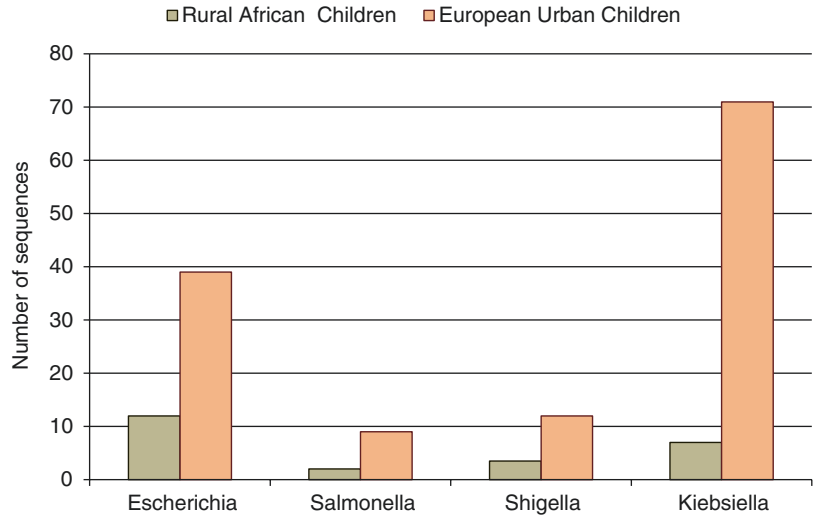

Fig. 3.5 Levels of potentially pathogenic intestinal bacteria in fecal samples of African and European children ($p < 0.05$) [29]

Adults

An international cross-sectional study (24 adults; mean age 58 years; 12 healthy African-Americans with urban Western diets; 12 age- and sex-matched healthy native Africans with rural traditional diets) found that the African-American diets were higher in protein and fat and lower in fiber with fundamentally different predominant core microbiota rich in *Bacteroides* compared to native Africans with fiber rich diets and microbiota dominated by *Prevotella* [24]. The native Africans had significantly higher total bacteria and fecal SCFAs than African-Americans as a result of higher fiber intake. Stool butyrate concentrations significantly correlated with the abundance of the butyrate producers *Clostridium* cluster IV and *Clostridium* cluster XIVa which were higher in the native Africans. Fecal secondary bile acid concentrations were higher in African-Americans because of higher animal fat intake.

Vegetarian vs. Omnivore Diets

There are at least five cross-sectional studies [21, 23, 26–28] and two intervention trials [31, 32] on the effects of vegetarian vs. omnivore diets on microbiota composition. The largest cross-sectional study (298 German adults; 149 healthy vegetarians and vegans vs. 149 healthy omnivores matched for sex and gender; mean age 52 years) observed that vegetarian and vegan diets were associated with significantly lower stool pH, *E. coli*, and *Enterobacteriaceae* levels and healthier microbiota ecosystems compared to omnivorous diets (Fig. 3.6) [26]. Additionally, several intervention trials further support the benefits of vegetarian-type diets on microbiota and inflammatory health [31, 32]. A US crossover RCT (ten adults; six males and four females; mean age 22 years; BMI 19–32; plant-based diet with whole grains, legumes, fruits, vegetables, and 26 g fiber/1000 kcals; animal-based diet with meat, eggs, cheeses, and 0 g fiber/day; 5-day duration; 6-day washout) demonstrated that plant-based

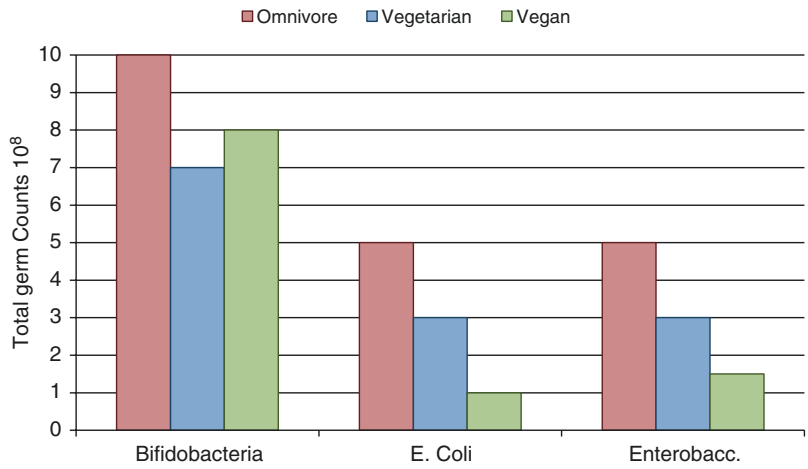

Fig. 3.6 Effect of vegetarian vs. omnivore dietary patterns on microbiota bacteria composition [26]

diets increased polysaccharide-fermenting bacteria and total fecal SCFAs, whereas animal-based diets increased the level of bile-tolerant microbes, decreased polysaccharide-fermenting *Firmicutes*, and increased amino acid fermentation metabolites and level of secondary bile acids within 24 hrs [31]. A Korean open-label trial (six obese adults; strict vegetarian diet; 1-month duration), found that a strict vegetarian diet beneficially changed the microbiota composition by reducing the *Firmicutes*-to-*Bacteroidetes* ratio, pathogenic bacteria such as the *Enterobacteriaceae*, and fecal lipocalin-2 levels and increased the commensal microbes such as *Bacteroides fragilis* and *Clostridium* species belonging to clusters XIVa and IV compared to baseline values [32]. This study also found strict vegetarian diets lowered body weight and fasting glucose hemoglobin A1c levels. In contrast, three small cross-sectional studies from the USA, India, and Slovenia observed vegetarians had only modest microbiota composition differences compared to omnivores [21, 23, 27].

Mediterranean Diet (MedDiet)

There are two cross-sectional studies on the effects of MedDiets on microbiota composition and fecal SCFAs [20, 22]. A Spanish study (31 adults; 23 females and eight males; mean age 42 years; higher MedDiet score ≥ 4 [14 g fiber/1000 kcals] vs. lower MedDiet score < 4 [11 g/1000 kcals]) observed a direct association between MedDiet fiber level and fecal SCFA concentrations (Fig. 3.7). A higher MedDiet score increased abundance of the phylum *Bacteroidetes*, the family *Prevotellaceae*, and the genus *Prevotella* and decreased levels of the phylum *Firmicutes* and the genus *Ruminococcus* [20]. An Italian study (153 healthy adults; composed of vegans, vegetarians, and omnivores with high MedDiet adherence; 7-day food diary) observed that the increased consumption of fruit, vegetables, legumes, and fiber by subjects with satisfactory adherence to the MedDiet resulted in increased levels of fecal SCFAs and increased *Prevotella* and some fiber-degrading *Firmicutes* compared to subjects with lower adherence to the MedDiet and fiber intake [22]. Low adherence to MedDiets was associated with higher urinary trimethylamine oxide levels, which has been associated with increased cardiovascular disease risk.

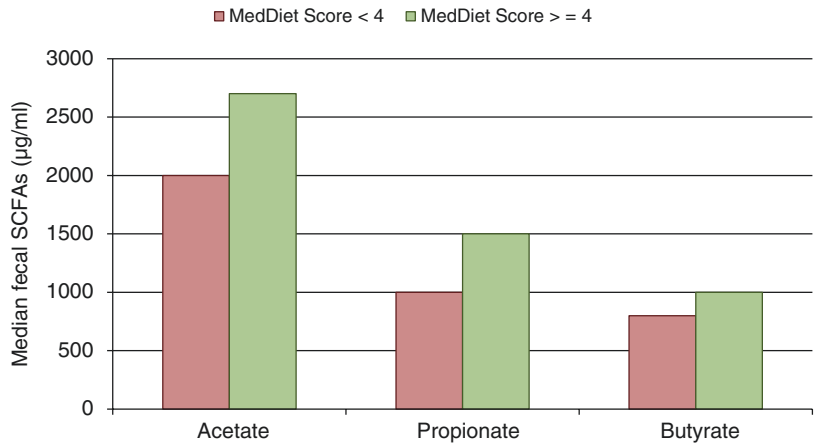

Fig. 3.7 Effect of Mediterranean diet (MedDiet) score on fecal short-chain fatty acid (SCFA) concentrations [20]

Higher-Fiber vs. Lower-Fiber Diets

Two RCTs indicate that high-fiber diets can positively influence microbiota diversity vs. low-fiber diets [27, 30]. A small US RCT (ten omnivorous adults; controlled-feeding study; low-fiber vs. high-fiber diets; 10 days) reported that detectable changes in microbiota species composition occurred within 24 h after consuming low-fiber or high-fiber diets but that core enterotype identity remained stable (e.g., no changing from *Bacteroides* to *Prevotella* during the 10-day study) [28]. A crossover RCT (19 healthy normal-weight adults; ten females/nine males; age 19–25 years; basal diet supplemented with 40 or 10 g fiber/day; 5 days; 15-day washout period) found that higher-fiber diets increased microbiota diversity and stability and promoted a higher *Prevotella*/*Bacteroides* ratio, increased fecal SCFAs, and modulated the expression of microbiota metabolic pathways such as glycan metabolism, with genes encoding carbohydrate-active enzymes active for fiber compared to lower-fiber diets within 5 days [30]. This was particularly true when subjects switched from their 10 g fiber diet to the 40 g fiber/day diet.

Whole Plant Food Randomized Controlled Trials (RCTs)

Eleven RCTs on the role of whole or minimally processed plant foods in promoting a healthy microbiota and related metabolites are summarized in Table 3.2 [33–43].

Table 3.2 Summary of RCTs on the effects of fiber-rich whole or minimally processed plant foods on microbiota and metabolites

Objective	Study Details	Results
Fruit and vegetables		
Klinder et al. Assess the impact of fruit and vegetable intake on gut microbiota (UK) [33]	**Parallel RCT (fruits and vegetables)**: 122 UK participants; 60% female; mean age 50 years; mean BMI 28; high-flavonoid and low-flavonoid fruit and vegetable intervention groups consumed 2, 4, and 6 portions vs. habitual control diet; 6 weeks each; fecal bacteria quantification by fluorescence in situ hybridization	There was a significant dose effect for fruit and vegetable intake on increasing *C. leptum-R. bromii/flavefaciens*, while a trend was reported for *Bifidobacterium* ($p = 0.090$) and *Bacteroides*/*Prevotella* ($p = 0.070$). Increased intake of fruit and vegetable portions and flavonoids was protective against the growth of potentially pathogenic *Clostridia* with a negative correlation ($r = -0.145$), and higher-fiber intake was weakly positively correlated with *Bacteroides*/*Prevotella* ($r = 0.091$). TNF-α was reduced with the fruit- and vegetable-induced microbiota changes
Eid et al. Assess the impact of palm date consumption, rich in both phenolics and fiber, on the growth of colonic microbiota (UK) [34]	**Crossover RCT (dates)**: 22 healthy human volunteers (age range between 18 and 55 years); 11 males and 11 females; were randomly assigned to either seven dates (50 g/day) or control maltodextrin-dextrose (37 g/day); 21-day duration; 14-day washout period	After consumption of dates relative to baseline, there were no significant changes in the growth of select microbiota bacterial groups or SCFAs. Dates improved bowel movement regularity and reduced DNA oxidative damage (comet assay) in the fecal material, which is suggestive of potential lower colorectal cancer risk

Table 3.2 (continued)

Objective	Study Details	Results
Vendrame et al. Examine the effects of wild blueberry beverage on microbiota composition (Italy) [35]	**Crossover RCT (wild blueberry beverage)**: 20 healthy males; mean age 46 years; mean BMI 25; wild blueberry drink (25 g of wild blueberry powder in 250 mL of water) or placebo drink (250 mL of water, 7.5 g of fructose, 7 g of glucose plus citric acid/blueberry flavor/colors) twice a day/fecal microbiota quantified by real-time polymerase chain reaction methodology	Wild blueberry beverage significantly increased total *Eubacteria* and *Bifidobacterium* spp. twofold. No significant differences were observed for *Bacteroides* spp., *Prevotella* spp., *Enterococcus* spp., and *Clostridium coccoides*. This study suggests that regular consumption of wild blueberry polyphenols and fiber can positively promote a healthy microbiota ecosystem
Shinohara et al. Investigate the effects of apples on the colonic microbiota (Japan) [36]	**Open-label clinical (whole apple)**: eight healthy men; two apples/day added to habitual diet for 14 days; microbiota quantified by sequencing of 16S rRNA genes	Compared to baseline, apple intake significantly increased fecal *Bifidobacteria* and decreased *C. perfringens* after 7 days. There was also an increase in fecal SCFAs and a decrease in fecal ammonia and sulfide levels. Apple pectin appears to be primarily responsible for this beneficial microbiota change
Costabile et al. Assess the impact of a very-long-chain inulin, derived from globe artichoke on the human intestinal microbiota (UK) [37]	**Double-blinded, crossover RCT (globe artichoke)**: 32 healthy adults; mean age 25 years; 18 females, 14 males; randomized into either 10 g/day of very-long-chain inulin, derived from approx. two medium globe artichokes or maltodextrin for two 3-week study periods, 3-week washout period; enumeration of fecal microbial populations by fluorescence in situ hybridization (FISH)	Globe artichoke inulin significantly increased fecal *Bifidobacteria* and *Lactobacilli* compared with the placebo. Additionally, levels of the *Atopobium* group significantly increased, while *Bacteroides*/*Prevotella* numbers were significantly reduced. No significant changes in fecal SCFA levels were observed. There was a significant increase in mild and moderate bloating upon globe artichoke inulin ingestion
Whole grains		
Heinritz et al. Examined the effect of two diets with different levels of fiber and fat on microbial composition and activity by using the pig microbiota as a model for humans (Netherlands) [38]	**Parallel RCT pig-human model (high-fiber whole grains/lower-fat vs. low-fiber diets/higher fat)**: eight pigs were equally allotted to two treatments, either fed a low-fat/high-fiber (whole wheat grain type) or a high-fat/low-fiber diet; 7 weeks; feces were sampled weekly; diet effects on fecal microbiota were quantified with real-time PCR, DNA fingerprinting, and metaproteomics	Significantly higher numbers of *Lactobacilli*, *Bifidobacteria*, and *Faecalibacterium prausnitzii* were found in the feces of the whole-wheat-grain-type (low-fat/high-fiber) diet-fed pigs, while pathogenic type *Enterobacteriaceae* were significantly increased in the high-fat/low-fiber diet-fed pigs. Significantly higher total and individual fecal SCFA levels, especially butyrate, were found with whole-wheat-grain-type diets vs. the low-fiber diets (Fig. 3.8)
Wang et al. Evaluate the effect of β-glucan-enriched breakfast cereals on microbiota composition and cardiovascular disease (CVD) risk factors (Canada) [39]	**Single-blind, crossover RCT (β-glucan-enriched breakfast cereals)**: 30 hyperlipidemic adults; American Heart Association (AHA) diet plus four breakfasts containing 3 g high molecular weight (MW) β-glucan, 3 g and 5 g low MW β-glucan, vs. refined wheat and rice (control); 5-week study period; 4-week washout; fecal samples were collected after each intervention phase; microbiota quantified by sequencing of 16S rRNA genes	The high MW β-glucan significantly increased *Bacteroidetes* and decreased *Firmicutes* abundance compared to control. At the genus level, consumption of 3 g/d high MW β-glucan increased *Bacteroides*, tended to increase *Prevotella*, but decreased *Dorea*, whereas neither of the low MW β-glucan diets altered the microbiota composition. The high MW β-glucan changes in microbiota composition were significantly correlated with shifts of CVD risk factors, including reduced BMI, waist circumference, blood pressure, as well as triglyceride levels. This study suggests the microbiota health effects of high MW β-glucan

(continued)

Table 3.2 (continued)

Objective	Study Details	Results
Martinez et al. Assess the effect of whole grains on both the colonic microbiome and human physiology (USA) [40]	**Crossover RCT (various whole grain foods)**: 28 healthy subjects; 11 males and 17 females; mean age 26 years; mean BMI 25; daily dose of 60 g of whole grain barley (19 g fiber), brown rice (4.4 g fiber), or an equal mixture of the two (11.5 g fiber); 4-week treatments with 2-week washout; fecal and blood samples were taken at baseline and after each treatment period; fecal microbiota was determined by 16 S rRNA sequencing	The barley whole grain foods increased overall microbiota diversity and specifically *Roseburia*, *Bifidobacterium*, and *Dialister*, and the species *Eubacterium rectale*, *Roseburia faecis*, and *Roseburia intestinalis*. Additionally, whole grain barley reduced IL-6, associated with increased *Dialister* and decreased *Coriobacteriaceae* in the microbiota. No significant differences were detected in fecal SCFAs, but this was because of colonic absorption
Carvalho-Wells et al. Evaluate the effects of maize whole grain and refined breakfast cereal on the microbiota (UK) [41]	**Double-blinded, placebo-controlled crossover RCT (maize whole grain vs. refined breakfast cereal)**: 32 subjects; 20 females/12 males; mean age 32 years; mean BMI 23; 48 g/day maize whole grain breakfast cereal or refined-grain cereal placebo; 3-week trial periods; 3-week washout; fecal microbiota analyzed by fluorescence in situ hybridization with 16S rRNA oligonucleotide-specific probes	Maize whole grain breakfast cereal significantly increased levels of fecal *Bifidobacteria* compared with the control cereal but returned to baseline levels after the washout period. There were no statistically significant changes of fecal SCFAs, bowel habit data, fasted lipids/glucose, blood pressure, BMI, and waist circumference
Costabile et al. Compare the effects of whole grain wheat breakfast cereal on the human microbiota compared to wheat bran (UK) [42]	**Double-blinded, crossover RCT (whole grain wheat breakfast cereal)**: 31 volunteers; average age 25 years; 16 females/15 males; BMI 20–30; two groups consuming either daily 48 g of whole grain wheat or wheat bran breakfast cereals; 3-week study periods, 2-week washout; fecal microbiota from 16S rRNA targeted oligonucleotide probes and fluorescence in situ hybridization	The whole grain wheat cereals significantly increased the numbers of fecal *Bifidobacteria* and *Lactobacilli* compared with wheat bran cereal. Ingestion of both breakfast cereals resulted in a significant increase in ferulic acid concentrations in blood but no discernible difference in feces or urine. No significant differences in fecal SCFAs, fasting blood glucose, insulin, total cholesterol, triglycerides, or HDL-C were observed upon ingestion of whole grain compared with wheat bran breakfast cereals
Almonds		
Liu et al. Evaluate the effects of almonds on the microbiota (Chinese) [43]	**Parallel RCT (almonds)**: 48 healthy adult volunteers; daily dose of roasted almonds (56 g) vs. commercial fructooligosaccharides (positive control; 8 g); 6 weeks; fecal samples were evaluated by classical bacteriological isolation and plating identification	Almond intake resulted in significant increases in the fecal populations of *Bifidobacterium* spp. and *Lactobacillus* spp., and the growth of the pathogen *Clostridium perfringens* was significantly lowered. Almond intake significantly changed fecal microbiota enzyme activities, by increasing fecal β-galactosidase activity and decreasing β-glucuronidase, nitroreductase, and azoreductase activities. Almonds had significantly lower overall prebiotic effects than fructooligosaccharides (Fig. 3.9)

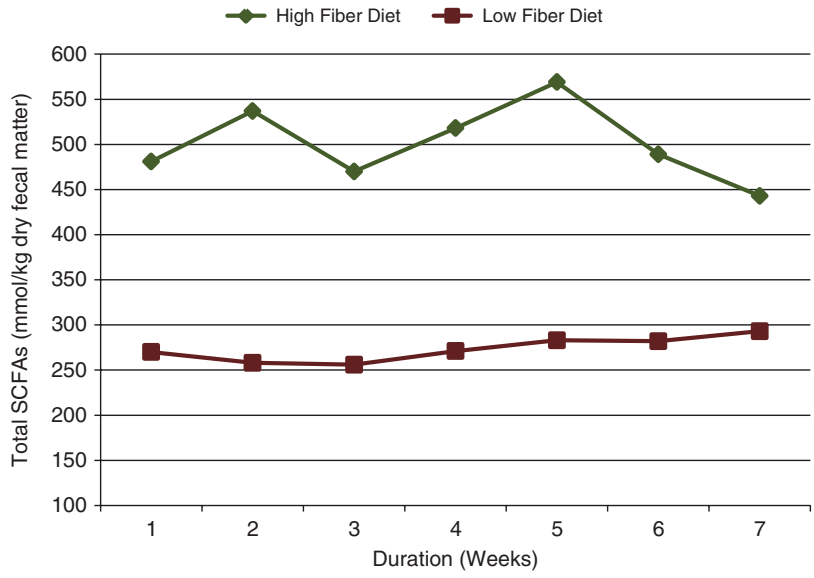

Fig. 3.8 Effect of fiber from wheat bran and cellulose on stool short-chain fatty acid (SCFA) levels in pig model study over 7 weeks ($p = 0.002$) [38]

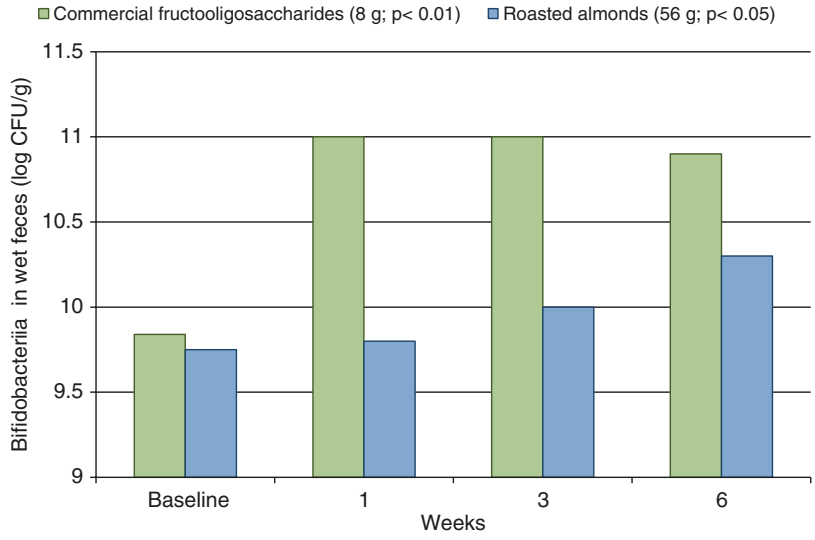

Fig. 3.9 Effect of almonds vs. fructooligosaccharides on fecal *Bifidobacteria* levels in healthy humans [43]

Fruits and Vegetables

RCTs have consistently shown increased fruit and vegetable intake promotes colonic microbiota health to varying degrees [33–37]. A UK-based dose-response RCT (122 adults 61% female; mean age 50 years; mean BMI 28; daily addition intake by 2, 4, and 6 portions vs. habitual diet control group; duration of 6 weeks) found that increasing the intake of fruits and vegetables significantly increased *C. leptum-R. bromii/flavefaciens* and borderline significantly increased *Bifidobacterium* ($p = 0.090$) and *Bacteroides/Prevotella* ($p = 0.070$) and was negatively associated with the growth of potentially pathogenic clostridia (e.g., *Clostridium histolyticum/perfringens*) [33]. The active fruit and vegetable protective components were identified as fiber and flavonoids. Lower TNF-α systemic inflammation was associated with the fruit- and vegetable-induced microbiota pattern. These findings are also supported by other specific fruit and vegetable RCTs on apples, blueberries, and artichokes, which were shown to promote healthier microbiota composition [35, 36] and on dates which were shown to improve bowel movement regularity and reduce DNA oxidative damage in the fecal material [34].

Whole Grains

RCTs on increased whole grain intake have consistently shown promotion of colonic microbiota health [38–42]. A pig-human model trial (16 pigs; fed a low-fat/high-fiber (whole wheat/cereal fiber) or a high-fat/low-fiber diet; 7 weeks; weekly fecal samples) found that whole wheat fiber-rich diets resulted in significantly higher numbers of *Lactobacilli*, *Bifidobacteria*, and *Faecalibacterium prausnitzii* compared to a significant increase in pathogenic type *Enterobacteriaceae* in the low-fiber diet-fed pigs [38]. Additionally, the higher-whole wheat/cereal-fiber diets significantly increased total fecal SCFA levels compared to the low-fiber diets (Fig. 3.8). Several RCTs show similar findings on the beneficial effects of whole grains on the microbiota and cardiometabolic health [39–42]. A Canadian crossover RCT (30 hyperlipidemic adults; age 27–78 years; American Heart Association core diet; four breakfasts containing 3 g high molecular weight (MW) β-glucan, 3 g and 5 g low MW β-glucan, or refined-grain control breakfast cereal for 5 weeks; 4-week washout) showed that the consumption of breakfast cereal with 3 g high MW β-glucan/day increased *Bacteroides* and *Prevotella*, decreased pathogenic *Dorea*, and was correlated with lower cardiovascular risk factors, including BMI, waist circumference, blood pressure, and triglyceride levels. This effect of β-glucan was also shown in a crossover RCT (28 healthy, young adults; mean age 26 years; 60 g whole grain barley; 4 weeks) which found that barley whole grain increased levels of the genera *Roseburia*, *Bifidobacterium*, and *Dialister* and the species *Eubacterium rectale*, *Roseburia faecis*, and *Roseburia intestinalis* and significantly reduced systemic IL-6 coinciding with higher proportions of *Dialister* and lower abundance of *Coriobacteriaceae* [40]. In two double-blinded crossover RCTs (63 healthy, young adults; mean age 25–32 years; 48 g of whole grain wheat or maize breakfast cereals; 3 weeks), whole grain breakfast cereal significantly increased levels of fecal *Bifidobacteria* compared with the control cereal without significant change in SCFAs levels or cardiovascular risk factors [41, 42].

Almonds

A RCT on roasted whole almonds (48 healthy adults; daily dose of 56 g roasted almonds vs. 8 g commercial fructooligosaccharides as a positive control; 6 weeks) demonstrated that whole almonds significantly increased the fecal populations of *Bifidobacterium* spp. (Fig. 3.9) and *Lactobacillus* spp. but to a lesser degree than commercial fructooligosaccharides [43].

Isolated or Synthetic Fiber Source Randomized Controlled Trials (RCTs)

Twelve published RCTs on the effects of soluble corn fiber, inulin, short-chain fructooligosaccharides, resistant starch, and polydextrose as food ingredients or supplements in promoting a healthy microbiota and related metabolites are summarized in Table 3.3 [44–56].

Table 3.3 Summary of RCTs on effects of isolated or synthetic fiber sources on microbiota and its metabolites

Objective	Study Details	Results
Soluble corn fiber (SCF)		
Costabile et al. Determine optimum SCF dose on tolerance, desired changes to microbiota and fermentation metabolites in healthy adults (Finnish) [44]	**Double-blinded, parallel RCT**: 24 healthy volunteers; 12 female/12 males; mean age 33 years; mean BMI 24; dose-response 8, 14, or 21 g SCF; 14 days	SCF significantly increased fecal *Bifidobacteria* at 8 g/day and was well tolerated in doses as high as 21 g/day
Hooda et al. Explore the impact of SCF on the composition of the microbiota (USA) [45]	**Double-blinded, placebo-controlled crossover RCT**: 20 healthy adult men; baseline mean fiber intake 14 g/day; consumed snack bars with 21 g SCF/day or 0 SCF/day; 21 days; no washout period; fecal microbiota DNA amplification of the V4–V6 region of the 16S rRNA gene and 454 pyrosequencing	The consumption of SCF led to greater fecal *Clostridiaceae* and *Veillonellaceae* and lower *Eubacteriaceae* compared with a no-fiber supplementation. The abundance of *Faecalibacterium*, *Phascolarctobacterium*, *Dialister*, and *Lactobacillus* was significantly greater in response to SCF intake. *Faecalibacterium prausnitzii*, known for its anti-inflammatory properties, was significantly increased with SCF intake
Inulin or short-chain fructooligosaccharides (FOS)		
Salazar et al. Evaluate the effects of inulin/oligofructose on the human microbiota (Belgium) [46]	**Double-blinded, placebo-controlled, parallel RCT**: 30 obese women; received either 16 g/day inulin/oligofructose 50/50 mix or maltodextrin; 3 months; 16S rRNA gene sequencing	The number of fecal *Bifidobacterium* was significantly increased by inulin/oligofructose 50/50 mix compared to the control group, and increasing *B. longum* negatively correlated with serum lipopolysaccharide endotoxin
Holscher et al. Assess effects of agave inulin on the microbiota of healthy adults (USA) [47]	**Double-blinded, placebo-controlled, crossover RCT (agave inulin):** 29 healthy adults; consumed 0, 5.0, or 7.5 g agave inulin daily for 21 days; 7-day washout; fecal samples were collected during days 16–20 of each period; 16S Illumina sequencing	Fecal *Actinobacteria* and *Bifidobacterium* were significantly enriched by three- and fourfold after 5.0 and 7.5 g agave inulin/day, respectively, compared with control. *Desulfovibrio* were depleted 40% with agave inulin compared with control. Also, the level of inulin intake was positively associated with fecal butyrate concentration
Dewulf et al. Examine the effects of inulin/oligofructose on microbiota and cardiometabolic health in obese women (Belgium) [48]	**Double-blinded, placebo-controlled RCT**: 30 obese women; mean age 48 years; mean BMI 36; 16 g/day of inulin/oligofructose 50/50 mix or placebo maltodextrin; 3 months; feces analyzed by phylogenetic microarrays and qPCR analysis of 16S rDNA; plasma and urine metabolic profiles were analyzed by1H-NMR spectroscopy	The consumption of 16 g of 50/50 mix of inulin/oligofructose increased *Bifidobacterium* and *Faecalibacterium prausnitzii*; both bacteria negatively correlated with serum lipopolysaccharide levels and decreased *Bacteroides intestinalis*, *Bacteroides vulgatus*, and *Propionibacterium*, an effect associated with a slight decrease in fat mass and with plasma lactate and phosphatidylcholine levels. However, no clear treatment effects were found in plasma or urine metabolomic profile analyses

(continued)

Table 3.3 (continued)

Objective	Study Details	Results
Bouhnik et al. Investigate the effects of FOS ingestion on the colonic microflora in older adults [49]	**Open-label trial**: 12 healthy older adults; six females/six males; mean age 69 years; three consecutive periods: basal period (2 weeks), FOS ingestion period (8 g/day for 4 weeks) and follow-up period (4 weeks); standard colony-forming units (cfu) plate count method	Fecal *Bifidobacteria* counts were significantly increased during the FOS period (9.2 log cfu/g vs. 8.5 log cfu/g during the basal period) and returned to their initial values at the end of follow-up (8.4 log cfu/g). Fecal pH decreased during FOS ingestion compared to the basal period. Flatus and bloating were significantly more frequent during FOS ingestion when compared to the basal period, but the intensity of these symptoms was mild
Bouhnik et al. Determine the dose-response bifidogenic effects of FOS (French) [50]	**Dose-response RCT**: 40 healthy volunteers; 18 males/22 females; mean age 29 years; five groups of eight subjects each consumed a dose of 2.5, 5.0, 7.5, and 10 g/day of FOS added to the habitual diet or a placebo; 7 days; fecal stools collected before day eight and at the end of day 15; classical bacteriological isolation and plating identification	*Bifidobacteria* count increase was higher in FOS than in placebo group for all doses tested. A significant correlation between the ingested dose of FOS and fecal *Bifidobacteria* counts was observed at day 15. Total anaerobes increased at the dose of 10 g/day. The frequency of digestive symptoms was not different between FOS at any of the doses tested and placebo
Bouhnik et al. Determine the threshold dose of FOS that leads to a significant increase in fecal *Bifidobacteria* and the possibility of a dose-response relationship in healthy volunteers consuming their usual diet (France) [51]	**Dose-response RCT**: 40 healthy volunteers; 18 males/22 females; mean age 30 years; eating their usual diets were randomly divided into five groups of eight subjects and received FOS at a dose of 0, 2.5, 5.0, 10, and 20 g/day for 7 days; stools were collected before day one and at the end of day eight; classical bacteriological isolation and plating identification	There was a significant correlation between the dose of FOS ingested and the fecal *Bifidobacteria* counts observed at day eight. Excess flatus was significantly more frequent in subjects consuming 20 g FOS than other FOS levels. The optimal and well-tolerated dose of FOS that significantly increased fecal *Bifidobacteria* in healthy volunteers consuming their usual diet is 10 g/day
Resistant starch		
Karimi et al. Determine the effects of resistant starch on metabolic endotoxemia and insulin resistance, known biomarkers of microbiota health (Iran) [52]	**Parallel, double-blinded, placebo RCT**: 56 females with type 2 diabetes mellitus; 10 g/day resistant starch subtype 2 vs. placebo control group; 8 weeks; marker of microbiota dysfunction endotoxemia	In women with type 2 diabetes, resistant starch subtype 2 significantly decreased endotoxin (−25%) and homeostasis model of insulin resistance (−33%) as indicators of improved microbiota function compared to placebo group. Other related improved biomarkers included reductions in levels of malondialdehyde (−34%), glycosylated hemoglobin (−9.4%), insulin (−29%), and a significant increase in total antioxidant capacity (18%) and glutathione peroxidase (12%) as compared with control
Aryana et al. Evaluate the effects of resistant starch on microbiota in children (USA) [53]	**Pilot open-label trial**: four children; three adolescent children/one prepubertal child; high-amylose maize (type 2)-enriched yogurt for 4 weeks to test its fermentability and potential microbiota effects	The three adolescent children had significantly reduced stool pH and increased stool SCFAs including increased fecal acetate and butyrate suggesting a favorable change to the gut microbiota

Table 3.3 (continued)

Objective	Study Details	Results
Haenen et al. Evaluate the effect of resistant starch on the microbiota ecosystem (the Netherlands) [54]	**Parallel RCT pig-human model**: 20 adult female pigs; diet with high resistant starch (retrograded tapioca starch; type 3) or digestible starch (pregelatinized potato starch); 2 weeks; fecal microbiota PITChip is a phylogenetic microarray with >2900 oligonucleotides based on 16S rRNA gene sequences	Resistant starch stimulation increased colonic-associated butyrate-producing *Faecalibacterium prausnitzii*, whereas potentially pathogenic members of the *Gammaproteobacteria*, including *Escherichia coli* and *Pseudomonas* spp., were reduced in relative abundance. Resistant starch significantly increased colonic SCFA concentrations
Martinez et al. Evaluate the effects of resistant starch types 2 (RS2) and 4 (RS4) on human fecal microbiota (USA) [55]	**Double-blinded, crossover RCT**: ten adults; five female/five male; age 23–38 years; 100 g crackers/day of either resistant starch type 2 (33 g), resistant starch type 4 (32 g), or native starch (5 g); 3 weeks each with a 2-week washout; multiplex sequencing of 16S rRNA tags	RS4 induced phylum-level changes, significantly increasing *Actinobacteria* and *Bacteroidetes* while decreasing *Firmicutes*. At the species level, the changes evoked by RS4 were increases in *Bifidobacterium adolescentis* and *Parabacteroides distasonis*, while RS2 significantly raised the proportions of *Ruminococcus bromii* and *Eubacterium rectale* when compared to RS4. RS4 resulted in a tenfold increase in *Bifidobacteria* in three subjects, enriching them to 18–30% of the fecal microbial community. The microbiota responses were reversible and tightly associated with the consumption of resistant starch
Polydextrose		
Costabile et al. Identify effect of polydextrose on the microbiota (Finnish) [56]	**Double-blinded, placebo-controlled, crossover RCT**: 33 healthy; normal-weight adults; polydextrose (8 g/day) vs. maltodextrin placebo; 3 weeks; 3-week washout; fluorescence in situ hybridization	Polydextrose significantly increased the known butyrate producer *Ruminococcus intestinalis* and bacteria of the *Clostridium* clusters I, II, and IV. Of the other microbial groups investigated, there were decreases in the level of fecal *Lactobacillus-Enterococcus* group. Polydextrose was shown to be slowly degraded in the colon, and the fermentation significantly reduced the genotoxicity markers (comet assay) in fecal water
Hooda et al. Explore the impact of polydextrose on the composition of the microbiota (USA) [45]	**Double-blinded, placebo-controlled crossover RCT**: 20 healthy adult men; baseline mean 14 g fiber/day; snack bars with 21 g polydextrose/day or 0 polydextrose/day; 21-day duration; no washout period; DNA amplification of the V4–V6 region of the 16S rRNA gene and 454 pyrosequencing	The consumption of polydextrose led to greater fecal *Clostridiaceae* and *Veillonellaceae* and lower *Eubacteriaceae* compared with a no-fiber supplementation. The abundance of *Faecalibacterium*, *Phascolarctobacterium*, and *Dialister* was significantly greater in response to polydextrose intake. *Faecalibacterium prausnitzii*, known for its anti-inflammatory properties, was also significantly increased

Soluble Corn Fiber

Soluble corn fiber (SCF) was found to increase fecal *Bifidobacteria* levels starting at 8 g/day with a gastrointestinal tolerance of approximately 21 g/day [44]. The intake of 21 g SCF/day was shown to significantly increase *Lactobacillus* and *Faecalibacterium prausnitzii*, known for its anti-inflammatory effects, and significantly decrease pathogenic *Eubacteriaceae* from the phylum *Firmicutes* [45].

Inulin

The consumption of 16 g/day of a 50/50 inulin/oligofructose mixture was demonstrated to significantly increase fecal *Bifidobacterium* and *Faecalibacterium prausnitzii* and was negatively correlated with serum lipopolysaccharide (LPS) levels [46, 48]. A dose-response trial with agave inulin found that fecal *Actinobacteria* and *Bifidobacterium* were significantly enriched by three and fourfold after 5.0 and 7.5 g agave inulin/day, respectively, compared with control [47]. Also, the level of inulin intake was positively associated with fecal butyrate concentration.

Short-Chain Fructooligosaccharides

Short-chain fructooligosaccharides at an optimal level of 10 g/day were shown to significantly increase fecal *Bifidobacteria* levels and lower colonic pH with only mild bloating and flatus [49–51].

Resistant Starch

Four intervention trials have consistently supported the benefits of resistant starch type 2, 3, and 4 on microbiota composition and metabolites [52–55]. A parallel, double-blinded, placebo RCT (56 females with type 2 diabetes mellitus; 10 g/day resistant starch subtype 2 vs. the placebo control group; 8 weeks) showed resistant starch significantly decreased endotoxin (−25%) and HOMA-IR (−33%) as indicators of improved microbiota function compared to the placebo group [52]. Type 2 resistant starch was also shown to decrease colonic pH and increase fecal SCFAs in adolescents when consumed with yogurt [53]. A pig-human model trial (20 female pigs; digestible vs. resistant starch) found that type 3 resistant starch stimulated butyrate-producing *Faecalibacterium prausnitzii* and fecal SCFA levels and reduced potentially pathogenic members of *Gammaproteobacteria*, including *Escherichia coli* and *Pseudomonas* spp. [54]. In a double-blinded, crossover RCT (ten adults; five female/five male; 100 g crackers with 32 g type 4 resistant starch; 3 weeks; 2-week washout), it was shown that type 4 resistant starch induced increases in *Bifidobacterium adolescentis* (e.g., tenfold increase in *Bifidobacteria* in three subjects) and *Parabacteroides distasonis* [55].

Polydextrose

Two double-blinded, placebo-controlled crossover trials found 8–21 g polydextrose/day was significantly beneficial to microbiota [45, 56]. The benefits of polydextrose intake included fecal increases in known butyrate producer *Ruminococcus intestinalis* and bacteria of the *Clostridium* clusters I, II, and IV. *Faecalibacterium prausnitzii*, known for its anti-inflammatory properties, was also significantly increased. Polydextrose is known to slowly degrade in the colon, and its fermentation significantly reduced the fecal water genotoxicity (comet assay) levels.

Recent Findings on the Benefits of Fiber on Colonic Microbiota and Human Health

Evidence Mapping

A 2017 evidence map identified 188 intervention fiber trials on modulation of colonic microflorae and/or colonic fermentation and short-chain fatty acid concentration [57]. These trials included oligosaccharides (20%), plant fibers (e.g., cereal, fruit, and vegetable; 19%), resistant starch (16%), and chemically synthesized fibers (e.g., polydextrose, dextrins, soluble corn fiber, and microcrystalline cellulose; 15%), inulin (13%), bran (13%), and high fiber diets (2%). The most frequently studied outcomes included SCFAs concentration (47%) and bacterial composition (88%). The physiological health outcomes evaluated included colonic microbiota and gastrointestinal health measures, including fecal bulking, laxation, and transit time, but there was limited evidence on satiety, adiposity, and blood pressure effects [57].

Oligosaccharides are short-chain saccharide polymers, known for their prebiotic activity in altering the composition and/or activity of the microbiota in such a way that promotes colonic health [57]. RCTs have consistently shown that oligosaccharides, and fructooligosaccharides in particular, increase Bifidobacterium, a genus of oligosaccharide-fermenting colonic bacteria that may be beneficial to human health. Despite the considerable number of studies showing this bifidogenic effect, few studies have actually examined the direct relationships of this modulation of the colonic microbiota and other physiological health outcomes. There is no clinical evidence supporting a link between soluble, nonviscous, readily fermentable fibers (such as oligosaccharides) and physiological health benefits on laxation and stool softening, or cholesterol and glycemic control, as these benefits are attributed to the physical properties of soluble, viscous/gel-forming, low-fermentable fibers (such as β-glucan and psyllium) [58]. In contrast, readily fermented fiber types, such as oligosaccharides and resistant starch, have other important physiologic effects via the metabolites produced from microbial fermentation such as SCFAs, (mainly butyrate, propionate, and acetate) which are absorbed by the colonocytes and have a role in health and prevention of disease, such as bowel disease, colon cancer, and metabolic syndrome and affect colonic health, immune function, energy metabolism, stimulation of the sympathetic nervous system, and serotonin release.

Calcium Bioavailability and Bone Health

The increased intake of soluble fermentable fiber has been shown to make positive colonic microbiota changes in increasing calcium absorption and retention, and improving indices of bone health [59, 60]. Fermentation of fibers also leads to increased production of short-chain fatty acids, which benefits mineral utilization associated with decreased colonic fecal pH, increased colonocyte function, and increased proportion of healthy bacteria such as Bifidobacterium. A pioneering clinical study showed that pubertal adolescents consuming 8 g/day mixed short- and long-chain inulin-type fructans increased calcium absorption at 8 weeks and whole-body bone mineral density at 1 year [61]. Similar outcomes were observed in young girls (10–13 years) consuming smoothie drinks containing 5 g/day galacto-oligosaccharides which significantly improved calcium absorption mediated by enhanced microbiota bifidobacteria [62]. A double-blind crossover study found that the daily intake of 10 g soluble corn fiber significantly increased adolescent female calcium absorption compared to placebo after 4 weeks in direct relationship to the increase in healthy microflora [63]. Soluble fermentable

fiber also improved calcium bioavailability in boys [59, 60]. An increase in peak bone mass by 10% has been estimated to delay osteoporosis by 13 years [59]. Soluble corn fiber may also help increase net calcium retention in those who have reached peak bone mass. A dose-response, crossover, double-blind RCT (14 postmenopausal women; mean age 60 years; 0, 10, and 20 g soluble corn fiber/day; 50 days) showed that 10 and 20 g soluble corn fiber/day significantly improved bone calcium retention by 4.8% and 7%, respectively [64]. There was also a significant 8% increase in bone-specific alkaline phosphatase (a bone-formation marker) detected with the intake of 20 g soluble corn fiber/day compared to control low-fiber diets (Fig. 3.10).

Prevotella vs. Bacteroides Enterotypes

Human colonic microbiota vary among individuals and the concept of "enterotypes" has been used to stratify microbiota compositions [65]. Different enterotypes are defined by their dominant bacteria such as *Prevotella* and *Bacteroides* genera and long-term dietary patterns, with *Prevotella* associated with complex carbohydrates, especially fiber-rich diets consumption or nonindustrialized populations; and the *Bacteroides* associated with diets rich in animal protein and fats or Western diets. These two microbiota enterotypes ferment fiber structures differently to produce different amounts and ratios of the SCFAs [65]. Among the SCFAs: (1) butyrate is a preferred energy source for the colonocytes and promotes colonic barrier protection to reduce intestinal and systemic inflammation; (2) propionate is metabolized in the liver and decreases hepatic lipogenesis, reduces serum cholesterol, and is potent in triggering the enteroendocrine L-cells to signal a satiety response; and (3) acetate is primarily an energy source but emerging studies indicate that it may have a circulating peripheral effect at the arcuate nucleus of the hypothalamus to reduce appetite [65]. *Prevotella* produce higher total SCFA levels compared to *Bacteroides* enterotype, which indicates higher fiber utilizing capacity, a reasonable outcome of plant-rich diets associated with the *Prevotella* enterotype. The *Prevotella*-dominated microbiota produce 2–3 times more propionate than the *Bacteroides*-dominated microbiota. Higher propionate increases the synthesis of the odd-chain fatty acid heptadecanoic acid by the liver and increases plasma circulating quantity which is a potential quantitative

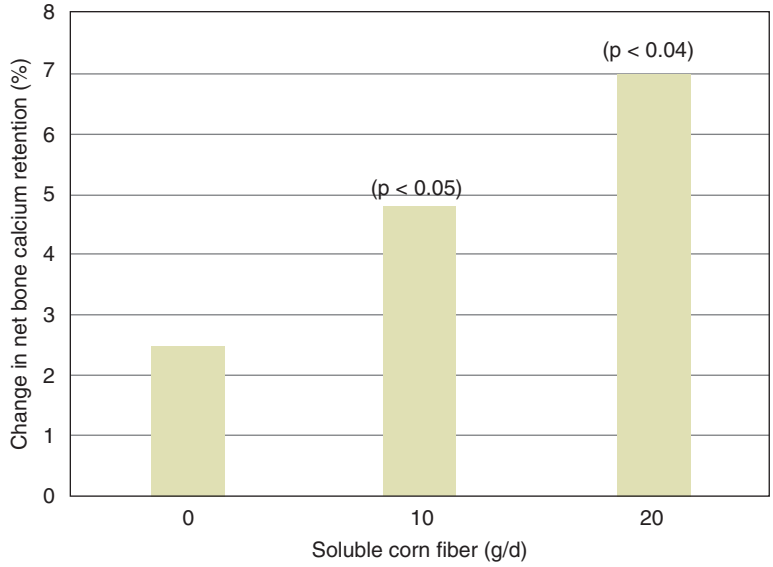

Fig. 3.10 Effect of soluble corn fiber on net bone calcium retention in postmenopausal women [62]

marker of fiber intake and inversely associated with risk of type 2 diabetes and ischemic heart disease [66]. A habitual MedDiet rich in fiber, vegetables, and fruits has been associated with a *Prevotella* enterotype [22, 67].

Whole vs. Refined Grains

Prospective studies suggest an inverse association between whole grain consumption and inflammation but the RCT evidence is limited, especially for cell-mediated immunity [68]. A 2017 RCT (49 men and 32 postmenopausal women; mean age 55 years; mean BMI 26; 16 g whole grain or 8 g refined grain per 1000 kcal; 6 weeks) found that the whole grain group had significantly increased stool weight, stool frequency, and SCFA producer *Lachnospira* but decreased pro-inflammatory *Enterobacteriaceae* compared to the refined grain group [68]. Changes in stool total SCFAs were higher in the whole grain group than in the refined grain group. Whole grains had positive effects on terminal effector memory T cells and acute innate immune response. Also, a 1999 RCT (23 subjects; metabolic ward; fine vs. coarse wheat bran; 1 month) found that fine wheat bran had similar effects on fecal bulking and laxation as the coarser bran but the fine bran promoted fermentation to increase butyrate levels to contribute to colonic microbiota heath and possibly other health benefits [69].

Conclusions

During the last decade, the number of human studies investigating the effects of diet on colonic microbiota composition has substantially increased because of the expanded use of molecular techniques, such as 16s rRNA sequencing and dedicated DNA chips. The diet has been estimated to contribute to as much as 60% of microbiota composition variation with fiber and animal products being the most influential food components. Fiber is the primary energy source for the microbiota and the fermentation substrate required for the bacterial production of SCFAs such as butyrate, required for colonic and human health. It has been hypothesized that the Western diet fiber gap is a major factor responsible for microbiota dysbiosis, which predisposes individuals to increased systemic and tissue inflammation associated with most noncommunicable diseases and increased frailty in older age. Changing from a low fiber, meat based diet to a high fiber, plant based diet can significantly improve microbiota health within 24 hrs, but it may take over 10 days for major enterotype identity changes to occur. There are at least three cross-sectional studies and two RCTs suggesting that fiber-rich dietary patterns such as the Mediterranean and vegetarian diets can promote a healthy microbiota ecosystem and numerous intervention trials suggesting that the increased intake of fiber-rich foods or fiber ingredients and supplements may support a healthier microbiota ecosystem. However, larger, higher-quality RCTs and observational studies are needed to more fully understand the complex interplay between fiber, microbiota, and human health.

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Chapter 4
Connection Between Fiber, Colonic Microbiota, and Health Across the Human Life Cycle

Keywords Dietary fiber • Dietary patterns • Microbiota • Short chain fatty acids • Butyrate • Symbionts • Pathobionts • Infants • *C. difficile* • Inflammatory bowel disease • Colorectal cancer • Obesity • Type 2 diabetes • Metabolic syndrome • Breast cancer • Aging • Frailty • Mortality

Key Points

- A symbiotic relationship has developed between fiber-rich dietary patterns and a healthy colonic microbiota over the course of millions of years of human evolution, which contributes to healthier energy metabolism and aging, and lower risk of chronic diseases, frailty in older age, and premature death. However, the present widespread intake of a Western pattern lower fiber diet has disturbed this relationship leading to a reversal of these health effects.
- There is a critical balance between microbiota health and dysbiosis depending on the level of fiber in the diet. Fiber is the primary dietary source of microbiota-accessible carbohydrates required for fermentation to short chain fatty acids, which are the main colonocyte energy source and an important source of bioactive metabolites.
- Adequate fiber intake supports a healthier colonic microbiota ecosystem, which decreases pathobionts, colonic permeability and endotoxemia, inflammation, colonic pH, and bowel transit time; increases symbionts, immune function, and fecal butyrate levels (an important colonic anti-inflammatory metabolite); and contributes to greater stool bulk to dilute potential toxic or carcinogenic compounds or metabolites.
- Fiber-rich healthy dietary patterns help to promote a diverse, healthy colonic microbiota that has a critical role throughout the human life span, beginning with the promotion of a healthy infant immune function and subsequently protecting the colon from infections such as *C. difficile*, inflammatory bowel disease, and colorectal cancer; decreasing the risk of weight gain and obesity, type 2 diabetes and metabolic syndrome, and breast cancer; and delaying the aging process, including frailty and premature death.

Introduction

Over the last decade, there has been increased human observational and clinical evidence supporting the role of dietary (fiber)-rich dietary patterns in promoting healthy microbiota and colonic function, promoting infant immunity, preventing chronic disease risk (e.g., cardiovascular diseases, type 2 diabetes, cancer) and weight gain, and supporting healthy aging and a longer life expectancy with less

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frailty compared to Western low-fiber dietary patterns [1–17]. The colonic microbiota serves a number of important human biological functions including aiding the absorption of nutrients, synthesizing vitamins, fermenting fiber to metabolically bioactive short-chain fatty acids (SCFAs), promoting barriers against pathogens, optimizing colonic and systemic immune function, and improving cardiometabolic health and glycemic control [17–22]. This human symbiotic relationship between fiber-rich diets, microbiota, and human health evolved over millions of years [23–28].

There is a balance between microbiota health and dysbiosis that depends on the level of fiber in the diet. Fiber is the primary source of microbiota-accessible carbohydrates for energy and fermentation metabolites such as SCFAs, primarily butyrate, acetate, propionate, and hydrogen, which are crucially involved in promoting a healthy microbiota ecosystem [28]. With an adequate fiber intake, there is more likely to be higher levels of butyrate-producing bacteria such as *Roseburia* spp., *F. prausnitzii*, *Anaerostipes* spp., *Coprococcus* spp., *Eubacterium rectale*, and *Eubacterium hallii* which maintain an acidic colon at 5.5 pH as butyrate tends to maintain a presence in the colon [6]. Butyrate is also an important energy source for colonocytes and is involved in the regulation of cell proliferation, differentiation to reinforcement of the colonic barrier, and colonic anti-inflammatory support. With lower-fiber diets, the colon pH can increase to 6.5, which coincides with a reduction in fermentation and butyrate-producing bacteria and an increasingly dysfunctional colonic microbiota. Additionally, with the higher pH, there is an increased opportunity for expansion of *Proteobacteria*, which includes a wide variety of pathogens such as *Escherichia*, *Salmonella*, and *Vibrio*, and increased endotoxemia risk [21, 28]. *Proteobacteria* is emerging as a marker for increased risk of chronic diseases and unhealthy aging (Fig. 4.1) [21]. The relationship between the level of fiber intake and the colonic microbiota balance between symbionts (bacteria with health-promoting functions) and pathobionts (bacteria that potentially induce pathology), fermentation metabolites such as SFCAs, and their effects on cardiometabolic health and aging quality (Fig. 4.2) [28–31]. The objective of this chapter is to review the relationship between fiber intake, colonic microbiota, and health across the human life cycle.

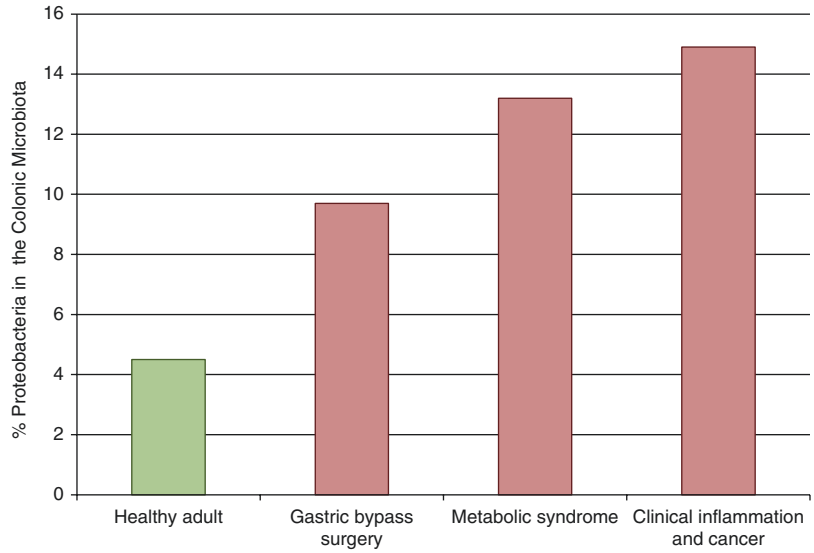

Fig. 4.1 Effect of health condition on the level of *Proteobacteria* in the colonic microbiota [21]

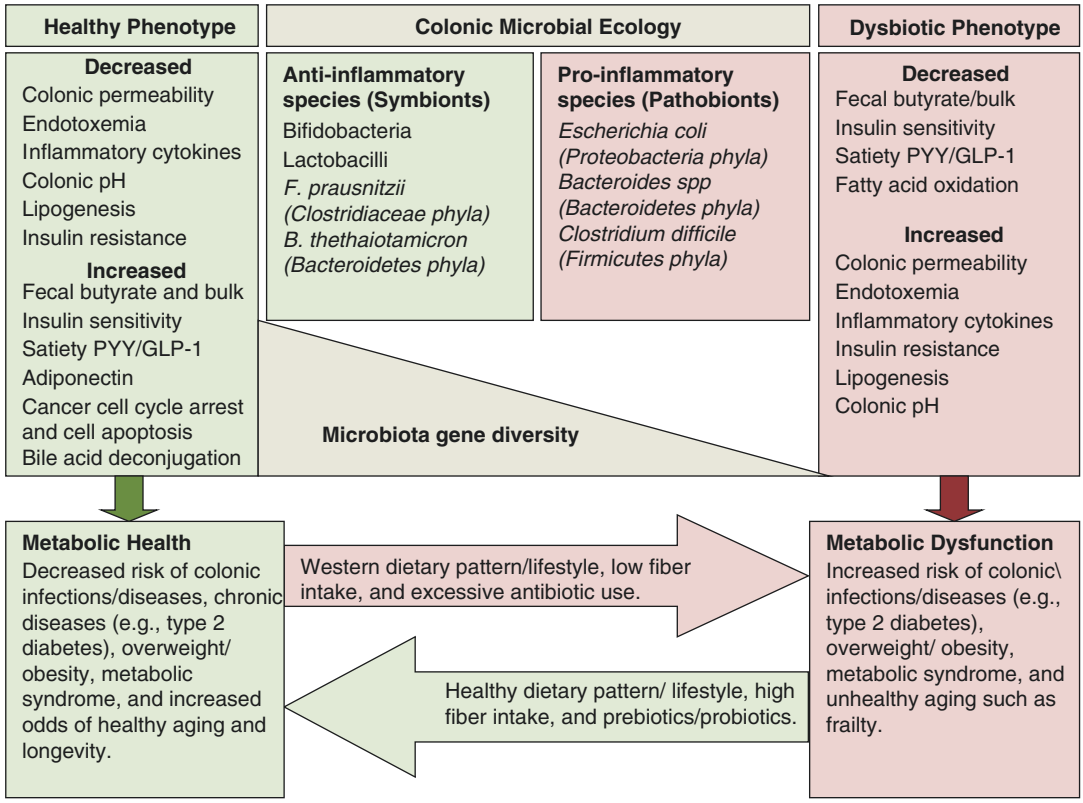

Fig. 4.2 Effect of healthy fiber-rich dietary patterns vs. Western low-fiber dietary patterns on colonic microbiota, cardiometabolic health, and aging [28–31]

Fiber-Rich Dietary Patterns in Colonic Microbiota Health

Populations with high adherence to the Western dietary pattern are at risk of having microbiota dysbiosis because they provide approximately half the adequate fiber level [9, 10, 23–31]. In contrast, populations with healthy fiber-rich dietary patterns (or 14 g per 1000 kcals) maintain a healthy microbiota ecosystem as mixed fiber from whole food sources are generally estimated to be 50–70% fermentable [28–32]. Top food sources of fiber are summarized in Appendix 1. The composition of several leading healthy or traditional dietary patterns that provide adequate fiber is summarized in Appendix 2.

Table 4.1 summarizes the observational studies and randomized controlled trials (RCTs) on the effects of fiber-rich dietary patterns in improving colonic microbiota health and reducing risk of major intestinal diseases [33–51]. Two large cohort studies, the Nurses' Health Study and Health Professionals Follow-up Study and the European Prospective Investigation into Cancer (EPIC) suggest that high adherence to healthy dietary patterns rich in fiber may reduce the risk of colorectal cancer and inflammatory bowel disease compared to high adherence to a Western or high sugar and soft drink pattern [33, 34]. Eight observational studies show varying degrees of an improved microbiota ecosystem by increasing fecal concentrations of SCFAs as illustrated by higher adherence to the Mediterranean diet (MedDiet) (Fig. 4.3) and increased probiotic and decreased pathogenic bacteria, especially with Mediterranean and vegetarian dietary patterns vs. more Western-type dietary patterns (Fig. 4.4) [35–42]. Nine RCTs consistently support beneficial microbiota effects within 5 days to 7 weeks of consuming fiber-rich healthy dietary patterns compared to lower-fiber Western diets [43–51].

Table 4.1 Summary of observational studies and randomized controlled trials (RCTs) on the effects of fiber-rich vs. Western dietary patterns on colonic microbiota health

Objective	Study Details	Results
Observational studies		
Mehta et al. Examine the effect of fiber-rich prudent/healthy vs. Western dietary patterns on colorectal cancer (CRC) risk according to presence of intestinal *Fusobacterium (F) nucleatum* in tumor tissue (Nurses' Health Study and Health Professionals Follow-up Study; USA) [33]	137,217 subjects; 35% male; mean age for men 54 years and women 46 years; 26–32 years of follow-up; 1019 CRC cases with *F. nucleatum*	The prudent/healthy dietary pattern (rich in whole grains and fiber) significantly lowered the multivariate risk of *F. nucleatum*-positive CRC by 54% (p-trend = 0.003; highest vs. lowest diet score) but not *F. nucleatum*-negative CRC, which had an insignificant lower risk by 5% (p-trend = 0.47)
Racine et al. Investigate the association between dietary pattern and inflammatory bowel disease (European Prospective Investigation into Cancer (EPIC) study; nested matched case-control study) [34]	366,351 participants with inflammatory bowel disease; 256 ulcerative colitis cases and 117 Crohn's disease cases with four matched controls per case	After excluding the first 2 years, there was a positive association for the "high sugar and soft drink" pattern with a 68% increased inflammatory bowel disease risk, which was only significant if there was high sugar and soft drink as well as low vegetable intake, which suggests a relationship between vegetable fiber intake and microbiota health
Gutierrez-Diaz et al. Assess the association between the adherence to a Mediterranean dietary (MedDiet) pattern and its components, with fecal microbiota in a cohort of adults (Spanish) [35]	31 adults; 23 females/8 males; mean age of 42 years; higher MedDiet score ≥4 [14 g fiber/1,000 kcals] vs. lower MedDiet score <4 [11 g fiber/1,000 kcals]; all diets contained 850 mg phenolic/1,000 kcal	Higher MedDiet fiber level was directly associated with higher fecal SCFA concentrations (Fig. 4.3), increased abundance of phylum *Bacteroidetes*, family *Prevotellaceae*, and genus *Prevotella* and decreased levels of phylum *Firmicutes* and the genus *Ruminococcus*. Higher cereal intake was associated with higher levels of *Bifidobacterium* and *Faecalibacterium*
Wu et al. Compare measures of dietary intake, gut microbiota composition, and the plasma metabolome between healthy human vegans and omnivores (US) [36]	21 urban adults;15 vegans/6 omnivores; fiber intake for vegans (35 g/day) and omnivores (18 g/day); 3 × 24 h dietary recalls	The differences in colonic microbiota between omnivores and vegans sampled in an urban environment in the Northeastern USA were quite modest, but the vegan plasma metabolome profile differed markedly from omnivores because of the phytonutrients from the whole foods. Higher consumption of fiber by vegans was not associated with significantly higher levels of fecal SCFAs
De Filippis et al. Evaluate the effect of the MedDiet on the microbiota and its metabolites (Italian) [37]	153 healthy adults; vegans, vegetarians, and omnivores with high MedDiet adherence; 7-day weighed food diary; fecal and urinary samples	Subjects with good adherence to the MedDiet with higher fiber, fruits, vegetables, and legumes intake showed higher levels of fecal SCFAs, *Prevotella*, and some fiber-degrading *Firmicutes* compared to those with lower adherence to the MedDiet. Western omnivore diets with adequate fiber intake are not necessarily detrimental to microbiota. Low adherence to MedDiets was associated with higher urinary trimethylamine oxide levels
Matijasic et al. Examine the effect of long-term omnivore vs. vegan and lacto-vegetarian dietary patterns on fecal microbiota composition (Slovenia) [38]	60 adults; 31 vegetarians (11 lacto-vegetarians, 20 vegans); 29 omnivores	Vegetarian diets were associated with higher ratios of *Bacteroides*/*Prevotella*, *Bacteroides thetaiotaomicron*, *Clostridium clostridioforme*, and *Faecalibacterium prausnitzii* compared to omnivores

Table 4.1 (continued)

Objective	Study Details	Results
Ou et al. Examine if the influence of diet on colon cancer risk is mediated by the microbiota through their metabolites (African American vs. Native African) [39]	12 healthy African Americans, urban Western diets; 12 native Africans, rural traditional diet; age and sex matched; mean age 58 years	African Americans consumed twice the protein, three times the dietary fat and less fiber than the native Africans. The African Americans and native African adults had fundamentally different predominance core microbiota, *Bacteroides* vs. *Prevotella*, respectively. The native Africans had significantly higher total bacteria and fecal SCFAs than the African Americans. Stool butyrate concentrations were significantly correlated with the abundance of the butyrate producers, *Clostridium* cluster IV and *Clostridium* cluster XIVa, in the native Africans. Fecal secondary bile acid concentrations were higher in African Americans
Zimmer et al. Assess the effects of vegetarian vs. omnivorous diets on microbiota composition (German) [40]	249 vegetarians or vegans vs. 249 control omnivores; matched for age and gender; mean age approx. 52 years	Total counts of *Bacteroides* spp., *Bifidobacterium* spp., *Escherichia coli*, and *Enterobacteriaceae* spp. were significantly lower in subjects on the vegan diet compared to those on the omnivorous diet. Subjects consuming the vegetarian diet ranked between vegans and omnivores. Also, subjects on a vegan or vegetarian diet showed significantly lower stool pH and counts of *E. coli* and *Enterobacteriaceae* than those with an omnivorous diet suggesting a healthy microbiota environment (Fig. 4.4)
Kabeerdoss et al. Compare effects of lacto-vegetarian and omnivorous diets on the fecal microbiota of young women (Southern India) [41]	32 lacto-vegetarian and 24 omnivorous women from a similar social and economic background; median age 19 years; median BMI 21; macronutrient intake and anthropometric data were collected	Omnivores had an increased relative abundance of *Clostridium* cluster XIVa bacteria, specifically *Roseburia-E. rectale* and butyryl-CoA-transferase gene, associated with microbial butyrate production, compared with lacto-vegetarians. Both diets had the same median crude fiber intake. The relative proportions of other microbial communities were similar in both groups
Wu et al. Investigate the effect of diet on colonic microbiota (USA) [42]	98 healthy volunteers; collected diet information using two questionnaires that queried recent diet and habitual long-term diet (food frequency questionnaire)	The *Bacteroides* enterotype was highly associated with higher meat intake (e.g., animal protein and saturated fats; Western diet) The *Prevotella* enterotype was associated with higher carbohydrates/fiber-based diet more typical of agrarian societies (Vegetarian diet)
RCTs		
Tap et al. Assess the short-term effects of increased fiber intake on microbial composition (crossover RCT; France) [43]	19 healthy normal weight adults; 10 females/9 males; age 19–25 years; basal diet supplemented with 40 or 10 g fiber/day; 5 days; 15-day washout period	Higher-fiber diets increased microbiota diversity and stability and promoted a higher *Prevotella*/*Bacteroides* ratio, increased fecal SCFAs, and modulated the expression of microbiota metabolic pathways such as glycan metabolism, with genes encoding carbohydrate-active enzymes active for fiber, compared to the low-fiber diets, within 5 days. This was particularly true when subjects switched from their 10 g fiber diet to the 40 g fiber/day diet
O'Keefe et al. Evaluate the acute effects on colonic microbiota after switching diets of African Americans (high colon cancer risk) and rural Africans (low colon cancer risk) (crossover RCT USA/South Africans) [44]	20 healthy middle-aged African Americans and 20 rural South Africans; first 2 weeks in their own home environment, eating their usual food, and then again in house they switched diets so the African Americans were fed a high-fiber, low-fat African-style diet and rural Africans a high-fat low-fiber Western-style diet under close supervision for 2 weeks	Diets with higher animal protein and fat and lower-fiber consumption resulted in higher colonic secondary bile acids, lower colonic short-chain fatty acid quantities, and higher mucosal proliferative biomarkers of cancer risk in South Africans, whereas a higher-fiber and lower-fat diet increased fecal butyrate concentration and suppressed secondary bile acid synthesis in the African Americans. Significant changes in mucosal inflammation and proliferation associated with potential colon cancer risk can occur within 2 weeks depending on the quality and fiber content of the dietary pattern

(continued)

Table 4.1 (continued)

Objective	Study Details	Results
David et al. Compare the effects of plant vs. animal-based diets on microbiota (crossover RCT; USA) [45]	10 US adults; 6 males and 4 female; ages 21–33 years; BMI range from 19 to 32;2 diets: a plant-based diet (rich in whole grains, legumes, fruits, and vegetables; 26 g fiber/1000 kcals); and an animal-based diet (consisting of meats, eggs, and cheeses; 0 g fiber/day); 5 days; 6 day washout	Plant-based diets increased saccharolytic bacteria and fecal SCFAs content, whereas animal food-based diets increased total count of bile-tolerant microorganisms, decreased the levels of *Firmicutes* able to ferment plant polysaccharides and increased levels of the products of amino acid fermentation and *Bilophila wadsworthia*, known to elevate the risk of inflammatory bowel disease. This study suggests that microbiota can rapidly respond to large changes in diet composition
Fruits and vegetables		
Klinder et al. Assess the impact of fruit and vegetable intake on gut microbiota (Parallel RCT; UK) [46]	122 UK participants; 60% female; mean age 50 years; mean BMI 28; high-flavonoid and low-flavonoid fruit and vegetable intervention groups consumed 2, 4, and 6 portions vs. habitual control diet; 6 weeks	There was a dose effect for fruit and vegetable intake on increasing *C. leptum-R. bromii/flavefaciens*, while a trend was reported for *Bifidobacterium* ($p = 0.090$) and *Bacteroides/Prevotella* ($p = 0.070$). Increased intake of fruit and vegetable portions and flavonoids was protective against the growth of potentially pathogenic clostridia with a negative correlation ($r = -0.145$), and higher-fiber intake was weakly positively correlated with *Bacteroides/Prevotella* ($r = 0.091$)
Whole grains		
Heinritz et al. Examined the effect of two diets with different levels of fiber and fat on microbial composition and activity by using the pig microbiota as a model for humans (Parallel RCT pig model; Netherlands) [47]	Eight pigs were equally allotted to two treatments, either fed a low-fat/high-fiber (whole wheat grain type) or a high-fat/low-fiber diet; 7 weeks; feces were sampled weekly	Significantly higher numbers of lactobacilli, bifidobacteria, and *Faecalibacterium prausnitzii* were found in the feces of the whole wheat grain type (low-fat/high-fiber) diet-fed pigs, while pathogenic-type *Enterobacteriaceae* were significantly increased in the high-fat/low-fiber diet-fed pigs. Significantly higher total and individual fecal SCFA levels, especially butyrate, were found with whole-wheat-grain-type diets vs. the low-fiber diets (Fig. 4.5)
Wang et al. Evaluate the effect of β-glucan-enriched breakfast cereals on microbiota composition and cardiovascular disease (CVD) risk factors (single-blind crossover RCT; Canada) [48]	30 hyperlipidemic adults; American Heart Association (AHA) diet plus four breakfasts containing 3 g high molecular weight (MW) β-glucan, 3 g and 5 g low MW β-glucan vs. refined wheat and rice (control); 5-week study period; 4-week washout	The high MW β-glucan significantly increased *Bacteroidetes* and decreased *Firmicutes* abundance compared to control. At the genus level, consumption of 3 g/d high MW β-glucan increased *Bacteroides*, tended to increase *Prevotella* but decreased *Dorea*, whereas neither of the low MW β-glucan diets altered the microbiota composition. The high MW β-glucan changes in microbiota composition were significantly correlated with shifts of CVD risk factors, including reduced BMI, waist circumference, blood pressure, as well as triglyceride levels. This study suggests the microbiota health effects of high MW β-glucan
Martinez et al. Assess the effect of whole grains on both the colonic microbiome and human physiology (crossover RCT; USA) [49]	28 healthy subjects; 11 males and 17 females; mean age 26 years; mean BMI 25; daily dose of 60 g of whole grain barley (19 g fiber), brown rice (4.4 g fiber), or an equal mixture of the two (11.5 g fiber); 4-week treatments with 2-week washout; fecal and blood samples were taken at baseline and after each treatment period	The barley whole grain foods increased overall microbiota diversity and specifically *Roseburia*, *Bifidobacterium*, and *Dialister*, and the species *Eubacterium rectale*, *Roseburia faecis*, and *Roseburia intestinalis*. Additionally, whole grain barley reduced IL-6, associated with increased *Dialister* and decreased *Coriobacteriaceae* in the microbiota. No significant differences were detected in fecal SCFAs but this was because of colonic absorption

Table 4.1 (continued)

Objective	Study Details	Results
Carvalho-Wells Evaluate the effects of maize-whole grain and refined breakfast cereal on the microbiota (double-blind crossover RCT; UK) [50]	32 subjects; 20 females/12 males; mean age 32 years; mean BMI 23; 48 g/day maize whole grain breakfast cereal or refined grain cereal placebo; 3-week trial periods; 3-week washout	Maize whole grain breakfast cereal significantly increased levels of fecal bifidobacteria compared with the control cereal, which returned to baseline levels after the washout period. There were no statistically significant changes in fecal SCFAs, bowel habit data, fasted lipids/glucose, blood pressure, BMI, or waist circumference
Costabile et al. Compare the effects of whole grain wheat breakfast cereal on the human microbiota compared to wheat bran (double-blind crossover RCT; UK) [51]	31 volunteers; average age 25 years; 16 females/15 males; BMI 20–30; 2 groups consuming daily either 48 g of whole grain wheat or wheat bran breakfast cereals; 3-week study periods, 2-week washout	The whole grain wheat cereal significantly increased the numbers of fecal bifidobacteria and lactobacilli compared with wheat bran cereal. Ingestion of both breakfast cereals resulted in a significant increase in ferulic acid concentrations in blood but no discernible difference in feces or urine. No significant differences in fecal SCFAs, fasting blood glucose, insulin, total cholesterol, triglycerides, or HDL-C were observed upon ingestion of whole grain compared with wheat bran breakfast cereals

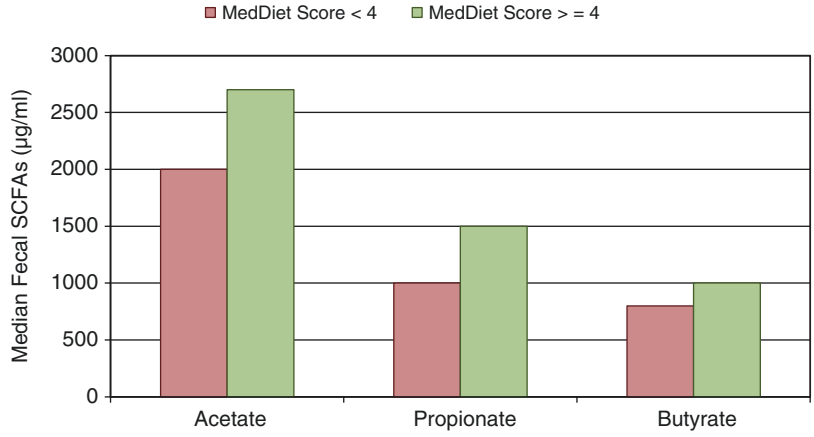

Fig. 4.3 Effect of Mediterranean diet (MedDiet) score on fecal short-chain fatty acid (SCFA) concentrations [35]

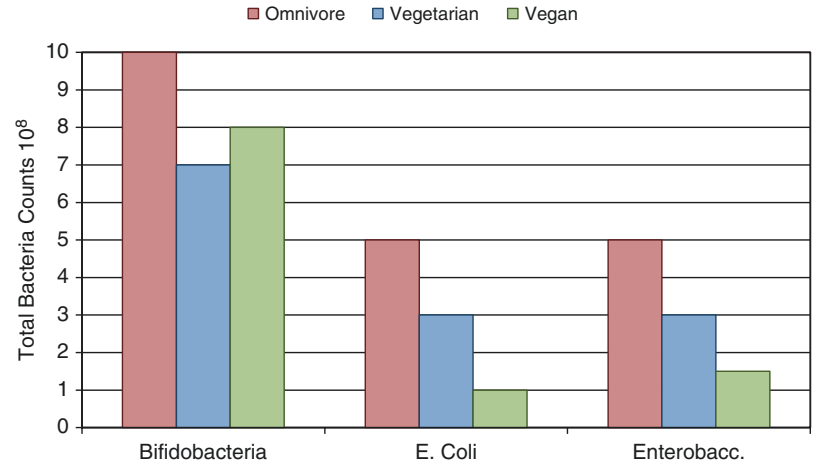

Fig. 4.4 Effect of vegetarian vs. omnivore dietary patterns on microbiota bacteria composition [40]

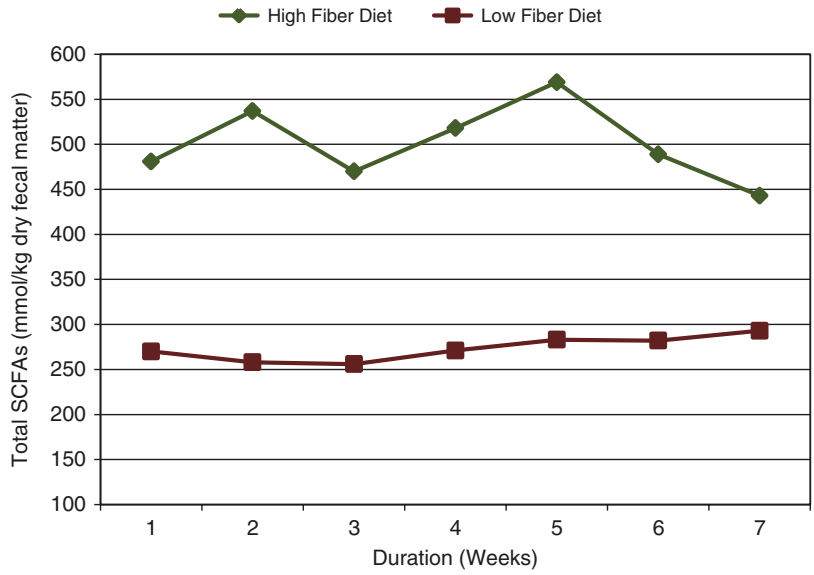

Fig. 4.5 Effect of fiber from wheat bran and cellulose on stool short-chain fatty acid (SCFA) levels over 7 weeks in pig model study ($p = 0.002$) [47]

A French crossover RCT (19 adults; 40 g vs. 10 g fiber/day dietary patterns) showed that the 40 g fiber diets increased microbiota diversity with a higher ratio of probiotic bacteria and increased SCFA concentrations compared to 10 g fiber diets within 5 days [43]. A US and South African crossover RCT in which 20 healthy middle-aged African Americans and 20 rural South Africans switched diets so that African Americans consumed a high-fiber and low-fat diet and rural Africans consumed a high-fat and low-fiber diet for 2 weeks found that the African Americans had increased fecal butyrate concentrations and suppressed secondary bile acid synthesis and the rural Africans had decreased butyrate concentrations and increased secondary bile acid synthesis [44]. A UK fruit and vegetable dose-response RCT (122 participants mean age 50 years; 2, 4, and 6 servings daily vs. habitual control diet; 6 weeks) demonstrated that higher intake of fruits, vegetables, and fiber had dose effects for a healthier microbiota bacteria profile and lower inflammation and flavonoid-rich fruits and vegetables provided greater protection from pathogenic bacteria [46]. A Dutch pig RCT to model human colonic changes (eight pigs; high-fiber (whole grains) and low-fat vs. low-fiber and high-fat dietary patterns; 7 weeks) showed that higher-whole-grain-fiber diet significantly increased fecal SCFAs, especially butyrate, vs. a low-fiber diet (Fig. 4.5) [47].

Infants

Human Milk/Infant Formula: Prebiotics

The recognition of the importance of fiber prebiotics in human milk and enriched infant formula for optimal colonic microbiota health is important in infant nutrition [4]. The gastrointestinal tract is the largest immune organ in the body with ≥65% of the overall immunologic tissues [52, 53]. Human milk contains >1000 distinct fiber oligosaccharides (prebiotics) as the third most abundant nutrient fraction after lactose and lipids, which are virtually absent from cow's milk [4, 54]. Human milk also contains many other immunomodulatory compounds, including IgG, IgM, and isoforms of

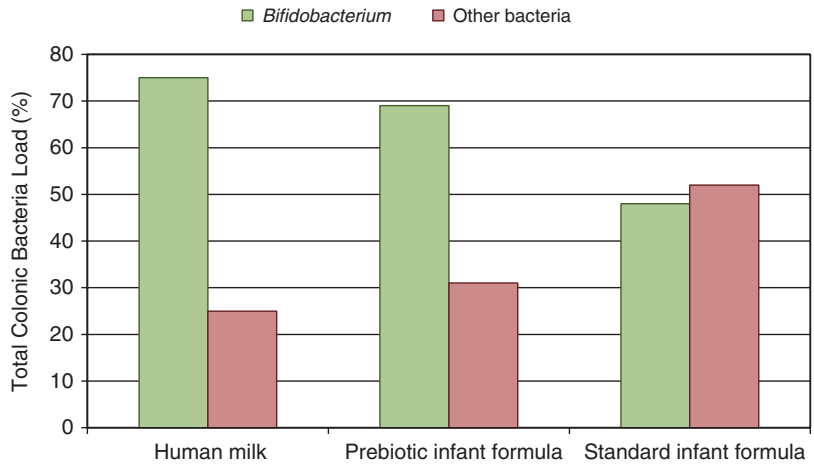

Fig. 4.6 Effect of human milk and prebiotic or standard infant formula on Bifidobacterium species vs. other bacteria in the stools of infants aged 1–3 months ($p < 0.05$) [56]

immunoglobulins (secretory IgA), nucleotides, n-3 fatty acids, antibacterial proteins/peptides, and intact immune cells. At birth the infant's gastrointestinal tract is sterile, but within a few days, microbes rapidly colonize the digestive tract in large number, with the highest amounts in the distal part of the colon. Early infant microbial colonization involves a series of stages initially involving facultative anaerobic bacteria (*Escherichia coli* and streptococci) that gradually consume all colonic oxygen which leads to a rapid increase in anaerobic *Bifidobacterium*, *Bacteroides*, and *Clostridium* within 1 week after birth. Generally, *Bifidobacterium* species become dominant as they are very effective at fermenting human milk prebiotics. As the newborn immune system progressively develops after birth, the digestive tract is a highly permissive environment where diverse bacterial populations quickly develop. Colonic bifidobacterial species play an important role in maintaining the general health of infants and young children as they are known to directly neutralize pathogenic bacteria and their toxins. The development of a healthy microbiota is critical in establishing the initial immune system. This symbiosis is important throughout life because the microbes contribute to the degradation of fiber and endogenous constituents, to the supply of SCFAs as an energy source for enterocytes, to the prevention of the colonization by or excessive development of pathogenic microorganisms, to detoxification of xenobiotic compounds, and to bioactivation of beneficial constituents such as polyphenols, which support the immune system. Since 2002, clinical investigations have shown that infant formula enriched with prebiotics such as mixtures of short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides have a bifidogenic change effect by decreasing stool pH and increasing SCFAs and bringing the immune system, stool consistency, and defecation frequency closer to those of breast-fed infants (Fig. 4.6) [4, 55, 56]. Between the ages of 2 and 3 years, a more functionally stable microbiota similar to adults is established.

Infant Allergies: Prebiotics

It has been hypothesized that prebiotics in infant formulas have the potential to prevent sensitization of infants to dietary allergens, but the ≥18 RCTs have been inconsistent [57, 58]. The 2015 World Allergy Organization evidence-based guideline panel recommended the use of prebiotic supplements to help in the prevention of allergies in non-exclusively breastfed infants and not in exclusively breastfed infants. The recommendation was conditional and based on suggestive evidence supporting

prebiotic supplementation in infants to reduce risk of developing recurrent wheezing and the development of food allergies, but there was very low certainty that prebiotics have an effect on other allergic outcomes. The panel chose not to provide a recommendation about prebiotic supplementation in pregnancy or during breastfeeding because of lack of experimental or observational study of prebiotic supplementation in pregnant women or in breastfeeding mothers.

Fiber-Rich Dietary Patterns in Aging and Disease

During the last few decades, there have been numerous human studies showing a high degree of synergy between healthy dietary patterns with adequate fiber intake and colonic microbiota with major beneficial effects on promoting colonic health, weight control, healthy aging, and chronic disease and frailty prevention.

Colonic Health

The microbiota is an important component in maintaining colonic health, which is engaged in a multitude of immunogenic and metabolic interactions that contribute to the maintenance of human health [17–19, 59–62]. However, when healthy microbiota composition is disturbed, dysbiosis or altered gut microbiota can trigger the development of various gastrointestinal diseases including *Clostridium difficile* infection, Crohn's disease, and colorectal cancer. There is a growing evidence suggesting that multiple factors, such as genetic variations, diet, stress, and medication, can significantly affect the balance of the gut microbiota. With the support of fiber, the microbiota act as a metabolic organ to interact with human cells and provide the functional support required for the maintenance of colonic homeostasis. The end products of fiber anaerobic bacteria fermentation in the colon are SCFAs, which have been shown to enhance the epithelial cell barrier and anti-inflammatory immune cell function. Among these SCFAs, butyrate is important for the maintenance of various aspects of colonic homeostasis, such as intestinal motility, visceral blood flow, and suppression of pathogen expansion [60, 61]. Additionally, the colon microbiota plays a role in the metabolism of bile acids to secondary bile acid metabolites, which has both beneficial and harmful effects in the colon by inhibiting the growth of pathogens or increasing the potential risk of mucosal and DNA oxidative damage or tumors [62].

Clostridium difficile Infections

Antibiotic-resistant bacteria, including *Clostridium difficile (C. difficile)*, has been on the rise for the past few decades with the increasing usage of antibiotics [63, 64]. Since the 1970s, *C. difficile* infection has become one of the most prominent sources of antibiotic-associated resistance diarrhea with increasing rates in elderly populations in both hospital and communities worldwide. *C. difficile* is an anaerobic, spore-forming bacterium with infection symptoms varying among patients, ranging from mild to severe diarrhea (>15 bowel movements/day) to death in severe cases. The *C. difficile* infection mortality rate has been increasing over the last few decades, due to the development of hypervirulent and antibiotic-resistant strains. *C. difficile* transmission is a major problem in hospitals throughout the developed world, as its spores are highly resistant to routine cleaning agents, including alcohol-based hand washes and can survive for months on aerobic surfaces (e.g., hospital walls, doors, surgical tools, cell phones, etc.) in spore form. When ingested, the multiple layers of the spore help protect it from

stomach acids and digestive enzymes, but in the colon the spores can be germinated into active cells by taurine-conjugated bile acid and colonize within the colonic microbiota to induce toxin-associated intestinal damage and inflammation. Low-fiber diets and chronic antibiotic use are considered to be major risk factors, as they can both lead to colonic microbiota dysbiosis [65, 66]. Some normally commensal bacteria, especially butyrate producers, are significantly depleted in *C. difficile*-infected patients. Two prebiotic fibers, fructo-oligosaccharides and polydextrose, have been shown to actively re-establish indigenous microbiota, particularly those bacteria yielding large amounts of SCFAs and decreased gut pH, which can contribute to the prevention of growth and toxin release by *C. difficile* [67]. Also, the combination of prebiotic fiber with antibiotics appears to have synergistic effects in fighting *C. difficile* infections [68].

Crohn's Disease

Crohn's disease is a chronic relapsing, multifactorial inflammatory bowel disease associated with abnormal T cell responses to the intestinal microbiota [69]. Although its etiology is still unclear, it is primarily thought to be the result of an excessive immune response to endogenous commensal bacteria, which occurs in genetically predisposed individuals. Crohn's disease patients tend to have microbiota with an increased number of *Proteobacteria* and a reduced amount of dominant commensal bacteria, such as *Firmicutes* and *Bacteroidetes*. The Crohn's and Colitis Foundation of America Partners Internet cohort dietary survey (1,619 participants in remission; dietary intake and disease activity index survey; 6 months) suggests that increased fiber intake during remission is associated with reduced disease flare-ups [70]. Compared with participants in the lowest quartile of fiber consumption (median intake 10 g/day), those with Crohn's disease in the highest quartile of fiber intake (median intake 34 g/day) were significantly 42% less likely to have a disease flare-up, but there was no association between fiber intake and flares in patients with ulcerative colitis. Similar results were observed in the Nurses' Health Study [71]. The consumption of fiber during active Crohn's disease is not recommended because it may aggravate existing symptoms [72]. A double-blind, placebo RCT (103 patients with active Crohn's disease; randomized to 15 g fructo-oligosaccharides (prebiotic) or placebo; 4 weeks) found no clinical benefit for patients consuming the prebiotic compared to the placebo group ($p = 0.067$) [73]. Although patients consuming the prebiotic did not significantly increase fecal bifidobacteria and *F. prausnitzii* bacteria, there was a significant improvement in intestinal dendritic cell function, a key regulator of the immune system, which is suggestive of potential better long-term management of colonic inflammatory activity. A systematic review, and dose response meta-analysis (5 cohort studies with 238,887 participants; 4 case-control studies with 311 Crohn's cases and 660 controls) showed that fiber intake was inversely associated with Crohn's disease risk (10 g fiber/day reduced risk by 15%) and sucrose intake was associated with increased risk (10g/day elevated risk by 9%) [74]. The potential anti-inflammatory role of fiber in Crohn's disease is intriguing and merits further investigation in adequately powered clinical trials. Currently, there is little evidence that fiber intake should be restricted in patients with Crohn's disease in remission as it may provide some long-term colonic health benefits associated with a healthier microbiota. A meta-analysis of observational studies (two cohort studies, one nested case-control study, and five case-control studies) found that higher-fiber intake significantly reduced Crohn's disease risk by 56% and marginally significantly lowered ulcerative colitis risk by 20% [75]. In addition, a significant dose-response relationship was observed between fiber intake and Crohn's disease risk with a 13% lower risk per 10 g of fiber intake. There are several mechanisms which support the effect of increased fiber intake on lowering the risk of inflammatory bowel disease by: (1) improving colonic microbiota health, which has a regulatory influence on the colon immune response and maintenance of immunological homeostasis; (2) promoting direct anti-inflammatory effects through its fermentation metabolite butyrate,

which is known to promote colon endothelial health; (3) mediating an aryl hydrocarbon receptor protective response against inflammatory bowel disease (IBD) pathogenesis; and (4) lowering levels of C-reactive protein (CRP) which is associated with increased Crohn's disease risk [75, 76]. An EPIC nested match case-control analysis (256 ulcerative colitis case; 117 Crohn's disease cases) observed that Western dietary patterns rich in sugar and soft drinks increased the risk of IBD by 68% in combination with low-vegetable intake [34].

Colorectal Cancer (CRC)

The potential importance of fiber and the colonic microbiota to protect against colorectal cancer was first hypothesized in the early 1970s by Dr. Burkitt, who observed lower rates of CRC among Africans who consumed a diet high in fiber [77]. Now, there is increased evidence that a higher fiber intake undergoes bacterial fermentation in the colonic microbiota to yield butyrate, which is a short-chain fatty acid and histone deacetylase (HDAC) inhibitor which suppresses the viability and growth of colorectal cancer cells [78, 79]. In 2011, a dose-response meta-analysis (16 cohort studies) estimated that there was a 10% lower risk of CRC per each 10 g of increased fiber intake, and the World Cancer Research Fund and American Institute of Cancer Research continuous update concluded that there was convincing evidence that increased fiber intake was protective against CRC risk [80, 81]. The large, population-based prospective Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (57,774 colorectal cancers, 16,980 adenoma, and 1667 recurrent adenoma cases; mean baseline age 63 years; flexible sigmoidoscopy at baseline; 3 or 5 years of duration) found that individuals consuming the highest intakes of fiber, especially cereal and fruit fiber, had significantly reduced risks of colorectal adenoma and distal colon cancer (Fig. 4.7) [82]. A cross-sectional study (688 subjects eligible; 50% female; age >50 years; healthy control vs. advanced colorectal adenoma groups), showed that high-fiber diets, higher fecal SCFAs concentration, and healthy colonic microbiota were associated with a reduced risk of advanced colorectal adenoma [83]. Healthy individuals with high-fiber intake had significantly higher butyrate than either healthy individuals with low-fiber intake or those individuals with advanced colorectal adenoma (Fig. 4.8) [83].

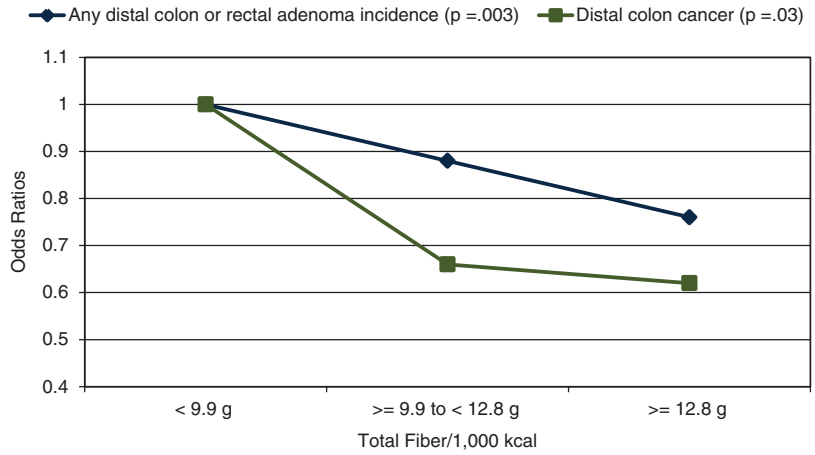

Fig. 4.7 Effect of total fiber density on distal colon or rectal adenoma or distal colon cancer risk [82]

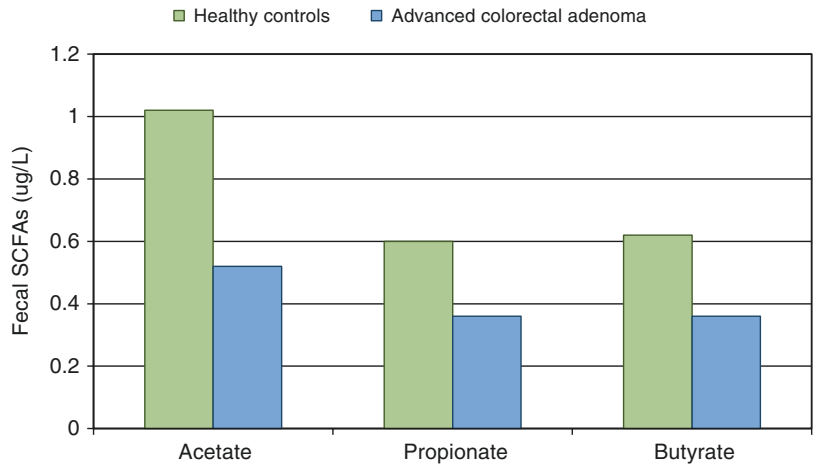

Fig. 4.8 Fecal short-chain fatty acids (SCFAs) in healthy and advanced colorectal adenoma subjects ($p < 0.05$) [83]

Weight Control and Obesity Prevention

Leaner individuals tend to consume higher fiber, healthy dietary patterns (low-energy density and fiber-rich foods such as fruits and vegetables) compared to overweight and obese individuals who tend to consume higher-energy-dense foods and have a lower daily fiber intake [86–93]. Higher-fiber diets are also associated with healthier, more diverse colonic microbiota ecosystems compared to high-energy-dense, low-fiber dietary patterns [28–52]. Studies consistently report that individuals with low microbiota diversity are characterized by higher body fat mass, insulin resistance, dyslipidemia, and low-grade systemic inflammation compared to individuals with higher microbiome diversity [84, 85, 94–98]. Overweight and obese individuals tend to consume more low fiber refined foods which are higher in metabolizable energy; have decreased abundance of butyrate-producing bacteria, in particular *F. prausnitzii*; and have increased proinflammatory functions such as mucus degradation and production of endotoxins such as lipopolysaccharides (LPS) from gram-negative endobacterium and an upregulation of genes to manage oxidative stress which are suggestive of increased weight gain, inflammation, insulin resistance, and metabolic disease risk [84, 85, 95–99]. On the contrary, lean, metabolically healthy individuals tend to consume more fiber-rich foods which leads to more diverse microbiota bacterial gene functions such as cell motility, metabolism of cofactors and vitamins, and increased abundance of *Bifidobacterium* species and butyrate-producing bacteria such as *F. prausnitzii*, a marker of a healthy microbiota due to its anti-inflammatory activity [94, 95, 99–105]. The most probable fiber-related microbiota metabolites associated with overweight/obesity and leanness are SCFAs [106–109]. Increased fiber intake helps to protect against weight gain and obesity, due to SCFAs' ability to act as ligands of free fatty acid receptors, which increases expression and secretion of satiety hormones glucagon-like peptide 1 or peptide YY and leptin from adipocytes [108, 109]. Butyrate and propionate are predominantly antiobesogenic as they may promote a lean profile of leptin, resistin, lower insulin resistance, and adipokines associated with satiety and weight control. Although acetate acts as a substrate for hepatic and adipocyte lipogenesis, elevated colonic fermentation of fiber to SCFAs appears to stimulate numerous hormonal and neural signals at different organ and tissue sites leading to cumulative suppressing of short-term appetite and energy intake [108, 109].

Type 2 Diabetes (Diabetes)

Diabetes, a consequence of an increase in the production of glucose in the liver and a deficit in the secretion and action of insulin, increases the risk for other chronic illnesses such as cardiovascular and renal disease, tuberculosis, and serious health complications such as retinopathy, neuropathy, and leads to shorter life expectancy and higher medical costs [110, 111]. Growing evidence suggests that colonic microbiota may play a role in the pathogenesis of both type 1 and type 2 diabetes [112–114]. Overweight and obesity are initiating factors for diabetes risk because of increased low-grade inflammation, which reaches tissues involved in metabolism regulation, such as the liver, adipose tissue, and muscles, and interferes with cellular insulin signals leading to insulin resistance. This low-grade inflammation and insulin resistance has been shown to be linked to dysbiosis of the colonic microbiota [114]. *Proteobacteria* have been shown to be significantly higher in diabetic compared to healthy persons and positively correlated with plasma glucose [115]. Two other studies also showed that diabetic subjects were characterized by a reduction in the number of *Clostridiales* bacteria (*Roseburia* species and *Faecalibacterium prausnitzii*), which produce butyrate [106, 116]. Adequate fiber intake may help to protect against the adverse effects of microbiota dysbiosis on insulin resistance which is associated with increased systemic inflammation associated with the colonic permeability of lipopolysaccharides (LPS) by gram-negative bacteria pathobionts, low incretin secretion and fecal butyrate production, macrophage influx into visceral fat tissue, and activation of hepatic Kupffer macrophage cells [28–31, 106, 115]. A 2017 German double-blind, crossover RCT (16 healthy subjects, mean age 40 years; 7 days) found that propionate from fiber fermentation increased heptadecanoic production by the liver which is associated with increased insulin sensitivity and lower diabetes risk [116, 117]. At least four RCTs support the role of fiber-rich dietary patterns such as vegetarian diets [118, 119] and diets rich in resistant starch in promoting a healthy microbiota ecosystem and lower biomarkers of diabetes risk [120, 121].

Metabolic Syndrome

Metabolic syndrome, which is associated with combinations of elevated blood pressure, dyslipidemia (defined by increased triglycerides and reduced high-density lipoprotein cholesterol), high fasting glucose, and/or central obesity, occurs in 20–40% of the worldwide adult population [122]. The colonic microbiota can have a major influence on the pathogenesis of metabolic syndrome, which can increase the rate of unhealthy aging [123]. Prospective studies suggest that low fiber Western dietary patterns, characterized by high consumption of meat or meat products, snacks, baked desserts, and sugar-sweetened beverages, are associated with higher metabolic syndrome risk, whereas fiber-rich healthy dietary patterns characterized by higher intake of vegetables, fruits, whole grains, nuts, and fish are associated with a reduced risk of metabolic syndrome [124]. Five RCTs suggest that a fiber-rich dietary pattern and healthy microbiota ecosystem can protect against the risk of developing metabolic syndrome [108–112]. For example, an Italian RCT (54 adults with metabolic syndrome; 31 females/23 males; mean age 58 years; mean BMI 31.5; whole grain group with 29 g cereal fiber/day vs. control group with 12 g cereal fiber/day; 12 weeks) found that the whole grain diet increased fasting plasma propionate, which correlated with lower postprandial insulin concentrations [125]. Another RCT showed that the absorption of colonic propionate has the potential to help control body weight gain and intra-abdominal fat accretion in overweight adults by stimulating the release of the anorectic gut hormones peptide YY and glucagon-like peptide 1 [126]. Although the pathogenesis of the metabolic syndrome is complex, increased intake of fiber-rich dietary patterns can reduce systemic and tissue inflammation through effects on microbiota health and promote lower body weight, and improve lipid homeostasis and insulin sensitivity to help reduce the risk of developing metabolic syndrome [127, 128].

Breast Cancer

Diets high in fiber have been hypothesized to reduce breast cancer (BC) incidence by inhibiting reabsorption of estrogen, which decreases circulating levels [129–131]. A 2012 meta-analysis (16 prospective studies) found a weak inverse association per 10 g fiber daily increment with a 5% lower BC risk [132]. A Nurses' Health Study II (44,263 premenopausal women; 20 years of follow-up; 2833 BC cases) showed a relationship between fiber intake during adolescence and early adulthood and BC risk [133]. In contrast to a 2012 meta-analysis' weak relationship, this study found that among all women, total fiber intake in early adulthood (highest versus lowest quintile) was associated with significantly lower future BC risk by 19% (p-trend = 0.002) and in adolescence by 16% (p-trend = 0.04) 133]. This study supports the hypothesis that higher-fiber intakes during adolescence and early adulthood may be especially important in reducing BC risk.

Aging and Premature Death

The colonic microbiota does not follow the same general trajectory of age-related chronological physiological decline as the human body because it is continually renewed with daily food intake and bowel movements [134–137]. As a consequence, maintaining a healthy microbiota with the habitual intake of fiber-rich healthy diets can support healthy aging and lower premature death.

Healthy aging may be defined as the absence of chronic disease, lack of good social engagement, and physical disability, and good mental health [138]. The level of fiber intake, antibiotic use, illness, and prebiotic and probiotic intake can impact the microbiota ecosystem with a significant influence on metabolic health mechanisms and healthy aging [139]. Adequate fiber intake is associated with a healthier microbiota diversity, including symbionts such as *Prevotella*, *Lactobacillales*, *Christensenellaceae*, *Bifidobacterium* groups, and butyrate-producing bacteria such as *Roseburia* spp., *F. prausnitzii*, and *Akkermansia muciniphila* [28–31, 136, 140]. Increased fiber intake provides the colon with the butyrate and lower pH needed to maintain a strong barrier to fight pathobionts and inflammaging compared to a low-fiber intake, which supports lower bacterial gene count diversity with fewer butyrate-producing bacteria and increased acetate- and propionate-producing *Bacteroides*-related bacteria, and elevated colonic pH. Several studies show that individuals with low microbiota diversity are characterized by more marked overall adiposity, insulin resistance, dyslipidemia, and inflammation when compared with high-bacterial-diversity individuals [95, 96]. Increased fiber intake from the regular diet has been shown to be directly associated with healthier microbiota profiles in comparison to lower-fiber diets, even in older age [140]. A meta-analysis including 14 RCTs showed that an increase of 8 g/day of fiber compared with a lower-fiber control diet significantly reduced systemic C-reactive protein by 0.5 mg/L [76]. A 1999–2010 US National Health and Nutrition Examination Survey (NHANES) analysis observed that increasing levels of fiber intake were found to significantly reduce the risk of elevated CRP levels and to reduce the risk of metabolic syndrome and obesity, two microbiota-related health conditions associated with inflammaging (Fig. 4.9) [141]. A cross-sectional analysis of the Nurses' Health Study (2,284 women; mean age 59 years; mean BMI 26; 87% postmenopausal) showed fiber was positively associated with leukocyte telomere length with a significant increase in telomere length by 0.19 units between the extremes of fiber intake, after multivariate adjustment [142]. A Canadian cost-of-illness analysis estimated that each 1 g fiber/day increase in consumption resulted in an annual $2.6–51.1 million in savings in type 2 diabetes care and $4.6–92.1 million in cardiovascular disease care [143]. A meta-analysis (25 cohort studies; 1,752,848 midlife individuals; average 12.4 years of follow-up) suggests that fiber is inversely associated with mortality risk (Fig. 4.10) [144]. The large US National

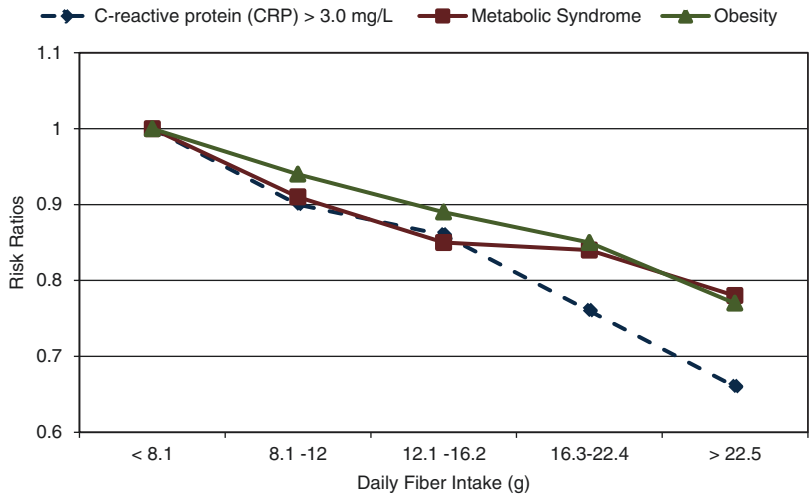

Fig. 4.9 Effect of increasing fiber intake on C-reactive protein (CRP), metabolic syndrome, and obesity from the 1999–2010 US National Health and Nutrition Examination Survey (NHANES); CRP had a significant *p*-trend <0.001, after multivariate adjustments [141]

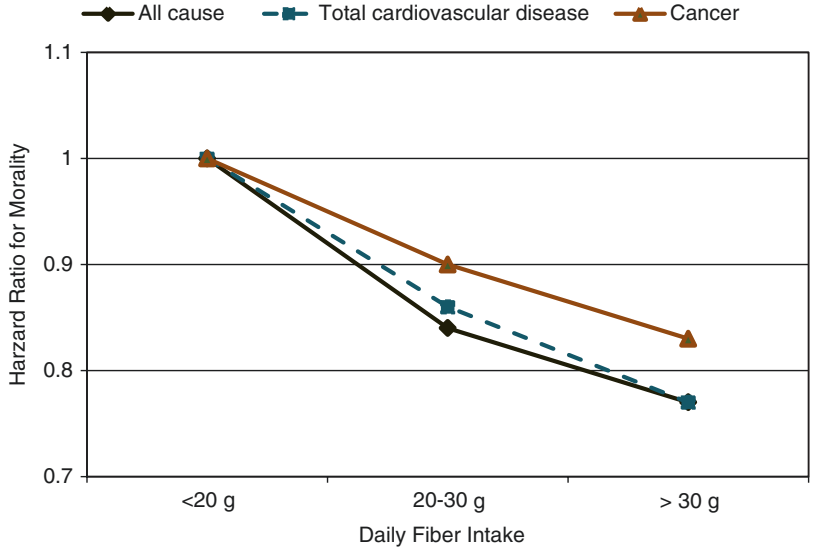

Fig. 4.10 Association between level of fiber intake and all-cause and disease-specific mortality risk based on a meta-analysis of 25 prospective cohort studies [144]

Institutes of Health (NIH)-AARP Diet and Health Study (567,169 men and women; mean age 62; mean BMI 27; 9-year follow-up; 20,126 deaths in men and 11,330 deaths in women) found that increased fiber intake by 15 g/day significantly reduced all-cause mortality rates by 22% in both men and women and CVD mortality in men by 24% and women by 34% (multivariate

adjusted) [145]. The European Prospective Investigation into Cancer and Nutrition (EPIC) prospective study (452,717 men and women; mean age 51 years; mean BMI 25.5; mean 12.7 years of follow-up; 23,583 deaths) found an inverse association with total mortality and circulatory morality risk of 10% reduction per 10 g fiber increased intake [146]. Fiber-rich foods such as whole grains, fruits, and vegetables have been consistently shown to reduce all-cause mortality risk [147, 148].

Frailty and Centenarian Phenotype

In elderly adults, a fiber-rich dietary pattern, especially in long-stay care facilities, is important to reduce the risk of frailty by avoiding the adverse effects of standardized low-fiber meals, which can subsequently reduce microbiota diversity and increase dysbiosis associated with accelerated inflammaging-related frailty [149, 150]. A cross-sectional study (371 elderly subjects; mean age 78 years; four groups, community dwelling, outpatient day hospitals, in short-term rehabilitation care (<6 weeks), or in long-term care facilities) observed that elderly from either the community or long-term care facilities consuming unhealthy diets (e.g., low in fiber and high in sugars and fats) had low microbiota diversity and increased signs of biological aging and frailty [150]. Additionally, elderly in long-term care facilities had a gradual change in their core community-based microbiota composition over approximately 18 months to a new core elderly type microbiota composition associated with dysbiosis and frailty. In another cross-sectional study (178 elderly adults; mean age 78 years; stratified by their current living situation; community dwelling (98% low-fat/high-fiber diets)); outpatients; short-term hospitalized subjects; long-term care residents (83% high-fat/low-fiber diets)) observed that elderly in long-term care facilities had significantly poorer frailty test scores compared to elderly living in a residential community [149]. The long-term care elderly consumed less diverse/lower-fiber diets and experienced microbiota dysbiosis and accelerated frailty. The residential community-living elderly consumed more diverse/higher-fiber diets, had healthier microbiota (higher diversity index with a higher proportion of *Firmicutes*/*Lachnospiraceae*), and high levels of fecal SCFAs and lower rates of frailty. Other studies indicate that the microbiota composition profile of unhealthy aging or frail elderly is generally associated with reduced levels of symbionts and increased levels of pathobionts such as marked reductions in lactobacilli, *Bacteroides*/*Prevotella*, or *F. prausnitzii*, increases in *Enterobacteriaceae*, and a major shift from *Firmicutes* to *Bacteroidetes* phyla [151–154].

The centenarian phenotype has a unique and complex microbiota composition, which counterbalances inflammaging processes and is necessary to establish a microbiota ecosystem for exceptionally healthy longevity. A cross-sectional study (24 semi-supercentenarians, average age 106 years, 18 females, six males; 15 young adults, average age 31 years, eight females, seven males) observed that longevity adaptation appears to involve enriched health-associated microbiota [155]. Extremely long-living people experience a parallel increase in several health-associated bacteria, especially from the family *Christensenellaceae*, which increases in prevalence in centenarians as health-associated bacteria are inversely correlated with BMI, positively associated with improved renal function, and significantly interacting with the human genome. Additionally, *Akkermansia* and *Bifidobacterium*, which have well-known health-associated benefits associated

with immunomodulation, protection against inflammation, and promotion of a healthy metabolism, are increased in centenarian's microbiota. An Italian cross-sectional study (84 subjects belonging to four different groups: 21 centenarians, 20 women, average 101 years; 22 elderlies (11 women, 11 men); average 73 years, genetically unrelated to the centenarians; 21 elderly (10 women, 11 men); average age 68 years offspring of the centenarians; and 20 younger adults (9 women, 11 men); average 31 years) observed that centenarians had a unique microbiota species pattern that significantly differed from the typical adult-like pattern [156]. In this study, it was shown that the centenarians, as all aging individuals, have an increased microbiota pathobiont population associated with an increased risk of inflammaging. However, centenarians also have a uniquely effective microbiota symbiont population with higher than normal anti-inflammatory activity. The major centenarian difference was a restructuring of their marked anti-inflammatory butyrate-producing bacteria population from *F. prausnitzii* to *E. limosum* (*Clostridium* cluster XIV), which was 15 times higher than in typical aging adults. In a Chinese study, age and high-fiber diets were associated with changes in the colonic microbiota of centenarians, suggesting that a high-fiber diet has a role in establishing a new structurally balanced microbiota that may benefit the health of centenarians [157].

Conclusions

A symbiotic relationship has developed between fiber-rich dietary patterns and a healthy colonic microbiota over the course of millions of years of human evolution, which contributes to healthier energy metabolism and aging and lower risk of chronic diseases, frailty in older age, and premature death. However, the present widespread intake of a Western pattern lower fiber diet has disturbed this relationship leading to a reversal of these health effects. There is a critical balance between microbiota health and dysbiosis depending on the level of fiber in the diet. Fiber is the primary dietary source of microbiota-accessible carbohydrates required for fermentation to SCFAs, which are the main colonocyte energy source and an important source of bioactive metabolites. Adequate fiber intake supports a healthier colonic microbiota ecosystem, which decreases pathobionts, colonic permeability and endotoxemia, inflammation, colonic pH, and bowel transit time; increases symbionts, immune function, and fecal butyrate levels (an important colonic anti-inflammatory metabolite); and contributes to greater stool bulk to dilute potential toxic or carcinogenic compounds or metabolites. Fiber-rich healthy dietary patterns help to promote a diverse, healthy colonic microbiota that has a critical role throughout the human life span, beginning with the promotion of a healthy infant immune function and subsequently protecting the colon from infections such as *C. difficile*, inflammatory bowel disease, and colorectal cancer; decreasing the risk of weight gain and obesity, type 2 diabetes and metabolic syndrome, and breast cancer; and delaying the aging process, including frailty and premature death.

Appendix 1. Fifty High-Fiber Whole or Minimally Processed Plant Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cups (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds, whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw, or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report. Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part D. Chapter 1: Food and nutrient intakes, and health: current status and trends. 2015;97–8; Table D1.8

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Appendix 2. Comparison of Western and Healthy Dietary Patterns Per 2000 Kcals (Approximated Values)[a]

Components	Western dietary pattern (USA)	USDA base pattern	DASH diet pattern	Healthy Mediterranean pattern	Healthy vegetarian pattern (Lacto-ovo based)	Vegan pattern
Emphasizes	Refined grains, low-fiber foods, red meats, sweets, and solid fats	Vegetables, fruits, whole grains, and low-fat milk	Potassium-rich vegetables, fruits, and low-fat milk products	Whole grains, vegetables, fruit, dairy products, olive oil, and moderate wine	Vegetables, fruits, whole grains, legumes, nuts, seeds, milk products, and soy foods	Plant foods: vegetables, fruits, whole grains, nuts, seeds, and soy foods
Includes	Processed meats, sugar-sweetened beverages, and fast foods	Enriched grains, lean meat, fish, nuts, seeds, and vegetable oils	Whole grains, poultry, fish, nuts, and seeds	Fish, nuts, seeds, and pulses	Eggs, nondairy milk alternatives, and vegetable oils	Nondairy milk alternatives
Limits	Fruits and vegetables, whole grains	Solid fats and added sugars	Red meats, sweets, and sugar-sweetened beverages	Red meats, refined grains, and sweets	No red or white meats, or fish; limited sweets	No animal products

Appendix 2 (continued)

Estimated nutrients/components						
Carbohydrates (% total kcal)	51	51	55	50	54	57
Protein (% total kcal)	16	17	18	16	14	13
Total fat (% total kcal)	33	32	27	34	32	30
Saturated fat (% total kcal)	11	8	6	8	8	7
Unsat. fat (% total kcal)	22	25	21	24	26	25
Fiber (g)	16	31	29+	31	35+	40+
Potassium (mg)	2800	3350	4400	3350	3300	3650
Vegetable oils (g)	19	27	25	27	19–27	18–27
Sodium (mg)	3600	1790	1100	1690	1400	1225
Added sugar (g)	79 (20 tsp.)	32 (8 tsp.)	12 (3 tsp.)	32 (8 tsp.)	32 (8 tsp.)	32 (8 tsp.)
Plant food groups						
Fruit (cup)	≤1.0	2.0	2.5	2.5	2.0	2.0
Vegetables (cup)	≤1.5	2.5	2.1	2.5	2.5	2.5
Whole grains (oz.)	0.6	3.0	4.0	3.0	3.0	3.0
Legumes (oz.)	–	1.5	0.5	1.5	3.0	3.0+
Nuts/seeds (oz.)	0.5	0.6	1.0	0.6	1.0	2.0
Soy products (oz.)	0.0	0.5	–	–	1.1	1.5

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Chapter 5
Fiber in Laxation and Constipation

Keywords Fiber-rich foods • Fiber supplements • Laxation • Bowel movement • Chronic constipation • Colon • Wheat bran • Oat bran • Polydextrose • Psyllium • Partially hydrolyzed guar gum • Konjac glucomannan • Prunes • Kiwi fruit

Key Points

- The consumption of adequate dietary fiber (>25 g/day), recommended fluid intake, and regular physical activity are especially beneficial in preventing and alleviating constipation.
- Fiber mechanisms associated with improved laxation and alleviated constipation include increasing stool weight and bulk volume (through fiber and microbiota physical volume and water holding capacity) and gas volume trapped in the stool to increase bowel movement frequency and quality, especially in constipated individuals.
- Adequate intake of fiber from whole-grain cereal rich in bran, fruits (especially prunes and kiwi fruit), vegetables, and common fiber-rich food ingredients, including polydextrose, psyllium, and chicory inulin, has the potential to increase population-wide levels of regularity and may play a role in providing constipation relief. In general, less fermentable food fibers tend to increase fecal weight to a greater amount than more fermentable fibers.
- Wheat bran is the most widely studied fiber source for laxation and constipation relief: when baseline transit time was >48 h, each extra g/day of wheat bran significantly increased total stool weight by 3.7 g and reduced transit time by 45 min. Further, in people with an initial transit time >48 h, transit time was reduced by approximately 30 min per gram of cereal, fruit, or vegetable fiber, regardless of fermentability. Increased fiber intake does not tend to significantly change transit time in individuals with an initial time of <48 h.
- Soluble, high viscosity and low fermentable fiber supplements such as psyllium and konjac glucomannan, have been shown to help soften stools, promote laxation and alleviate constipation symptoms.

Introduction

Constipation is a commonly underreported complaint in adults and children in all countries as most people are affected by it at some time in their lives [1, 2]. Up to 25% of people experience constipation that is more than a minor annoyance and can be chronic, sometimes severe, and have significant and often debilitating effects on their quality of life [2]. When individuals are asked about their

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perception of constipation, they frequently discuss infrequent bowel movements, straining, passage of hard stools, or difficulty in passing stools with the specific combination of symptoms varying from person to person [3]. However, physicians frequently define constipation as fewer than three bowel movements/week based on a 1990 UK study in which 99% of the interviewed working population maintained a bowel frequency between three bowel movements/day and 3/week [4]. In Western countries, about 30% of the general adult population experiences problems with constipation during their life time, with elderly people and women being most affected [1]. Chronic constipation is more commonly diagnosed in female patients at two to three times the rate of males. Only a minority of patients (approximately 25%) seek medical treatments. Epidemiological studies estimate that about 2–3% of the general population report a lower than normal number of evacuations (<3 times) per week [5]. However, this single symptom tends to underestimate the considerably larger number of patients actually suffering from variations of constipation [6]. The prevalence of constipation increases with age with about 34% in women and 26% in men considering themselves to be constipated by around 80 years of age [1]. The prevalence of childhood constipation is challenging to estimate, but worldwide about 16% of mothers of toddlers report some degree of constipation in their children [7, 8].

Diet and lifestyle modifications, including increased intake of fiber-rich foods, fiber supplements, or other types of laxatives plus fluids are traditionally considered the initial stage of a comprehensive treatment program to effectively manage constipation, as this increases colonic stool volume and water content directly or stimulates motility leading to shortened colonic transit and decreased water absorption [1–3]. Constipation can come occasionally (acute) or last for weeks, months, or years (chronic), as a result of a variety of potential factors including low-fiber diets, inadequate fluid intake, inactivity, or certain medicines, such as opiates used to control pain [1–3, 9, 10]. Adequate fiber from foods (>25 g/day) plus water intake and regular physical activity may especially represent an effective, inexpensive, and feasible therapeutic way to prevent and alleviate constipation [11, 12]. The objective of this chapter is to review the role of fiber in promoting softer stools, laxation and alleviating constipation.

Overview of Fiber, Laxation, and Constipation

Leading medical associations recommend the consumption of fiber-rich foods and fiber laxative supplements as potentially effective treatments for constipation management. However, bloating, distension, flatulence, and cramping may limit their use, especially if increases in fiber intake are not introduced gradually [9, 10, 13]. The American Medical Association recommends the consumption of adequate fiber intake of at least 25 g/day as a first step that may improve or eliminate constipation by increasing the intake of fiber containing fruit, vegetables, whole grains (e.g., wheat bran breakfast cereals), legumes, and nuts and seeds or appropriate fiber supplement products such as psyllium [9, 10]. The American College of Gastroenterology suggests that fiber supplements, especially from soluble fibers such as psyllium, may be effective in the management of chronic constipation in adults [13]. The Academy of Nutrition and Dietetics called for the public to consume adequate amounts of fiber from a variety of plant foods and stated that fiber aids in laxation by increasing fecal biomass, increasing stool frequency, and reducing intestinal transit time [14]. The European Food Safety

Authority (EFSA) panel recommended that the consumption of at least 25 g fiber/day from food was adequate for normal laxation in adults [15]. The American Academy of Pediatrics recommends a fiber intake of 0.5 g/kg/day for all children or alternatively for children older than age 2 years, an amount equivalent to their age in years plus 5 g/day (to a maximum of 25–35 g/day for older children or adolescents) as low-fiber intake may be a risk factor for chronic constipation and obesity [16].

Adequate water intake is important for fiber laxation mechanisms to work optimally, and low water intake may increase the prevalence of constipation [17, 18]. An intervention trial (117 subjects with chronic functional constipation, mean age 39 years, 64% women, duration 2 months, baseline diet: 7 g fiber/1000 kcal vs. study diet, 10 g fiber/1000 kcals) demonstrated that increased fiber intake is more effective at reducing chronic constipation if adequate daily water is consumed [19]. Specifically, this trial demonstrated that the consumption of 2 L of liquids/day with added fiber intake was significantly more effective at increasing stool frequency and decreasing laxative use than consuming only 1 L of fluid/day (Fig. 5.1).

Adequate intake of fiber, especially from a variety of plant foods and fiber supplements, along with adequate fluid intake, is the cornerstone for normal bowel health and regularity. Fiber sources from a variety of fiber-rich whole foods, minimally processed foods, fiber supplements, or foods enriched with wheat bran, psyllium seed husk fiber, and methylcellulose, which combine low fermentability and high water-binding capacity, tend to be the most effective fiber sources for softening stools and promoting laxation [20]. Low fiber intake is often associated with constipation in epidemiologic studies [11, 12, 21]. The Nurses' Health Study (62,036 women, age range 36 to 61 years, laxative users, 3,327 reported bowel movement frequency every 3rd day or less) observed that women with a median intake of about 20 g fiber daily had a 36% lower prevalence of constipation compared with women who consumed about 7 g of fiber daily (Fig. 5.2) [11]. Further, when women were simultaneously classified by both physical activity and dietary fiber intake, a multivariate analysis showed that those in the highest quintile of physical activity (two to three times/week) and fiber intake had a 68% lower prevalence of constipation, compared with those in the lowest quintile of physical activity (< once weekly) and fiber intake. In a study of Canadian adults, each 1 g/day increase in fiber from foods was

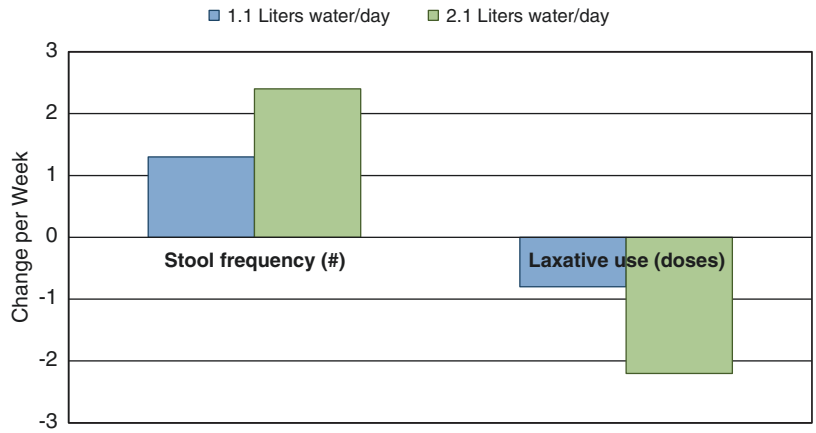

Fig. 5.1 Effect of level of water intake with a standard diet providing 25 g fiber/day on stool frequency and laxative usage in 117 patients with chronic functional constipation ($p < 0.001$) [19]

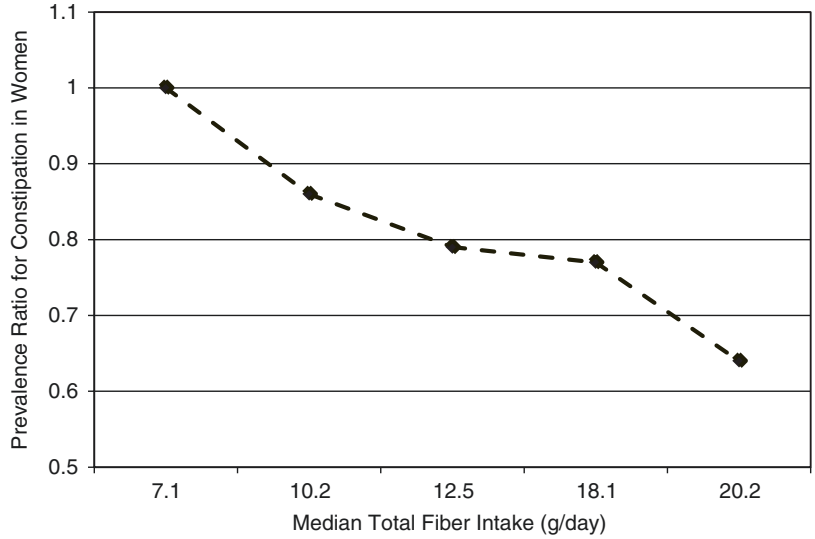

Fig. 5.2 Effect of level of fiber intake and constipation prevalence in women ($p < 0.0001$, multivariate adjusted) [11]

projected to reduce constipation rates by about 2% [22]. Similarly, in the USA, it was estimated that if fiber intake was increased by 9 g/day from bran (equivalent to one serving of high-fiber breakfast cereal/day), there could be approximately a billion dollars in annual savings in medical costs due to decreased constipation [23].

Fiber-Related Laxation Mechanisms

The way in which fiber affects bowel habit cannot be explained on the basis of one simple hypothesis [24]. There are several ways by which fiber increases laxation. First, plant cell walls especially rich in lignin with moderate water-holding capacity and low to moderate fermentability such as found in wheat bran, or soluble fibers with high water-holding capacity and incompletely fermented to significantly increase colonic volume such as found in psyllium, are among the most effective options for increasing fecal bulk and stimulating colonic laxation. Second, prebiotics, especially highly fermentable soluble fibers such as inulin, can stimulate increased microbiota numbers and add volume to the colonic fecal mass. Third, fiber fermentation to hydrogen, methane, and carbon dioxide gases, which can be trapped within colonic contents, add volume to increase fecal bulk. All of these mechanisms can additively increase bulk in the colon, often speeding up the rate of passage through the bowel. Each fiber source has a different bulking and fermentation capacity. There is a fecal bulking index for standardized measurement of the relative colonic bulking efficacy of foods relative to a typical edible serving size [25]. The fecal bulking index values for most foods range between zero for some starch-based foods to about 50 for wheat bran-enriched breakfast cereals. Fiber laxative supplements based on fermentation-resistant hydrated soluble polysaccharides have values in excess of 100, with psyllium having a value of 500. Coarse wheat bran and other insolube fibers are fairly resistant to fermentation to retain their three-dimensional fiber structure and water-binding capacity of 5–6 g water/g fiber in the distal colon. More fermentable fibers provide some bulk mainly due to increased bacterial mass and trapped gas [26]. Coarse wheat bran increases stool volume 2 1/2 times more than fine bran when consumed at the same dose. In general, the greater the weight of the stool and the more rapid the rate of passage through the colon, the better the laxative effect. Table 5.1 provides an

Table 5.1 Fecal bulking index and total fiber content per 100 g of plant foods [27]

Food	Fecal bulking index (%)	Total fiber content (g/100 g)
Ingredients		
Wheat bran	100	44
Wheat germ	37	16
Rye flour	21	12
Pea flour	11	16
Soy flour	9	18
Oat bran	8	11
Corn meal	2	7
Breakfast cereals		
All-Bran	51	30
Bran Flakes	26	19
Muesli	17	7
Rolled oats	17	9
Puffed wheat	8	8
Special K	8	4
Wheat Chex	3	2
Puffed rice	−0.4	6
Cornflakes	−2	3
Bakery products		
Ryvita crisp bread	23	14
Whole wheat bread	12	6
Multigrain bread	4	6
White bread	1	3
Vegetables/pulses		
Lentils, boiled	9	2
Green Peas, boiled	7	6
Spinach, cooked	6	2
Cabbage, boiled	4	2
Carrots, cooked	3	3
Fruit		
Pear, dried	27	7
Apricot, dried	3	3

estimation of the fecal bulking capacity of whole and processed plant foods relative to wheat bran from a validated model system [27]. Generally, this assay suggests that food fiber content is directly related to fecal bulking, but type of fiber and food matrix can also play a role in influencing fecal bulking.

Laxation Effects of Fiber-Rich Diets and Specific Foods

Although the beneficial effects of whole grain and wheat bran on laxation were known since Hippocrates in 370 BC, the advancement of the dietary fiber hypothesis refocused interest on the effects of dietary fiber and digestive health in a wider range of diets and foods [28]. The laxative and constipation alleviating effects of 29 fiber-rich diets and foods meta-analyses and specific representative RCTs are summarized in Table 5.2 [24, 29–51].

Table 5.2 Summary of intervention trials on the effects of fiber-rich foods and foods and ingredients in laxation and constipation relief

Objective	Study details	Results
Systematic reviews and meta-analyses		
DeVries et al. Summarize the effects of cereal, vegetable and fruit food fiber on fecal weight and transit time [30]	136 experimental studies in healthy subjects	Cereal and vegetable fiber had similar effects on fecal weight, whereas fruit fibers were less effective. Lower fermentable fibers increased fecal weight to a greater degree than more fermentable fibers. Fiber did not change transit time in those with an initial time of <48 h. In those with an initial transit time ≥ 48 h, transit time was reduced by 30 min per gram of cereal, fruit or vegetable fiber, regardless of fermentability
DeVries et al. Review and quantitatively examine the effects of cereal fiber-rich foods and ingredients on bowel function [31]	65 intervention studies among generally healthy populations	Each extra g/day of wheat fiber increased total stool weight by 3.7 g ($p < 0.0001$), dry stool weight by 0.75 g ($p < 0.0001$), and stool frequency by 0.004 times ($p = 0.0346$). Transit time decreased by 0.78 h per additional g/day ($p < 0.0001$) of wheat fiber among those with initial transit times >48 h
Thies et al. Systematically review intervention studies on the effects of oats or oat bran on bowel function [38]	14 intervention trials	Trials in healthy subjects suggest that oats or oat bran can significantly increase stool weight and decrease constipation. Oat consumption significantly increased wet and dry stool weight in six out of nine studies (from 15 to 88% increase) and five out of six studies (from 15 to 101% increase), respectively. Stool frequency did not change significantly in five studies, improved in two studies, and reduced in one study relative to wheat bran and rice bran interventions. Transit time decreased significantly by 17% in only one out of four studies
Lever et al. Assess the effect of prunes on stool frequency and consistency [42]	Four RCTs, one in constipated and three in non-constipated subjects	For constipation subjects, 3 weeks of prune consumption (100 g/day) improved stool frequency (3.5 vs. 2.8 per week ($p = 0.006$) and stool consistency (3.2 vs. 2.8 on Bristol stool form scale, $p = 0.02$) compared with psyllium (22 g/day). In non-constipated subjects, prunes softened stool consistency and increased stool weight (628 g vs. 514 g/ 72 hs wet weight, $p = 0.001$) compared with control. Meta-analysis was not supported due to heterogeneity in subject populations and methods
Yang et al. Investigate the effects of dietary fiber on stool weight and transit time [24]	Five placebo-controlled, double-blinded RCTs, limited to bran and glucomannan primarily	Increasing fiber showed significant increased mean stool frequency by 19% vs. placebo ($p < 0.05$), but there was no significant difference in stool consistency, laxative use, and painful defecation between the two groups. Improved stool frequency was reported by all five RCTs, with either a trend or a significant improvement for the fiber group vs. control
Suares and Ford Assess the efficacy of soluble and insoluble fiber supplementation in the management of chronic idiopathic constipation [50]	Six RCTs (three psyllium, one bran, one rye bread, and one inulin)	Compared with placebo, psyllium improved global symptoms (86% vs. 47%), straining (56% vs. 29%), pain on defecation, stool consistency, an increase in the mean number of stools per week (3.8 stools per week after therapy compared with 2.9 stools per week at baseline), and reduced the number of days between stools. Evidence for any benefit of insoluble fiber was conflicting. Formal meta-analysis was not undertaken due to concern about methodological quality of identified studies

Table 5.2 (continued)

Objective	Study details	Results
Muller-Lissner et al. Investigate the effects of wheat bran on stool weight and transit [32]	20 RCTs	Wheat bran increased the stool weight and decreased the transit time in healthy controls and in patients with irritable bowel syndrome and chronic constipation. However, bran was shown to be only partially effective in restoring normal stool weight and transit time in constipated subjects
Mixtures of fiber-rich plant foods		
Wisten and Messner Study the effects of a daily consumption of a fruit- and fiber-rich porridge on stool frequency, perceived well-being, and laxative usage, when compared with traditional treatment with laxatives, in geriatric patients (parallel RCT, Sweden) [40]	20 patients in secondary geriatric hospitals, porridge (flaxseed, chopped prunes and apricots, raisins, rolled oats, and oat bran) vs. control standard diet without porridge, 1-week run-in and 2-week study	Patients in the fruit-and-fiber-rich porridge group had a daily defecation without laxatives on average 76% of the time (11/14 days) compared with 23% of the time (3.3/14 days) in the non-porridge group ($p = 0.003$). Discomfort was less in the porridge group (2.5 vs. 6.5 on a 10-degree visual analogue scale ($p = 0.008$) when compared with the control group. The cost for laxatives was 93% lower in the porridge group
Haack et al. Determine the responses of healthy adult men to increased intakes of fiber provided in fiber-rich foods provided by foods, <15, 30, and 45 g/day (crossover RCT, USA) [33]	Nine healthy, young men; consumed constant diets with 3 amounts of fiber provided by a mixture of fruit, vegetables, and grains diets which contained 16, 30, and 42 g total fiber/day, of which 2.9, 4.8, and 7.7 g was soluble; 1 month each diet	Fiber provided by a mixed-food diet: (1) increases stool weight as effectively as cereal bran; (2) even high amounts of fiber do not change transit time or defecation frequency if they are already between 1 and 3 daily bowel movements; (3) food patterns containing legumes and whole grains are necessary to achieve recommended fiber intakes of 14 g/1000 kcal; and (4) mixed-food fiber has little effect on calcium balance when calcium intakes are high (≥1.5 g/day)
Astrup et al. Examine the effect of increased plant fiber intake on bowel function during the intake of very low caloric diets (crossover RCT, Denmark) [34]	22 obese subjects, very low caloric diets with and without added 30 g plant fiber/day, 4 weeks	Bowel movements reduced from 1.9/day on the habitual study diet to 0.7/day on the low-fiber diet and 1.0/day on the high-fiber diet ($p < 0.01$)
Cereal brans		
Lawton et al. Investigate the effect of wheat bran on subjective digestive feelings, general well-being, and bowel function (open-label trial, UK) [35]	153 low-fiber consumers (baseline <15 g/day), one bowl of ready-to-eat breakfast cereal containing at least 5.4 g fiber (3.5 g from wheat bran), 14 days, completed a daily symptom diary	The inclusion of one bowel of bran cereal over 2 weeks, significantly improved subjective perception of (1) bowel function (e.g., ease of defecation) and digestive feelings (bloating, constipation, feeling sluggish, and digestive discomfort) and (2) general well-being (feeling less fat, more mentally alert, slim, happy and energetic while experiencing less stress, mental and physical tiredness, difficulty concentrating, and fewer headaches)
Sturtzel et al. Determine effects of adding oat bran to a low-fiber habitual diet on use of laxatives and improvement in the well-being and bodyweight of inhabitants of a long-term-care facility (single blind, parallel RCT, Austria) [39]	30 frail inhabitants of a geriatric hospital; aged 57–100 years with laxative use; 15 subjects received 7-8 g oat bran/day (fiber group) mixed up in the daily common diet of the ward and 15 received no oat bran (control group); 12 weeks	Laxatives were successfully discontinued by 59% ($p < 0.001$) in the fiber group; in the control group there was an increase of 8% ($p = 0.218$). Body weight remained constant in the fiber group and decreased in the control group ($p = 0.002$). The oat-fiber supplementation was well tolerated

(continued)

Table 5.2 (continued)

Objective	Study details	Results
Vuksan et al. Assess the effects of increasing fiber intake on bowel habits and gastrointestinal tolerance in healthy persons (crossover RCT, Canada) [36]	23 free-living participants consumed a typical Canadian or US diet (35% fat, 12 g fiber/day) and received 25.0–28.7 g fiber/day from each of 5 breakfast cereals: All-Bran, Bran Buds with corn, Bran Buds with psyllium, with viscous fiber blend, or a low-fiber control; 3 weeks, with each study arm separated by a washout of ≥1 week; 7-day stool collections and a symptom diary were obtained during the last week of each study arm	All study cereals induced significant ($p < 0.05$) increases in fecal bulk US the control diet, less intestinal transit time, and significantly ($p < 0.05$) greater bowel movement frequency, while maintaining a good level of tolerance. Bran Buds with psyllium was more effective than other cereals in terms of increasing fecal wet weight ($p < 0.05$)
Hongisto et al. Investigate the effects of fiber-rich rye bread and yogurt containing *Lactobacillus* rhamnosus GG (LGG) on intestinal transit time and bowel function (parallel RCT, Finland) [37]	59 healthy women with self-reported constipation: four diet groups: (1) rye bread plus LGG yogurt, (2) rye bread, (3) LGG yogurt, and (4) control; 3-weeks	The rye bread shortened total intestinal transit time by 7 days ($p = 0.007$), increased fecal frequency by 0.3 per day (<0.001), softened feces by 0.3 units ($p < 0.001$), made defecation easier by 0.4 units ($p < 0.001$), and also increased gastrointestinal symptoms score by 1.6 units ($p < 0.001$) compared to the low-fiber toast consumed in the LGG and control groups. There were fewer gastrointestinal symptoms in the rye bread plus LGG group compared to the rye bread group by 1.3 units ($p = 0.027$)
Jenkins et al. Test the effects of wheat bran particle size on colonic function (crossover RCT, Canada) [29]	Two studies, each with three phases in healthy subjects: (1) 23 subjects; 19 g/day fiber from wheat bran with mean particle size (MPS) 50 or 758 mm in bread or a control low-fiber bread; 2 week study with 2 week washout and (2) 24 healthy subjects, breakfast cereal (ad libitum) with wheat bran MPS 692 and 1158 mm and the control was low fiber. 1 month; 2 week washout metabolic ward; fecal collections last week of each diet	In both studies, wheat bran supplemented bread and breakfast cereal significantly increased fecal bulk compared to the control ($p < 0.004$), with no significant differences between brans of different particle size and no differences in fecal water content. However, higher fecal butyrate concentrations ($p < 0.007$), butyrate output, and breath CH4 levels ($p = 0.025$) were seen with the finer MPS wheat bran compared to the larger MPS bran, suggesting increased bacterial fermentation. Fine wheat bran is an effective fecal bulking agent and may have added advantages in promoting colonic microbiota health
Whole fruits and vegetables vs. *fruit and vegetable juices*		
Kelsay et al. Assess the effect of high-fiber vs. low-fiber fruits and vegetables on bowel function (crossover RCT, USA) [41]	12 men, age range 37–58 years, weight range 68–95 kg, high-fiber fruit and vegetable diet vs. a low-fiber diet containing fruit and vegetable juices, 26 days, no washout	High-fiber fruit and vegetables vs. low-fiber fruit and vegetable juice intake significantly reduced fecal transit time (38 vs. 52 h), increased the number of daily bowel movements (1.4 vs. 1), and increased daily wet fecal weight (208 g vs. 90 g)
Prunes (dried plums)		
Attaluri et al. Assess and compare the effects of dried plums and psyllium in patients with chronic constipation (single-blind, randomized crossover RCT, USA) [43]	40 constipated subjects, 37 females, mean age 38 years, dried plums (50 g twice per day; fiber = 6 g/day) or psyllium (11 g twice daily; fiber = 6 g/day) for 3 weeks/1-week washout period, daily symptom and stool diary	The number of complete spontaneous bowel movements per week and stool consistency scores improved significantly ($p < 0.05$) with dried plums when compared to psyllium (Fig. 5.3). Straining and global constipation symptoms did not differ significantly between treatments ($p > 0.05$). Dried plums and psyllium were rated as equally palatable and both were safe and well tolerated

Table 5.2 (continued)

Objective	Study details	Results
Kiwi fruit		
Chang et al. Examine the impact of kiwifruit on bowel function in patients diagnosed with constipated irritable bowel syndrome (IBS-C) patients (parallel RCT, Taiwan) [46]	54 patients with IBS-C and 16 healthy adults, two Hayward green kiwifruits vs. two placebo capsules/day, 4 weeks	The intake of kiwifruit significantly improved weekly defecation frequency ($p < 0.05$) and decreased colon transit time ($p = 0.026$) in the IBS-C group. This study suggests that kiwifruit improves bowel function in adults diagnosed with IBS-C
Chan et al. Investigate the effect of increased kiwifruit on Chinese constipated patients (open label trial, China) [45]	33 constipated patients and 20 healthy volunteers, kiwifruit twice daily, 4 weeks	Responder rate was 54.5% in the constipated group. The mean complete spontaneous bowel movements per week increased after treatment from 2.2 to 4.4 ($p = 0.013$) and an improvement in transit time ($p = 0.003$). There was also significant improvement in the scores for bothersomeness of constipation, satisfaction of bowel habit, and decrease in days of laxative used
Rush et al. Evaluate the effect of regular kiwifruit intake on laxation in elderly people (crossover RCT, New Zealand) [44]	38 healthy adults of age > 60 years consumed their normal diet plus one kiwifruit per 30 kg bodyweight vs. no kiwifruit; 3 weeks, followed by a 3-week crossover period; daily records were taken on frequency of defecation and characteristics of the stools	Kiwifruit consumption was associated with a significant increase in frequency of defecation ($p = 0.012$), volume or bulk of stool produced ($p = 0.002$) and softness of stools ($p < 0.0001$)
Polydextrose and soluble corn fiber		
Shimada et al. Evaluate the effects of polydextrose on constipated dialysis patient (parallel, triple-blind RCT, Japan) [49]	50 constipated dialysis patients, 51–79 years of age, laxative for >3 months and dialysis >6 months, food products containing 10 g polydextrose vs. 0 polydextrose control, 8 weeks	The polydextrose group showed significant improvement in stool frequency from 3.0 to 7.5 times weekly and no gastrointestinal problems such as abdominal distension, cramps, or diarrhea ($p < 0.001$) (Fig. 5.5)
Timm et al. Compare the laxative effects of polydextrose and soluble corn fiber (SCF) to a low-fiber control eaten daily as a muffin and cereal (double-blind, crossover RCT, USA) [47]	36 healthy men and women; 20 g/day of polydextrose and SCF vs. low-fiber control (LFC) (about 14 g fiber/day) control diet; 10-day treatment with a 2-week washout period; collected fecal samples during the last 5 days of each treatment and completed food diaries and gastrointestinal tolerance questionnaires on day 1, 2, and 10	5-day fecal wet weight was higher after the polydextrose and SCF treatments than the LFC treatment ($p \leq 0.0007$). The number of stools per day and daily fecal output were also significantly greater during the polydextrose period compared with the LFC treatment (Fig. 5.4). The whole gut transit time did not differ among treatments. The polydextrose treatment resulted in a softer stool ($p = 0.002$) than the SCF and LFC treatments. Fecal pH was lowered by the polydextrose treatment ($p = 0.02$), whereas SCF tended to lower it compared with the LFC group ($p = 0.07$). Polydextrose and SCF at a dose of 20 g/day results in mild laxative effect with nominal colonic tolerance issues

(continued)

Table 5.2 (continued)

Objective	Study details	Results
Vester Boler et al. Evaluate digestive physiological outcomes elicited by functional polydextrose and soluble maize fiber in healthy adults (crossover RCT, USA) [48]	21 healthy adult men, 21 g/day polydextrose or soluble maize fiber (SCF) vs. no supplemental fiber (NFC) in a snack bar, 21 days with fecal collection during the last 5 days	Both SCF and polydextrose promoted colonic health with low to moderate gastrointestinal discomfort. Compared to the no fiber control, SCF and polydextrose increased fecal bulk with only slight discomfort or distention but flatulence was significantly increased. Fecal pH was significantly lower when subject consumed SCF
Chicory Inulin		
Micka et al. Determine the effect of chicory inulin on stool frequency in healthy constipated subjects (double-blind, crossover RCT, Germany) [51]	44 healthy constipated subjects, 75% women, mean age 47 years, 12 g/day inulin from chicory or 12 g/day maltodextrin, 4 weeks	Consumption of chicory inulin significantly increased stool frequency compared to placebo (median 4.0 vs. 3.0 stools/week ($p = 0.038$) and softened stools with a trend toward higher subject satisfaction vs. placebo ($p = 0.059$)

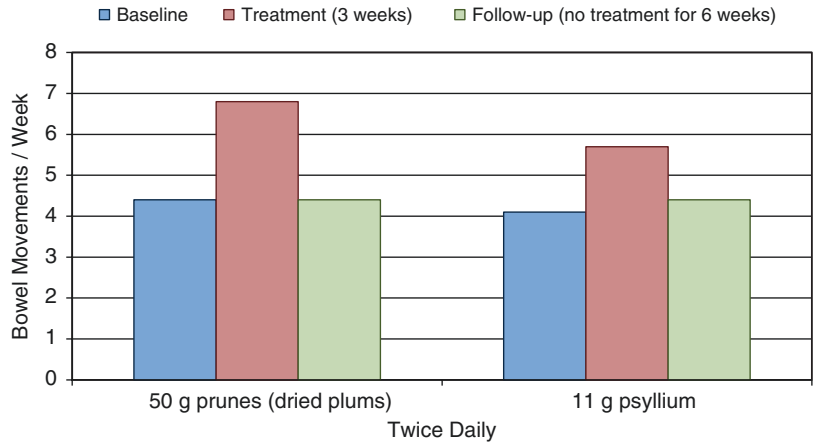

Fig. 5.3 Effect of dried prunes vs. psyllium supplement (6 g fiber/day each) on bowel movements/frequency ($p = 0.002$) [43]

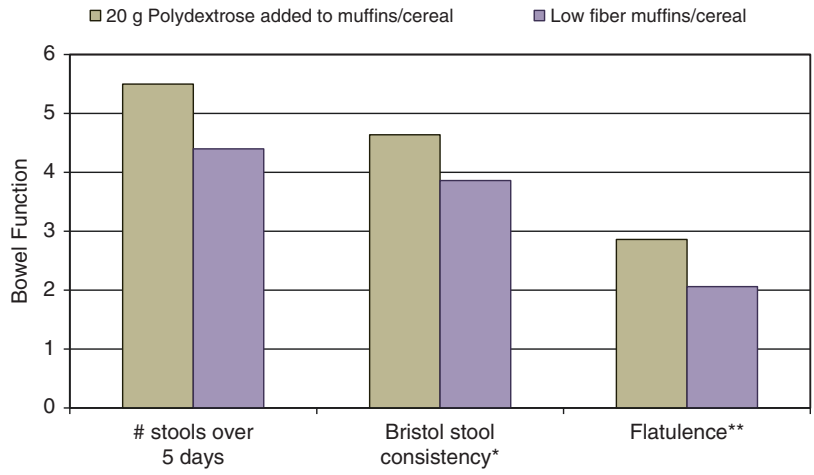

Fig. 5.4 Effect of adding polydextrose to muffins and cereal vs. low-fiber muffins and cereal ($p < 0.05$ for all) [47]. * 1 (separate hard lumps) and 7 (entirely liquid) and ** 0 (none) and 10 (extreme)

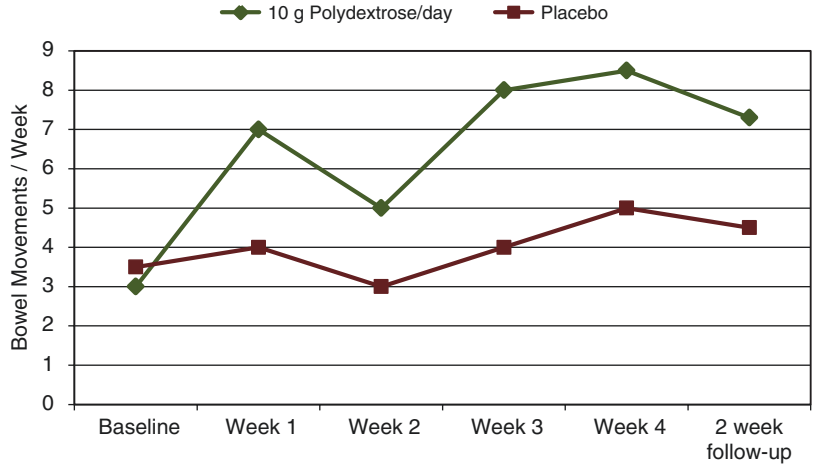

Fig. 5.5 Triple-blinded RCT on the laxative effects of jelly with added polydextrose intake on 50 constipated Japanese hemodialysis outpatients (51–79 years of age) ($p < 0.05$) [49]

Systematic Reviews and Meta-Analyses

Seven systematic reviews and meta-analyses provide an important overview of the best fiber-rich foods for laxation and alleviation of constipation [24, 30–32, 38, 42, 50]. These systematic reviews suggest that adequate intake of fiber from cereal, fruits (prunes), vegetables, and common fiber-rich food ingredients and supplements including cereal brans and psyllium has the potential to increase population-wide levels of regularity and may play a role in providing constipation relief.

Cereal, Fruit, and Vegetable Sources

A 2016 systematic review of intervention trials on cereal, fruit, and vegetable fibers (136 experimental studies, healthy subjects) found that cereal and vegetable fiber resulted in similarly increased fecal weight with fruit fiber being less effective [30]. Less fermentable food fibers increased fecal weight to a greater amount than more fermentable fibers. Fiber did not change transit time in individuals with an initial time of <48 h. In those with an initial transit time ≥ 48 h, transit time was reduced by approximately 30 min per gram of cereal, fruit, or vegetable fiber, regardless of fermentability. This analysis indicates that slow transit time (≥48 h) may be normalized by increasing fiber, regardless of the type consumed.

Cereal Sources

Four specific systematic reviews and/or meta-analyses have evaluated the effects of cereal fiber-rich food sources on bowel function [24, 31, 32, 38]. A 2015 systematic review of cereal fiber intervention in studies with healthy subjects (65 trials, 90% wheat bran) found that wheat bran improved measures of bowel function [31]. Specifically, when baseline transit time was >48 h, each extra g/day of wheat bran significantly increased total stool weight by 3.7 g and reduced transit time by 45 min. A meta-analysis of wheat bran trials (20 RCTs, healthy and constipated subjects) showed that bran increased the stool weight and decreased the transit time in healthy controls and in individuals with chronic constipation, but in constipated individuals, their stool weight and transit time were not completely restored to normal [32]. A systematic review of oat product intervention studies (14 trials) found that in healthy oats or oat bran can significantly increase stool weight and decrease constipation [38]. Oat consumption significantly increased wet and dry stool weight in six out of nine studies (from 15 to 88% increase) and in five out of six studies (from 15 to 101% increase), respectively. Stool frequency did not change significantly in five studies, improved in two studies, and reduced in one study relative to wheat bran and rice bran interventions. Transit time decreased significantly by 17% in only one out of four studies. A meta-analysis of placebo-controlled, double-blinded RCTs (five RCTs, primarily bran and glucomannan) demonstrated that increased fiber intake significantly improved stool frequency by 19% (p <0.05), but there was no significant improvement in stool consistency or painful defecations [24].

Prunes (Dried Plums)

A systematic review of prunes and gastrointestinal function (four RCTs,165 participants, mean age 36–54 years, 73% women, three studies in healthy and one in constipated subjects, duration 2 weeks–3 months, 84–100 g prunes/day, controls included grape juice, dried apples, cookies, psyllium plus water) suggested that in constipated subjects prunes were superior to psyllium in increasing stool frequency and improving stool consistency and in non-constipated subjects prunes softened stool consistency and increased stool weight [42].

Psyllium

A systematic review of the efficacy of soluble and insoluble fiber supplementation in the management of chronic idiopathic constipation (six RCTs (three psyllium, one bran, one rye bread, and one inulin)) found that psyllium was the most effective of the fibers in promoting bowel function [50]. Compared with placebo, psyllium improved global symptoms (86% vs. 47%), straining (56% vs. 29%), reduced pain on defecation, improved stool consistency, increased the mean number of stools per week (3.8 stools per week after therapy compared with 2.9 stools per week at baseline), and a reduced the number of days between stools. Evidence for any benefit of insoluble fiber was conflicting.

Specific Trials

Mixed Fiber-Rich Diets

Three RCTs provide important insights on the benefits of fiber-rich diets on bowel function in both regular and low caloric diets [33, 34, 40].

Dose Response

A US crossover, dose-response RCT (nine healthy, young male students; 16 g, 30 g, and 42 g fiber/day from a mixture of fruits, vegetables and cereal grains; duration 1 month for each dose with 15-day washout) found that mean daily stool weights increased directly with the amount of fiber consumed; wet fecal mass was 109 g, 156 g, and 195 g for 16 g, 30 g, and 42 g fiber intake, respectively [33]. Increasing dietary fiber intake from 16 g/day to 30 g/day increased mean stool frequency from 0.7 to about 1 per day, but increasing fiber intake from 30 g/day to 42 g/day did not further increase stool frequency. Increasing fiber intake from a mixture of whole plant food sources tended to be as effective as consuming cereal bran, but there was no improvement in stool frequency if the baseline stool frequency rate was already $\geq$1 per day.

Very Low-Calorie Diets

A 1990 crossover RCT (22 obese adults, mean age 31 years, 80% women, 2 weeks, no washout) showed that adding 30 g insoluble plant fiber/day into a very low-calorie diet reduced hunger and increased stool weight and the number of daily bowel movements from 0.7 to 1.0/per day compared to a fiber free very low calorie diet, without affecting rate of weight loss, flatulence, or calcium, iron, or magnesium balance [34].

Pajala Porridge

Pajala porridge containing rolled oats, oat bran, flax seeds, chopped prunes, apricots, and raisins has been shown to be a well-tolerated fiber food option for addition to elderly diets in long-term care facilities alleviating constipation [40]. A parallel RCT (20 adults, age > 65 years, breakfast porridge with 7.5 g fiber vs. breakfast without porridge, 1-week run-in, 2 weeks) demonstrated that the fiber-rich porridge was effective, well-liked, and tolerated and reduced the need for laxatives in geriatric patients. Specifically, the porridge group had bowel movements without laxatives 76% of the time

vs. 23% for the control group ($p = 0.003$), and bowel discomfort was significantly 40% lower in the porridge vs. the control group ($p = 0.008$).

Cereal Bran-Rich Foods

Five publications and six intervention trials assess the effects of cereal bran-rich foods [29, 35–37, 39].

Breakfast Cereals

Three intervention trials evaluate the effect of increased wheat bran in breakfast cereal [29, 35, 36]. An open label trial (153 subjects, 81 females and 72 males, mean age 34 years, mean BMI 24.5, mean baseline total fiber intake 10.5 g/day, one bowel of wheat bran-containing ready-to-eat-breakfast cereal with 5.4 g/day fiber [3.5 g from wheat bran], 14 days) found that wheat bran cereal significantly improved subjective perception of bowel function (e.g., ease of defecation), digestive feelings (less bloating, constipation, feeling sluggish, and digestive discomfort) and general well-being (feeling less fat, more mentally alert, slim, happy and energetic, while experiencing less stress, mental and physical tiredness, difficulty concentrating, and fewer headaches) [35]. A parallel RCT (23 subjects; mean age 35 years; 12 women and 11 men; four different fiber-rich breakfast cereals including All-Bran or Bran Buds with fiber blends of corn and psyllium at 2.5 servings/day to provide about 25 g fiber/day added to the habitual Western diet with 12 g fiber/day; 3 weeks; 1-week washout) showed that all the fiber-enriched breakfast cereals significantly increased wet bulk (by 55% or 71 g/day), reduced transit times (by 30% or 12 hrs), and increased bowel movement frequency (25% or 0.2g/day) compared to the low-fiber control diet, while maintaining a good level of tolerance [36]. Bran cereal with psyllium was more effective than the other breakfast cereal in increasing stool wet weight for softer consistency. A three-phase crossover RCT evaluating the effect of bran particle size (24 healthy subjects, 12 females and 12 males, mean age 36 years, breakfast cereal with 19 g fiber from wheat bran/day made from medium and coarse particle size bran vs. a low-fiber cereal control, 1 month metabolic ward) showed that both medium and coarse wheat bran breakfast cereals similarly increased daily wet stool bulk compared to the low-fiber breakfast cereal [29]. Smaller particle size bran fiber did not adversely affect stool bulking or frequency of bowel movements.

Breads

Two RCTs evaluated the effects of bran-enriched bread on bowel function [27, 37]. A three-phase metabolic, crossover RCT (23 healthy subjects, 12 women and 11 men, mean age 58 years, bread with 19 g fiber/day from very fine or medium wheat bran vs. a low-fiber control bread, 2 weeks) found that both fine and medium wheat bran particle size enriched bread significantly increased fecal bulk by 58–68 g/day compared to the low-fiber bread [27]. There was a small but significantly increased bowel movement frequency for the medium bran fiber bread (1.5/day) compared to the fine bran fiber bread (1.4/day) and to low-fiber bread (1.3/day). This study showed that bread with fine wheat bran in improving fecal bulk and laxation. Additionally, the fine bran was significantly fermented to produce butyrate, an indicator of colonic microbiota health, compared to the medium particle size bran. A parallel RCT (59 women with constipation; mean age 41 years; four diets, (1) rye bread (30 g fiber/day), (2) rye bread plus Lactobacillus rhamnosus GG (LGG)-enriched yogurt, (3) LGG-enriched yogurt, and (4) a control low-fiber bread; 3 weeks) found that rye bread shortened total intestinal transit time by 17 hrs, increased fecal frequency by 0.3 per day, softened feces by 0.3 units, made

defecation easier by 0.4 units and also increased gastrointestinal symptom (bloating and flatulence) score by 1.6 units compared to the low-fiber bread (control) on LGG yogurt groups [37]. However, consuming high fiber rye bread with LGG yogurt prevented the bloating and flatulence associated with high fiber bread alone.

Oat Bran in Soups and Desserts

A blinded parallel RCT (30 assisted living subjects, mean age 85 years, 5.1 g oat bran fiber/day vs. 0 fiber control, 12 weeks) found that oat bran blended into the daily lunch soup or dessert served in a standard diet or incorporated into the afternoon cake significantly reduced laxative usage by 59%, whereas the control group slightly increased laxative use by 8% [39]. The oat bran was well tolerated.

Fruits and Vegetables

Whole Fruit and Vegetables vs. Fruit and Vegetable Juice

A crossover RCT (12 men, age range 37–58 years, weight range 68–95 kg, high-fiber fruit and vegetable diet vs. a low-fiber diet containing fruit and vegetable juices, 26 days, no washout), showed that the high-fiber intake from fruit and vegetables vs. low-fiber juice intake significantly reduced fecal transit time (by 27% or 14 hrs), increased the number of daily bowel movements (by 40% or 0.4g), and increased daily wet fecal weight (by 118 g) [41].

Prunes (Dried Plums)

A crossover RCT comparing prunes vs. psyllium (40 constipated subjects, 92% women, mean age 38 years, 50 g prunes or 11 g psyllium twice daily, total 6 g fiber each, 3 weeks, 1-week washout) found that prunes significantly improved constipation symptoms as reflected by a significant increase in the number of complete and spontaneous bowel movements/week (Fig. 5.3) and improved stool consistency (softer stools) compared with a psyllium fiber supplement [43]. This study showed that psyllium was also useful in improving bowel symptoms in individuals with mild to moderate constipation and affirmed prior studies on psyllium in chronic constipation. The laxative effects of prunes (dried plums) are most likely due to a combination of sorbitol (14.7 g per 100 g) and dietary fiber (6 g per 100 g).

Kiwifruit

Three RCTs assess the laxative effects of kiwifruit intake on bowel function, which is associated with the kiwifruit cell wall unique viscous polysaccharides with exceptionally high swell or water-binding capacity for fecal bulking and stool softening properties similar to that of psyllium [44–46]. A 2002 crossover RCT with elderly adults (38 healthy, overweight subjects, mean age 73 years, 25 females and 13 males, two-kiwifruit/day vs. no kiwifruit, 3-week duration with a 3-week washout) showed that kiwifruit significantly enhanced laxation, including bulkier and softer stools, ease of defecation, and more frequent bowel movements [44]. A second RCT in constipated Chinese subjects (33 constipated subjects, mean age 50 years, 24 females, 20 healthy subjects with regular bowel movements, mean age 51 years, 16 females, kiwifruit twice daily, 4 weeks) found that kiwifruit significantly

doubled complete spontaneous bowel movements from two times to four times per week along with significantly improved transit time and satisfaction with bowel habits [45]. However, in the subjects with normal regularity, kiwifruit resulted in no significant changes in normal bowel function. In a third RCT, subjects with a combination of irritable bowel syndrome with constipation (IBS-C) (54 subjects, 49 females, 2-kiwifruit/day, 4 weeks) reported that kiwifruit consumption significantly shortened colon transit time, increased defecation frequency, and improved overall bowel function [46]. This study suggests that kiwifruit (taken as a routine dietary constituent) appears to be a safe and effective natural laxative for individuals with IBS-C.

Common Fiber-Rich Food Ingredients

Polydextrose

Three RCTs evaluated the effect of polydextrose, a common synthetic low energy, low-moderate fermentability fiber ingredient, on bowel function [47–49]. A double-blind, crossover RCT (36 healthy adults, mean age 26 years, 18 females and 18 males, 20 g polydextrose/day in muffins and cereal vs. low-fiber control, 10 days with a 2 week washout) showed that polydextrose enriched foods significantly improved laxation activity compared with the low-fiber control foods (Fig. 5.4) [47]. This study shows that the addition of 20 g polydextrose in foods is well tolerated and has moderate laxative effects. Similar findings were observed for consuming 21 g/day of polydextrose in a snack bar compared to a no fiber control snack bar [48]. A triple-blind, parallel RCT (50 constipated Japanese hemodialysis patients, mean age 65 years, 60% with diabetes, 34 men and 16 women, 10 g polydextrose/day in foods vs. control, 4 weeks) demonstrated that polydextrose significantly improved stool frequency, softened the stool, and improved ease of defecation, without inducing adverse gastrointestinal effects (Fig. 5.5) [49].

Chicory Inulin

A 2017 German double-blind, crossover RCT (44 healthy constipated subjects, 75% women, mean age 47 years, 12 g/day inulin from chicory or 12 g/day maltodextrin, 4 weeks) found that chicory inulin significantly increased stool frequency compared to placebo (median 4.0 vs. 3.0 stools/week ($p = 0.038$), softened stools and resulted in a trend toward higher subject satisfaction vs. placebo ($p = 0.059$) [56]. This RCT also showed that chicory inulin significantly increased flatulence from 1.1 for the placebo to 1.9 on a scale of 0–4 units.

Soluble Fiber Supplements

Soluble fiber-based dietary supplements are widely used and recommended by health-care professionals as an option to help alleviate constipation [9, 10]. A systematic review of fiber supplementation in the management of chronic idiopathic constipation (6 RCTs including three psyllium, one bran, one rye bread, and one inulin trials) found that compared with placebo, psyllium improved global symptoms by 39%, reduced straining by 27%, pain on defecation, enhanced stool consistency, and increase the mean number of stools per week (3.8 stools per week after therapy compared with 2.9 stools per week at baseline) [50]. Table 5.3 summarizes the intervention trials for psyllium Konjac glucomannan and partially hydrolyzed guar gum [52–61].

Table 5.3 Summary of intervention trials on soluble fiber supplements for laxation and chronic constipation relief

Objective	Study details	Results
Psyllium		
Nunes et al. Evaluate the effects of a psyllium laxative preparation in adults with chronic constipation (double-blind RCT, Brazil) [52]	60 adults, 65% women, 10 g psyllium daily vs. placebo, 2 weeks	87% of individuals receiving psyllium vs. only 30% of those in the placebo group had normal bowel movement frequency ($p < 0.001$). Psyllium was shown to be effective in relieving chronic constipation
McRorie et al. Compare the effects of psyllium and docusate sodium on chronic constipation (double-blind RCT, USA) [53]	170 adults, mean age 37 years, 90% women, 5.1 g psyllium twice daily vs. docusate sodium, 2 weeks	Psyllium was superior to docusate sodium for softening stools by increasing water content and improving overall laxative efficacy
Ashraf et al. Evaluate the effects of psyllium therapy on stool characteristics and colon transit in chronic constipation (double-blind RCT, USA) [54]	22 adults, 14 females, 5 g psyllium twice daily vs. placebo, 8 weeks	In individuals with chronic constipation, psyllium increased stool frequency compared with placebo and improved stool consistency, reduced pain on defecation, straining and sense of complete evacuation compared to baseline
Stevens et al. Compare the effects of psyllium and wheat bran on colonic transit time and stool characteristics (parallel RCT, USA) [55]	12 subjects; psyllium, wheat bran, or low-fiber diet; 2 weeks	Both fiber sources decreased transit time and increased the daily number of defecations and wet and dry weight of stools. Bran increased transit time greater than psyllium, and psyllium had a greater effect on stool weight and % bound water. The fiber sources reduced the subjective ratings of hard stools by 40% compared to the control low-fiber group
Fenn et al. Assess the effect of psyllium on chronic constipation (single-blind RCT, UK) [56]	201 subjects, 150 females, psyllium vs. placebo primary outcome improvement in global symptoms, 2 weeks	87% of subjects allocated to psyllium reported an improvement in global symptoms compared with 47% of subjects receiving placebo ($p < 0.001$). Also, psyllium significantly reduced abdominal pain and straining on defecation Psyllium was twice as effective in reducing chronic constipation symptoms compared to placebo
Konjac glucomannan (KGM)		
Loening-Baucke et al. Evaluate the effect of KGM on children with chronic constipation (double-blind RCT USA/Italy) [62]	46 children with chronic constipation, mean age 7 years, 24 boys and 22 girls, 5 g KGM/day with 500 mL fluid vs. placebo, 4 weeks	KGM significantly improved the number of bowel movements, decreased soiling episodes and abdominal pain (45%) compared to placebo control (13%). No significant side effects were reported
Chmielewska et al. Assess the effect of KGM as a sole treatment of chronic constipation in children (double-blind RCT, Poland) [57]	80 children, 3–16 years, 2.5 g KGM vs. placebo with water, 4 weeks	Overall 2.5 g KGM/day did not significantly improve constipated children compared to placebo control, which indicates a need for a higher dose in older children
Chen et al. Evaluate the effects of KGM on laxation in healthy adults (parallel RCT, China) [58]	Eight adults, 4.5 g KGM/day vs. low-fiber Chinese diet, 21 days	KGM supplement significantly increased defecation frequency by 27% and wet stool weight by 30%

(continued)

Table 5.3 (continued)

Objective	Study details	Results
Partially hydrolyzed guar gum (PHGG)		
Russo et al. Investigate the effect of PHGG on constipation in individuals with irritable bowel syndrome with constipation (IBS-C) (prospective open label trial, Italy) [59]	86 constipated IBS-C subjects, mean age 37 years, mean BMI 24, 69 females, 5 g PHGG consumed daily with water after breakfast, 4 weeks	PHGG was significantly associated with improved symptom scores, lower use of laxatives, and improved stool consistency and colonic transit time in individuals with IBS-C
Polymeros et al. Evaluate the effect of PHGG on chronic constipation (prospective open label trial, Greece) [60]	49 chronic constipated subjects, mean age 56 years, mean BMI 24, 43 females, 5 g PHGG daily with water, 4 weeks	PHGG significantly reduced colon transit time by 21%, laxative use, and days with abdominal pain and improved number of complete spontaneous bowel movements, number of bowel movements without straining, and improved stool form
Ustundag et al. Compare the effects of PHGG vs. lactulose (osmotic laxative) in children with constipation (parallel RCT, Turkey) [61]	61 children, 4–16 years; 1 mL lactulose/kg/day in divided doses; PHGG; 3 g/day for children between 4–6 years; 4 g/day for children 6–12 years; 5 g/day for children 12–16 years with water; 4 weeks	Bowel movement frequency/week and stool consistency improved significantly in both treatment groups ($p < 0.05$). The % of children with abdominal pain also decreased in both groups ($p < 0.05$). Lactulose was associated with bad taste and flatulence but PHGG was not

Soluble Fiber, Gel-Forming, Viscose, Limited Fermentable Supplements

Psyllium

Psyllium is a soluble, viscous, relatively low-fermentable fiber with high water-holding capacity, which forms an effective stool bulking gel in the colon to promote softer stools, laxation and help normalize bowel movements.

Five RCTs support psyllium's effectiveness as a relatively low-fermentable, stool bulking gel in promoting laxation and alleviating chronic constipation [52–56]. A double-blind placebo-controlled RCT (60 adults with chronic constipation, 65% women, 10 g psyllium daily, 2 weeks) found that 87% of individuals receiving psyllium vs. only 30% of those in the placebo group had normal bowel movement frequency ($p < 0.001$) [52]. The other psyllium RCTs all showed similar effects in relieving chronic constipation [53–56]. These trials consistently show that psyllium improves the stool frequency and softness as well as improving global symptoms including stool consistency and reduced pain and straining on defecation in individuals with constipation. In a comparison study of psyllium and wheat bran, psyllium was shown to be more effective than wheat bran at increasing stool water (softening) and overall stool weight, but wheat bran was more effective in speeding up fecal transit time verses a low-fiber control [55].

Konjac Glucomannan (KGM)

Konjac glucomannan (KGM) is a soluble, fermentable, and highly viscous fiber derived from the root of the elephant yam or konjac plant, which is native to Asia [63]. KGM has a high molecular weight ranging from 200,000 to two million daltons (average: 1,000,000 daltons) with linkages that prohibit fermentation by the microbiota, which allows for a very high water-holding capacity for effective colonic bulking and laxation. Two double-blinded RCTs in children suggest that 3–5 g KGM/day can provide constipation relief with minimal side effects [57, 62]. In one RCT, 4.5 g KGM/day was found to be an effective laxative for Chinese adults consuming low-fiber diets [58].

Soluble, Non-Gelling, Fermentable Fiber

Partially Hydrolyzed Guar gum (PHGG)

Partially hydrolyzed guar gum (PHGG) is a fermentable, soluble, non-gelling fiber, which supports bifidogenic and lactogenic growth, and increases the concentration of short-chain fatty acids (SCFAs) in the distal colon [64]. In two prospective open label trials in adults with irritable bowel syndrome associated constipation or chronic constipation, it was shown that 5 g PHGG taken daily with fluids significantly improved symptoms of constipation [59, 60]. One RCT in children demonstrated that 3–5 g PHGG, depending on age, was as effective as lactulose in relieving constipation and abdominal pain and improving stool consistency with fewer side effects [61].

Conclusions

The consumption of adequate dietary fiber (>25 g/day), recommended fluid intake, and regular physical activity are especially beneficial in preventing and alleviating constipation. Fiber mechanisms associated with improved laxation and alleviated constipation include increasing stool weight and bulk volume (through fiber and microbiota physical volume and water holding capacity) and gas volume trapped in the stool to increase bowel movement frequency and quality, especially in constipated individuals. Adequate intake of fiber from whole-grain cereal rich in bran, fruits (especially prunes and kiwi fruit), vegetables, and common fiber-rich food ingredients, including polydextrose, psyllium, and chicory inulin, has the potential to increase population-wide levels of regularity and may play a role in providing constipation relief. In general, less fermentable food fibers tend to increase fecal weight to a greater amount than more fermentable fibers. Wheat bran is the most widely studied fiber source; when baseline transit time was >48 h, each extra g/day of wheat bran significantly increased total stool weight by 3.7 g and reduced transit time by 45 min. Further, in people with an initial transit time >48 h, transit time was reduced by approximately 30 min per gram of cereal, fruit, or vegetable fiber, regardless of fermentability. Increased fiber intake does not tend to significantly change transit time in individuals with an initial time of <48 h. Soluble high viscosity, low fermentable fiber supplements such as psyllium and konjac glucomannan, have been shown to help soften stools promote laxation and alleviate constipation symptoms.

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Chapter 6
Fiber and Low FODMAP Diets in Irritable Bowel Syndrome

Keywords Irritable bowel syndrome • Dietary fiber • Low FODMAP diets • Bloating • Bowel distension • Microbiota dysbiosis • Psyllium • Wheat bran • Celiac disease • Mucosal inflammation • Mast cells • Intestinal permeability • Enteric nerves

Key Points

- Irritable bowel syndrome (IBS) is the most common gastrointestinal disorder occurring in people <45 years.
- IBS is a chronic and relapsing functional colonic disorder characterized by abdominal pain, bloating, distension, and changes in bowel habits that lack visible structural or anatomic abnormalities.
- IBS pathophysiology is associated with colonic microscopic and molecular abnormalities from low-grade inflammation, neuronal hyperexcitability, and microbiota dysbiosis including reduced bacteria diversity, lower levels of butyrate-producing bacteria and increased levels of pathogenic bacteria.
- Celiac disease and bile acid malabsorption may be confounding and difficult to distinguish from IBS symptoms.
- Although certain foods can be triggers for IBS symptoms, some types of fiber supplements and low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diets and traditional IBS dietary guidance (avoidance of large meals, moderate dietary fat intake, limits on high lactose milk products and gas producing foods such as beans, cabbage and onions) have been shown to reduce the risk of acute IBS symptoms.
- Of the supplemental fiber options, psyllium has been most consistently shown to provide moderate relief of IBS symptoms.

Introduction

Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder occurring in people <45 years [1–4]. It is a chronic and relapsing functional colonic disorder characterized by abdominal pain, bloating, distension, and changes in bowel habits that lack visible structural or anatomic abnormalities. Previously, IBS was called colitis, mucous colitis, spastic

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colon, nervous colon, and spastic bowel. IBS affects 10–15% of the global population with peak prevalence in people from 20 to 39 years of age, and it is twice as common in females as males [5]. Studies estimate that the IBS rate in North American children is 14% of high school students and 6% of middle school students [1, 4]. IBS accounts for as much as 12% of total visits to primary care providers with between 2.4 and 3.5 million annual physician visits for IBS in the USA alone [3].

IBS is generally diagnosed when a person has had abdominal pain or discomfort at ≥3 times a month for the previous 3 months without other disease or injury that could explain the pain [1].

The pathogenesis of IBS is multifactorial and not completely understood, but potential dysfunctions that have been reported in patients with IBS include altered gastrointestinal motility, increased gastrointestinal fermentation, abnormal gas transit, colonic hypersensitivity, stress, brain-gut axis dysregulation, and microbiota dysbiosis [1, 2, 5–8]. Abdominal pain is the most common symptom and often is described as a cramping sensation. Among patients about 40% of people have mild IBS, 35% moderate IBS, and 25% severe IBS [3]. IBS has four different subtypes: IBS with constipation, IBS with diarrhea, mixed IBS alternating constipation and diarrhea, and unsubtyped with a milder degree of abnormal stool consistency [1].

Food can be a trigger for IBS symptoms, and diet management has a potentially important role in alleviating symptoms. However, there is an incomplete understanding about how food affects IBS symptoms since there are few rigorous, blinded RCTs [6–14], so it is not uncommon for IBS individuals to generate their own theories to explain this phenomenon or seek guidance from other, usually unsupported, dietary remedies [9]. Certain foods and drinks that are most commonly linked to IBS symptoms in some people are beans, cabbage, and other foods that may cause gas, foods high in fat, some higher lactose milk products, or drinks with large amounts of low-calorie sweeteners [1]. Between 60 and 80% of patients with IBS report postprandial worsening symptoms and adverse reactions to one or more foods, and many patients avoid specific foods to reduce symptoms [11–13]. These symptoms tend to occur or worsen within 3 h after meal consumption in patients with IBS [11]. The relationship between fiber intake and IBS is complex and dependent on the subtype of IBS. In people with IBS-constipation, fiber can improve constipation symptoms and may help with reducing colonic pain as fiber softens stool so that it moves smoothly through the colon [1]. Fiber intake should be slowly increased with recommended levels of water to reduce the risk of increased gas and bloating, and medications should be consumed at least 2 h after consuming fiber-rich meals or supplements to avoid any potential drug interactions. FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) appear to increase symptoms, and low FODMAP diets may improve bloating and abdominal pain or discomfort, but they do not consistently improve bowel diarrhea or constipation [6, 10, 15]. The objective of this chapter is to review the effects of fiber and low FODMAP diets on IBS symptoms.

Other Colonic Conditions with Symptoms Similar to IBS

There are several conditions that can be difficult to distinguish from IBS, including bile acid malabsorption and celiac disease.

Bile Acid Malabsorption

Excessive bile acids entering the colon may cause increased colonic water and resulting diarrhea [15]. A meta-analysis suggests that 10% of patients with IBS-diarrhea like symptoms have severe bile acid malabsorption [16]. A recent survey in the UK suggests that bile acid diarrhea accounts for nearly one in four IBS patients referred to secondary care with diarrhea [17].

Celiac Disease

It is difficult to clinically distinguish IBS from adult-onset celiac disease [18–20]. Both IBS and celiac disease patients can have abdominal symptoms triggered by the ingestion of wheat products. In celiac disease patients, this is due to wheat gluten intolerance, while in IBS, the effect is attributed to fructans and galactans in the wheat products [18, 19]. A meta-analysis found that the pooled prevalence of IBS symptoms in patients with treated celiac disease on a gluten-free diet was up to 40%, in part because of the fructans and galactans present in gluten-free diets [20]. Baked goods such as breads generally contain low quantities of fructan (0.61–1.94 g/100 g), with rye bread being the richest source (1.94 g/100 g) [21]. Surprisingly, gluten-free bread contains similar quantities of fructan (0.36–1.79 g/100 g) to other breads. Consequently, the widespread consumption of bread products including gluten-free products may make a significant contribution to fructan intakes and IBS symptoms. Despite adhering to a gluten-free diet, patients with celiac disease exhibit a fivefold higher odds of IBS symptoms compared to healthy individuals as IBS may coexist with celiac disease in some patients [10, 18–20].

IBS Pathophysiology

IBS is characterized by increased susceptibility to bloating and bowel distension [18, 22, 23]. In a study (20 patients with IBS, 20 healthy volunteers, 75% women) 90% of patients with IBS developed colonic gas retention compared to only 20% of the control subjects ($p < 0.01$). The IBS patients had excessive gas retention and impaired gas clearance from the proximal colon, as opposed to the distal colon [23]. Increased susceptibility to gas production and bloating occurs in nearly all patients with IBS especially after the consumption of fermentable carbohydrates [14, 15, 22–24]. Although IBS colons generally lack visible structural or anatomic abnormalities, emerging research shows that there are colonic microscopic and molecular abnormalities from low-grade colonic inflammation and neuronal hyperexcitability, and microbiota dysbiosis now identified in IBS patients.

Low-Grade Colonic Inflammation and Neuronal Hyperexcitability

Multifactorial low-grade colonic inflammation is involved in the pathogenesis of IBS with studies showing colonic microscopic and molecular abnormalities mainly characterized by an increased infiltration of mast cells [25–29]. Mast cells are innate immune cells involved in food allergies,

wound healing, and protection against pathogens [25]. The digestive tract contains an extensive enteric neuron network to control mucosal transport and motility, and in response to persistent colonic inflammation, incoming mast cells communicate with the central nervous system to release mediators, such as histamine, tryptase, and chymase, which can evoke neuronal hyperexcitability, a major factor for IBS pain [26–29]. Abnormalities in the colonic enteric nervous system may alter digestion, gastrointestinal motility, and cause hypersensitivity which appear to have a pivotal role in the pathogenesis of IBS in susceptible individuals [25]. Food such as those containing FODMAPs increase the levels of inflammatory compounds in the urine associated with the pathophysiology of IBS [30, 31]. A single-blinded, parallel RCT (40 IBS patients, 83% IBS mixed or diarrhea, 35 females, mean age 51 years; 3 weeks) found that low FODMAP diets can reduce urinary histamine eightfold compared to high-FODMAP diets [31].

Microbiota Dysbiosis

Emerging research supports the link between colonic microbiota dysbiosis and the development and maintenance of IBS symptoms [32]. One of the key features of IBS is the erratic pattern of stool form, with both hard and loose stool within a time period as short as 24 h, indicating that stool microbiota is unstable in IBS [15]. It has been hypothesized that IBS may develop in predisposed individuals following an acute bout of infectious gastroenteritis, which has been linked to disturbance of the colonic microbiota with overgrowth of pathogens such as *Escherichia coli*, *Salmonella*, *Shigella*, and *Pseudomonas*, a twofold increase in the ratio of Firmicutes to Bacteroidetes and a marked reduction in diversity [32–36]. A dysbiotic colonic microbiota including increased pathogenic bacteria and decreased butyrate-producing bacteria such as *F. prausnitzii* may activate innate mucosal immune responses which increase colonic epithelial permeability, activate nociceptive sensory pathways, and dysregulate the enteric neuromotor sensory function and brain-gut axis leading to IBS symptoms. It has been suggested that dysbiotic bowel syndrome could be another name for IBS [37].

Fiber for the Management of IBS

Empirical thinking suggests that increased fiber may help to promote long-term alleviation of IBS symptoms because of fiber's known ability to promote digestive health by promoting regular bowel movements, increasing stool bulk, lowering colonic pH to protect against pathogens, supporting healthier microbiota, and controlling colonic permeability and inflammation [38, 39]. However, according to the American College of Gastroenterology monograph on IBS, fiber's effectiveness in relieving IBS symptoms is inconsistent. Insoluble fibers such as wheat bran provide minimal relief, while some soluble fibers, especially psyllium, provide moderate relief to IBS symptoms [9]. A 2014 meta-analysis (14 RCTs evaluated fiber in IBS; 940 subjects; six trials used bran, 441 subjects; seven trials used psyllium, 499 subjects) found significant benefits for fiber in reducing the pooled mean IBS risk by14% compared to a placebo, with no significant heterogeneity between studies [40].

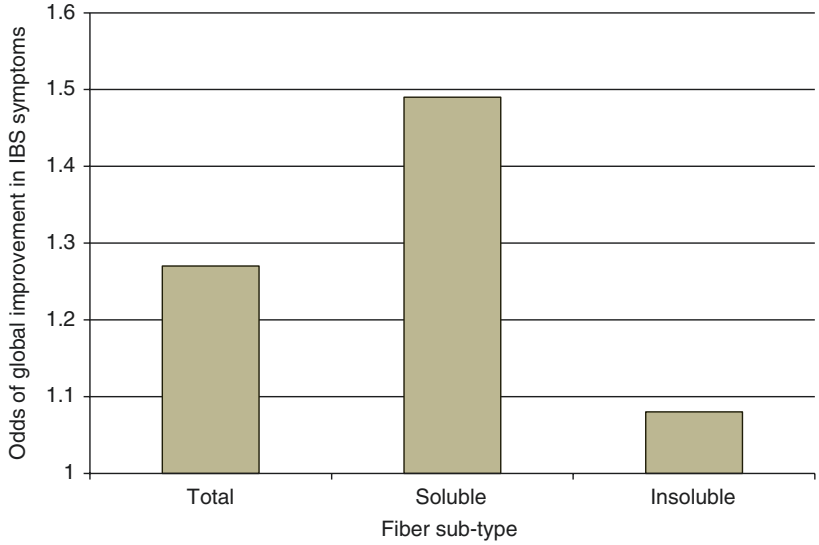

Fig. 6.1 Effect of fiber type on managing irritable bowel syndrome (IBS) symptoms [41]

A stratified analysis showed that bran had an insignificant effect on the treatment of IBS by lowering risk by10%, whereas psyllium resulted in a significant 17% reduction in IBS. A 2015 systematic review and meta-analysis (22 RCTs, 1299 participants; 4.1–40 g fiber/day; 3–16 weeks), showed that fiber, especially soluble fiber, appears to have a role in improving the symptoms of IBS with a low risk of harm [41]. There was a significant improvement in global assessment of symptoms among those randomized to soluble fiber by 49% or total fiber by 27% (Fig. 6.1). Soluble fiber also reduced abdominal pain score by 1.84 units, whereas insoluble fiber did not improve any outcome. The analysis concludes that soluble fiber appears to improve symptoms of IBS, whereas there is no evidence for recommending insoluble fiber for IBS. These meta-analyses identify soluble fiber especially psyllium, if consumed with adequate water, as being possibly helpful in alleviating IBS symptoms and promoting regularity [40, 41].

Table 6.1 provides a comprehensive summary of RCTs on the effects of fiber on IBS symptoms [42–58]. A double-blind RCT (275 patients in primary care, 164 completers, mean age 34 years, 78% women, 10 g psyllium or 10 g ground wheat bran added to yogurt and ingested twice daily vs. placebo yogurt with rice flour, 3 months) found that psyllium, but not wheat bran, added to yogurt was effective in the clinical management of IBS symptoms compared to the placebo (Fig. 6.2) [42]. Other soluble fibers with potential IBS protective effects similar to psyllium include partially hydrolyzed guar gum [50–52] and pectin [53]. The RCTs summarized in Table 6.1 show a moderate level of evidence that psyllium is moderately effective in alleviating IBS symptoms [42–49], whereas wheat bran fiber supplementation did not improve IBS symptoms [42, 54–58]. The 2015 IBS global perspective guidelines recommend a fiber-rich diet or a soluble bulk former such as psyllium combined with sufficient fluids intake for potential IBS relief given that fiber is inexpensive and generally thought to be safe, especially compared with the available drugs approved for IBS [40, 59]. Overall, there is limited evidence that most fiber sources alleviate IBS symptoms compared to placebo.

Table 6.1 Summary of RCTs on fiber and irritable bowel syndrome (IBS) symptoms [42–58]

Objective	Study details	Results
Psyllium		
Bijkerk et al. Evaluate the effects of psyllium supplement for the treatment of IBS (double-blind RCT, Netherlands) [42]	275 patients in primary care with 164 completers, mean age 34 years, 78% female, 10 g psyllium added to yogurt twice daily vs. placebo yogurt with rice flour for 12 weeks	Psyllium provided improved relief of IBS symptoms compared to wheat bran or placebo (Fig. 6.2). After 3 months, symptom severity was reduced with psyllium by 34% compared with 18% for the placebo ($p = 0.03$)
Jalihal and Kurian Assess the effects of psyllium on IBS symptoms (double-blind RCT, India) [43]	22 patients in secondary care with 9% loss to follow-up, 20% female, 75% constipation, 30 g psyllium vs. placebo daily, 4 weeks	Psyllium significantly improved global symptoms and resulted in satisfying bowel movements vs. the placebo but produced no change in abdominal pain or flatulence
Prior and Whorwell Evaluate the effects of psyllium on managing IBS symptoms (double-blind RCT, England) [44]	80 patients in tertiary center with 29% loss to follow-up, 90% female, 49% constipation, 3.6 g psyllium vs. placebo 3× daily, 12 weeks	Psyllium significantly improved global IBS vs. placebo (82% vs. 53% improvement). Also, psyllium significantly improved constipation, but it did not reduce abdominal pain or bloating significantly
Kumar et al. Determine the optimal dose of psyllium for IBS management (dose response, crossover RCT, India) [45]	14 female/19 male patients; continuous psyllium 10, 20, and 30 g/day;14-day study; 3 days of stool collection for each dose, no washout period; 14 days with a 1-week washout	Psyllium significantly improved three major IBS symptoms, constipation, abdominal pain, and diarrhea. The 20 and 30 g doses were more effective than the 10 g dose, but compliance was reduced with the 30 g dose The optimum dose of psyllium in the treatment of IBS was 20 g/day
Nigam et al. Determine the effect of psyllium on alleviating IBS symptoms (double-blind RCT, India) [46]	42 patients in secondary care with no loss to follow-up, 45% female, psyllium vs. placebo, 12 weeks	Psyllium significantly reduced risk of global IBS symptoms by 38% Psyllium may help to alleviate IBS symptoms
Arthurs and Fielding Evaluate the effects of psyllium on controlling IBS symptoms (double-blind RCT, Ireland) [47]	80 patients in secondary care with 2.5% loss to follow-up, 78% female, two psyllium sachets vs. placebo, 4 weeks	Psyllium significantly reduced global IBS symptoms by 25%. Psyllium may help to alleviate IBS symptoms
Longstreth et al. Assess the effect of psyllium on IBS alleviation (double-blind RCT, USA) [48]	77 patients in secondary care with 60 completers, 83% female, psyllium vs. placebo, 8 weeks	Both psyllium and placebo significantly improved subjective global IBS symptoms by 70% A strong placebo effect occurs in patients with painful IBS
Ritchie and Truelove Determine the effects of psyllium on treating IBS (double-blind RCT, England) [49]	100 patients in tertiary care with 4% loss to follow-up, 77 females, two sachets psyllium/day, 12 weeks	Psyllium significantly reduced risk of IBS symptoms by 42%. Psyllium helps alleviate IBS symptoms
Partially hydrolyzed guar gum (PHGG)		
Niv et al. Study the effects of PHGG on symptoms of IBS patients (double-blind RCT, Israel) [50]	121 patients with 108 completers 59% mixed, 25% diarrhea, and 16% constipation IBS; 66% female; mean age 43 years; 6 g PHGG or placebo; 12 weeks; 4 weeks of follow-up	After 12 weeks on PHGG, there was a significant lower bloating score vs. placebo by 2.9 and bloating + gas score by 3.2. The effect lasted for at least 4 weeks after the last PHGG dose. PHGG had no effect on other IBS symptoms or quality of life scores. There was a significantly higher rate of dropouts in the placebo compared with the PHGG group (49% vs. 22%)

Table 6.1 (continued)

Objective	Study details	Results
Russo et al. Investigate the effect of PHGG on constipation-predominant IBS (prospective open label trial; Italy) [51]	86 constipated IBS subjects, mean age 37 years, mean BMI 24, 82% female, 2-week run-in baseline evaluation, 4-week intervention with 5 g PHGG consumed daily with water after breakfast	PHGG was significantly associated with improved symptom scores, stool form/consistency, colonic transit time, and reduced use of laxatives
Parisi et al. Compare the effects of wheat bran and PHGG on IBS symptoms (multicenter open RCT, Italy) [52]	188 patients with 59% IBS-constipation; mean age 40 years; 74% female; wheat bran diet 30 g/day vs. PHGG 5 g/day in a beverage; 12-week duration; after 4 weeks patients were allowed to change groups depending on symptoms	Per protocol analysis showed that both wheat bran and PHGG were effective in improving pain and bowel habits ($p > 0.05$) Intention-to-treat analysis of core IBS symptoms (abdominal pain and bowel habits) showed a significantly greater success in the PHGG group (60%) than in the wheat bran fiber group (40%)
Pectin		
Xu et al. Evaluate the efficacy of pectin on diarrhea predominate IBS (parallel RCT, China) [53]	87 patients with IBS-diarrhea, 24 g pectin/day vs. placebo, 6-week intervention	Patients on pectin had a significantly greater reduction in global symptom scores, Bristol stool scale scores, and improved quality of life scores compared to placebo scores. Also, pectin acted as a prebiotic and no significant adverse effects were observed
Wheat Bran		
Bijkerk et al. Assess the effects of wheat bran vs. psyllium supplement for the treatment of IBS (double-blind RCT, Netherlands) [42]	275 patients in primary care with 164 completers, mean age 34 years,78% female, 10 g ground wheat bran added to yogurt twice daily vs. placebo yogurt with rice flour for 12 weeks	Wheat bran was less effective at relieving IBS symptoms than psyllium (Fig. 6.2). After 3 months, symptom severity was reduced for the wheat bran by 22% ($p = 0.61$) compared with 18% for the placebo Wheat bran had insignificant benefits in patients with IBS in primary care
Rees et al. Evaluate the effect of coarse wheat bran on IBS symptom management (single-blinded RCT, England) [54]	28 patients from tertiary center with 21% lost to follow-up, 86% female, mean age 36 years, 100% constipation predominant, 10–20 g/day of coarse wheat bran supplement added to the normal diet vs. a low-fiber placebo, 8–12 weeks	Wheat bran significantly increased fecal wet weight by 28 g/24 h compared with the placebo group, but other bowel function measures and symptoms were insignificant Wheat bran was ineffective in alleviating IBS symptoms
Lucey et al. Study the effects of wheat bran on IBS symptoms (double-blind crossover RCT, England) [55]	44 patients from tertiary center with 36% lost to follow-up, 79% female, mean age 32 years, wheat bran 15.6 g fiber/day vs. placebo <0.5 g fiber/day in biscuits, 12 weeks	There were no significant differences in IBS symptoms between wheat bran and placebo groups. Wheat bran was ineffective in alleviating IBS symptoms
Kruis et al. Assess the effects of wheat bran on alleviating IBS symptoms (parallel RCT, German) [56]	80 patients from tertiary center with 17.5% lost to follow-up, 62.5% female, wheat bran 15 g fiber/day vs. placebo, 16 weeks	Wheat bran significantly improved IBS symptoms vs. placebo after 12 weeks, but not after 16 weeks The long-term effect of wheat bran vs. placebo on IBS symptoms was not confirmed

(continued)

Table 6.1 (continued)

Objective	Study details	Results
Manning et al. Determine the effect of wheat bran on IBS symptoms (parallel RCT, England) [57]	26 patients from tertiary center with 8% lost to follow-up, 46% female, 20 g/day from bran and whole wheat bread vs. low-fiber diet, 6 weeks	Wheat bran significantly improved IBS symptoms and resulted in beneficial effects of pain symptoms
Soltoft et al. Evaluate the effect of Miller's wheat bran on IBS treatment (double-blind RCT, Denmark) [58]	59 patients from tertiary center with 12% lost to follow-up, 64% women, bran 30 g/day in biscuits vs. low-fiber wheat biscuits, 6 weeks	52% of patients in the Miller's wheat bran group had subjective improvement of IBS symptoms compared with 65% in the low-fiber wheat control group

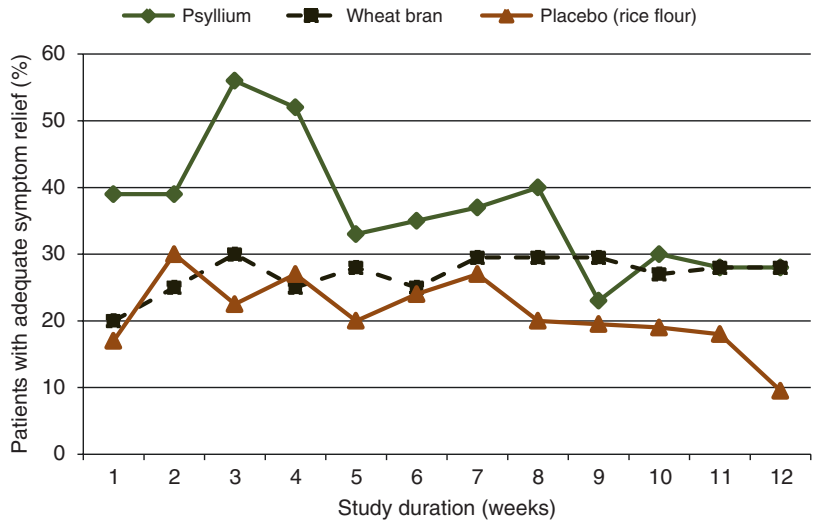

Fig. 6.2 Effect of psyllium vs. wheat bran (10 g/day each) on irritable bowel syndrome (IBS) symptom relief ($p < 0.05$) [42]

FODMAPS and IBS

Consuming moderate amounts of FODMAPs in healthy individuals generally has very limited adverse effects, but for patients with IBS, they often cause IBS symptoms because they are all rapidly fermented, poorly absorbed, and osmotically active and rapidly increase gas production, with additive effects contributing to IBS symptoms [6, 10]. Sources of low and high-FODMAP foods are listed in Table 6.2. The protocol for assessing the need for a low FODMAP diet is as follows: (1) in an initial period of 6–8 weeks, all known or suspected types of food with high content of FODMAPs are eliminated from the diet to determine the benefit of FODMAP restriction, and (2) individual FODMAPs are reintroduced to test the individual's tolerance of each via a series of food challenges [60]. One important long-term challenge is that restricting the intake of FODMAPs excludes a wide variety of foods from the diet with the potential risk for poor dietary nutrient quality. Several systematic reviews of RCTs and observational studies suggest that low FODMAP diets may be effective in the shorter management of IBS symptoms, especially

Table 6.2 Potential food sources of FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) [14, 21, 60, 61]

Component	High-FODMAP food source	Low-FODMAP food source
Fructose	Fruit: apple, pear, peach, mango, watermelon Other: honey or other sweeteners with fructose	Fruit: banana, blueberry, durian, grapefruit, grape, honeydew, melon, kiwifruit, lemon, lime, mandarin, orange, passion fruit, raspberry, and strawberry Other: honey substitutes (maple syrup, golden syrup)
Lactose	Dairy: milk (cow, goat, sheep), ice cream, soft cheeses, regular yogurt	Dairy: lactose free milk, hard and camembert cheese, Greek yogurt, butter Dairy substitutes: ice cream substitutes, sorbet, rice, and almond milk
Polyols (e.g., sorbitol, mannitol, maltitol, xylitol, erythritol, polydextrose, and isomalt)	Vegetable: artichoke, asparagus, beet root, Brussels sprout, broccoli, cabbage, cauliflower, fennel, garlic, leeks, okra, onion, peas, mushrooms, shallots Legume: chickpeas, lentils, red kidney beans, baked beans Fruit: watermelon, apple, pear, white peach, persimmon, avocado Cereal: wheat and rye when eaten in large amounts Chewing gum/hard candies	Vegetable: bamboo shoots, bok choy, carrot, celery, capsicum, corn, eggplant, green beans, lettuce, chives, parsnip, pumpkin, spring onion, tomato Cereal: gluten-free and spelt bread/cereal products
Fructans and/or galactans	Fruit: nectarine, white peach, grapefruit, honey dew melon watermelon, longan, persimmon, cantaloupe Vegetable: artichoke, leeks, onions, Brussel sprouts, garlic, beet root Grain products: both gluten containing and gluten-free	Fruit: banana, blueberry, durian, grapefruit, grape, honeydew, melon, kiwifruit, lemon, lime, mandarin, orange, passion fruit, raspberry Vegetable: most vegetables Sweeteners: sucrose, glucose

with IBS-diarrhea but more rigorous trials are needed to establish long-term efficacy and safety [10, 61]. A systematic review of six RCTs on the effect of low FODMAP vs. control diets showed significantly reduced IBS symptom severity scores by 66%, abdominal pain by 81%, bloating by 75%, overall symptoms by 81%, and increased quality of life by 84% [62].

A summary of nine RCTs on the effect of low FODMAP diets and IBS symptoms is reported in Table 6.3 [24, 31, 63–67]. The findings of these RCTs support the potential benefits of restricting a spectrum of FODMAPs in the diet to various degrees to improve IBS symptoms. A single-blinded, parallel RCT (40 IBS patients, 83% mixed or diarrhea predominate, 87% female, mean age 51 years; 3 weeks) showed that the IBS symptom severity scores were significantly reduced with a low FODMAPs compared to high-FODMAP diet (Fig. 6.3) [31]. In a multicenter, single-blind, parallel RCT (75 IBS patients, mean age 43 years, mean BMI 24, 82% female), a low FODMAP diet had the same effectiveness as traditional IBS guidance which is to avoid large meals and reduce dietary fat, high lactose milk products, and gas producing foods such as beans, cabbage and onions (Fig. 6.4) [63]. Also, a New Zealand prospective observational trial (192 IBS patients, average age 47 years, low FODMAP diet, 84% female, 47% completers, average follow-up 15.7 months) found that IBS symptoms were significantly improved at follow-up with 72% of completers [68]. A low FODMAP diet with a restriction phase of 3–6 weeks may be efficacious in the treatment of IBS symptoms when the diet is planned with a dietitian [69].

Table 6.3 Summary of RCTs on low-FODMAP diets and IBS symptoms [24, 31, 63–67]

Objective	Study design	Results
McIntosh et al. Evaluate effects of low- and high-FODMAP diets on IBS symptoms (single-blinded, parallel RCT, Canada) [31]	40 IBS patients, 83% mixed or diarrhea predominate, with 93% completers, 87% female, mean age 51 years, low- vs. high-FODMAP diets, 3 weeks	Low-FODMAP diet significantly reduced IBS symptom severity scores vs. high-FODMAP diet (Fig. 6.3). Low-FODMAP diets significantly reduced urinary histamine levels by eightfold and potential unhealthy changes in the microbiota that might impact longer-term colonic health
Böhn et al. Compared the effects of a diet low in FODMAPs with traditional dietary advice in patients with IBS (multicenter, single-blind, parallel RCT, Sweden) [63]	75 IBS patients, 46% mixed/unsubtyped, 67 completers, mean age 43 years, mean BMI 24, 82% female, low-FODMAP diet vs. traditional IBS dietary guidance for 4 weeks	About 50% of patients in both the low-FODMAP and traditional IBS diet groups had reductions in IBS severity scores by ≥50 compared with baseline ($p = 0.72$; Fig. 6.4). Food diaries demonstrated good adherence to both diets. Combining elements from these two diet strategies might further reduce symptoms of IBS
Yoon et al. Examine the dose effects of FODMAP level on IBS symptoms (multicenter, double-blind, parallel RCT, Korea) [64]	100 IBS-diarrhea hospital patients, 84 completers; mean age 60 years; mean BMI 20; 70% male; three enteral diets with 1 g (low), 2.2 g (moderate), and 3.7 g (high) of FODMAPs; 14 days	Diarrhea in patients receiving low FODMAPs was significantly improved compared with those receiving moderate or high FODMAPs. These results support the hypothesis that low-FODMAP formula may reduce diarrhea leading to an improvement in nutritional status and IBS recovery
Halmos et al. Investigate the effects on IBS symptoms of a diet low in FODMAPs compared with an Australian diet (single-blind, crossover RCT, Australian) [65]	45 outpatients with IBS with 30 completers, 43% IBS-constipation, secondary care, 70% female, median age 28 years, mean BMI 24, low <0.5 FODMAPs per meal diets vs. Australian diet (high in FODMAPs) and supplemented with psyllium and resistant starch, 3 weeks with 3 week washout	IBS subjects had significantly lower overall gastrointestinal symptom scores while on a diet low in FODMAPs, compared with the Australian diet. Bloating, pain, and gas also were reduced, while IBS patients were on the low-FODMAP diet. A diet low in FODMAPs and supplemented with psyllium and resistant starch was effective in managing IBS symptoms
Pedersen et al. Investigate the effects of low FODMAP diets and probiotics on IBS symptoms (parallel RCT, Denmark) [66]	123 outpatients; secondary care; 108 completers; 85% IBS-diarrhea or mixed; median age 37 years; 73% female; low-FODMAP diet, probiotic *Lactobacillus rhamnosus* GG (LGG) supplement, and Western diet; 6 weeks	The low-FODMAP diet significantly decreased the overall IBS severity scores vs. the Western diet. LGG probiotic significantly lowered IBS symptoms but to a lesser extent than the low-FODMAP diet. Significant improvements were observed for the IBS-diarrhea and IBS-mixed subtypes only. Low-FODMAP diet and probiotic LGG are effective in controlling IBS symptoms in the IBS-diarrhea or mixed subtypes but not IBS-constipation

Table 6.3 (continued)

Objective	Study design	Results
Biesiekierski et al. Investigate effects of gluten and a FODMAP diet on IBS symptoms (double-blind, crossover RCT, Australia) [67]	40 IBS patients with non-celiac gluten sensitivity; primary/secondary care outpatient setting; 37 completers; 43% IBS-diarrhea, 35% IBS-constipation; median age 45 years; 84% female; low FODMAP diets, high-gluten [16 g gluten/day], low-gluten [2 g gluten/day], or control [16 g whey protein/day] diets; 1-week trial; 2 weeks of washout	IBS symptoms consistently and significantly improved on low-FODMAP diets and significantly worsened to a similar degree on regular diets including gluten or whey protein. Gluten-specific IBS effects were observed in only 8% of participants
Ong et al. Compare patterns of breath hydrogen and methane and symptoms produced in response to diets that differed only in FODMAP content (single-blind, crossover RCT, Australia) [24]	15 IBS patients in secondary care, median age 41 years, 87% female; 15 healthy subjects, median age 23 years, 60% women; FODMAP-restricted diet (9 g/day) or a high-FODMAP diet (50 g/day); 2-day trial; 7-day washout; diets were matched for total energy, starch, protein, fat and resistant starch, and fiber; all food was provided to the subjects	Patients with IBS produced significantly more hydrogen gas than healthy controls while on the high-FODMAP diet vs. the FODMAP-restricted diet. For IBS patients, all symptoms were significantly lower while on the FODMAP-restricted diet, including abdominal pain, bloating, passage of gas, nausea, heart burn, and lethargy

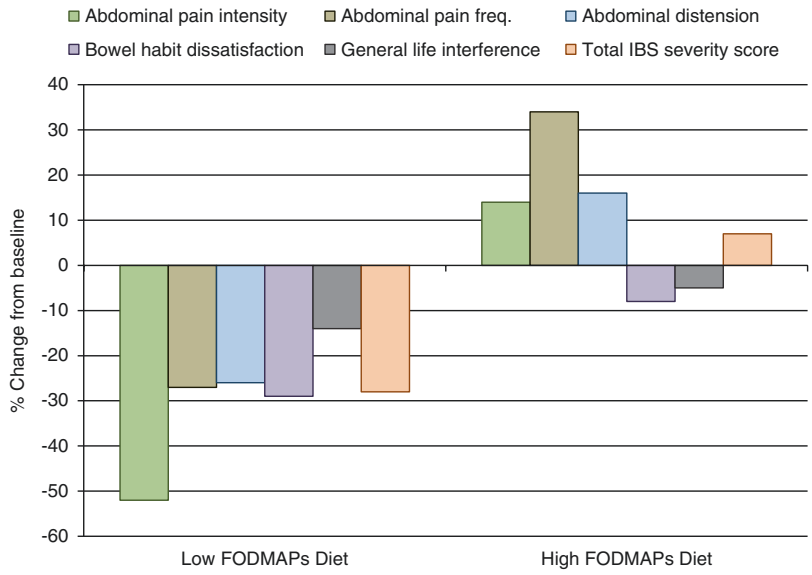

Fig. 6.3 Effect of low- vs. high-FODMAP diets on a range of irritable bowel syndrome (IBS) symptoms [31]

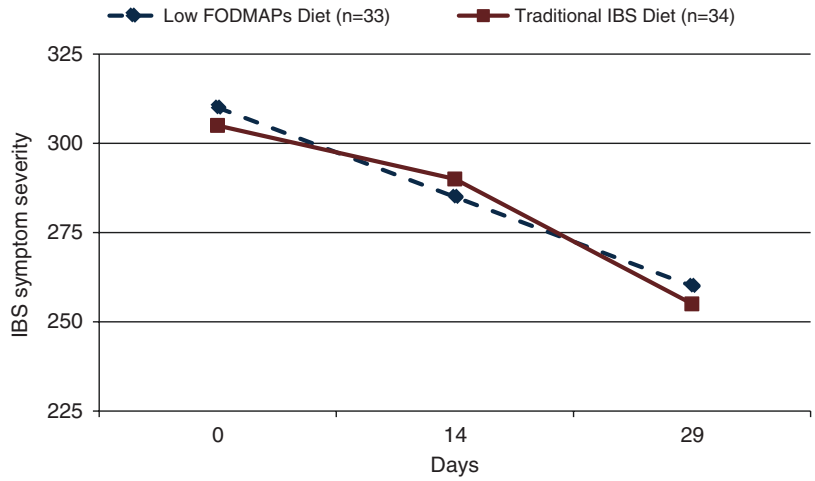

Fig. 6.4 Effect of low-FODMAP diet compared to traditional irritable bowel syndrome (IBS) dietary guidance* on IBS patient symptom severity score (p = 0.72) [63].*Traditional IBS dietary guidance is to avoid large meals and reduce intake of fat, high lactose milk products, caffeine, and gas-producing foods such as beans, cabbage, and onions

Conclusions

IBS is the most common gastrointestinal disorder occurring in people <45 years. IBS is a chronic and relapsing functional colonic disorder characterized by abdominal pain, bloating, distension, and changes in bowel habits that lack visible structural or anatomic abnormalities. IBS pathophysiology is associated with colonic microscopic and molecular abnormalities from low-grade inflammation, neuronal hyperexcitability, and microbiota dysbiosis including reduced bacteria diversity, lower levels of butyrate-producing bacteria and increased levels of pathogenic bacteria. Celiac disease and bile acid malabsorption may be confounding and difficult to distinguish from IBS symptoms. Although certain foods can be triggers for IBS symptoms, some types of fiber supplements and low FODMAP diets and traditional IBS dietary guidance (avoidance of large meals, moderate fat intake, limits on high lactose milk products and gas producing foods such as beans, cabbage and onions) have been shown to reduce the risk of acute IBS symptoms. Of the supplemental fiber options, psyllium has been most consistently shown to provide moderate relief of IBS symptoms.

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Chapter 7
Fiber and Inflammatory Bowel Disease

Keywords Inflammatory bowel disease • Ulcerative colitis • Crohn's disease • Microbiota • Butyrate • Prebiotics • Dietary fiber • Psyllium • Symbiotics

Key Points

- Inflammatory bowel disease (IBD) consists of two major phenotypes, ulcerative colitis and Crohn's disease, which are characterized by chronic relapsing gastrointestinal tract inflammation (e.g., irritation or swelling), primarily in the colon or ileum.
- Globally, IBD affects up to 0.5–1.0% of the population, especially in Western countries, with the number of cases increasing in all countries. Some case-control data suggest that dietary patterns associated with low fiber Western diets and high intake of animal protein, fatty foods, and sugar may increase the risk of IBD onset. Diet-related colonic microbial dysbiosis is considered to be an important precondition for the development of IBD in susceptible individuals.
- There is little evidence that fiber should be restricted in IBD patients' diets, except during an active flare-up, as low fiber diets may increase colonic microbiota dysbiosis. Fiber supplements such as psyllium, prebiotics and symbiotics, semi-vegetarian diets, and other fiber-rich dietary patterns appear to have potential use in improved long-term clinical symptom management, in reducing colonic inflammation, and as adjunctive therapy with IBD medications.
- Westernized diets, characterized by increased intake of the amount of foods, fried foods, red and processed meats, and refined carbohydrates with lower fiber foods and reduced intake of fruits and vegetables, appear to be associated with the development of both Crohn's disease and ulcerative colitis, or trigger flare-ups.
- Adequate fiber intake is beneficial to colon health by stimulating fiber fermentation to short-chain fatty acids such as butyrate (anti-inflammatory and a major energy source for colonocytes), lowering colonic pH as a defense against pathogenic bacteria, and promoting a healthier more diverse microbiota ecosystem required to help maintain colonic immunological homeostasis.

Introduction

Inflammatory bowel disease (IBD) is an intestinal inflammatory condition with two major phenotypes, ulcerative colitis and Crohn's disease [1, 2]. IBDs are characterized by chronic relapsing gastrointestinal tract inflammation (e.g., irritation or swelling), primarily in the colon or ileum.

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Globally, IBD affects up to 0.5–1.0% of the population, especially in Western countries, with the number of cases increasing in all countries [2]. Specifically, in the USA, IBDs affect >2 million people of all ages [3]. The age of IBD onset is decreasing with a significant increase in morbidity observed among children and adolescents [4]. Some case-control data suggest that dietary patterns associated with low-dietary fiber (fiber) Western diets and high intake of animal protein, fatty foods, and sugar may increase the risk of IBD onset [4].

Although the etiology and pathogenesis of IBD is complex and not completely understood, colonic microbial dysbiosis interactions are considered a precondition for the development of IBD [3–8]. IBD develops as a result of interactions of genetic, epigenetic, environmental, and immunological factors. Individuals with IBD often have a genetic predisposition or epigenetic gene expression altered by DNA methylation or histone modifications that can disrupt encoded proteins targeted to preserve the colonic mucosal barrier and lead to colonic inflammatory dysbiosis. This increases susceptibility to colonic infection by pathogenic bacteria by allowing an increased number of surface-adherent and intracellular pathogenic bacteria access to the underlying mucosa cells that can perpetuate the type of colonic inflammatory response and nerve damage associated with IBD. Crohn's disease is characterized by increased intestinal permeability promoting bacterial translocation in the ileum and colon, which could reflect mucosal defects through the formation of fistulae and strictures [7]. Ulcerative colitis is associated with an altered intestinal mucus barrier in terms of mucus composition such as decreased membrane phospholipid concentrations [7]. During the active phases of IBD, symptoms can have a profound impact on quality of life due to resulting diarrhea and abdominal pain [9]. IBD colonic inflammation is a major risk factor for the pathogenesis of colorectal cancer or other types of cancer [10, 11]. Longer duration, especially in aging populations, of IBD may lead to increasing risk of colorectal cancer as a result of prolonged colonic inflammation [11].

The potential protective effect of fiber-rich diets on intestinal disorders such as IBD was postulated by Dr. Burkitt in the early 1970s based on his medical experiences in Africa where he observed a significant increase in noninfectious intestinal diseases among native inhabitants whose diets had been normally rich in fiber foods but were changed to low-fiber Western diets [12]. Since fiber has a number of physiological properties that may have an impact on IBD risk, the objective of this chapter is to review the potential role of fiber in the prevention and management of IBD symptoms.

Inflammatory Bowel Disease (IBD) Risk Factors

Potential IBD risk factors, include dietary patterns, sedentary lifestyle, chronic smoking, NSAIDs or antibiotic use, and pathogenic microbial exposure [1–3, 5–7, 13]. The relationship between diet and IBD is an active area of research [14–16]. A population case-control study, in the Barwon area in Australia which has one of the highest incidence rates of IBD (132 incident cases, 104 controls), suggests that smoking, frequent fast-food intake, chicken pox, or tonsillectomy increases IBD risk, whereas high fruit and caffeine intake and pet ownership as a child are protective against IBD (Fig. 7.1) [14]. Other observational studies also suggest a potential role for the Western diet as a pre-illness diet and the risk of development of IBD possibly related to dietary components, such as increased risk associated with low fiber and high intake of refined carbohydrates, total fats, PUFAs, omega-6 fatty acids, meat and animal fat, and reduced risk associated with healthy diets emphasizing vegetables, fruits, olive oil, fish, whole grains, and nuts [1, 3, 15–17]. A Swedish population-based case-control study of IBS and dietary habits (152 cases with Crohn's disease, 145 cases with ulcerative colitis, and 305 controls; 50% women), found a 1.6 times increased IBD risk for participants consuming ≥55 g sucrose/day, a 50% decreased risk for subjects consuming ≥15 g fiber/day, and a ≥2.4 times increased

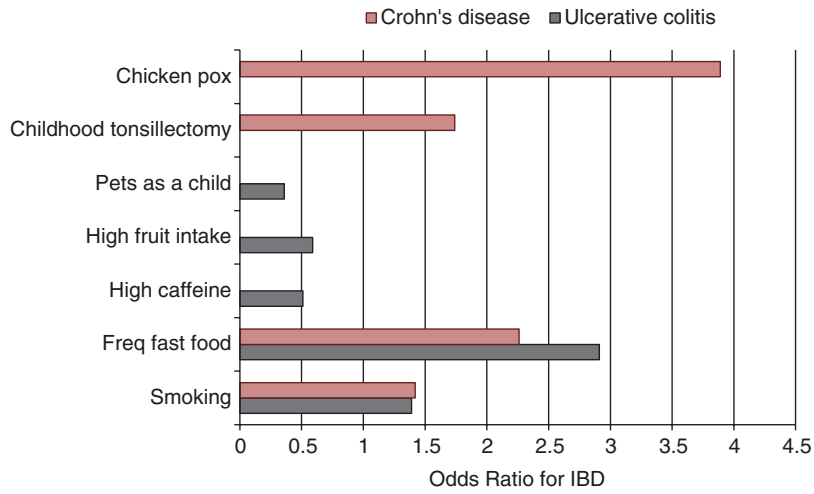

Fig. 7.1 Effect of food and lifestyle on the risk of developing inflammatory bowel disease (IBD) (all $p \leq 0.003$) [14]

risk associated with consumption of fast foods at least two times/week [18]. A 2017 systematic review and dose-response meta-analysis (5 cohort studies with 238,887 participants; 4 case-control studies with 311 cases and 660 controls) showed that fiber intake was inversely associated with Crohn's disease (10 g fiber/day reduced risk by 15%) and sucrose intake was positively related to Crohn's disease (10 g sucrose/day increased risk by 9%) [19]. However, intervention trials are inconsistent on the effect of high-sugar and low-fiber diets on IBD risk [20, 21]. A 2015 review of published data on pre-IBD diets found evidence to support the concept that the "Westernized" diet, characterized by increased intake of the amount of food, higher fat, and refined carbohydrates with lower fiber foods and by reduced intake of fruits and vegetables, appears to be associated with the development of both Crohn's disease and ulcerative colitis [22].

Dietary Guidelines for Inflammatory Bowel Diseases

Patients with IBDs have significant diet challenges in both the active IBD phase and during remission in order to prevent a relapse for as long as possible. Table 7.1 provides an overview of dietary guidance for managing active IBD and mildly active or inactive IBD [23]. General dietary suggestions include avoiding foods that worsen symptoms, eating more frequent and smaller meals, drinking adequate fluids, avoiding or limiting alcohol, taking vitamin and mineral supplementation, eliminating dairy foods if lactose intolerant or sensitive, limiting excess fat, reducing refined carbohydrates, and reducing high-fiber foods during flares. In general, fiber-restricted diets should only temporarily be used during the active period of IBD with fiber-rich diets or psyllium supplements reintroduced during periods of remission [17, 23–25]. The global operative definition of fiber is according to the 2009 Codex Alimentarius Commission definition: "fiber consists of carbohydrate polymers with ≥3 monomeric units, which are neither digested or absorbed in the human small intestine" [26]. Fiber-rich foods or supplements may favorably influence fermentation, microbiota, GI inflammation, and progression and management of IBD as an adjunct to pharmacological treatment [17].

Table 7.1 Common clinical practice dietary guidelines for inflammatory bowel disease (IBD) management [17, 22–24]

IBD status	General guidelines	Recommended foods
Periods with active symptoms or after surgery (e.g., colectomy surgery)	Eat small meals or snacks every 3–4 h during the day Consume low-fiber diets (less than 2 g/serving), avoiding whole-grain products, brown rice, corn, popcorn, nuts and chunky nut butters, seeds, raw or dried fruits with seeds or prune juice, beans, peas, or raw vegetables including potatoes with skins Avoid or limit whole milk, half-and-half, or cream; fried, processed, tough, or chewy cuts of meats; or fried eggs Limit sugar-sweetened beverages or canned fruit with heavy syrup Avoid FODMAPS (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) or sugarless gums and candies Limit fats and oils to <8 teaspoons/day and limit fried foods Drink recommended fluid levels (eight cups or about 2 L/day) Use a multivitamin supplement	**Dairy products**: yogurt (with probiotic), low-fat cheeses, lactose-free low fat milk, buttermilk **Meat and plant proteins**: tender, lean, well-cooked unprocessed red meats, poultry, fish, eggs or soy prepared without added fat, smooth nut butters **Grains**: bread, bagel, rolls, crackers, cereal, pasta made with white/refined flour **Vegetables**: most well-cooked vegetables without seeds, potatoes without skins, lettuce, strained vegetable juice **Fruit**: ripe bananas, peeled apples or melons, fruit juice without pulp (except prune juice, or canned fruit in light syrup **Beverages**: water, decaffeinated coffee or tea, soft drinks lower in sugar, rehydration beverages lower in sugar
Periods with no symptoms or mildly active symptoms	Gradually, reintroduce high-fiber foods one at a time in small amounts to meet the fiber adequate intake levels (14 g fiber per 1000 kcals or 25 g/day for women or 38 g/day for men)	Whole fiber-rich foods or psyllium or prebiotic fiber supplements

Fiber and Inflammatory Bowel Disease (IBD)

Observational Studies

Meta-Analysis

Two meta-analysis of observational studies show that fiber intake is significantly associated with a decreased risk of IBD symptoms, which is consistent with the "fiber hypothesis" regarding colonic health and decreased risk of IBD [19, 27]. A 2015 meta-analysis (two cohort studies; one nested-control study; five case-control studies) found that fiber reduced the mean risk for ulcerative colitis by 20% and Crohn's disease by 56%, between the highest and lowest categories of fiber intake [27]. A linear inverse dose-response relationship was found between fiber intake and Crohn's disease risk with a significant risk reduction of 13% for every 10 g/day increment in fiber intake (Fig. 7.2). The previously summarized 2017 systematic review and dose-response meta-analysis showed that fiber intake is inversely associated with Crohn's disease with a 15% reduced risk per 10 g fiber/day intake [19].

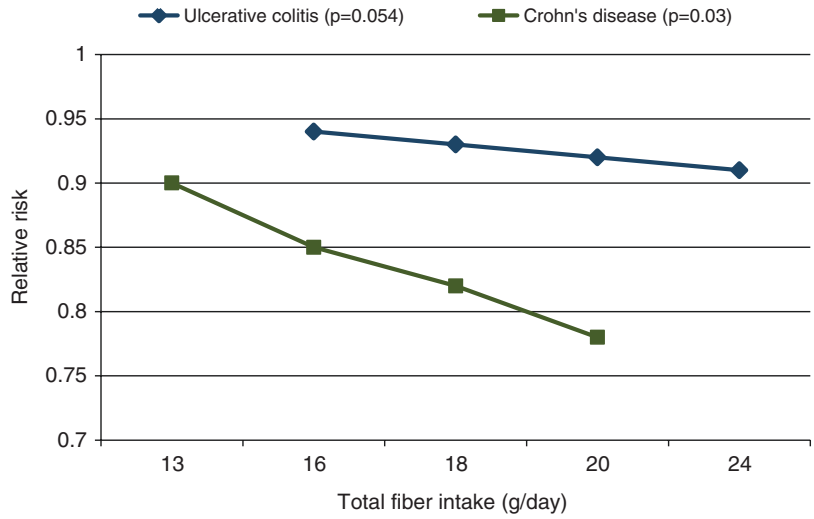

Fig. 7.2 Effect of total fiber intake on inflammatory bowel disease (IBD) risk [27]

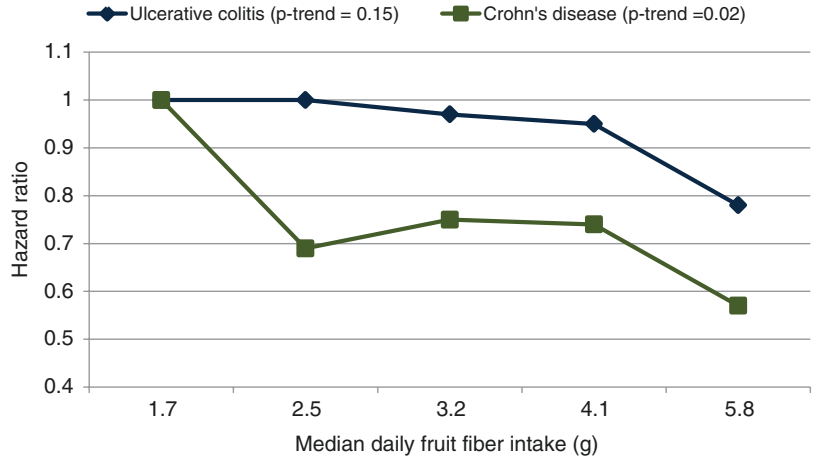

Fig. 7.3 Effect of fruit fiber intake on inflammatory bowel disease (IBD) risk (multivariate adjusted) [28]

Specific Observational Studies

There are eight prospective and case-control studies on the effects of total and specific carbohydrates on IBD risk [15, 28–35]. Three large prospective cohort studies are reviewed in more detail [15, 28, 34]. The Nurses' Health Study (170,776 women; mean baseline age 43 years; 607 IBD cases; 26 years of follow-up) suggests that the long-term intake of fiber, especially from fruit fiber, is associated with a 41% lower risk of Crohn's disease flare-ups but not ulcerative colitis (Fig. 7.3) [28]. A European Prospective Investigation into Cancer and Nutrition (EPIC) study (401,326 men and women;

244 incident cases, mean age at diagnosis 57.5 years, 57% female; median interval between recruitment and diagnosis 5 years) observed no significant effect of total carbohydrate, sugars, or starch on IBD risk [34]. However, a 2016 EPIC study found that a high-sugar and soft drink dietary pattern increased the risk of ulcerative colitis by 68%, especially for subjects consuming low levels of vegetables [15].

Internet-Based Dietary Survey

Data from the Crohn's and Colitis Foundation of America Partners Internet cohort dietary survey (1,619 participants; 70% Crohn's disease/30% ulcerative colitis in remission; 6 months) observed that the intake of fiber is associated with reduced disease flares in participants with Crohn's disease, but not ulcerative colitis [36]. Compared with participants in the lowest quartile of fiber consumption (median intake 10 g/day), those with Crohn's disease in the highest quartile of fiber intake (median intake 34 g/day) were significantly 42% less likely to have a flare-up. However, there was no association between fiber intake and flares in patients with ulcerative colitis. A 2015 literature review concluded that high fiber intake was favorable in preventing Crohn's disease flare-up during remission [37].

Fiber Intervention Trials

Systematic Review

A systematic review (23 RCTs, 10 ulcerative colitis, 12 Crohn's disease, 1 pouchitis; 1,296 patients in remission or active, 65% female; 17 supplement trials, psyllium, germinated barley, wheat or oat bran, prebiotics, and symbiotics; six high- vs. low-fiber diet trials, semi-vegetarian, high- vs. low-fiber oligosaccharide/inulin mix; 2 weeks to 29 months) demonstrated the potential for the efficacy of fiber on improving IBD symptoms and clinical outcomes [24]. Fiber supplements such as psyllium, prebiotics, and symbiotics appear to have potential as adjunctive therapy with IBD medications. The best evidence was for the effectiveness of psyllium in maintenance of remission of ulcerative colitis. However, the key issue with fiber and IBD clinical trials is that they consist of a limited number of high-quality studies. There were no serious adverse events or bowel obstructions reported in any of these fiber interventions. Overall, the review found no evidence that fiber should be restricted in IBD patients except during flare-ups. The potential for fiber to improve clinical symptom management and colonic anti-inflammatory effects merits more research in high-quality RCTs.

Ulcerative Colitis

Table 7.2 provides summaries of intervention trials assessing the effects of fiber-rich diets and supplements during ulcerative colitis remission and during active disease states [38–48].

Table 7.2 Summary of RCTs and open-label trials with fiber supplements and fiber-rich foods on ulcerative colitis (UC)

Objective	Study details	Results
Remission		
Psyllium		
Fujimori et al. Compare the effects of psyllium vs. symbiotic on treatment of UC (Japan) [38]	**Parallel RCT**: 120 UC patients in remission or with mildly active symptoms; 78% completers; mean age 36 years; 59% female; 3 treatments: 8 g psyllium daily; *B. longum* 9^9 cfu daily; or symbiotic combination of psyllium and probiotic; 4 weeks	UC symptom scores improved for all treatment groups but only significantly for the symbiotics. Individual scores improved as follows: *B. longum*, emotional function ($p = 0.03$); psyllium, bowel function ($p = 0.04$); and symbiotics and systemic and social functions ($p = 0.008$ and $p = 0.02$). C-reactive protein decreased significantly only with symbiotic therapy compared to baseline
Copaci et al. Evaluate the effect of psyllium on UC remission rate (Romania) [39]	**Parallel RCT**: 31 patients; 100% completers; mesalamine with no added fiber; mesalamine plus psyllium or probiotic *S. boulardi;*12 months	Mesalamine with psyllium significantly reduced remission failure rate vs. no added fiber (35% vs. 28%) and increased the number of asymptomatic nights
Fernandez-Banares et al. Assess the efficacy and safety of psyllium vs. mesalamine in maintaining UC remission (Spain) [40]	**Parallel RCT**: 105 patients; 97% completers; mean age 43 years; 55% males; 10 g psyllium twice daily;500 mg mesalamine 3 × daily; or combination of both; 12 months	Psyllium might be as effective as mesalamine in maintaining remission in UC as there were nonsignificant differences between remission maintenance failure with psyllium (40%), mesalamine (35%), and the combination (30%), which suggests an adjunctive role for psyllium. Psyllium was well tolerated and significantly increased butyrate concentrations in the stools of patients, which is associated with colon health
Hallert et al. Evaluate the effect of psyllium on UC remission rate (Sweden) [41]	**Crossover double-blind, RCT**: 29 patients; mean age 43 years; 60% female; 81% completers; 7 g psyllium daily vs. placebo; 2 months	Psyllium was significantly superior in maintaining UC remission to the placebo (69% vs. 24%)
Germinated barley foods		
Faghfoori et al. Determine the effect of administration of germinated barley-enriched foods on serum systemic inflammation in UC patients in remission (Iran) [42]	**Parallel RCT**: 41 patients; 100% completers; mean age 34 years; about 50% males; standard meds with germinated barley foods, rich in β-glucans vs. control; 2 months	Levels of TNF-α, IL-6, and IL-8 all decreased in the GBF group compared with baseline during the 2-month trial, while in the control group all values increased. For IL-6 and IL-8, this effect was significant, $p = 0.034$ and 0.013, respectively
Wheat and oat bran		
Hallert et al. Examine the effect of oat bran on UC remission and colonic butyrate levels (Sweden) [43]	**Open-label trial**: 22 patients; mean age, 44 years; 45% women; median time from last relapse 1 year; 60 g oat bran (20 g total fiber) added to the daily diet, mainly as bread slices; 12 weeks	During the oat bran intervention, the fecal butyrate concentration significantly increased by 36% at 4 weeks (from 11 to 15 mol/g feces). The mean butyrate concentration over the entire test period remained significantly increased at 14 mol/g feces. No patient showed signs of UC relapse, and patients with abdominal pain and reflux complaints at entry showed significant improvement at 12 weeks that returned to baseline 3 months after the study

(continued)

Table 7.2 (continued)

Objective	Study details	Results
Davies and Rhodes Assess the effects of wheat bran on UC relapse (UK) [44]	**Parallel RCT**: 39 patients; 90% completers; mean age 40 years; 25 g of wheat bran from breakfast cereal/day vs. no changes in diet or sulfasalazine; evaluations at 1,3, and 6 months	Wheat bran-supplemented diets caused significant increases in UC relapses (75%) vs. sulfasalazine medication (20%). Wheat bran cereal was not effective in maintaining remission
Active		
Germinated barley foods		
Bamba et al. Determine the effect of barley intake on mild to moderately active UC (Japan) [45]	**Open-label trial**: 18 patients with mild to moderate active UC; mean age 37 years; standard meds plus 20–30 g germinated barley foods (β-glucan) vs. standard meds no fiber; 4 weeks	At 4 weeks, germinated barley foods significantly improved clinical symptoms and endoscopic colonic health. The improvement was associated with an increase in stool butyrate concentrations. The potency of germinated barley on promoting a healthier microflora ecosystem, as well as the high water-holding capacity, may play important roles in treatment and remission of UC
Prebiotics		
Casellas et al. Test the effect of a prebiotic in patients with active UC (Spain) [46]	**Double-blind, RCT**: 19 patients with active UC; 79% completers; mean age 36 years; 68% female; 3 g mesalazine/day were randomized to 12 g/day of oligofructose/inulin (prebiotic) or placebo (maltodextrin); 2 weeks	Oligofructose-enriched inulin was well tolerated and significantly reduced UC symptoms vs. placebo. At day 7, a significant reduction of calprotectin was observed in the prebiotic vs. placebo
Symbiotics		
Ishikawa et al. Evaluate the effect of a symbiotic on the treatment of mild to moderate UC (Japan) [47]	**Open-label trial**: 41 mild to moderate UC patients; 95% completers; mean age 45 years; symbiotic *B. breve* strain Yakult (3×9^9 cfu) plus 5.5 g/day galacto-oligosaccharides (GOS); 1 year	After a 1 year of consuming the symbiotic, the clinical status of the UC patients, as assessed by colonoscopy, significantly improved. Also, colonic levels of myeloperoxidase, *Bacteroidaceae*, and fecal pH were significantly reduced
Furrie et al. Assess the effectiveness of symbiotic treatment for active UC (Scotland) [48]	**Double-blind, RCT**: 18 patients with active UC; 89% completers; mean age 41 years; 50% male; 12 g of symbiotic fructo- oligosaccharide/inulin plus *B. longum* 2×10^{11} cfu daily vs. placebo; 4 weeks	Colonic biopsies in the symbiotic group showed reduced inflammation and regeneration of epithelial tissue vs. placebo. Symbiotic usage reduced sigmoidoscopy scores and TNF- α and IL-1α

Remission

Psyllium

The most effective fiber supplement was psyllium with four trials providing various degrees of support for improved ulcerative colitis management [38–41]. A double-blind crossover RCT showed psyllium was significantly superior by 45% in maintaining ulcerative colitis remission compared to placebo [41]. A parallel RCT found that psyllium was as effective as the drug mesalamine in maintaining remission; in addition, psyllium significantly increased fecal butyrate concentrations, which is associated with colonic health [40]. The other two trials found that psyllium was an effective adjunctive supplement with mesalamine and probiotics to reduce remission failure rates and support reduced symptoms and improved bowel function [38, 39].

β-Glucan-Rich Cereal

Two trials showed positive effects for β-glucan-rich cereal fiber on ulcerative colitis remission [42, 43]. The consumption of germinated barley-enriched foods was found to reduce systemic TNF-α, IL-6, and IL-8 levels compared to increased values for the control group during the 2-month trial [42]. Additionally, the consumption of 60 g oat bran in bread was shown to significantly increase fecal butyrate concentration, prevent relapse, and improve abdominal pain and reflux complaints over 12 weeks [43].

Wheat Bran

One RCT found no clinical benefit or a possible worsening of remission maintenance when consuming 25 g of wheat bran from breakfast cereal daily over 6 months [44].

Active Disease

Germinated Barley Foods

Germinated barley foods significantly improved clinical symptoms, endoscopic colonic health, and stool butyrate concentrations to promote a healthier microbiota ecosystem after 4 weeks [45].

Prebiotic

A double-blind RCT showed that oligofructose-enriched inulin was well tolerated and significantly reduced UC symptoms and fecal calprotectin (elevated levels are a marker of colonic inflammation associated with IBD) [46].

Symbiotics

There are several trials that suggest beneficial effects of symbiotics on active ulcerative colitis [47, 48]. An open-label trial with *B. breve* and galacto-oligosaccharides reported improved colonoscopy assessment and significantly reduced levels of colonic fecal pH, myeloperoxidase, and *Bacteroidaceae* after 1 year [47]. A double-blind placebo-controlled RCT found that symbiotic fructo-oligosaccharide/inulin plus *B. longum* reduced sigmoidoscopy scores and inflammation, showed regeneration of epithelial tissue from biopsies and significantly reduced TNF-α and IL-α cytokines compared with placebo [48].

Crohn's Disease

Table 7.3 provides summaries of intervention trials assessing the effects of fiber-rich diets and supplements during Crohn's disease remission and during active disease states [20, 21, 49–55].

Remission

Semi-vegetarian Diets

A Japanese RCT (22 patients; 2 years) showed a high-fiber semi-vegetarian diet was significantly more effective at preventing relapse compared to a lower fiber omnivorous diet [49]. Remission rate with the semi-vegetarian diet was 100% at 1 year and 92% after 2 years vs. 33% in the omnivorian group ($p = 0.0003$).

Table 7.3 Summary of RCTs and open-label trials with fiber supplements and fiber-rich foods on Crohn's disease (CD)

Objective	Study design	Results
Remission		
Semi-vegetarian diet		
Chiba et al. Investigate whether a semi-vegetarian diet has a preventive effect against relapse of CD in patients who have achieved remission (Japan) [49]	**Parallel RCT**: 22 Japanese CD patients; 70% completers; 64% males; median age 26.5 years; semi-vegetarian (32 g fiber/day; $n = 16$) vs. omnivorous diets (15 g fiber /day; $n = 6$) with mesalamine or sulfasalazine meds; 2 years	Remission rate with a semi-vegetarian diet was 100% at 1 year and 92% at 2 years vs. 33% in omnivorian group ($p = 0.0003$). The concentration of C-reactive protein was normal at the final visit in more than half of the patients in remission who were consuming semi-vegetarian diets
High- vs. low-fiber diets		
Brotherton et al. Investigate the effects of wheat bran consumption on health-related quality of life and gastrointestinal function in individuals diagnosed with CD (US) [50]	**Single blind parallel RCT**: 7 CD patients; 6 females and 1 male; mean age 29 years; dietary guidance to consume wheat bran and reduce refined carbohydrates vs. general dietary guidance; 4 weeks	Consuming a wheat bran-inclusive diet was feasible and caused no adverse effects. Participants reported improved health-related quality of life ($p = 0.028$) and GI function ($p = 0.008$) compared to the control group
Ritchie et al. Compare the long-term effects of fiber-rich/low-sugar vs. lower-fiber/high-sugar diets on CD activity (UK)[20]	**Parallel RCT**: 352 CD patients; 51% completers; 63% female; mean age 35 years; 31 g fiber/14 g sugar daily vs. 17 g fiber /100 g sugar daily; 2 years	There was no significant difference in clinical outcomes detected among patients in the two dietary treatment groups
Heaton et al. Assess the effects of a lower-sugar, higher-fiber diet vs. a higher-sugar, lower-fiber diet on CD prognosis (UK)[21]	**Parallel RCT**: 32 CD patients; mean age 36 years; about 50% female; fiber-rich diet (33 g fiber and 39 g sugar/day) vs. no dietary instruction (<20 g fiber and 90 g sugar/day); 4 years	An unrefined-carbohydrate, fiber-rich diet appears to improve CD patient prognosis. Hospital admissions were significantly fewer and shorter in the fiber-rich diet-treated patients, who spent a total of 111 days in the hospital compared with 533 days in the lower-fiber control group
Active		
High- vs. low-fiber diets		
Bartel et al. Study the effect of a high-fiber restricted diet vs. a low-fiber Western diet on CD active lesions (Austria) [51]	**Parallel RCT**: 18 mild to moderate, active CD patients; 78% completers; 64% male; mean age 48 years; high-fiber diet (46 g fiber daily), or a control Western low-fiber, high-carbohydrate diet (16 g fiber daily); 6 weeks	At 6 weeks, the mean intestinal imaging score significantly improved in the high-fiber group but remained unchanged in the low-fiber group. MRI, endoscopy, and sonography showed significant improvement of intestinal lesions in about 75% of patients in the high-fiber group and 11% in low-fiber group patients
Levenstein et al. Examine the effect of a very low fiber vs. a typical Western diet on UC activity (Italy) [52]	**Parallel RCT**: 85 active CD patients, 84% completers; mean age 40 years; 63% males; low residue (3 g fiber diet/day) vs. normal Western diet (13 g fiber/day); 29 months	There was no difference in outcomes between the two groups, including symptoms, need for hospitalization, need for surgery, new complications, nutritional status, or postoperative recurrence
Prebiotics		
Joossens et al. Evaluate the effects of a prebiotic on CD activity (Belgium)[53]	**Parallel RCT**: 67 patients with inactive and mild to moderately active CD; twice daily 10 g oligofructose-enriched inulin vs. placebo; 4 weeks	The prebiotic was positively correlated with improved CD symptoms and an increase in the number of *Bifidobacterium longum* in the microbiota compared to placebo

Table 7.3 (continued)

Objective	Study design	Results
Benjamin et al. Evaluate the effects of a prebiotic on CD activity (UK) [54]	**Parallel RCT**: 103 patients with active Crohn's disease; 83% completers; mean age 40 years; 39% males; 15 g/day fructo-oligosaccharides (FOS) (Synergy1) vs. non-prebiotic placebo; 4 weeks	FOS showed no clinical benefit or improvements in fecal concentration of bifidobacteria and *F. prausnitzii* after the 4-week intervention in patients with active CD. However, the FOS group had significantly reduced IL-6 and increased IL-10 levels
Symbiotics		
Steed Investigate the effects of symbiotic consumption on disease processes in patients with CD (UK) [55]	**Double-blind, parallel RCT**: 35 patients with Crohn's disease; 97% completers; mean age 47 years; 54% male; 2×10^{11} freeze-dried viable *B. longum* in a gelatin capsule, and a sachet containing either 6 g oligofructose-enriched inulin or a placebo given twice daily 6 months	Compared to placebo, the symbiotic significantly reduced clinical CD activity indices, histological scores, and TNF-a expression. Mucosal bifidobacteria proliferated in symbiotic patients

High- vs. Low-Fiber Diets

A large UK RCT (352 patients; 63% women; 2 years) reported no difference in the number of patients with deteriorating disease between those consuming diets high in fiber (daily mean 31 g) and low in sugar (daily mean 14 g) vs. diets low in fiber (daily mean 17 g) and high in sugar (daily mean 100 g) [20], whereas another UK RCT (32 patients; 50% women; 4 years) found that similar higher-fiber and lower-sugar diets significantly reduced GI symptoms and hospitalizations compared to low-fiber and high-sugar diets [21].

Wheat Bran

A US single-blind RCT (7 patients; 86% women; 4 weeks) showed that consuming a wheat bran-rich diet vs. a general diet caused no adverse effects. Participants consuming the wheat bran diet reported significantly improved health-related quality of life and gastrointestinal functions compared to the control group [50].

Active Disease

High- vs. Low-Fiber Diets

Two RCTs show that increasing dietary fiber intake has no adverse effects and may improve clinical outcomes if the level of fiber intake is adequate. An Italian RCT (85 patients; 29 months) comparing a low residue fiber-restricted diet (3 g fiber/day) and a typical Italian diet (13 g fiber/day) found no difference in clinical outcomes [52]. This trial indicates that individuals with active Crohn's disease can effectively consume normal diets without adversely affecting symptoms over time. An Austrian RCT (18 patients; 6 weeks) showed that high-fiber and low-refined carbohydrate diets are more effective in managing persistent active Crohn's lesions than the Western diet [51].

Prebiotics

Two trials using 10–15 g/day of prebiotic fiber (oligofructose/inulin) reported mixed beneficial effects on disease outcomes [53, 54]. The first RCT (67 patients; 4 weeks) found improved clinical GI symptoms and increased fecal *Bifidobacterium longum* [53]. The second RCT (103 patients; 4 weeks)

found no differences between groups in clinical symptoms or inflammatory markers or probiotic bacteria, but there was a shift to greater mucosal immunoregulation in the prebiotic group, including significantly higher IL-10- and lower IL-6-positive dendritic cells [54].

Symbiotics (Symbiotic B. longum *and Oligofructose/Inulin)*

A double-blind UK RCT (25 patients; 6 months) showed significantly improved clinical symptoms and histological scores, increased bifidobacteria, and lower colonic inflammation compared to placebo [55].

Overall Summary

No two intervention trials used the exact same fiber and control treatment and the number of subjects was generally small. Despite these and other variables, psyllium, B-glucan foods (oat bran, germinated barley), fructans, and higher fiber diets may support gastrointestinal symptom relief especially in combination with medication or probiotics [56].

Fiber Mechanisms

In susceptible individuals, high adherence to a low-fiber Western dietary pattern and lifestyle may promote colonic microbiota dysbiosis and negatively impact colonic health and immune homeostasis which may increase the risk of IBD [22, 37]. There is growing evidence that healthy dietary patterns such as semi-vegetarian or other types of higher-fiber diets may reduce the risk of IBD by promoting a healthy microbiota ecosystem with low colonic inflammation and permeability, lower pH and levels of potentially pathogenic bacteria, and increased levels of symbiotic bacteria such as butyrate-producing species [49, 57]. Fiber may exert an anti-inflammatory effect through increasing colonic butyrate levels and promoting healthy microbiota composition, which may reduce the risk of IBD by increasing tissue healing.

An increase in the production of healthy short-chain fatty acids (SCFAs) in stool from fiber fermentation can aid in the nourishment of the colonic mucosa and improve mucus production. Butyrate and the other SCFAs, including acetate and propionate, also exert trophic effects on the colon, stimulate water and electrolyte absorption, and increase colonic blood flow [49, 57]. Butyrate is especially effective at decreasing colonic inflammation at the systemic and cellular levels [49, 57]. Butyrate is thought to reduce colonic permeability and maintain colonocyte health by acting as a primary energy source, lowering colonic pH to protect against pathogenic bacteria and through its activation of peroxisome proliferator-activated receptor C [58–60]. Butyrate might be especially important for individuals with Crohn's disease because they may be genetically predisposed to increased colonic permeability. Butyrate can also exert direct immunomodulatory effects by suppression of nuclear factor kappa B (NF-κβ) activation, which is a transcription factor that controls the expression of genes encoding proinflammatory cytokines, chemokines, and inducible inflammatory enzymes associated with IBD. Of the soluble fiber ingredients or supplements, inulin produces significantly more fecal butyrate (Fig. 7.4) compared to psyllium or wheat dextran [61], and fruit and vegetable fiber have been shown to produce significantly more fecal butyrate per gram than cereal fiber [62]. Adequate fiber intake, especially prebiotics, can promote activity of health-promoting bacteria and lower colonic

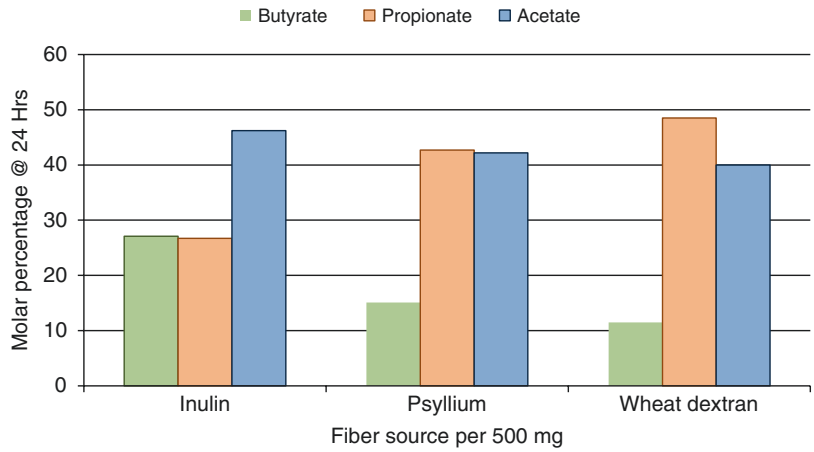

Fig. 7.4 Relative effects of common soluble fiber sources on fermentation to short-chain fatty acids (SCFA) per 500 mg [61]

pH, which inhibits the growth of gram-negative *Enterobacteriaceae* including familiar pathogens *Salmonella* spp. and *Escherichia coli* and by increasing beneficial bifidobacteria or block bacterial-epithelial adherence [63].

Conclusions

IBD is an intestinal inflammatory condition with two major phenotypes, ulcerative colitis and Crohn's disease, which are characterized by chronic relapsing colonic tract inflammation (e.g., irritation or swelling). Globally, IBD affects up to 0.5–1.0% of the population, especially in Western countries, with the number of cases increasing in all countries. Some case-control data suggest that dietary patterns associated with low fiber Western diets and high intake of animal protein, fatty foods, and sugar may increase the risk of IBD onset. Diet-related colonic microbial dysbiosis is considered to be an important precondition for the development of ulcerative colitis and Crohn's disease in susceptible individuals. There is little evidence that fiber should be restricted in IBD patients' diets, except during an active flare-up, as low fiber diets may increase colonic microbiota dysbiosis. Fiber supplements such as psyllium, prebiotics and symbiotics, semi-vegetarian diets, and other fiber-rich dietary patterns appear to have potential use in improved long-term clinical symptom management, in reducing colonic inflammation, and as adjunctive therapy with IBD medications. Westernized diets, characterized by increased intake of the amount of foods, fried foods, red and processed meats, and refined carbohydrates with lower fiber foods and reduced intake of fruits and vegetables, appear to be associated with the development of both Crohn's disease and ulcerative colitis, or trigger flare-ups. Adequate fiber intake is beneficial to colon health by stimulating fiber fermentation to short-chain fatty acids such as butyrate (anti-inflammatory and a major energy source for colonocytes), lowering colonic pH as a defense against pathogenic bacteria, and promoting a healthier more diverse microbiota ecosystem required to help maintain colonic immunological homeostasis.

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Chapter 8
Fiber and Diverticular Disease

Keywords Diverticulosis • Diverticulitis • Diverticular disease • Colon microbiota • Dietary fiber • Western dietary pattern • Vegetarian diets • Butyrate • Obesity

Key Points

- Diverticular disease is among the most clinically and economically significant gastroenterological conditions in people ≥ 65 years of age. Most people > 65 years of age will develop colonic diverticulae (herniate pouches) potentially caused by high colon intraluminal pressure. While 80% of the population with colonic diverticula remain asymptomatic, approximately 20% may develop abdominal symptoms (symptomatic uncomplicated diverticular disease), and in some individuals there may be eventual complications such as severe bouts of diverticulitis or bleeding that may lead to sepsis and death.
- In aging populations, the widespread intake of low fiber Western diets; increased intake of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) naturally from whole foods or added to processed foods; and weight gain leading to obesity are several factors that may increase the risk of diverticular disease, bouts of symptoms, or its complications.
- Five prospective studies suggest that fiber-rich healthy diets and low red or processed meat consumption significantly decrease the risk of diverticular disease.
- Although a number of intervention trials suggest that fiber-rich diets and foods or supplements containing wheat bran, psyllium, or methylcellulose may help to alleviate diverticular disease symptoms and/or improve bowel function, there are presently a limited number of high-quality trials.
- Fiber-related mechanisms associated with potentially reduced diverticular disease risk or alleviation of symptoms are related to improved colonic health including improved laxation and stool bulk and a healthier microbiota ecosystem with higher fecal concentration of probiotic bacteria and butyrate, lower inflammation, and improved body weight and visceral fat regulation.

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Introduction

Diverticular disease is among the most clinically and economically significant gastroenterological conditions in older people, which was virtually unknown before the introduction of highly processed food in the twentieth century [1–3]. Diverticula, colonic submucosal herniated pouches, or diverticulosis incidence increases with age affecting 5–10% of adults under 40 years, 30% by age 50 years, and 70% by the age of 85 years. Some 80% of individuals with colonic diverticula remain asymptomatic, showing no or few complications over their lifetime [3–8]. Eighty percent of the population with colonic diverticula remain asymptomatic. The other 20% may develop symptomatic uncomplicated diverticular disease or diverticulitis characterized by recurrent abdominal symptoms several times per year such as abdominal pain and bloating similar to or overlapping symptoms present in irritable bowel syndrome and attributed to alterations in the diverticula [6–8]. The impact of these complaints is variable, and the severity and frequency of symptoms may range from mild and rare episodes to a severe, chronic, recurrent disorder, affecting daily activities and the quality of patients' lives. Some 15% of the patients with acute diverticulitis may experience complications with the development of varying levels of abscesses, perforation, fistula, peritonitis, spasms, and/or bleeding which can be associated with weakness, dizziness or light-headedness and abdominal cramping, and in extreme cases sepsis and death [1, 4–8]. A meta-analysis (11 cross-sectional, one case-control and two cohort studies) found that diverticular disease can significantly increase the odds of developing colonic adenomas by 68% and a trend for increased odds of colorectal cancer by 36% [9]. In the USA, complications associated with diverticular disease account for >300,000 hospital admissions, 1.5 million inpatient care days, and ≥$2.5 billion in direct costs [1–3].

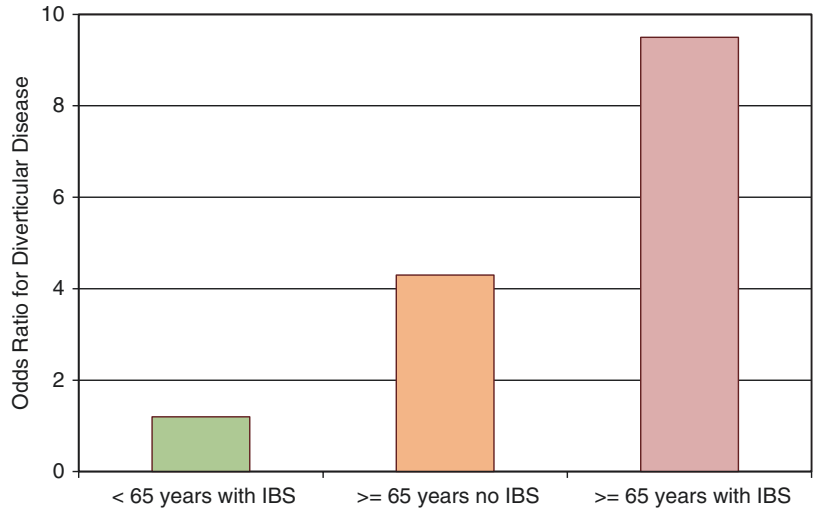

Fig. 8.1 Association between irritable bowel syndrome (IBS) and diverticular disease risk with age [23]

The combination of aging populations, low dietary fiber (fiber) Western diets, and higher intake of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) often added to processed foods are factors that may increase the risk of diverticular disease, which may be related to colonic structural defects caused by bouts of high colonic intraluminal pressure [1, 6, 10–22]. Also, people with a history of irritable bowel syndrome were shown to be associated with an increased risk of developing diverticular disease at ≥65 years of age (Fig. 8.1) [23].

It is estimated that 60% of diverticular disease risk is associated with modifiable factors [1, 4–6]. The highest prevalence rates for diverticular disease are reported for Europe and North America, but the prevalence is increasing globally as populations adapt a Western style diet and lifestyle. There are a number of non-dietary lifestyle factors including physical activity, smoking, and medications such as non-steroidal anti-inflammatory drugs (NSAIDs) that may affect diverticular disease risk however, the influence of fiber, including fiber-rich dietary patterns and fiber supplements, on diverticular disease risk and symptoms has been the most widely studied [24–31]. The primary objective of this chapter is to comprehensively evaluate the effects of increased fiber intake on diverticular disease risk and symptom alleviation.

Dietary Factors

A list of specific dietary patterns and foods and their association with diverticular disease risk are summarized in Table 8.1 [13, 30, 31].

Table 8.1 Dietary patterns and foods associated with symptomatic diverticular disease risk [13, 30, 31]

Dietary patterns/specific foods	Decrease risk	Increase risk
Western dietary pattern		√
Healthy dietary pattern (with adequate fiber)	√	
Beef, pork, or lamb (main dish)		√
Processed meat, one slice or piece		√
Bacon, two slices		√
Hot dog		√
Green leafy vegetables	√	
Peaches, apricots, or plums, one fresh or 100 g canned	√	
Whole orange	√	
Whole apple	√	
Blueberries, 100 g	√	
Large cookie		√
Potato or corn chips, one serving		√
French fried potatoes, one serving		√
White bread, one slice		√

Specific Foods and Beverages

Some foods and beverages are highlighted because of historically popular connections to diverticular risk. There was the notion that undigested particles from nuts, seeds, and popcorn might lodge in portions of the diverticulum and hypothetically lead to diverticular disease complications and patients were often advised in the past to avoid these foods [31, 32]. However, the Health Professionals Follow-Up Study (47,228 men; mean age ranging from 51 to 60 years at baseline; mean BMI 25;18-year follow-up; 801 incident cases of diverticulitis) observed that nuts, corn, and popcorn consumption did not significantly increase the risk of diverticulitis (Fig. 8.2) [32]. This suggests that recommendations to avoid these foods to prevent diverticular complications should be reconsidered as these foods may actually lower risk of diverticular disease. Two common adult beverages, coffee and alcohol, have different effects on diverticular disease risk [24–26]. Coffee consumption has not been observed to have any effect on diverticular disease [24, 25]. However, alcoholism appears to be associated with a three times greater risk of hospitalization for people with diverticular disease than the general population [24]. In a prospective study, no relationship was shown between diverticular disease and beer or wine, but daily consumption of spirits or liqueurs resulted in a 65% increased diverticular disease risk [25]. In the EPIC cohort, the effect of alcohol consumption on hospitalization due to diverticular disease was no longer significant after correction for smoking habits [33].

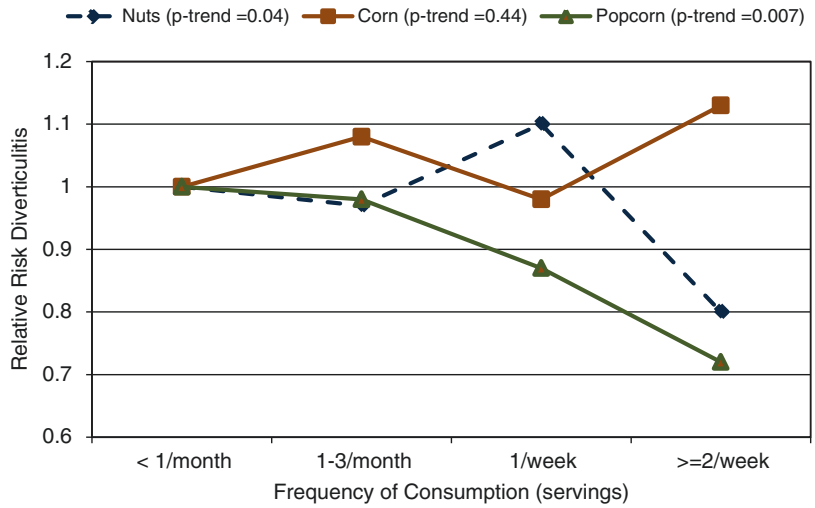

Fig. 8.2 Association between nuts, corn, and popcorn intake frequency and diverticulitis risk [32]

Dietary Fiber

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) publication on diverticular disease indicates that the symptoms of diverticular disease may be treated with an appropriate combination of high-fiber diet or fiber supplements, medications, and possibly probiotics [34]. NIDDK suggests a (1) slow increase in fiber-rich foods to minimize gas and abdominal discomfort and (2) fiber supplements methylcellulose or psyllium one to three times a day and the consumption of adequate water. A 2002 review concluded that diets high in fiber and low in total fat and red meat and a lifestyle with more physical activity might help prevent diverticular disease [17]. A 2011 review concluded that "despite the lack of high-quality supportive evidence, on the basis of low risk and theoretical benefit, a high fiber diet and/or fiber supplementation should be considered in asymptomatic diverticulosis to reduce the likelihood of disease progression and in symptomatic diverticulosis to reduce symptom episodes and prevent acute diverticulitis" [35]. FODMAP highly fermentable fiber sources should be limited due to their risk of increasing colonic pressure because of flatulence and osmotic load, which may lead to colonic defects or diverticular disease symptoms or complications [12].

Fiber-Rich Dietary Patterns

Observational Studies

Table 8.2 summarizes the eight observational studies on higher fiber and lower red or processed meat consumption or vegetarian diets on the risk of diverticulosis and diverticular disease [13, 33, 36–41].

Diverticulosis (Benign Diverticula). Three observational studies assessed the association between fiber-rich dietary patterns and diverticulosis risk [36–38]. A UK case-control study (56 vegetarians for >10 years and 264 nonvegetarians; age > 45 years) found that diverticulosis was significantly higher in nonvegetarians (33%) than in vegetarians (12%) [36]. Vegetarians had a significantly higher mean fiber intake (41.5 g/day) than nonvegetarians (21.4 g/day). Two US cross-sectional studies observed no association between total dietary fiber intake and diverticulosis incidence, but the mean fiber intake was relatively low between 15 and 19 g/day, and the mean age of the subjects was in the mid-50 years [37, 38]. Scientifically, the association between diet and diverticulosis is difficult to prove because of the long latency of diverticula formation, the often lack of symptoms of diverticulosis, and the challenges of obtaining accurate dietary fiber intake.

Diverticular Disease. Five prospective studies examined the association between dietary patterns higher in fiber and lower in red or processed meat consumption, or vegetarian diets, on diverticular disease risk [12, 33, 39–41]. A 2017 Health Professionals Follow-Up Study (46,295 men; mean baseline age 53 years; 26 years of follow-up; 1063 incident cases of diverticulitis) found that after adjustment for other risk factors, men with the highest prudent/healthy scores were associated with decreased risk of diverticulitis by 26–33%, whereas men with the highest Western dietary pattern scores had an increased multivariate risk of diverticulitis by 55% (Fig. 8.3) [13]. The association between dietary patterns and diverticulitis was predominantly attributable to intake level of fiber and red meat.

The 2014 UK Million Women Study (690,075 women; mean age 60 years; 17,325 were admitted to the hospital or died with diverticular disease; 6 years of follow-up) observed that fiber significantly reduced diverticular disease risk with cereal and fruit fiber having the strongest effects (Fig. 8.4) [39]. An EPIC UK/Oxford cohort (47,033 adults; 76% female; median BMI 23; 33% vegetarians; mean

Table 8.2 Summary of observational studies on fiber-rich dietary pattern effects on diverticulosis and diverticular disease risk

Objective	Study details	Results
Diverticulosis		
Case-control study		
Gear et al. Determine the effect of fiber in vegetarian and nonvegetarian diets on diverticulosis prevalence (UK) [36]	56 vegetarians (members of the UK Vegetarian Society for ≥10 years, > 45 years, and 60% female); 264 nonvegetarians (≥ 45 years, 55% female); barium enema; food frequency questionnaire	Vegetarians had a significantly higher mean fiber intake (41.5 g/day) than nonvegetarians (21.4 g/day). Diverticulosis was significantly higher in nonvegetarians (33%) than in vegetarians (12%). Low intake of cereal fiber was associated with the presence of diverticulosis, especially for women
Cross-sectional studies		
Peery et al. Examine the link between low fiber intake and the risk of asymptomatic diverticulosis (US) [37]	539 individuals with colonic diverticula; mean age of 60 years; 1,569 controls without diverticula; mean age 57 years; 60% males; mean BMI 29; mean total fiber intake 15 g/day	No association was observed between total fiber intake and diverticulosis in comparing the highest quartile to the lowest (mean intake 25 vs. 8 g/day)
Peery et al. Study the association between high fiber intake and the risk of asymptomatic diverticulosis (US) [38]	878 cases of diverticulosis; mean age 59 years; 1,226 controls without diverticula; mean age 54 years; mean total fiber intake 19 g/day	Higher-fiber diets were not protective against asymptomatic diverticulosis
Diverticulitis/diverticular disease		
Prospective studies		
Strate et al. Examine the association of major dietary patterns on the risk of diverticulitis (Health Professionals Follow-Up Study; US) [13]	46,295 men; mean baseline age 53 years; 26 years of follow-up; 1,063 incident cases of diverticulitis	After adjustment for other risk factors, men in the highest quintile of Western dietary pattern scores had an increased multivariate risk of diverticulitis by 55% vs. men in the lowest quintile. In contrast, men with higher prudent/healthy scores were associated with decreased risk of diverticulitis by 26–33% (Fig. 8.3). The level of fiber and red meat intake were the primary dietary factors associated with diverticulitis risk
Crowe et al. Characterize the effect of different fiber sources on diverticular disease risk (The Million Women Study, UK) [39]	690,075 women; mean age 60 years; 17,325 were admitted to hospital or died with diverticular disease; stable diet for the last 5 years; mean total fiber intake 14 g/day; 6 years of follow-up	Fiber significantly reduced risk of diverticular disease with cereal and fruit fiber having the strongest effects (Fig. 8.4)
Crowe et al. Assess the effect of vegetarian diets and fiber intake on risk of diverticular disease (European Prospective Investigation into Cancer and Nutrition [EPIC]-Oxford, UK) [33]	47,033 health conscious adults; 1/3 reported consuming a vegetarian diet; 76% female; median BMI 23; mean follow-up time of 11.6 years; 812 cases of diverticular disease	Vegetarian diets and a high intake of fiber were both associated with a reduction in diverticular disease-related hospital admission or death risk. There was a significant inverse association with total fiber intake and diverticular disease risk (≥26 g/day vs. <14 g/day), after multivariate adjustments (Figs. 8.5 and 8.6)
Aldoori et al. Evaluate specific fiber types and diverticular disease risk in men (Health Professionals Follow-up Study; US) [40]	43,881 male health professionals; 40–75 years of age at baseline; 362 cases of symptomatic diverticular disease; 4 years of follow-up	Insoluble fiber was significantly associated with a decreased risk of diverticular disease by 37%, and this inverse association was particularly strong for cellulose which reduced risk by 48%

Table 8.2 (continued)

Objective	Study details	Results
Aldoori et al. Examine the association between fiber and sources of fiber with the diagnosis of symptomatic diverticular disease in men (Health Professionals Follow-up Study; US) [41]	47,888 male health professionals; 40–75 years of age; 385 cases of symptomatic diverticular disease; 4 years of follow-up	Total fiber intake was inversely associated with the risk of diverticular disease, after adjustment for age, energy-adjusted total fat intake, and physical activity, with a significant 42% lower risk at the extreme of fiber intake. Fruit and vegetable fiber were the most effective fiber sources. A high-red-meat, low-fiber diet increased risk over twofold compared with those on a low-red-meat, high-fiber diet

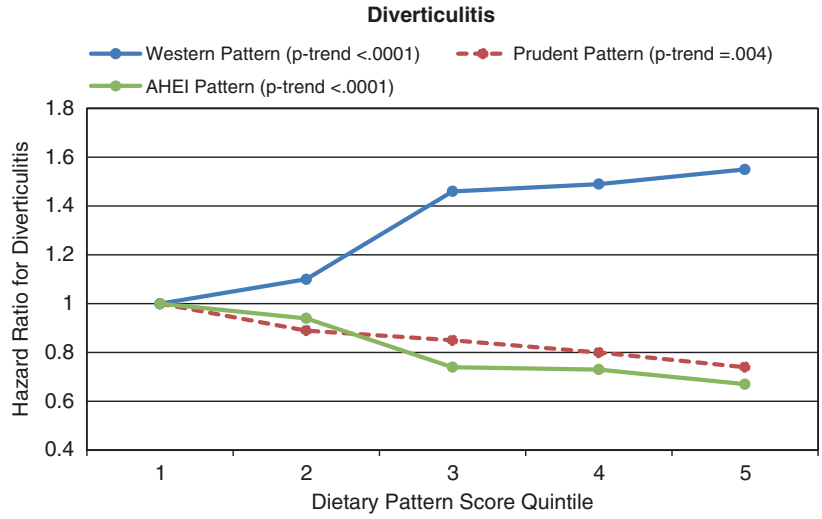

Fig. 8.3 Risk of diverticulitis and dietary pattern quality score in men [13]

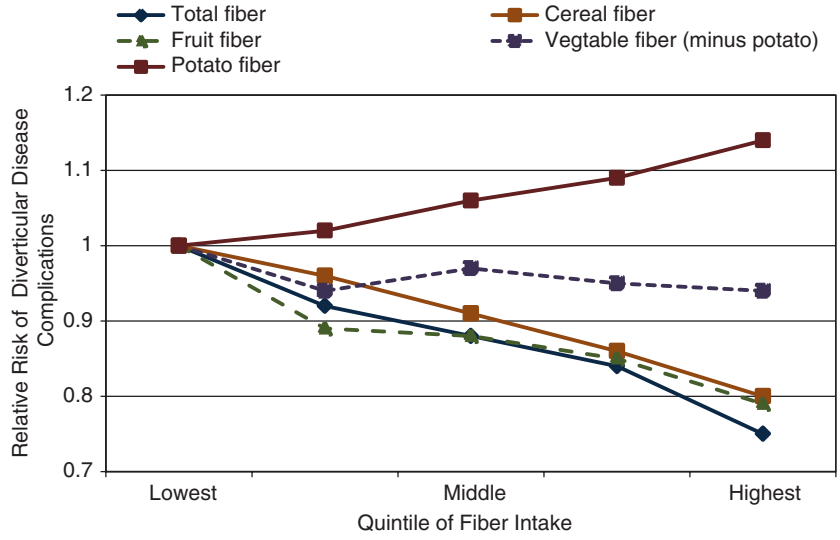

Fig. 8.4 Effect of fiber type on diverticular disease-related hospitalization or death risk from the UK Million Women Study ($p < 0.0001$ for total, cereal, and fruit fiber) [39]

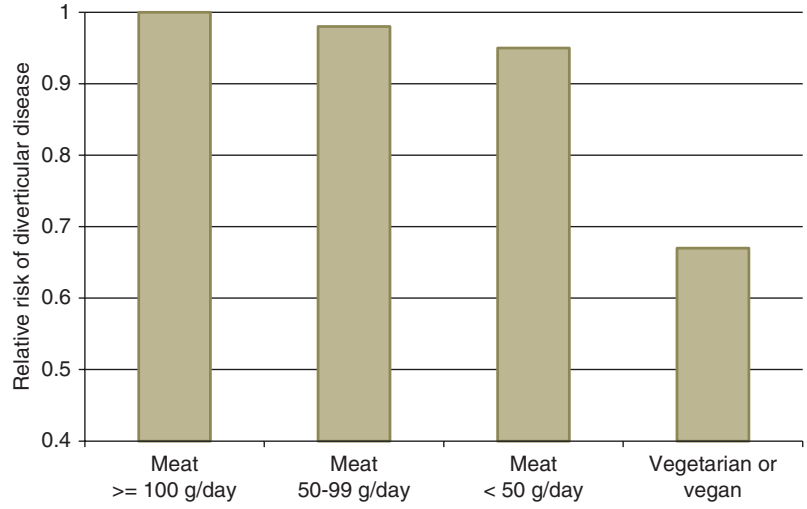

Fig. 8.5 Association between the level of meat or plant food intake and diverticular disease risk [33]

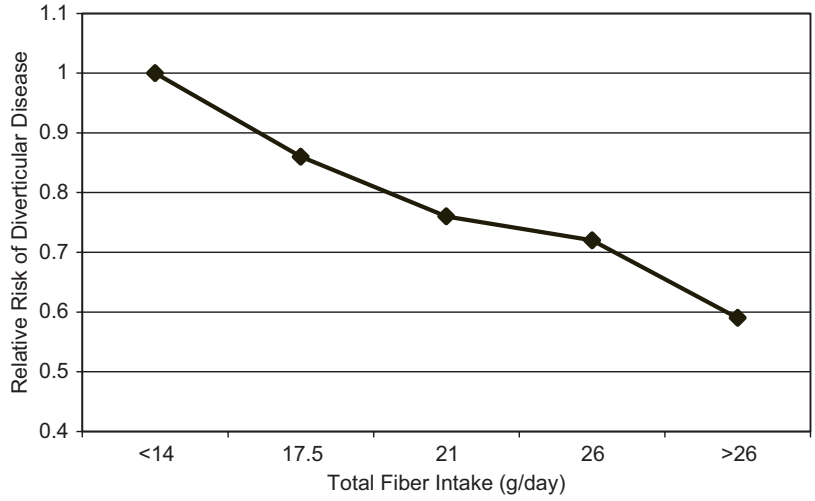

Fig. 8.6 Association between total fiber intake and diverticular disease risk ($p < 0.001$; multivariate adjusted) [33]

11.6 years of follow-up; 812 diverticular disease hospital admissions or deaths) showed that consuming a vegetarian diet significantly lowered the multivariate adjusted risk of diverticular disease by 31% vs. meat eaters (Fig. 8.5) [33]. There was also an inverse association between fiber intake and diverticular disease with a significant 41% lower risk (≥26 g fiber/day vs. <14 g fiber/day) (Fig. 8.6) [33]. Two US Health Professionals Follow-Up Studies from the 1990s showed similar inverse relationships between fiber intake and diverticular disease risk [40, 41].

Intervention Trials

Table 8.3 summarizes 11 intervention trials (six randomized controlled trials (RCTs) and five open-label trials) on the effects of fiber-rich diets and foods and supplements with wheat bran, bran crisps, psyllium, and methylcellulose on symptomatic uncomplicated diverticular disease [42–52]. All six

Table 8.3 Summary of intervention trials on the effects of fiber-rich diets and foods on diverticular disease (DD) symptoms

Objective	Study details	Results
RCTs		
Lahner et al. Evaluate the effects of high-fiber diets with and without a symbiotic supplement in the treatment of symptomatic DD (Italy) [42]	*Multicenter, parallel RCT*: 45 patients; mean age 66 years; 66% female; base ≥30 g daily fiber alone or plus 7 g Flortec© symbiotic formulation containing 5×10^9 CFU viable *L. paracasei B12060* plus a mixture of xylo-oligosaccharides (700 mg) and arabinogalactone (1243 mg) or no supplement; ≥ 1.5 L of water/daily; 6 months	A high-fiber diet is effective in relieving abdominal symptoms. The combination of high-fiber diet and synbiotic can relieve abdominal bloating as well as abdominal pain
Smits et al. Compare the efficacy and tolerance of lactulose and a high-fiber diet in the treatment of symptomatic DD (UK) [43]	*Parallel RCT*: 43 patients; high-fiber diet (30–40 g fiber daily) vs. lactulose (30 mL daily); 12 weeks	Bowel frequency and stool consistency improved similarly with both treatments. Pain on bowel movement and abdominal pain improved with both treatments in respect to frequency and severity
Ornstein et al. Compare the effects of bran and psyllium on symptomatic DD (UK) [44]	*Cross-over, double-blind RCT*: 58 patients; median age 64 years; 62% female; bran crisp bread (7 g fiber), psyllium beverage (9 g fiber), and placebo (2.3 g fiber) added to a daily habitual 15 g fiber diet; 16 weeks	The bran crisp bread and psyllium drink significantly improved symptoms of constipation when compared to the initial score. No significant differences in pain, lower bowel symptoms, and total symptom scores were reported since there was a only 5–7 g difference between the test fibers and placebo
Brodribb Evaluate the effects of wheat bran on symptomatic DD [45]	*Double-blind RCT*: 18 patients; 6.7 g fiber wheat bran crisp bread daily vs. 0.6 g fiber placebo crisp bread; 3 months	Daily wheat bran crisp bread significantly decreased mean overall symptom scores vs. placebo. Although wheat bran crisp bread significantly lowered overall pain score, there were no significant differences in bowel function scores. No adverse effects were recorded
Hodgson Assess the effect of methyl cellulose on symptomatic DD (UK) [46]	*Double-blind RCT*: 30 patients; two tablets methylcellulose vs. two tablets placebo; 3 months	Patients in the methylcellulose group had significantly greater symptom decrease than those in the placebo group
Taylor and Duthie Determine the effect of bran tablets on symptomatic diverticular disease [47]	*Crossover RCT*: 20 patients; high-fiber diet, Normacol plus, and bran tablets; 1 month	Bran proved to be the most effective treatment, not only in improving the symptoms but also in returning to normal the abnormal pathophysiological changes. Bran tablets were both convenient and acceptable as well as effective
Open-label trials		
Leahy et al. Compare the effects of higher vs. lower-fiber diets on DD symptoms (UK) [48]	31 patients on high-fiber diets; 25 patients; typical Western fiber diets; average follow-up 57 months	High-fiber diets significantly reduced symptoms recurrence (19% vs. 44%) and complications (6% vs. 20%) and required less surgery (6% vs. 32%) compared to the low-fiber control group
Hyland and Taylor Evaluate the long-term effects of a high-fiber diet on symptomatic diverticular disease (UK) [49]	100 patients; 75% consumed high-fiber diets; 5–7 years	Of the patients consuming high-fiber diets, 90% remained symptom-free

(continued)

Table 8.3 (continued)

Objective	Study details	Results
Eastwood et al. Assess the effects of different types of fiber on symptomatic DD (UK) [50]	31 patients; mean age 60 years; 20 g coarse wheat bran, two sachets of psyllium, and 20–40 mL/day lactulose; 4-week duration	All supplements equally alleviated symptoms
Brodribb and Humphreys Examine the effects of wheat bran on symptomatic DD (UK) [51]	40 patients; 24 g wheat bran daily; 6 months	Wheat bran decreased all symptoms by 60%, accelerated transit times in patients with >60 h, and reduced intracolonic pressure. Barium enema studies showed less spasm in eight patients and no diverticula in three patients after taking bran
Painter et al. Evaluate the effect of high fiber on symptomatic DD (UK) [52]	70 patients; 86% completers; high-fiber, low-sugar diet including unprocessed bran; average 22 months	High fiber intake relieved DD Symptoms in 89% of patients, and none of the completers required surgery

RCTs showed beneficial effects on symptoms and/or bowel function [42–47]. Three RCTs found that high-fiber diets can improve symptoms and/or bowel function [42, 43, 47]. Three RCTs suggest that wheat bran-, psyllium-, or methylcellulose-supplemented diets can improve symptoms and bowel function [44–46]. Five open-label trials all support the beneficial effects of fiber-rich diets and wheat bran on alleviating symptoms [48–52]. However, presently three systematic reviews conclude that quality evidence on the efficacy of fiber treatment for the reduction of symptoms associated with uncomplicated diverticular disease and for the prevention of acute diverticulitis is limited [53–55]. Well-designed studies, specifically focusing on the efficacy of dietary and supplemental fibers in alleviating the symptoms in uncomplicated diverticular disease still need to be confirmed [54].

Fiber Mechanisms

Fiber is known for its effects on promoting colonic health and weight control, which may contribute to reducing diverticular disease risk through a number of biological mechanisms [56–79].

Colonic Health

Fiber may improve colonic health to reduce diverticular disease by two primary mechanisms: (1) promoting stool bulk and regular laxation and (2) maintaining a healthy colonic microbiota ecosystem [63–68]. Consistent with the original fiber hypothesis on diverticular disease, fiber promotes laxation by increasing fecal bulk and stool frequency, and reducing intestinal transit time by increasing fecal water-holding capacity, and improves the microbiota ecosystem for overall colonic health. Fiber sources that from fiber-rich diets containing a variety of whole or minimally processed plant foods or from wheat bran-, psyllium fiber-, and methylcellulose-containing foods or supplements combine low fermentability and high water-binding capacity are particularly effective in promoting laxation [56–63]. A 1988 RCT (12 subjects, 2 weeks) showed that both wheat bran and psyllium husk fiber decrease transit time and increase daily stool regularity as well as promote healthier stool weights and structure, compared to low-fiber controls [62]. Wheat bran was more effective at reducing transit time, and psyllium was more effective at increasing stool water content (softer stools) and weight. A systematic

review of 65 intervention studies found that wheat bran improves bowel function by significantly increasing total wet stool weight by 3.7 g/gram intact wheat fiber and reduces transit time by 45 min/g when baseline transit time is greater than 48 h [63]. Alterations in colonic microbiota composition related to low-fiber Western diets can have an adverse effect on colonic health, especially with aging, leading to increased incidence of colonic dysbiosis, whereas the consumption of adequate fiber can lower the colonic lumen pH, increase the balance of healthy metabolites, and inhibit the growth of pathogenic bacteria to lower colonic inflammation [64–69]. Bacterial fermentation of fiber to maintain an adequate colonic butyrate concentration is critical for maintaining distal colonic health. Butyrate exerts potent effects on a variety of colonic mucosal functions such as inhibition of inflammation, by reinforcing various components of the colonic defense barrier and the inhibition of nuclear factor kappa B (NF-κβ) activation and histone deacetylation, and the activation of G-coupled receptors.

Body Weight Regulation

Elevated BMI and obesity increases the risk of diverticular disease and its complications [70–72]. Central obesity is an independent risk factor for complications due to the release of proinflammatory cytokines from visceral fat [70]. A 2012 prospective cohort study (36,592 Swedish women; follow-up of 12 years) found that women with a BMI between 25 and >30 had a 30% higher risk of diverticular disease and a two times higher risk of abscess or perforation compared to women with a BMI of 20–24.99 [27]. A 2009 American prospective study (47,000 men; followed over 18 years) found that men with a BMI > 30 had 78% increased risk of diverticulitis and a three times higher risk for diverticular hemorrhage compared to men with a BMI < 21 [72]. Populations with fiber-rich diets tend to be leaner than those with low-fiber diets [73–79]. In the Nurses' Health Study, women in the highest quintile of fiber intake had a significant 49% lower risk of major weight gain than women in the lowest quintile and weight gain was inversely associated with the intake of high-fiber and whole-grain foods [75]. A systematic review (43 prospective cohort, case-control, and randomized trials) found probable evidence that increased fiber intake was predictive of less weight gain and higher intake of refined grains, sweets, desserts and high-energy diets were predictive of elevated weight gain and waist size [76]. A Finnish trial of overweight middle-age men and women found that lower dietary fat and higher fiber intake is a significant predictor of sustained weight reduction, even after adjustment for other risk factors [77]. A long-term RCT suggests that consuming >30 g fiber/day can effectively promote weight loss similar to that of reduced energy diet regimens [78]. After weight loss is achieved, healthy fiber-rich dietary patterns can slow weight regain to maintain a 4–10 kg weight loss after 1 year and 3–4 kg after 2 years [79].

Conclusions

Diverticular disease is among the most clinically and economically significant gastroenterological conditions in people ≥ 65 years of age. Most people > 65 years of age will develop colonic diverticulae (herniate pouches) potentially caused by high colon intraluminal pressure. While 80% of the population with colonic diverticula remain asymptomatic, approximately 20% may develop abdominal symptoms (symptomatic uncomplicated diverticular disease), and in some individuals there may be eventual complications such as severe bouts of diverticulitis or bleeding that may lead to sepsis and death. In aging populations, the widespread intake of low fiber Western diets, increased intake of FODMAPs, naturally from whole foods or added to processed foods, and weight gain leading to

obesity are several factors that may increase the risk of diverticular disease, bouts of symptoms, or its complications. Five prospective studies suggest that fiber-rich healthy diets and low red or processed meat consumption significantly decrease the risk of diverticular disease. Although a number of intervention trials suggest that fiber-rich diets and foods or supplements containing wheat bran, psyllium, or methylcellulose may help to alleviate diverticular disease symptoms and/or improve bowel function, there are presently a limited number of high-quality trials. Fiber-related mechanisms associated with potentially reduced diverticular disease risk or alleviation of symptoms are related to improved colonic health including improved laxation and stool bulk and a healthier microbiota ecosystem with higher fecal concentration of probiotic bacteria and butyrate, lower inflammation, and improved body weight and visceral fat regulation.

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Chapter 9
Fiber and Healthy Dietary Patterns in Weight Regulation

Keywords Dietary fiber • Fiber-rich diets • Fiber supplements • Weight loss • Energy density • Dietary patterns • Mediterranean diet • Western diet • Obesity • Overweight • Body weight • Waist circumference • Body mass index • Visceral fat

Key Points

- During the last several decades, there has been an increased exposure to higher energy-dense and lower fiber-containing foods and increasingly sedentary lifestyles, which have led to net habitual positive energy balances and weight gain in Western populations. For overweight or obese individuals who successfully lose weight, as many as 80% typically drift back to their original weight or more because after weight loss there are an array of metabolic regulatory processes at work to promote weight regain, so it is difficult to maintain weight loss. Consequently, maintaining a healthy weight is a daily effort but healthy fiber-rich dietary patterns can help to promote satiety and reduce overall dietary energy density to assist in weight control.
- Dietary fiber intake is inversely associated with obesity risk, and populations with higher fiber diets tend to be leaner than those with low fiber diets.
- The human gastrointestinal and energy metabolism regulatory systems evolved on pre-agriculture high fiber diets.
- Prospective cohort studies suggest that increased total fiber intake by ≥12 g/day to >25 g fiber/day, especially as a replacement for refined low fiber food, can prevent weight gain by 3.5–5.5 kg each decade.
- Randomized controlled trials (RCTs) show that adequate fiber intake ≥28 g fiber/day from fiber-rich diets can significantly reduce body weight and waist circumference (WC) compared to low fiber Western diets (≤20 g fiber/day). Fiber-rich diets are usually more effective at promoting weight loss than are fiber supplements.
- RCTs show that healthy fiber-rich dietary patterns such as the Mediterranean (MedDiet), Dietary Approaches to Stop Hypertension (DASH), New Nordic, and vegetarian diets do not result in weight gain and high adherence to these diets can support weight loss and lower WC compared to control diets such as low fat or Western diets in overweight or obese individuals.
- Biological mechanisms associated with adequate fiber intake and healthy dietary patterns, in body weight regulation include effects on lowering diet energy density directly or by displacing higher energy-dense processed foods, promoting postprandial satiety, reducing metabolizable energy, and triggering other colonic microbiota or metabolic factors.

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Introduction

The worldwide overweight and obesity pandemic is among the greatest public health challenges of our time [1, 2]. Since 1980, the global prevalence of overweight and obesity increased by >28% for adults and >47% for children, resulting in a doubling of this population to over two billion people currently [1]. Overweight and obesity are complex multifactorial conditions resulting from chronic positive energy balance from higher energy intake and/or lower energy expenditure, involving primarily lifestyle factors, but also genetic, environmental, and emotional factors [3–5]. During the last several decades, there has been an increased exposure to higher-energy dense and lower dietary fiber (fiber)-containing foods and increasingly sedentary lifestyles, which have led to net habitual positive energy balances and weight gain in Western populations [1, 4–14]. A small positive energy balance of 50 kcal/day, by increased energy intake and/or reduced activity, can lead to an annual weight gain of 0.4–0.9 kg/year [5–7]. Further, a higher habitual intake of 200 kcal/day above energy balance in overweight or obese women may increase weight gain by as much as 9 kg/year [8]. Energy dense diets, common in the Western-style diet, are positively associated with higher BMI and risk of obesity [8–14]. Moreover, since people tend to eat approximately the same amount or volume of food on a day-to-day basis, regardless of the food energy density, the common advice of just eating less of all foods may not be the optimal approach for weight management [7]. A 2017 systematic review of longitudinal studies found that during adolescence, adhering to a Western dietary pattern high in fast foods and sugar sweetened beverages and low in fiber intake is associated with a 25% elevated body fat in early adulthood [15]. Elevated body mass index (BMI) or excessive adiposity in adulthood and increasingly in childhood is a growing risk factor for major chronic diseases such as diabetes, cardiovascular disease, nonalcoholic fatty liver disease, chronic kidney disease, and a number of obesity-related cancers [16–18].

For overweight or obese individuals who successfully lose weight, as many as 80% typically drift back to their original weight or more [19–21]. This is because after weight loss there are an array of metabolic regulatory processes at work to promote weight regain, so it is difficult to maintain weight loss [21–24]. After fat loss, thermogenesis reduces and leads to fat loss resistance, which may also be related to changes in leptin and thyroid hormone levels. Weight loss triggers strong overeating signals sent to the brain's hypothalamus to increase appetite. Also, in this period, adipocytes face cellular stress associated with the physical forces that arise within the shrinking cells, causing them to actively promote renewed fat storage. The determinants of weight maintenance are genetics, behavior, and environment with diet behavior thought to be the most important factor that influences weight regain. A cross-sectional study of weight loss maintainers who lost >10% of their body weight and maintained that loss for ≥5 years reported that they consumed a diet with lower energy density (1.4 kcal/g) than the weight regain individuals (1.8 kcal/g) [21]. These weight maintainers consumed more fiber-rich foods such as vegetables (4.9 servings/day) and whole-grain products (2.2 servings/day) compared to less than 1 daily serving of vegetables and whole grains for the weight regainers. In addition to eating a low-energy dense and high-fiber diet, successful long-term weight loss maintenance is associated with five additional strategies to help counteract weight regain metabolic processes: (1) engaging in physical activity, (2) eating breakfast, (3) self-monitoring weight on a regular basis, (4) limiting consumption of higher-energy dense foods, and (5) catching dietary "miss-steps" before they turn into a habit [20, 21, 24]. Two common dietary approaches for weight loss include: (1) reducing daily energy intake by 20–35% of energy for a negative energy balance or (2) eating lower-energy dense and healthy fiber-rich dietary patterns [21, 24]. A 2007 US randomized controlled trial (RCT) (32 healthy overweight women; age 20–42 yrs; 6 months) found that foods craved at baseline were more than twice the energy density of the habitual diet (3.7 kcal/g vs. 1.7 kcal/g [19]. These craved foods were lower in protein and fiber and higher in fat. Women who lost a greater percentage of weight after 6 months on the energy restricted diet reported less frequently giving in to food cravings and eating smaller portion sizes. In a 2015 RCT with obese adults with metabolic syndrome, it was

Fig. 9.1 Effect of a high-fiber diet (≥30 g/day) vs. an American Heart Association (AHA)* multicomponent weight loss program in 240 obese adults with metabolic syndrome over 1 year ($p > 0.05$) [25]. *AHA weight loss diet included increasing fiber. Energy intake goals were calculated and provided to the participant by estimating the daily calories needed to maintain the participant's baseline weight and subtracting 500–1000 calories per day to achieve a weekly weight loss of 0.5–0.9 kg. Each participant was given a customized goal of saturated fat grams allowed per day (7% of estimated calories), and no physical activity recommendations were made

shown that those who simply consumed a high-fiber diet had similar weight loss to those on a more complex multicomponent, hypocaloric diet plan after 1 year (Fig. 9.1) [25]. The objective of this chapter is to review the effects of fiber and healthy fiber-rich dietary patterns on body weight regulation.

Effect of Fiber on Body Weight and Composition

Fiber-Rich Diets

The human gastrointestinal and energy regulatory systems evolved on pre-agricultural diets containing ≥50 g fiber/day [26]. These preagricultural high-fiber dietary patterns are in sharp contrast to the present low-fiber, high-energy dense Western diets, a relatively recent occurrence in human evolution (Table 9.1) [27]. Ancestral fiber-rich whole food diets stimulated the evolution of the important colon microbiota ecosystem, which is equivalent to a symbiotic "organ" that supports optimal energy and cardiometabolic processes for weight control associated with a complex interplay between specific probiotic bacteria, fiber fermentation to short-chain fatty acid (SCFAs) satiety hormones, and increased excretion of fecal metabolizable energy [28, 29]. About 95% of Americans or other Western populations do not consume an adequate level of fiber daily (14 g fiber/1000 kcal or 25 g/day for women and 38 g/day for men) [30–32]. Total fiber intake was inversely associated with obesity risk among US adults in an analysis of NHANES 1999–2010 (Fig. 9.2). Populations with higher-fiber diets tend to be leaner than those with low-fiber diets [34–36]. A systematic review of 43 prospective cohort, case-control and randomized trials found moderately strong evidence that fiber-rich foods have a protective role against weight gain and increased waist size [34]. In 2010, the European Food Safety Authority (EFSA) recommended that adults should consume >25 g fiber per day (from whole-grain cereals, fruit, and vegetables) to improve weight maintenance and sustain weight reduction in overweight and obese individuals [37].

Table 9.1 Daily nutritional intake of preagricultural vs. present-day Western dietary pattern [27]

Nutritional components	Preagricultural diet	Current Western diet
Diet energy density (kcal/g)	Low	High
Dietary bulk (satiating)	More	Less
Sugar and sweeteners (% energy)	Limited amount of honey	17%
Grain products	Low (all whole grain)	High (mostly refined)
Fruit, vegetables, and nuts (% energy)	65%	8%
Fiber intake (g/day)	50–100	<15–17
Protein intake (% energy)	37% from lean game, eggs, fish, shellfish, or nuts	15% from meat, poultry, dairy, fish, eggs, legumes, or nuts
Fat intake (% energy)	22	32
Physical activity (kcal/d)	Active >1000 kcal/day	Sedentary (<150–490 kcal/day)

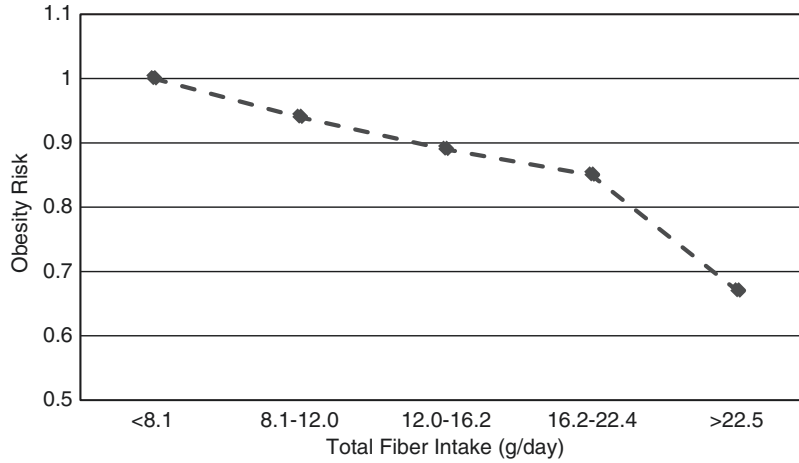

Fig. 9.2 Relationship between increasing fiber intake and adult obesity risk from the US National Health and Nutrition Examination (NHANES) Survey (1999–2010) [33]

Observational Studies

Observational studies generally support an inverse association between total fiber intake from minimally processed plant foods/diets and body weight, waist circumference (WC), and body and visceral fat (Table 9.2) [38–48]. Adequate fiber intake of ≥25 g fiber/day or 14 g fiber/1000 kcal from whole plant-based diets is a suggested target to reduce risk of weight gain, prevent risk of obesity, and promote modest weight loss [31, 37]. Specific studies suggest that increased total fiber intake above the usual Western diet fiber intake by ≥12 g/day, especially as a replacement for refined low-fiber food, can significantly prevent long-term (8–12 years) weight gain by 3.5–5.5 kg in both men and women [45, 47, 48]. A study in 252 women (mean age 40 years; 20-month follow-up) found that each 1 g/1000 kcal increase in total fiber significantly reduced body weight by 0.25 kg and body fat by 0.25%, by reducing total metabolizable energy intake [44]. The US Women's Health Study (18,146 women; baseline age ≥ 45 years; normal baseline BMI; 15.9-year follow-up) found that women with higher fiber intake did not have significant changes in body weight or BMI [38]. Studies show an inverse association with increased total fiber intake and WC [40–42, 46]. The European Prospective Investigation into Cancer and Nutrition (EPIC) study (89,432 participants; mean baseline age 53 years;

Table 9.2 Summary of observational studies on effects of increased fiber intake on body weight, waist circumference, and total and visceral fat

Objective	Study details	Results
Rautiainen et al. Investigate the effect of fiber intake on weight change and the risk of becoming overweight or obese (Women's Health Study; USA) [38]	18,146 women, baseline age ≥ 45 years; BMI 18.5 to <25; mean 15.9-year follow-up; Food Frequency questionnaire (FFQ) and self-reported body weight on annual questionnaire	This study found no significant association with total fiber intake and weight gain or becoming overweight or obese after multivariate adjustment including BMI (p-trend = 0.13)
Fischer et al. Assess how usual patterns of nutrient intake are associated with visceral adipose tissue (VAT), subcutaneous, abdominal, and trunk adipose tissue (Cross-sectional study; German adults) [39]	583 adults; mean age 61 years; VAT volumes from MRI; nutrient intake estimated by a 112-item food-frequency questionnaire linked to the German Food Code and Nutrient Database; foods, nutrients, or total energy intake associations with adipose tissue compartments via multiple linear regression	VAT was positively associated with nutrients characteristic of animal (except for dairy) products, (β: 0.25; $p < 0.0001$), but negatively with total fiber (β: −0.17; $p < 0.0001$), and nutrients found in milk. Subcutaneous abdominal and trunk adipose tissue were mainly associated with total energy intake
Lin et al. Assess the effect of total fiber and sources on BMI and waist circumference (WC) (Cross-sectional study; Belgian) [40]	3,083 individuals (1,546 men and 1,537 women); age ≥ 15 years. 42% of women and 29% of men were abdominally obese. The main contributors to total fiber intake were cereals and cereal products (34%), potatoes and other tubers (18.6%), fruits (14.7%), and vegetables (14.4%)	In fully adjusted multivariate models, WC was inversely related to total fiber intakes ($\beta = -0.118$, $p < 0.001$) and positively related to fruit fiber intakes ($\beta = -0.731$, $p = 0.001$). After adjustment for age, sex, region, and education level; intake of cereals and cereal product fiber were significantly associated with lower BMI ($\beta = -0.045$, $p = 0.025$), but the association was attenuated by energy intake adjustments
Du et al. Investigate the association of total dietary fiber, cereal fiber, and fruit and vegetable fiber with changes in body weight and WC European Prospective Investigation into Cancer and Nutrition (EPIC) Study [41]	89,432 participants; mean age 53 years; average 6.5-year follow-up	Higher intake of total fiber, especially cereal fiber, helps to prevent body weight and WC gain. For a 10 g/day higher total fiber intake, the mean weight loss was 39 g/year and WC loss was 0.08 cm/year. A 10 g/d higher cereal fiber intake was associated with −77 g body weight/year and −0.10 cm WC /year. Fruit and vegetable fiber were not associated with weight change but had a similar association with WC change when compared with intake of total fiber and cereal fiber
Romaguera et al. Assess the association between dietary factors and prospective changes in WC and visceral adiposity (EPIC Study) [42]	48,631 participants; mean age 50 years; mean BMI 26; median 5.5-year follow-up	In women, an increased fiber intake by 10 g fiber/day significantly reduced WC by 0.06 cm. WC was also significantly increased for every 1 kcal/g higher energy density by up to 0.15 cm and for every ten glycemic index units by up to 0.06 cm
Davis et al. Evaluate the relation between changes in dietary intake, specifically sugar and fiber intakes, with changes in adiposity and risk factors for type 2 diabetes in overweight Latino youth (longitudinal study; USA) [43]	85 overweight Latino youth; aged 11–17 years; body composition by dual-energy X-ray absorptiometry and magnetic resonance imaging; 2-year follow-up	Reduced fiber intake by 3 g/1000 kcal significantly increased visceral fat by 21% vs. an increase in fiber intake of 3 g/1000 kcal which reduced visceral fat by 4%

(continued)

Table 9.2 (continued)

Objective	Study details	Results
Tucker et al. Evaluate the effects of total fiber intake on risk of gaining weight and body fat in women over time (prospective Study; USA) [44]	252 women; mean baseline age 40 years; mean weight 65.6 kg; 20-month follow-up; 7-day weighed food records	For each 1 g/1000 kcal increase in fiber intake, there was a significant decrease in body weight by 0.25 kg and fat by 0.25%. After adjustment for energy intake, there was a reduction of about 33%, but the value still retained significance. Fiber's influence occurs primarily through reducing energy intake over time
Koh-Banerjee et al. Evaluate the associations between changes in cereal fiber intake and weight change (Health Professionals' Follow-up Study (HPFS); USA) [45]	27,000 men; mean baseline age 52 years; 8-year follow-up	Total fiber intake was inversely related to weight gain independent of whole grains (p-trend < 0.0001). The men consuming an increased 17 g fiber/day gained 1.40 kg, whereas the men with 26 g fiber/day gained 0.39 kg. After measurement error and multivariate adjustments, there was reduced weight gain by 5.5 kg (12 lbs) for each 20-g/day increment in total fiber intake
Koh-Banerjee et al. Determine the associations of changes in diet and physical activity, on waist circumference (WC) among men (HPFS; USA) [46]	16,587 men; mean baseline age 44–65 years; 9-year follow-up	An increase of 12 g total fiber/day was associated with a 0.63 cm decrease in WC ($p < 0.001$). Comparatively, WC was significantly reduced by increasing physical activity (25 ME h/week) by 0.38 cm and weight training (≥30 min/week) by 0.91 cm. Also, WC was significantly increased with smoking cessation by 1.98 cm and television watching (20 h/week) by 0.59 cm. All associations remained significant after further adjustment for BMI
Liu et al. Investigate the associations between the intakes of fiber and whole- or refined-grain products and weight gain over time (Nurses' Health Study; USA) [47]	74,000 female nurses; mean baseline age 50 years; 12-year follow-up	Over 12 years, women consuming a mean total fiber intake of 20 g vs. 13 g total fiber/day gained an average of 1.52 kg (3.4 lbs) less weight (p-trend < 0.0001) independent of body weight at baseline, age, and changes in covariate status; over 2–4 years, women gained less weight by 0.76 kg and BMI by 0.28 units. An increase in total fiber intake by 12 g/day is estimated to reduce weight gain by 3.5 kg (8 lb) in 12 years. Women in the highest quintile of total fiber intake had a 49% lower risk of major weight gain than women in the lowest quintile (p-trend < 0.0001)
Ludwig et al. Examine the role of fiber intake on weight gain, insulin status, and cardiovascular disease (CVD) risk factors (The Coronary Artery Risk Development in Young Adults [CARDIA]; USA) [48]	2,909 healthy adults; mean baseline age 26 years; >10.5 g fiber vs. <5.9 g fiber/1000 kcal; 10-year follow-up	After adjustment for potential confounding factors, total fiber intake was significantly inversely associated with body weight ($p = 0.001$), waist-to-hip ratio, and fasting insulin. Increased total fiber reduced weight gain by 8 lbs, waist-to-hip ratio by 0.1, and fasting insulin by 0.8–1.4 μU/mL in young adults. CVD risk factors were also significantly lowered

6.5-year follow-up) found that 10 g/day increase in total and cereal fiber reduced WC by approximately 1 cm/year [41]. For visceral fat, several studies show an inverse association with increased fiber intake, with children appearing to be especially responsive to the effects of low-fiber dense diets on visceral fat gain [43].

Randomized Controlled Trials (RCTs)

A systematic review of clinical studies found that increasing fiber intake by 14 g fiber/day in overweight or obese individuals, with ad libitum energy intake, was associated with a mean 10% decrease in energy intake and a reduction of weight by 1.9 kg after 4 months [49]. Seven RCTs support the consumption of adequate fiber intake ≥28 g fiber/day, or ≥14 g fiber/1000 kcal from fiber-rich diets combined with or without low fat was found to reduce body weight and improve body composition compared to a low-fiber (≤20 g fiber/day) Western control diet (Table 9.3) [25, 50–55]. A randomized trial (240 metabolic syndrome subjects; mean baseline age 52 years and BMI 35; 1 year) found that a high-fiber diet (goal to consume >30 g fiber/day) was as effective as a reduced energy

Table 9.3 Summary of RCTs on fiber-rich diets and body weight and composition regulation

Objective	Study details	Results
Karimi et al. Assess how weight maintenance, lipid profiles, and glycemic control differ between a low-energy density (LED) diet vs. a usual diet in subjects after recent weight reduction (Iran) [50]	70 subjects with recent history of weight reduction; mean age 55 years; 50% male; LED diet contained 30% fat, 15% protein, and 55% carbohydrate (20 g fiber, fruit 3.7 servings, and vegetables 5.5 servings) vs. usual diet including 35% fat, 15% protein, and 50% carbohydrate (14 g fiber; fruit 2.5 servings and vegetables 3.3 servings); dietary intake was assessed by using 3-day food records; 7 months	Subjects on the LED diet reduced weight by 0.3% vs. subjects on the usual diet control who gained 1.3% more weight ($p = 0.002$). The results were similar for WC with a loss of 0.4 cm on the LED vs. a gain of 0.3 cm on the usual diet ($p = 0.004$). Also, the LED diet group decreased fasting blood glucose by 9.5% vs. an increase by 0.4% on the usual diet ($p = 0.0001$). These findings support the beneficial effects of a LED diet derived from higher consumption of fruits, vegetables, and fiber on attenuating weight regain
Ma et al. Evaluate the effects of a simple high-fiber diet compared to a multicomponent American Heart Association (AHA) weight loss plan on body weight, waist circumference (WC), and BMI (USA) [25]	240 metabolic syndrome subjects; mean baseline age 52 years; mean BMI 35; goal ≥30 g fiber/day diet or an AHA weight loss program diet plan including caloric reduction of 500–1000 kcal/day; 1 year	At 12 months: (1) mean body weight was reduced by 2.1 kg in the high-fiber diet group vs. 2.7 kg in the AHA weight loss program, (2) mean WC was increased by 0.1 in. for the high-fiber diet vs. a loss of 0.4 in. for the AHA weight loss program, and (3) mean BMI was reduced by 0.8 units for the high-fiber diet and 1.0 units for the AHA weight loss program (Fig. 9.1). There was no significant difference in weight loss, BMI, or WC between the groups. This study suggests that simply consuming a high-fiber diet may be a reasonable alternative to a traditional, challenging, hypocaloric weight loss diet plan

(continued)

Table 9.3 (continued)

Objective	Study details	Results
Turner et al. Examine the effect of two high-fiber hypocaloric diets on weight loss (USA) [51]	20 subjects; mean age 47 years, 18 females and two males; mean BMI 31; high-fiber, reduced energy by 300–400 kcal/day diets with 1.5 cups beans/day vs. a variety of fruits, vegetables, and whole grains; 25–35 g fiber; 4 weeks	Both fiber-rich diets increased fiber intake from about 17 g/day to about 29 g fiber/day and lowered energy density by 38% for the bean group and 29% for the variety of fiber foods group. Both diets significantly reduced body weight, with the bean diet by 1.6 kg and the variety of fiber food diet by 1.1 kg. Combined mean weight loss was 1.4 kg ($p < 0.001$)
Mecca et al. Investigate the effectiveness of a high-fiber lifestyle intervention on overweight obese adults (Brazil) [52]	50 subjects; 11 males and 39 females; mean age 50 years; mean BMI 33.0; high-fiber diet group (daily 32 g fiber; 540 g fruits and vegetables) vs. control group receiving general nutrition education (17 g fiber/day); 10 weeks	Subjects on high-fiber diet lost 4% more weight, BMI by 4% and WC by 7% vs. the lower fiber control diet ($p < 0.05$; all)
Pal et al. Assess the effects of increased fiber intake from a healthy diet, psyllium, or their combinations on body weight and composition (Australia) [53]	72 participants; mean age 43 years; mean BMI about 34; diets: control diet plus placebo (20 g fiber/day), control diet plus psyllium (55 g fiber/day), healthy fiber-rich food diet plus placebo (31 g fiber/ day), or healthy fiber-rich food diet plus psyllium (59 g fiber/day);12 weeks	Compared to the control 20 g fiber/day usual diet group, the 31 g fiber healthy diet group significantly reduced body weight, BMI, and % body fat after 12 weeks (Fig. 9.3)
Ferdowsian et al. Study the effects of a high-fiber, low-fat vegan diet on body weight and composition in overweight subjects (US GEICO Corporate Site) [54]	113 adults; BMI >25; randomized into a low-fat, vegan diet group at 29 g fiber/day vs. Western habitual diet at 15 g fiber/day; 22 weeks	The higher-fiber diet group lost significantly more weight by 5.2 kg and waist size by 5.5 cm compared to the lower fiber Western diet control group ($p < 0.0001$). Weight loss of 5% of body weight was more frequently found for subjects in the high-fiber group by 49% vs. control group by 11% ($p < 0.0001$)
Lindstrom et al. Investigate the effect of total dietary fiber and fat and energy density on body weight and waist circumference (WC) (Finnish Diabetes Prevention Study) [55]	522 participants with impaired glucose tolerance; mean age 55 years; 67% female; mean BMI 31; standard lifestyle vs. high-fiber, low-fat diets and exercise counseling; 15 g fiber vs. 11 g fiber/1000 kcal; 4 years	Participants consuming the low-fat, high-fiber diet lost significantly 2.4 kg more weight than those on the high-fat, low-fiber diet. The fiber density of the diet was inversely associated with weight and waist size (Figs. 9.4 and 9.5)

multicomponent AHA weight loss program after 1 year (Fig. 9.1) [25]. Four RCTs show that the consumption of 29–32 g vs. 15–20 g total fiber/day significantly reduced body weight, BMI, and/or WC over 4–22 weeks [51–54]. An Australian RCT (72 subjects; mean age 43 years and BMI 34; 12-week duration) demonstrated that the intake of 31 g fiber or various combinations of diets with psyllium significantly reduced body weight, BMI, and % body fat compared to a 20 g fiber/day control (Fig. 9.3) [53]. Low-energy dense diets derived from higher consumption of fruits, vegetables, and fiber were shown to limit weight regain in subjects with a history of recent weight reduction to 0.3% compared to an increase of 1.3% for those on the usual diet after 7 months ($p = 0.002$) [50]. The Finnish Diabetes Prevention Study (522 prediabetic subjects; 67% females; mean baseline age 55 years; 4-year duration) showed total fiber intake (>15.5 g/1000 kcal vs. <11 g/1000 kcal) significantly reduced body weight by 2.6 kg (p-trend = 0.001) and WC by 1.3 cm (p-trend = 0.033) (Fig. 9.4) after multivariate adjustments [55]. Also, in this study, the adjusted 3-year weight reduction among those whose diets were both low in fat and high in fiber was 3.1 kg compared to 0.7 kg for subjects on the high-fat and

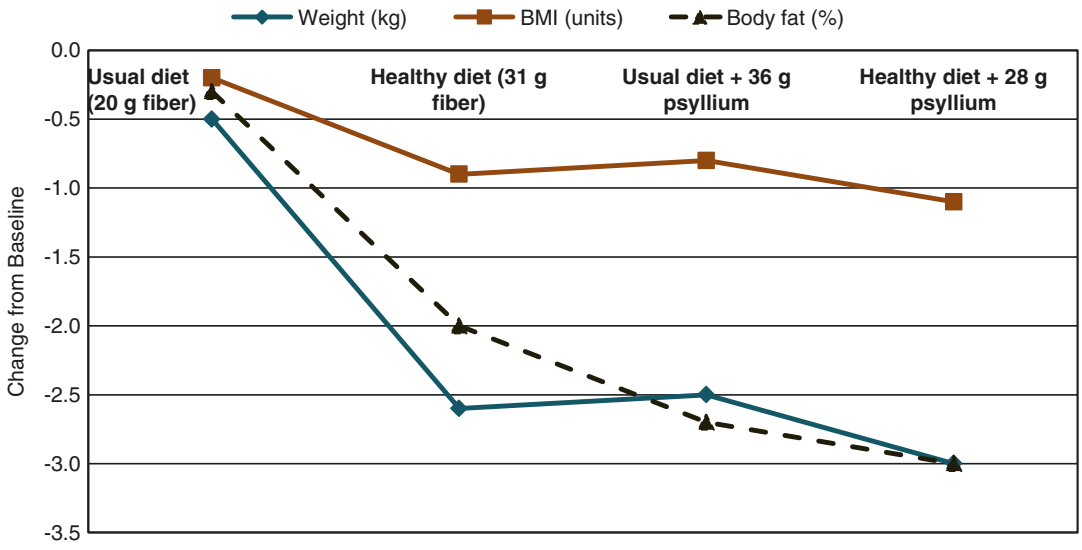

Fig. 9.3 Effect of usual diet and healthy diet with and without added psyllium (12 g 3×/day) in 72 obese adults (mean age 43 years; BMI 34) after 12 weeks ($p < 0.05$) [53]

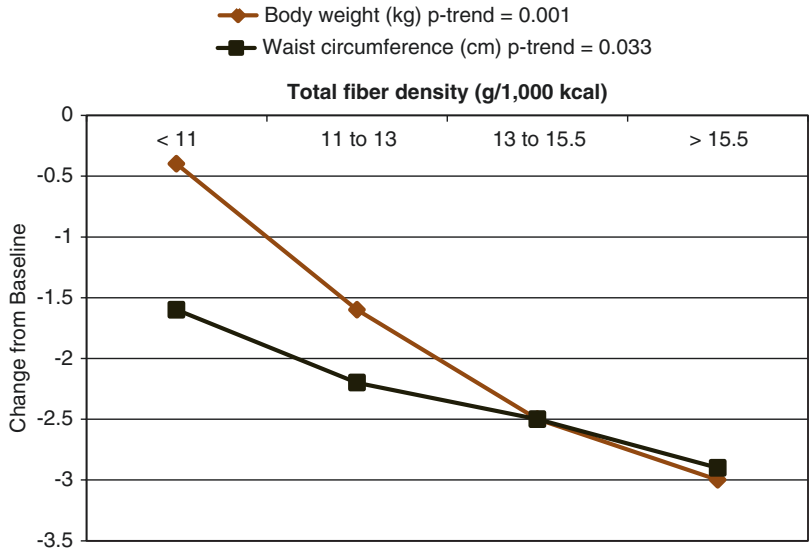

Fig. 9.4 Effect of dietary fiber density on body weight and waist circumference in 522 overweight/obese prediabetic adults over 3 years from the Finnish Diabetes Prevention Study (multivariate adjusted) [55]

low-fiber diet (Fig. 9.5). The daily substitution of a fiber-rich food for a lower fiber, energy dense food item at each meal and one snack is one approach to changing from a Western diet (15–17 g of daily fiber) to a healthy weight controlling diet with ≥30 g fiber/day. Examples of potential food switches to achieve >30 g/fiber/day and lower energy density needed to help prevent weight gain or to promote or maintain weight loss may include: (1) replacing a low-fiber, high glycemic breakfast cereal with a fiber-rich bran breakfast cereal; (2) eating an apple instead of a cookie at lunch; (3) adding artichokes or chickpeas to a salad; and (4) snacking on nuts, sunflower seeds, or popcorn instead of potato chips or candy. A list of 50 of the top fiber-containing foods is listed in Appendix 1.

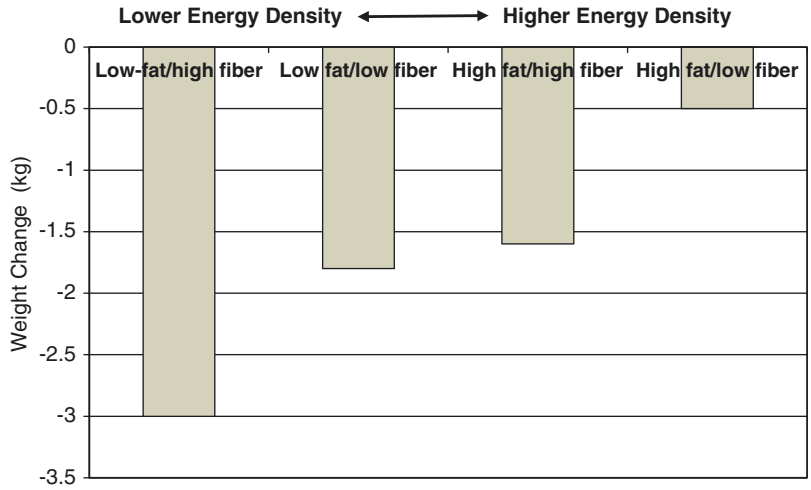

Fig. 9.5 Effect of dietary energy density on weight loss in 522 overweight/obese prediabetic adults over 3 years from the Finnish Diabetes Prevention Study (multivariate adjusted) [55]

Fiber Supplements and Ingredients

Three systematic reviews and four specific RCTs on the effects of isolated fiber supplements or ingredients on weight regulation are summarized in Table 9.4 [53, 56–61]. These RCTs showed that isolated fiber supplements were very heterogeneous and generally less effective than whole foods and fiber-rich diets. In a systematic review of 66 randomized trials that examined the effects of isolated fibers used as supplements or for food ingredients, the overall weight reduction was a modest 0.1 kg per 10 g fiber after 4 weeks with a high degree of variability [57]. A systematic review of inulin-type fructans RCTs showed insignificant or inconsistent weight loss effects [56]. Adding 12 g psyllium fiber mixed with 250 mL water, 3 times daily 5–10 min before breakfast, lunch, and dinner to a Western diet (20 g fiber/day), significantly lowered body weight and % body fat ($p < 0.05$) with an effect similar to consuming a plant-based healthy diet with 31 g fiber/day (Fig. 9.3) [53]. A 2016 double-blind RCT (159 subjects; mean age 50 yrs; mean BMI 32; 12 months) found that 5 g of high viscosity, moderately low fermentable soluble fiber supplements including PolyGlycopleX® (xanthan gum, Konjac glucomannan, and alginate) or psyllium significantly reduced body weight, waist circumference (WC), and DXA body fat after 12 months compared to the rice flour control [58]. A Chinese trial (39 college students; mean age 23 years and BMI 26; 12 weeks) found that biscuits supplemented with 27.5 g isolated soy fiber significantly reduced body weight by 0.7 kg and BMI by 0.44 vs. a control biscuit ($p < 0.05$) [59]. A Spanish double-blind, placebo-controlled trial with fiber-supplemented hypocaloric diets (200 overweight or obese subjects; mean age 48 years and BMI 31; 78% women; 16 weeks) showed that a relatively low supplementation blend of 4 g psyllium and glucomannan two or three times/day insignificantly reduced body weight 4.6 kg compared to 3.8 kg for the placebo ($p = 0.43$), suggesting that higher levels of fiber supplementation may be required for significant additional weight loss [60]. A US crossover trial (11 subjects; age range 23–46 years; 3 weeks with 4 week washout) found that ad libitum diets with the addition of 27 g/day of fermentable, soluble gel-forming/viscous fibers (pectin and β-glucan) and non-fermentable fiber (methylcellulose) consumed in a noncaloric beverage 30 min before each meal was shown to insignificantly reduce body weight by 0.13 kg for both fermentable and non-fermentable fibers and body fat for the fermentable fibers by 0.1% and for the non-fermentable fiber by 0.3% [61].

Table 9.4 Summary of RCTs on isolated fiber supplements and ingredients for body weight regulation

Objective	Study details	Results
Systematic reviews and meta-analysis		
Liber et al. Systematically evaluate the effects of inulin-type fructan supplementation on appetite, energy intake, and body weight (BW) in children and adults [56]	For the pediatric population; 4 RCTs; 232 children. For the adult population; 15 RCTs; 545 subjects	Very inconsistent effects on weight loss with limited data suggest that long-term use of inulin-type fructans may contribute to weight reduction
Wanders et al. Systematically investigate fiber types on appetite, energy intake, and body weight (systematic review) [57]	RCTs comparisons for appetite (58), acute energy intake (26), long-term energy intake (38), or body weight (66)	Overall, effects on energy intake and body weight were relatively small, and distinct dose-response relationships were not observed. Short- and long-term effects of fiber appear to differ and have multiple mechanisms relating to their different physicochemical properties. Fibers characterized as being more viscous (e.g., pectins, β-glucans, and guar gum) reduced appetite or energy intake more often than those less viscous fibers
Specific RCTs		
Pal et al. Investigate the effects of PolyGlyopleX® (xanthan gum, Konjac glucomannan, and alginate) vs psyllium on body weight and composition (Australia; double blind, parallel RCT) [58]	159 subjects; mean age 50 years; mean BMI 32; PolyGlyopleX®, psyllium US rice flour at 5 g added to 500 mL water before usual meals (total 15 g/day); 12 months	Compared to rice flour control, subjects reduced weight on PolyGlyopleX® by 2.8% and psyllium by 1.5%. Also, both viscous fiber reduced body fat and WC
Hu et al. Examined the effects of soy fiber on body weight and body composition in overweight and obese participants (China; parallel RCT) [59]	39 college students; mean age 23 years; mean BMI 26; biscuits supplemented with 27.5 g soy fiber/day for breakfast vs. control low-fiber biscuits; 12 weeks	Soy fiber supplemented breakfast biscuits significantly reduced body weight by 0.7 kg and BMI 0.44 vs. a control biscuit ($p < 0.05$)
Pal et al. Compare the effects of fiber intake from a healthy diet vs. a control diet plus psyllium or a healthy diet plus psyllium on body composition (Australia, parallel RCT) [53]	72 participants; mean age 43 years; mean BMI about 34; diets, control diet plus placebo (20 g fiber/day), control diet plus 36 g psyllium/day, healthy fiber-rich food diet plus placebo (31 g fiber/day), or healthy fiber-rich food diet plus approx. 28 g psyllium/day); 12 weeks	Adding 12 g psyllium fiber 3 times/day to a Western diet (20 g fiber/day) significantly lowers body weight and % body fat ($p < 0.05$) with a similar effect to a 31 g fiber/day healthy diet (Fig. 9.3)
Salas-Salvado et al. Compare the effect of the administration of a mixture of fibers on body weight loss, satiety, lipid profile, and glucose metabolism in a parallel, double-blind, clinical trial (Spain) [60]	200 overweight or obese subjects; mean age 48 years; mean BMI 31; 78% female; reduced calorie diet with mixed fiber dose 3 g psyllium and 1 g glucomannan either twice or three times daily vs. placebo; 16 weeks	Weight loss was higher after both doses of fiber by 4.5 and 4.6 kg than with placebo by 3.8 kg; the differences in changes between groups were not statistically significant ($p = 0.43$) However, post-prandial satiety increased in both fiber groups compared to the placebo
Howarth et al. Assess the effect of high fermentable and low fermentable fiber supplements on hunger, energy intake, and weight loss (USA; crossover RCT) [61]	11 subjects; age 23–46 years; BMI 20–34; 27 g/day of fermentable fiber (FF) (pectin and β-glucan) and non-fermentable (NFF; methylcellulose); ad libitum diets; 3 weeks; 4 weeks of washout; daily fiber supplements were divided into approximately three 10 g portions to be taken 30 min before each meal with 355 mL of a noncaloric liquid, to achieve a maximum effect as a preload	In ad libitum diets over 3 weeks, fiber supplements insignificantly reduced energy intake for FF by 7% ($p = 0.31$) and NFF by 9.5% ($p = 0.11$), body weight by 0.13 kg ($p > 0.05$), and % body fat for NFF by 0.3% ($p = 0.56$); FF by 0.1% ($p = 0.66$). This study showed a limited role for short-term use of FF and NFF supplements in promoting weight loss in humans consuming an ad libitum diet

Healthy Dietary Patterns

Overview

Compared with the usual Western diet, the consumption of healthy dietary patterns, including the US dietary guidelines diet, Mediterranean diet (MedDiet), Dietary Approaches to Stop Hypertension (DASH) diet, and healthy vegetarian (lacto-ovo) diets, by overweight and obese individuals can result in weight loss or at least prevent weight gain depending on the degree of adherence and fiber level [14]. Appendix 2 summarizes the food and nutrient composition of some major healthy dietary patterns vs. the American Western dietary pattern. The 2015 US Advisory Guidelines Advisory Committee scientific report concluded that there was strong evidence showing that overweight and obese adults, preferably as part of a comprehensive lifestyle intervention, can achieve clinically meaningful weight loss ranging from 4 to 12 kg after 6 months through a variety of healthy dietary patterns that achieve an energy deficit [14]. Thereafter, slow weight regain is observed, with total weight loss at 1 year of 4–10 kg and at 2 years of 3–4 kg. All these healthy dietary patterns double the fiber content from about 16–17 g/day in the usual Western diet to ≥30 g/day and decrease added sugar intake by more than half by emphasizing the increased consumption of plant-based foods, such as whole grains, fruits, vegetables, pulses, and nuts.

Observational Studies

The effect of dietary pattern nutrient quality and specifically the MedDiet, DASH diet, and vegetarian diets on body weight and abdominal fat regulation and obesity risk are summarized in Table 9.5 [62–80].

Overall Diet Quality

Observational studies consistently show that habitual intake of higher overall diet quality, especially with adequate fiber intake from whole plant foods and lower red meat and high-energy dense processed foods and beverages, are inversely associated with weight gain and central obesity in both men and women, especially in nonobese subjects at baseline (Table 9.5) [62–70]. A cross-sectional analysis of the Multi-Ethnic Study of Atherosclerosis [MESA] (5,079 adults; mean age 61 years; 47% men) demonstrated that higher intake of fiber-containing fruits, vegetables, whole grains and seeds/nuts, and yogurt were associated with decreased adiposity, while red/processed meats were associated with greater adiposity (Fig. 9.6) [62]. A study of US adolescence (2,656 adolescents recruited in middle/high schools; mean age 15 years; 10-year follow-up to mean age 25 years) showed that a 15-point higher diet quality score at age 15 years was associated with 1.5 kg less weight gain and lower BMI by 0.5 over 10 years ($p < 0.001$), independent of lifestyle factors and energy intake [63]. The Women's Health Initiative Observational Study (67,175 postmenopausal women with WC measurements; 3 years of follow-up) found that a 10% improvement in diet quality significantly reduced multivariate WC by up to 0.1 cm over 3 years [64]. A pooled analysis of the large Nurses' Health Study I and II and Health Professionals Follow-Up studies (123,098 women and 22,973 men; women mean age 36–48 years; men mean age 58; normal BMI; 20 years of follow-up) showed that higher adherence to all types of high-quality diet patterns was significantly associated with less weight gain over each 4-year weight assessment period in both men and women, especially in younger women or overweight individuals [65]. The Framingham Offspring and Spouse Study (590 normal-weight women; 16-year follow-up) found that lower-quality diets were associated with a 76% increased risk of becoming overweight or obese compared to high-quality diets [67]. The 2003 Baltimore Longitudinal Study of Aging (459 men and women;

Table 9.5 Summary of observational studies on dietary patterns in body weight and composition regulation

Objective	Study details	Results
Overall dietary pattern quality		
Shah et al. Investigate the relationship between dietary quality and regional adiposity in a cross-sectional analysis (Multi-Ethnic Study of Atherosclerosis [MESA]; USA) [62]	5,079 subjects; mean age 61 years; 47% males	Those with higher diet quality scores, AHA goals and adherence to the MedDiet were generally older and female, with a lower BMI, CRP, and markers of insulin resistance. After adjustment, a higher diet quality score (highest vs. lowest dietary score quartile) was associated with lower visceral fat: 523.6 vs. 460.5 cm^2/m (p-trend <0.01; Fig. 9.6), less pericardial fat 41.3 vs. 47.5 cm^3/m (p-trend <0.01), and hepatic steatosis (by hepatic attenuation; 58.6 vs. 60.7 Hounsfield units (p-trend <0.01). Greater intake of fiber-containing fruits, vegetables, whole grains and seeds/nuts, and yogurt were associated with decreased adiposity, while red/processed meats were associated with greater adiposity
Hu et al. Examine the previously validated diet quality score and weight change among adolescents transitioning into young adulthood (Prospective study, USA) [63]	2,656 adolescents recruited in middle/high school; mean age 15 years; 10-year follow-up to mean age 25 years; the dietary quality (without alcoholic items) was based on Mediterranean/prudent diets, focusing on foods that are varied, based on nutritionally rich plants, and less processed foods	The mean weight increased from 61 to 76 kg. Independent of lifestyle factors and energy intake, a 15-point higher diet quality score at age 15 years was associated with 1.5 kg less weight gain and lower BMI by 0.5 over 10 years ($p < 0.001$). A higher diet quality score can be achieved by increasing the intake of seeds (beans, whole grain, nuts), white meat (fish, poultry), fruits and vegetables, and low-fat dairy while decreasing the intake of processed foods, red meat, and sweet and salty foods (e.g., salty snacks, soft drinks, sweet breads, grain desserts). Establishment of high-quality dietary patterns in adolescence may help reduce excess weight gain by young adulthood
Feliciano et al. Examine whether changes in diet quality predicts changes in central adiposity among postmenopausal women (Women's Health Initiative Observational Study; USA) [64] Dietary patterns assessed included (Healthy Eating Index-2010, Alternate Healthy Eating Index-2010, Alternate MedDiet, and Dietary Approaches to Stop Hypertension (DASH))	67,175 postmenopausal women; mean baseline age 63 years, WC 83 cm (34.6 in.), and BMI 27; 3-year follow-up; waist circumference (WC) and trunk fat was measured in 4,254 women; dual-energy X-ray absorptiometry (DXA)	A 10% improvement in any dietary pattern quality score was associated with 0.07 to 0.43 cm smaller increase in WC over 3 years (all $p < 0.05$). After adjusting for weight change, associations attenuated to 0.02–0.10 cm but remained statistically significant for all patterns except Alternate MedDiet. Results were similar for DXA trunk fat. Improvements in diet quality are modestly protective against gain in WC, which is partially due to lesser weight gain. Achieving and maintaining a higher quality diet after menopause may help protect against gains in central adiposity
Fung et al. Evaluate the association between change of diet quality indexes and concurrent weight change over 20 years (Nurses' Health Study [NHS]) I and II, and Health Professionals Follow-up Study [HPFS]; USA) [65]	123,098 women and 22,973 men; mean baseline age 49 years for NHS I and 36 years for NHS II, 48 years for HPFS; mean BMIs ranged from 23 to 24.7; 20-year follow-up; weight measures every 4 years	There was significantly less weight gain over a 4-year cycle with each standard deviation (SD) increase of diet quality score in both men and women. Improvement of diet quality was associated with less weight gain, especially in younger women and overweight individuals

(continued)

Table 9.5 (continued)

Objective	Study details	Results
Lassale et al. Assess and compare the predictive value of six different dietary scores on risk of weight gain and obesity (Supple'mentation en Vitamines et Mine'raux Antioxydants; France) [66]	3,151 participants; 1,680 men and 1,471 women; mean baseline age 52 years; 13-year follow-up	This study suggests that baseline diet quality, measured by different dietary scores, is a good predictor of weight gain across genders. Dietary quality score appears to be especially predictive of obesity risk in middle-aged men. These findings support the broader use of dietary scores for weight gain prevention at the population level
Wolongevicz et al. Determine how diet quality effects risk of being overweight or obese in women (Framingham Offspring and Spouse Study; USA) [67]	590 normal-weight women; BMI <25, aged 25–71 years;16-year follow-up	Women with lower diet quality were significantly 76% more likely to become overweight or obese compared with those with higher diet quality (p-trend = 0.009)
Esmaillzadeh and Azadhakht Evaluate major dietary patterns and the prevalence of general obesity and central adiposity among women (crosssectional study; Iranian) [68]	486 women, mean age 50 years; usual dietary intakes were evaluated by FFQ; with the use of factor analysis three major dietary patterns were extracted: healthy (9.5 g fiber/1000 kcal), Western (3 g fiber/1.000 kcal, and Iranian 8.5 g fiber/1000 kcal)	Women in the upper category of the healthy pattern score were less likely to be obese by 59% and centrally obese by 52% ($p < 0.05$), whereas those in the upper quintile of Western pattern had greater risk for general obesity by 250% and for central obesity by 533% ($p < 0.01$), after adjustments. The Iranian dietary pattern was not significantly associated with general or central obesity
Schulz et al. Identify a dietary pattern predictive of subsequent annual weight change by using diet composition information (European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam cohort; Germany) [69]	24,958 participants; mean age 50 years, mean BMI 26; 4.4-year follow-up	Mean annual weight gain gradually decreased with increasing pattern score (p-trend < 0.0001). A diet pattern characterized by low-fat, high-fiber (13.5 g fiber vs. 8.8 g fiber/1000 kcal) foods such as whole-grain bread, fruits, vegetables, and cereals was associated with body weight maintenance or prevention of excess body weight gain in nonobese subjects at baseline. This study supports the importance of adequate fiber intake for weight control
Newby et al. Assess the effect of dietary pattern on BMI and waist circumference (WC) (Baltimore Longitudinal Study of Aging; USA) [70]	459 healthy men and women; 52% men; 95% whites/5% blacks; mean age for women 57 years and men 61 years; healthy diet (high fruit, vegetables, whole grains, low in red meat, fast foods, and soda; 27 g fiber/day vs. lower fiber by ≥20% for the other diet clusters; 7-day dietary records	Five dietary pattern clusters were derived (healthy, white bread, alcohol, sweets, and meat and potatoes) (Fig. 9.7). The mean annual gain in BMI was 0.30 for subjects in the meat-and-potatoes cluster compared to 0.05 for those in the healthy cluster ($p < 0.01$). The mean annual gain in WC was three times as great for subjects in the white bread cluster with 1.32 cm vs. those in the healthy cluster by 0.43 cm ($p < 0.05$)
Mediterranean diet (MedDiet) – Prospective studies		
Li et al. Study long-term changes in anthropometric measures in a generally healthy population (Swedish women) [71]	27,544 women; mean age 40; mean BMI 22; MedDiet score 0–9; 12-year follow-up	Among Swedish women, higher adherence to the MedDiet was not associated with increased body weight and WC compared to the average median gain in body weight by 5 kg and WC by 7.0 cm
Funtikova et al. Evaluate the association of adherence to the MedDiet and changes in WC and 10-year incidence of abdominal obesity (Spain) [72]	3,058 subjects; 51% women, mean baseline age 49 years; 10-year follow-up	High adherence to the MedDiet was inversely associated with WC by 1.5 cm ($p = 0.024$; fully adjusted models). The 10-year risk of abdominal obesity insignificantly decreased across the tertile score by 10–21%

Table 9.5 (continued)

Objective	Study details	Results
May et al. Investigate the combined effect of physical activity, dietary pattern, and smoking status on prospective gain in body weight and waist circumference (WC) (EPIC-PANACEA) [73]	325,537 participants; 94,445 men and 231,092 women, mean age 51–58 years; mean BMI 25–27; median 5-year follow-up	Men and women who reported to be physically active, never-smoking, and adherent to the MedDiet gained less weight over a 5-year period for men by 537 g and women by 200 g and about 1 cm less WC compared to participants with zero healthy behaviors
Beunza et al. Investigate the risk of weight gain (≥5 kg) or the risk of developing overweight or obesity (The Seguimiento Universidad de Navarra Follow-up University of Navarra (SUN) Cohort; Spain) [74]	10,376 men and women; university graduates; mean age 38 years; mean 5.7-year follow-up	Subjects with the lowest MedDiet adherence had an average 0.3 kg annual weight gain, whereas those with highest adherence had a loss of 0.059 kg/year and a 24% lower risk of gaining ≥5 kg over the first 4 years of follow-up
Romaguera et al. Assess associations between adherence to the MedDiet, weight change, and the incidence of overweight or obesity (EPIC-Physical Activity, Nutrition, Alcohol, Cessation of Smoking, Eating out of home and obesity project PANACEA; EU) [75]	325,537 participants; 94,445 men and 231,092 women, mean age 51–58 years; mean BMI 25–27; median 5-year follow-up	This study found that eating a MedDiet may help to prevent weight gain and the development of overweight and obesity. High adherence to the MedDiet reduced mean weight by 0.16 kg and risk of becoming obese by 10% compared to low adherence. A similar association between adherence to the MedDiet and weight change was observed in men and women (p-interaction = 0.823). The protective effect of MedDiet against weight gain was stronger in younger people (<40 y of age) and in nonobese (BMI <30) individuals at baseline (p-interactions < 0.0001)
Sanchez-Villegas et al. Evaluate the potential relation between compliance with traditional MedDiet score and subsequent weight maintenance and changes (SUN Cohort; Spain) [76]	6319 participants; mean age 34–40 years; mean BMI 23; 28-months follow-up; 7.9 g fiber/1000 kcal vs. 14.9 g/fiber/1000 kcal	In young, normal-weight adults, those in the lowest quartile of MedDiet score gained 0.73 kg compared to those in the top quartile who gained 0.45 kg. Although there was an initial inverse dose-response relationship (p-trend = 0.016), the results were not statistically significant after multivariate adjustment (p-trend = 0.291)
Mendez et al. Examine whether a MedDiet pattern is associated with reduced 3-year incidence of obesity (EPIC-Spain) [77]	17,238 women, mean baseline age 47 years; 10,589 men; mean baseline age 50 years; mean of 3.3-year follow-up	Higher adherence to the MedDiet was associated with a 30% lower risk of becoming obese. Associations were similar in women and men. MedDiet adherence was not associated with incidence of overweight or obesity in initially normal-weight subjects
Dietary approaches to stop hypertension (DASH) diet		
Barak et al. Investigate adherence to DASH diet and general and central obesity in female nurses (cross-sectional study; Iran) [78]	293 female nurses aged >30 years; general and abdominal obesity were defined as BMI ≥25 and WC ≥88 cm; usual dietary intakes were assessed using a validated FFQ; DASH diet score was based on foods and nutrients emphasized or minimized in the DASH diet	Increased adherence to the DASH diet was associated with older age ($p < 0.01$) and lower WC ($p = 0.04$). Initially, there was no statistically significant difference in the prevalence of general obesity between extreme quartiles of the DASH diet score, but after fully adjusting for dietary factors, those in the highest quartile of DASH diet score were 71% less likely to have general obesity. A marginally significant trend toward decreasing prevalence of central obesity was seen with increasing quartile of the DASH diet score with a 63% lower WC ($p = 0.09$)

(continued)

Table 9.5 (continued)

Objective	Study details	Results
Berz et al. Study the effects of the DASH eating pattern on BMI throughout adolescence (National Growth and Health Study; USA) [79]	2,327 girls with ten annual visits starting at age 9 years; 10 year follow-up	Adolescent girls with higher adherence to the DASH eating pattern had smaller gains in BMI. Girls in the highest vs. lowest quintile of the DASH score had significantly lower adjusted mean BMI of 24.4 vs. 26.3. The strongest individual food group predictors of BMI were total fruit with a mean BMI of 26.0 vs. 23.6 for <1 vs. ≥2 servings/ day ($p < 0.001$) and low-fat dairy with a mean BMI of 25.7 vs. 23.2 for <1 vs. ≥2 servings/day ($p < 0.001$). Whole-grain consumption was more weakly but beneficially associated with BMI
Vegetarian diet		
Tonstad et al. Assess the effects of different types of vegetarian diets on body weight and diabetes risk compared with nonvegetarians (USA; The Adventist Health Study-2 cohort) [80]	22,434 men and 38,469 women; mean age 58 years; 5 year follow-up data from Seventh-Day Adventist church members across North America; type of vegetarian diet was categorized based on a food frequency questionnaire (FFQ)	Mean BMI was lowest in vegans (23.6) and incrementally higher in lacto-ovo vegetarians (25.7), pesco-vegetarians (26.3), semi-vegetarians (27.3), and nonvegetarians (28.8). Prevalence of type 2 diabetes increased from 2.9% in vegans to 7.6% in nonvegetarians; the prevalence was intermediate in participants consuming lacto-ovo (3.2%), pesco- (4.8%), or semi-vegetarian (6.1%) diets. This study demonstrates potential for vegetarianism to protect against obesity and diabetes
Berkow and Barnard Review of published observational studies on the associations between vegetarian diets and reduced body weight (review article; US) [81]	40 studies reporting the weight status of vegetarians and nonvegetarians	29 of 40 observational studies reported that vegetarians weighed significantly less than nonvegetarians as measured by BMI or body weight. These studies found that the weight and BMI of both male and female vegetarians were 3–20% lower than that of nonvegetarians. Obesity prevalence ranges from 0 to 6% in vegetarians and from about 5 to 45% in non-vegetarians

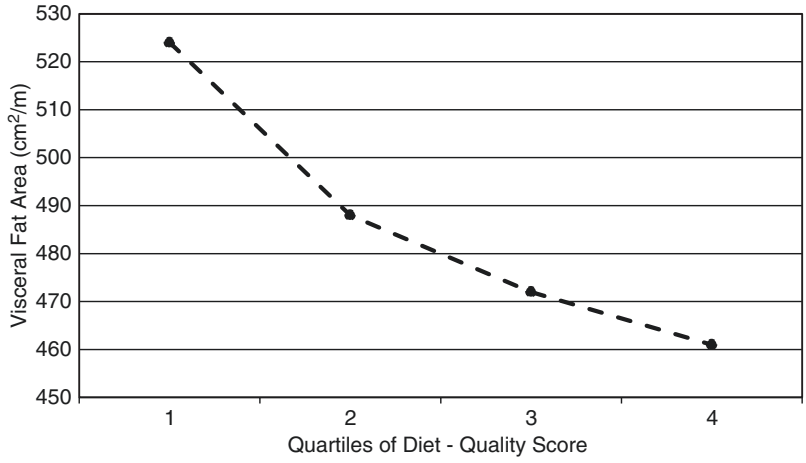

Fig. 9.6 Adjusted mean visceral fat area measures across quartiles of diet quality score from 5,079 USA subjects, mean age 61 years and 47 % men ($p < 0.01$) [62]

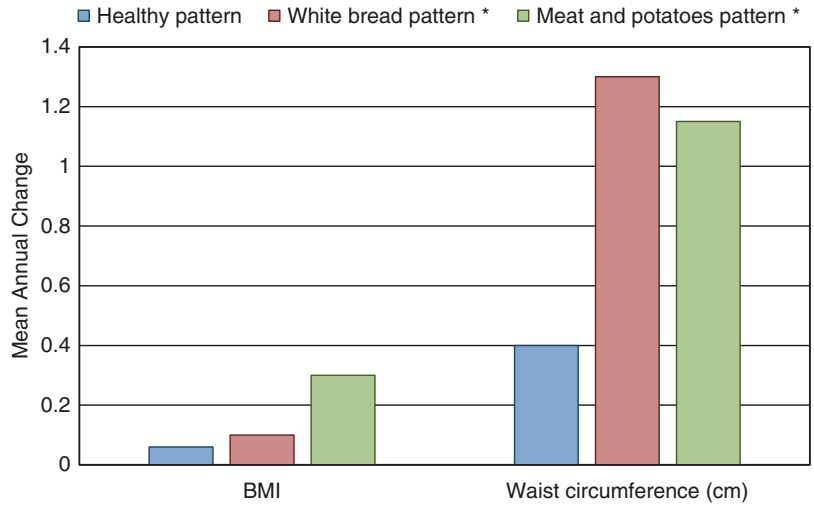

Fig. 9.7 Effect of healthy vs. Western-type derived food dietary pattern on BMI and waist circumference in men and women from the Baltimore Longitudinal Aging Study (*$p < 0.05$) [70]. *Healthy pattern*: contained relatively greater contributions from "healthy" foods, including fruit, high-fiber cereal, and reduced fat dairy, and relatively smaller contributions from fast food, nondiet soda, and salty snacks. *White bread pattern*: higher levels of refined carbohydrates and baked goods. *Meat and potatoes pattern*: higher levels of meats and higher-energy dense vegetables such as potato products

mean age about 60 years; healthy diet (27 g fiber/day; high in fruit, vegetables, and whole grains and low in red meat, fast foods, and sugary soda) vs. other types of Western diets (≥20 g/fiber/day) observed significantly less annual BMI and WC gain for the healthy vs. Western diet clusters (Fig. 9.7) [70].

Mediterranean Dietary Pattern (MedDiet)

Of the healthy dietary patterns, the MedDiet was the most studied for weight control. Higher adherence to the MedDiet was consistently shown to be inversely associated with weight gain or risk of general or central obesity in both men and women [71–77]. Several Spanish EPIC studies show that higher adherence to the MedDiet significantly reduced risk of obesity by 10–30% with mean weight reduction by 0.16 kg over 3.3–5.0 years [75, 77]. A similar association between adherence to the MedDiet and weight change was observed in men and women, but the protective effect against weight gain was stronger in younger people (<40 y of age) and in nonobese (BMI <30) individuals at baseline (p-interactions <0.0001). A 2010 Spanish university study (10,376 men and women; mean baseline age 38 years; 5.7-year follow-up) found that those subjects with the lowest MedDiet adherence had an average 0.3 kg annual weight gain, whereas those with highest MedDiet adherence lost 0.06 kg/year and had 24% lower risk of gaining ≥5 kg over the first 4 years of follow-up [74]. Another Spanish study (3,058 subjects; 51% women; mean baseline age 49 years; 10-year follow-up) found that high adherence to the MedDiet lowered WC by 1.5 cm ($p = 0.024$; fully adjusted models) [72].

Dietary Approaches to Stop Hypertension (DASH) Dietary Pattern

Two studies indicate that the high adherence to the DASH diets helps to prevent weight gain in adolescent girls and women (Table 9.5) [78, 79]. A 2014 cross-sectional study (293 female nurses; >30 years) showed that women with increased adherence to the DASH diet were 71% less likely to

have general obesity and had a marginally significant trend toward a lower prevalence of central obesity as measured by WC by 63% ($p = 0.09$) [78]. A 2011 US cohort study in adolescent girls (2,327 girls; annual visits starting at age 9 years; 10-year follow-up) found that higher adherence to the DASH eating pattern was associated with a significantly lower BMI by 1.9 units [79].

Vegetarian Dietary Pattern

High adherence to a vegetarian diet is generally shown to reduce BMI and risk of obesity [80, 81]. The Adventist Health Study-2 prospective study (60,903 subjects; mean age 58 years; 60% female 5 year-follow-up) found that the degree of vegetarian diet strictness was inversely associated with BMI with vegans having a 5-unit lower BMI than nonvegetarians [80]. A literature review analysis showed that 29 of 40 observational studies reported that a vegetarian diet significantly reduced BMI or body weight by 3–20% compared with nonvegetarians diets [81]. Also, the incidence of obesity ranged from 0 to 6% in vegetarians and from about 5 to 45% in nonvegetarians.

Randomized Controlled Trials (RCTs)

Table 9.6 summarizes RCTs on the effects of healthy dietary pattern including the MedDiet, DASH, and Nordic and vegetarian diets on weight and body composition [82–96].

Table 9.6 Summary of randomized controlled trials (RCTs) on dietary patterns in body weight and composition regulation

Objective	Study details	Results
Mediterranean diet (MedDiet)		
Systematic reviews and meta-analyses		
Mancini et al. Systematic review of the effect of the MedDiet on weight loss and waist circumference (WC) [82]	5 RCTs, 998 subjects; trials compared the MedDiet ($n = 492$) to low-fat diet ($n = 312$), a low-carbohydrate diet ($n = 109$), and the American Diabetes Association (ADA) diet ($n = 85$); ≥12 months (12–48 months)	The MedDiet resulted in greater weight loss than a low-fat diet (mean changes, −4.1 to −10.1 kg vs. 2.9 to −5.0 kg), but produced similar weight loss as low carbohydrate or ADA diets (mean values, −4.1 to −10.1 kg vs. −4.7 to −7.7 kg). Also, the MedDiet lowered BMI vs. the other diets (mean changes, −1.0 to −3.3 kg/m^2 vs. 1.4 to −1.8 kg/m^2) and WC vs. low-fat diets (mean values, −3.5 to −9.3 cm vs. 2.6 to −3.5 cm)
Huo et al. Meta-analysis of the effects of MedDiets on glycemic control, weight loss, and cardiovascular risk factors in type 2 diabetes patients [83]	9 RCTs; 1,178 subjects; age range at baseline 26–77 years; 4 weeks to 4 years	Compared with control diets, those on the MedDiet had greater reductions in BMI (mean difference −0.29), body weight (−0.29 kg), hemoglobin A1c (−0.30), fasting plasma glucose (−0.72 mmol/L), fasting insulin (−0.55 μU/mL), total cholesterol (−0.14 mmol/L), triglycerides (−0.29 mmol/L), and both systolic and diastolic BP (−1.4 mm Hg). Also, HDL-C was increased (0.06 mmol/L). MedDiet improves outcomes of body weight, glycemic control, and cardiovascular risk factors in diabetic patients

Table 9.6 (continued)

Objective	Study details	Results
Esposito et al. Evaluate the effect of MedDiets on body weight using meta-analysis [84]	16 RCTs; 3,436 participants (1,848 MedDiet/1,588 control diets); mean age 35–69 years and BMI 26–35; 1 month to 2-year duration	MedDiets can be effective in lowering body weight, especially with energy restriction, increased physical activity, and >6 months in duration. Overall, the MedDiet significantly reduced weight by 1.75 kg and BMI by 0.57 units. In studies lasting longer than 6 months, mean weight loss was 3.9 kg. Also, MedDiet accompanied with either a restricted energy diet or increased physical activity reduced weight by approximately 4 kg
Kastorini et al. Meta-analysis of the effect of a MedDiet on metabolic syndrome and its components [85]	50 original research studies (35 RCTs, two prospective and 13 cross-sectional studies) through April 30, 2010; 534,906 participants	Adherence to the MedDiet was associated with significantly reduced metabolic syndrome prevalence by 31%, WC by 0.42 cm, triglycerides by 6.1 mg/dL, systolic blood pressure (BP) by 2.4 mm Hg, diastolic BP by 1.6 mm Hg and fasting glucose by 3.9 mg/dL, and increased HDL-C by 1.2 mg/dL
Specific RCTs		
Estruch et al. Assess the long-term effects of ad libitum, high-fat, high-vegetable-fat MedDiets on bodyweight and WC in older people at risk of cardiovascular disease, most of whom were overweight or obese (parallel primary care multicenter RCT PREDIMED; Spain) [86]	7,447 adults with type 2 diabetes or ≤3 CV risk factors; mean age 67 years and BMI 30; three different ad libitum diets: MedDiet plus extra-virgin olive oil; MedDiet plus tree nuts (total dietary fat approx. 100 g/day for both or advice for reduced fat control diet) (96 g fat/day) (advice to restrict dietary energy or promote physical activity was not advised); measured body weight and WC at baseline and annually for 5 years; intention to treat	This study showed that the long-term intake of plant-based, unrestricted-calorie, high-fat diets, such as the traditional MedDiet, does not promote weight gain. The adjusted difference in 5-year loss in body weight in the MedDiet plus extra-virgin olive oil group was 0.43 kg ($p = 0.044$) and in the plus nut group was 0.08 kg ($p = 0.730$), compared with the reduced fat control group. The adjusted difference in 5-year reduction in WC was 0.55 cm ($p = 0.048$) in the MedDiet with extra-virgin olive oil group and 0.94 cm ($p = 0.006$) in the nut group, compared with the reduced fat control group (Fig. 9.8)
Alvarez-Perez et al. Assess effect of the MedDiet pattern on anthropometric and body composition parameters (PREDIMED trial; Spain) [87]	351 free-living subjects, mean age 67 years and BMI 31; 64% women; with type 2 diabetes or ≤3 CV risk factors; three different ad libitum diets: MedDiet plus extra-virgin olive oil, MedDiet plus mixed tree nuts, or a control reduced-fat diet; changes in anthropometric measures of body weight, BMI, WC, total body fat %; 1 year	This study found that unrestricted MedDiets that contain approximately 40% total fat can be alternative options to reduced-fat diets for weight maintenance. Significant reductions in body weight by 1 kg, BMI by 0.5 units and WC by 1.1 ($p < 0.05$; all) were observed for the MedDiet plus extra-virgin olive oil vs. the control group. The MedDiet plus nuts group exhibited a significant reduction in WC by 2.3 cm ($p < 0.001$). The control group showed a significant increase in total body fat by 1% ($p = 0.02$)
Damasceno et al. Investigate effect of MedDiets on changes in adiposity and lipoprotein subfractions vs. reduced fat control diet (PREDIMED trial; Spain) [88]	169 subjects with type 2 diabetes or ≤3 CV risk factors; mean age 67 years; 75% women; BMI 29.5; lipoprotein subclasses (particle concentrations and size) were determined by NMR spectroscopy; three different ad libitum diets: MedDiet plus extra-virgin olive oil, MedDiet plus mixed tree nuts (30 g walnuts, almonds, and hazelnuts/day), or a control reduced-fat diet; 1 year	Compared to the MedDiet-extra-virgin olive oil and reduced-fat control, participants in the tree nut-enriched MedDiet showed significantly reduced WC by 5 cm ($p = 0.006$) and increased LDL size with a net increase by 0.2 nmol/L ($p < 0.05$). Also, there were increased large HDL concentrations in both the olive oil- and nut-supplemented MedDiets

(continued)

Table 9.6 (continued)

Objective	Study details	Results
Shai et al. Compare the effectiveness of weight-loss diets (parallel RCT; USA) [89]	322 moderately obese subjects; mean age 52 years; mean BMI 31; males 86%; three restricted-calorie diets: low fat, MedDiet, or low carbohydrate; 2 years	Compared to other diet groups, the MedDiet group consumed the largest amounts of dietary fiber, and the low-carbohydrate group consumed the smallest amount of carbohydrates and the largest amounts of fat, protein, and cholesterol ($p < 0.05$ for all). The mean weight loss was 4.4 kg for the MedDiet group, 4.7 kg for the low-carbohydrate group, and 2.9 kg for the low-fat group ($p < 0.001$) (Fig. 9.9). The MedDiet and low-carbohydrate diets appear to be effective alternatives to low-fat diets for weight loss with more favorable effects on glycemic control with the MedDiet and on lipids with the low-carbohydrate diet. The rate of adherence to these diets was 95% at 1 year and 85% at 2 years
Esposito et al. Assess the effect of a MedDiet on weight and cardiometabolic markers associated with metabolic syndrome (parallel RCT; Italy) [90]	180 metabolic syndrome patients (99 men and 81 women); two diets: MedDiet advice about how to increase daily consumption of whole grains, fruits, vegetables, nuts, and olive oil (32 g fiber/day); control group followed a prudent diet (carbohydrates, 50–60%; proteins, 15–20%; total fat, 30%; 17 g fiber/day); 2 years	Compared to the control diet, the MedDiet had a significantly greater mean decrease in body weight by 11 kg and BMI by 4.2 units ($p < 0.001$) (Fig. 9.10). Also, compared to the control group, the MedDiet group had significantly reduced serum concentrations of hs-CRP ($p = 0.01$), insulin resistance ($p < 0.001$), and 50% fewer patients with metabolic syndrome ($p < 0.001$)
Esposito et al. Determine the effect of energy restricted MedDiet and physical activity on body weight, systemic inflammation, and insulin resistance (parallel RCT; Italy) [91]	120 premenopausal women; mean age 35 years and BMI 35; intervention group received detailed advice to reduce weight by ≥10% with reduced energy MedDiet and increase physical activity vs. control group given general info on healthy food choice and exercise; 2 years	The intervention group consumed 9 g fiber/day more and 310 kcal less than the usual diet control group ($p < 0.001$). Changes in body weight and BMI are shown in Fig. 9.11 . The intervention was also associated with reduction in CRP by 0.8 mg/L and HOMA-insulin resistance by 0.9 unit vs. control ($p = 0.008$; both)
DASH diet		
Systematic review and meta-analysis		
Soltani et al. Assess the effect of the DASH dietary pattern on body weight and composition in adults [92]	13 RCTs; 1,291 overweight and obese subjects; 8–52 weeks	Compared with the Western diet, subjects on the DASH diet lost more weight by 1.42 kg in 8–24 weeks, BMI by 0.42 units in 8–52 weeks and WC by 1.05 cm in 24 weeks. Lower caloric DASH led to more weight reduction when compared with other low-energy diets
Nordic diets		
Nordic weight loss diet for lactating women		
Bertz et al. Assess the effect of energy restricted diet on weight loss among overweight/obese lactating women (Lifestyle Weight Loss During Lactation Trial; Sweden) [93, 94]	68 women; prepregnancy BMI 25–35; mean age 33 years and BMI 30; intervention weight loss diet based on Nordic Nutrition Recommendation: restrict energy intake by 500 kcal, limit sweets and snacks to 100/week, substitute lower fat and sugar alternative for usual foods, cover ½ the lunch and dinner plate with vegetables, and reduce portion size vs. usual diet; 12-week duration plus 9-month follow-up	This dietary treatment was sufficient to significantly and clinically meaningfully promote weight, BMI, and total fat loss in lactating women and to sustain weight loss at 9-month follow-up after the intervention ended. Intervention diet lowered energy by approx 400–500 kcal and increased fiber by 3 g/1000 kcal. Changes in body weight are shown in Fig. 9.12. BMI was reduced by ≥3 units and total body fat was reduced by 5.5–6.7 kg ($p < 0.001$)

Table 9.6 (continued)

Objective	Study details	Results
New Nordic Diet		
Paulsen et al. Evaluate health effects of the New Nordic Diet (NND), developed in the Nordic countries in collaboration with Copenhagen's gourmet restaurant NOMA. The NND is based on regional foods in season, with a strong emphasis on palatability, healthiness, and sustainability, while aligning with regional food culture and dietary preferences (parallel RCT; Denmark) [95]	181 centrally obese men and women; 71% women; mean age of 42 years (20–66 years) and BMI 30.2 and waist circumference (WC) 100 cm (39 in.); received either the NND (high in fruit, vegetables, dairy products, whole grains, and fish and low in sugar, cakes, pastries, and biscuits) or an average Danish diet (ADD); NND diet contained 19 g/day more total fiber and 21 kcal (87.5 kJ) less energy/100 g than ADD; 26 weeks	Free-living intake of the NND reduced mean body weight by 3.2 kg (Fig. 9.13) and mean WC by 2.9 cm ($p < 0.001$; both) compared to the ADD. Also, the NND produced greater reductions in systolic blood pressure by 5.1 mm HG compared to the ADD ($p < 0.001$). The weight loss was shown despite the fact that the diet was developed as highly palatable and offered ad libitum, and the study was not specifically designed as a weight-loss study
Vegetarian diet		
Systematic review and meta-analysis		
Huang et al. Investigate the effects of lacto-ovo vegetarian and vegan diets on weight reduction [96]	12 RCTs; 1,151 subjects; median duration of 18 weeks	Overall, individuals assigned to the vegetarian diet groups lost significantly 2 kg more weight than those assigned to the nonvegetarian diet groups. Subgroup analysis detected significant weight reduction in subjects consuming a vegan diet by 2.5 kg and, to a lesser extent, in those given lacto-ovo vegetarian diets by 1.5 kg. Trials on subjects consuming vegetarian diets with energy restriction revealed a significantly greater weight reduction of 2.2 kg than those without energy restriction of 1.7 kg
		The weight loss for subjects with follow-up of <1 year was greater than those with follow-up of ≥1 year (−2.05 kg vs. −1.13 kg)
Barnard et al. Estimate the effect of vegetarian diets on body weight [97]	15 RCTs; 755 participants (197 lacto-ovo vegetarians and 558 vegans); ≥4 weeks without energy intake limitations	Vegetarian diets were associated with a mean weight loss by 3.4 kg ($p < 0.001$) in an intention-to-treat analysis vs. control diet. Greater weight loss was shown in studies with higher baseline weights, smaller proportions of female participants, older participants, or longer durations, and in studies in which weight loss was a goal
Specific comparative RCT of different types of vegetarian diets		
Turner-McGrievy et al. Determine the effect of plant-based diets on weight loss (parallel RCT; USA) [98]	63 overweight and obese adults; 19% nonwhite; 27% men; mean baseline age 48 years and BMI 35; randomized into five arms: a low-fat, low-glycemic index diet: vegan, vegetarian, pesco-vegetarian, semi-vegetarian, or omnivorous; 6 months	After 6 months, weight was significantly reduced in the vegan group by 7.5% and ovo-lacto vegetarian by 6.3% compared to the omnivorous, semi-vegetarian, and pesco-vegetarian groups by approximately 3% ($p = 0.03$) (Fig. 9.14). Vegan diets may result in greater weight loss than more modest recommendations

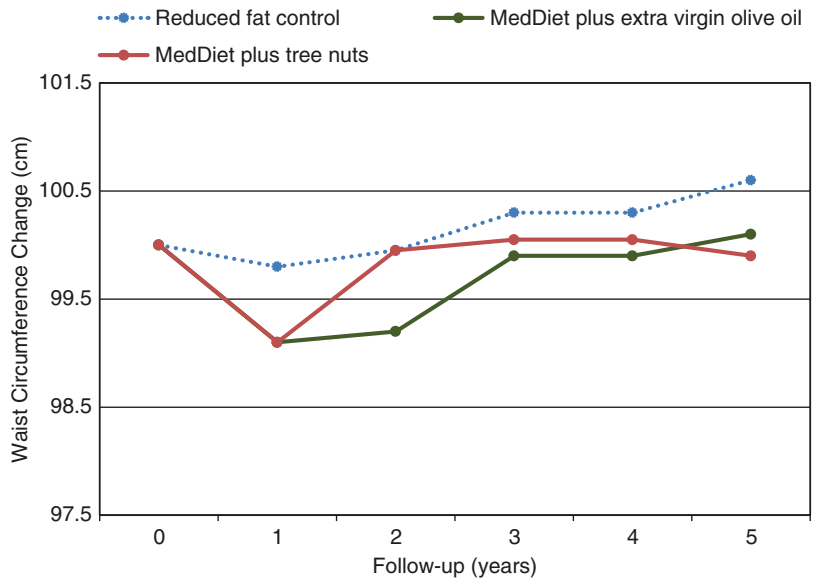

Fig. 9.8 Effect of unrestricted MedDiets and reduced fat control diet on mean waist circumference from the PREDIMED trial over 5 years (multivariate adjusted values) [86]

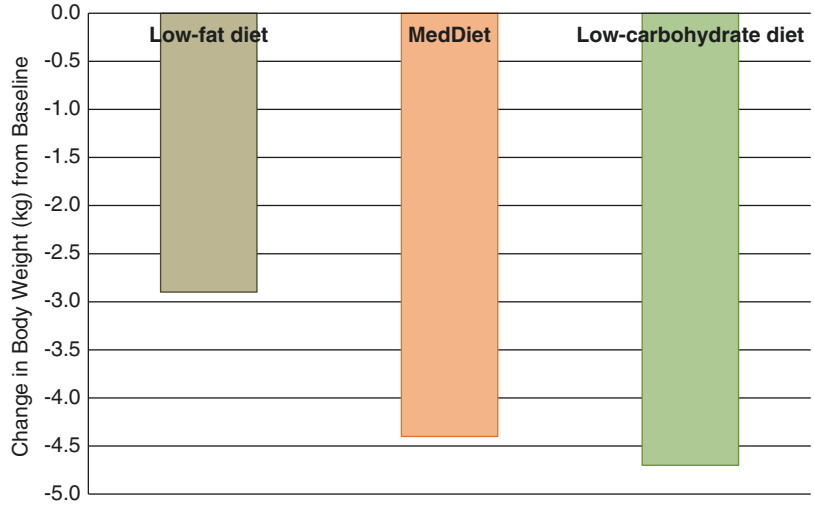

Fig. 9.9 Effect of the non-energy restricted Mediterranean diet (MedDiet) vs. low-fat and low-carbohydrate non-energy restricted diets in 322 obese adults (about 90% men) over 2 years ($p < 0.001$ for all) [89]

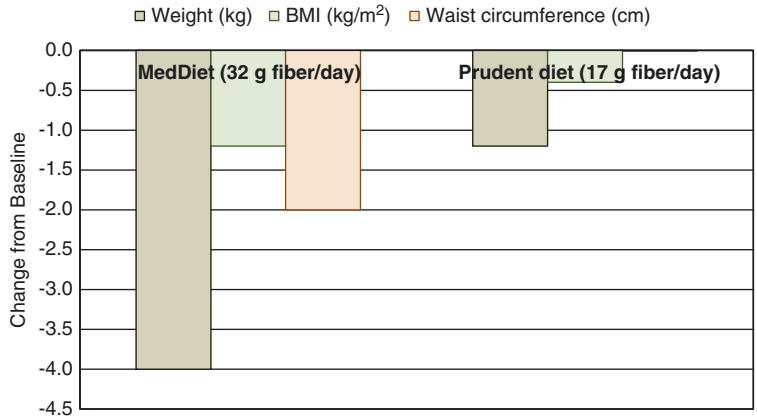

Fig. 9.10 Effect of a high fiber MedDiet compared to a moderate fiber prudent diet in 180 adults with metabolic syndrome over 2 years ($p < 0.001$; all) [90]

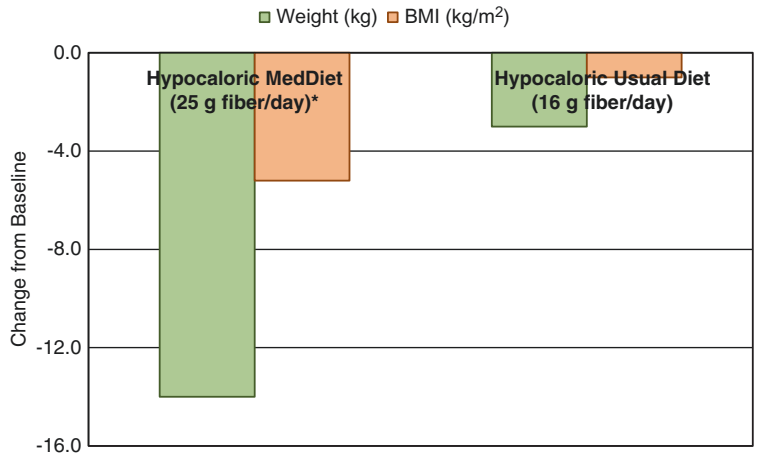

Fig. 9.11 Effect of a hypocaloric Mediterranean diet (MedDiet) vs. hypocaloric usual diet on body weight and BMI in 120 obese women over 2 years ($p < 0.001$ for both) [91]

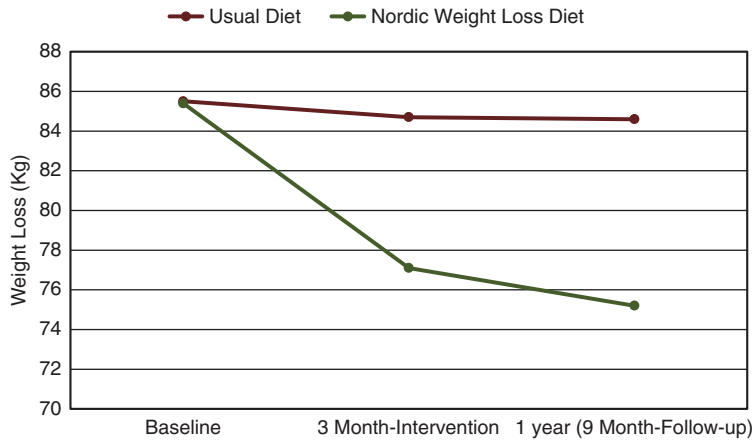

Fig. 9.12 Effects of Nordic energy-restricted and higher-fiber diet intervention on body weight in lactating overweight and obese women ($p < 0.001$) [93, 94]

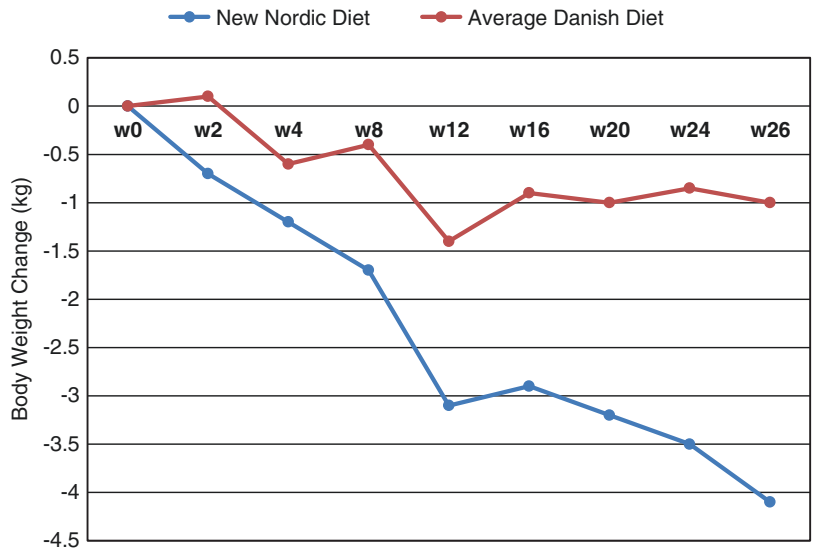

Fig. 9.13 Change in body weight (intention-to-treat) for the New Nordic Diet compared to the average Danish diet over 26 weeks ($p < 0.001$) [95]

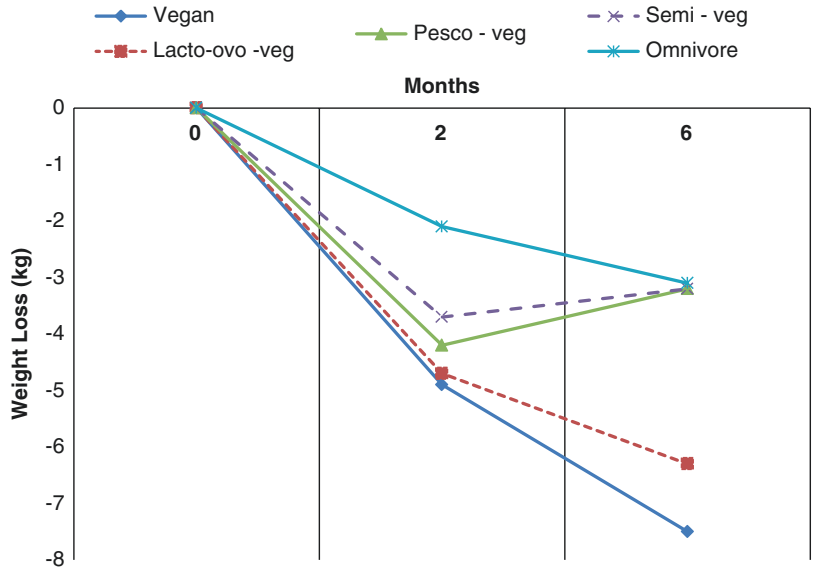

Fig. 9.14 Effect of type of vegetarian (veg) diets on weight loss in adults after 6 months (p-trend = 0.01 for vegan and lacto-ovo vegetarian diets) [98]

Mediterranean Diet (MedDiet)

Systematic Reviews and Meta-analyses

Four systematic reviews and meta-analyses of RCTs consistently show that ad libitum intake of MedDiets does not result in weight gain and high adherence to MedDiets supports weight loss and lowers WC compared to control diets such as low-fat and Western diets especially in overweight, obese, or type 2 diabetic individuals, intrials of longer duration (>6 months), or in conjunction with restricted energy diets or increased physical activity [82–85]. A meta-analysis (16 RCTs; 3,436 participants; 1 month to 2 years) found a significant mean reduction in weight with the MedDiet by 1.75 kg and BMI by 0.6 kg/m^2 compared to the control diet [84]. The effect of the MedDiet on weight loss was further improved with an energy restricted diet (−3.9 kg), with increased physical activity by −4.0 kg, or with trial durations >6 months by −2.7 kg. This analysis, also, showed that unrestricted intake of MedDiets does not promote weight gain, which helps to alleviate concerns about the MedDiet's liberal use of olive oils effect on weight control. A meta-analysis of long-term MedDiet intake (5 RCTs; 998 subjects; comparator diets low fat, low carbohydrate, and American Diabetes Association (ADA); ≥12 months) showed MedDiets resulted in greater weight loss, BMI and WC reductions than a low-fat diet, but produced similar weight loss as low carbohydrate or ADA diets [82]. A meta-analysis in people with type 2 diabetes (9 RCTs; 1,178 adults; age 26–77 years; 1 month to 4 years) found a small but significant mean loss of weight by 0.3 kg and BMI by 0.3 kg/m^2 compared to control diets along with significant improvements in glycemic control and reductions in cardiovascular disease risk factors [83]. A meta-analysis of metabolic syndrome subjects (35 RCTs and two cohort and 13 cross-sectional studies; 534,906 subjects) demonstrated that the MedDiet significantly reduced WC, blood pressure, fasting blood glucose and the prevalence of metabolic syndrome, and increased HDL-C [85].

Specific RCTs

Six RCTs describe various aspects of the effect of MedDiets, including the importance of adequate fiber intake, on reducing and managing body weight and composition [86–91]. Three Spanish PREDIMED trials show impressive long-term effects of the MedDiet on maintaining and moderately lowering body weight and WC [86–88]. The PREDIMED trial (7,447 subjects with type 2 diabetes or high cardiovascular risk; mean baseline age 67 years and BMI 30; MedDiet plus extra virgin olive oil or tree nuts and reduced-fat control diet; 5-year duration) showed in a long-term intervention that the unrestricted MedDiets are not associated with weight gain [86]. MedDiet plus extra virgin olive oil significantly reduced mean body weight by 0.43 kg compared to the reduced fat control diet. Both MedDiets showed lower WC vs. the control diet after 5 years (Fig. 9.8). Two sub-cohort PREDIMED trials found that (1) the tree nut-enriched MedDiet (169 subjects with type 2 diabetes or ≤3 CV risk factors; mean baseline age 67 years and BMI 29.5; 75% women; 1 year) significantly reduced WC by 5 cm and increased LDL size by 0.2 nmol/L compared to the MedDiet-extra virgin olive oil, and the lower-fat control diet [88] and (2) MedDiets (351 free-living subjects with type 2 diabetes or ≤3 CV risk factors, mean age 67 years and BMI 31; 64% women; 1 year)

significantly lowered body weight, BMI, and WC compared to the lower fat control diet [87]. A US parallel RCT of unrestricted energy diets (322 obese subjects; 86% men; mean baseline age 52 years and BMI 31; 2 years) found that the MedDiet, reduced body weight by 4.4 kg, which was as effective as low-fat or low-carbohydrate diets in promoting significant weight loss over 2 years ($p < 0.001$) (Fig. 9.9) [89]. Two long-term Italian trials also showed significant benefits for fiber-rich diets in body weight and composition regulation body [90, 91]. In 180 adults with metabolic syndrome, consuming an ad libitum 32 g fiber/day MedDiet (including about 500 g of whole grains, vegetables, fruit, legumes, and nuts) compared to a 17 g fiber/day prudent diet (including about 200 g of whole grains, vegetables, fruit, legumes, and nuts) found significantly lower body weight, BMI, and WC after 2 years (Fig. 9.10) [90]. In 120 premenopausal women, an energy-restricted MedDiet (25 g fiber/day) significantly lowered body weight and BMI compared to an energy-restricted usual diet (16 g fiber/day) after 2 years (Fig. 9.11) [91].

Other Diets

DASH Diet

A meta-analysis (13 RCTs; 1,291 overweight or obese subjects; 8–52 weeks) showed that the DASH diet significantly reduced weight by 1.42 kg and BMI by 0.42 kg m^2 in 8–24 weeks and WC by 1 cm in 24 weeks compared with Western or usual diet controls [92].

Nordic Diets

Nordic Weight Loss Diet for Lactating Women. Childbearing is associated with weight gain because of gestational weight gain and postpartum weight retention, which can exacerbate prepregnancy weight and associated conditions [93, 94]. The Swedish Lifestyle Weight Loss During Lactation Trial (68 women; prepregnancy BMI 25–35; mean age 33 years and BMI 30; intervention weight loss diet based on Nordic Nutrition Recommendation vs. usual diet; 12 weeks duration plus 9-month follow-up) found significant and clinically meaningful weight, BMI, and total fat loss in lactating women and sustained weight loss at 9-month follow-up after the intervention ended compared to the usual diet [93, 94]. The primary guidelines for this Nordic diet are to target restricted energy intake by 500 kcal, limit sweets and snacks to 100 kcals/week, substitute lower fat and sugar alternatives for usual foods, cover half of the lunch and dinner plate with vegetables, and reduce portion size which reduces energy intake by approx 400–500 kcal and increases fiber by 3 g/1000 kcal compared to the usual diet. Changes in body weight are shown in Fig. 9.12. BMI was reduced by ≥3 units and total fat was reduced by 5.5–6.7 kg ($p < 0.001$).

New Nordic Diet (NND). This food-based dietary concept was developed in the Nordic countries in collaboration with the world-leading Copenhagen gourmet restaurant, NOMA [95]. This diet is based on regional foods in season, with a strong emphasis on palatability, healthiness, and

sustainability, which are aligned with regional food culture and dietary habits. The basic food components of the NND include fruit and vegetables (especially berries, cabbages, root vegetables, and legumes), potatoes, fresh herbs, mushrooms, nuts, whole grain, meats from livestock and game, fish and shellfish, and seaweed, which provide 19 g fiber/day more than the average Danish diet. A Danish trial (181 adults; 71% women; mean age 42 years and BMI 30; 26-week duration) found that the unrestricted NND significantly reduced body weight (Fig. 9.13) and WC by 2.9 cm compared to the average Danish diet [95].

Vegetarian Diets

Two meta-analyses of vegetarian diets show that all vegetarian diets protect against weight gain [96, 97]. A 2016 systematic review and meta-analysis (12 RCTs; 1,151 subjects; 18-week mean duration) found that individuals on vegetarian diets lost significantly 2 kg more weight than those assigned to the nonvegetarian diets [97]. Subgroup analysis detected significant weight reduction in subjects consuming a vegan diet by 2.5 kg and, to a lesser extent, in those given lacto-ovo vegetarian diets by 1.5 kg. Trials on subjects consuming energy restricted vegetarian diets found a significantly greater weight reduction by 2.2 kg than those without energy restriction by 1.7 kg. The weight loss for subjects with follow-up of <1 year was greater than those with follow-up of ≥1 year (−2.05 kg vs. −1.13 kg). A 2015 meta-analysis (15 RCTs; 755 adults; 197 lacto-ovo vegetarians and 558 vegans; 75% females; no energy restricted diets; ≥4 weeks) showed that combined lacto-ovo vegetarian and vegan diets significantly reduced weight by 3.4 kg, despite the absence of specific guidance on energy intake or exercise [97]. Greater weight loss was found in studies with higher baseline weights, older participants, or longer durations. A five-arm plant-based weight loss RCT (63 subjects; mean age 48 years; mean BMI 35; 73% female; vegetarian vs. omnivorous diets; 6 months) reported that vegan and lacto-ovo vegetarian diets have similar greater effects on weight loss compared to omnivorous and semi- and pesco-vegetarian diets (Fig. 9.14) [98].

Fiber Biological Mechanisms

Postulated biological mechanisms associated with adequate fiber intake (>25 g/day) and healthy dietary patterns for the prevention of weight gain and the promotion of reduction in body weight, WC, body and visceral fat are summarized in Fig. 9.15 [99–128].

Adequate Fiber Intake

Energy Density:
Lowers energy density; fiber (2 kcals/g) vs refined carbohydrates (4 kcals/g)

Post-prandial Satiety Signaling:
Increases food volume, bulk, or viscosity
Prolongs chewing time to slow eating rate
Slows gastric emptying and reduces hunger

Circulatory System:
Attenuates blood glucose, insulin and C-reactive protein
Promotes insulin sensitivity
Promotes satiety hormones such as cholecystokinin (CCK), glucagon-like peptide-1(GLP-1) and peptide YY

Colon Fermentation and Microbiotia:
Fosters healthier, colonic microbiota and colon short chain fatty acids levels to promote satiety and leaner energy metabolism

Net Metabolizable Energy:
Higher macronutrient fecal excretion (e.g. dietary fat) for lower net metabolizable energy

Lowers Risk of Weight Gain and Obesity
Reduces Risk of Abdominal and Visceral Fat
Promotes Weight Loss

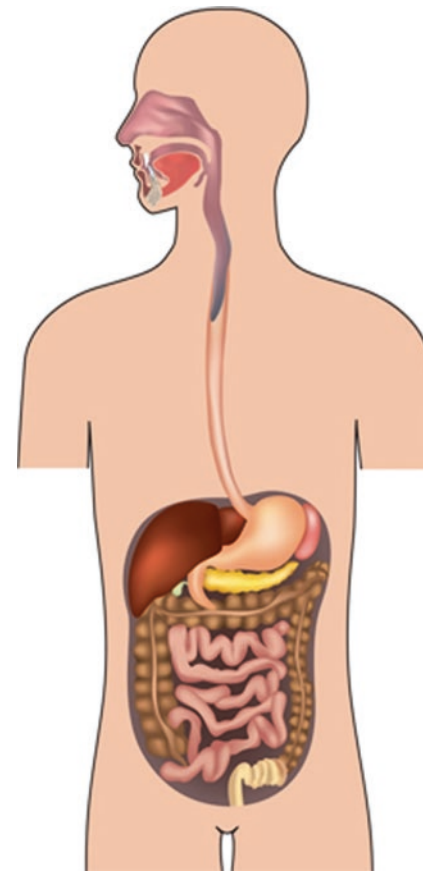

Fig. 9.15 Fiber and healthy dietary pattern mechanisms associated with body weight and abdominal fat regulation [99–128]

Energy Density

Lower-energy dense fiber-rich diets, as replacements for higher-energy dense diets, help to promote balanced energy intake to prevent weight gain or negative energy intake to help promote weight loss depending on the level of dietary fiber intake [8, 33, 42, 43, 49, 50, 97]. This is because (1) fiber is considered to be 2 kcal/g or less as compared to 4 kcal/g for digestible carbohydrates such as sugar and starch as fiber is not digested in the small bowel and (2) lower-energy dense fiber-rich foods displace higher density foods [99–102]. Fiber's lower energy content results from fiber being fermented by colonic bacteria to varying degrees into SCFAs and gases (carbon dioxide, hydrogen, and methane) and/or excreted in the stool [99–104].

Eating and Digestion Rates

Fiber-rich meals tend to be more mouth filling and harder to swallow because of their higher bulk, physical density, volume, or viscosity compared with energy-matched, low-fiber meals, and more rapidly reduce hunger after ingestion [99, 104]. Fiber-rich foods or clinically proven fiber supplements, especially with bulky, viscous soluble fibers, increase intraluminal concentration or viscosity,

slow gastric emptying, and create a mechanical barrier to enzymatic digestion of macronutrients such as starch in the small intestine.

Postprandial Satiety Signaling

Increased fiber intake has been shown to trigger a number of hormonal satiety inducing activities [108, 109]. High-fiber meals or β-glucan and psyllium supplements compared to energy-matched low-fiber control diets can (1) decrease plasma ghrelin, a stomach hunger promoting hormone, and slow the rate of postprandial increases in glucose and insulin blood levels to prevent reactive hypoglycemia known to promote hunger [99, 104–109]; (2) trigger the increased secretion of the hormone cholecystokinin (CCK), a brain neuropeptide known to decrease food intake, from the proximal small intestine to slow gastric emptying and increase satiety [105, 110, 111]; and/or (3) delay the absorption of nutrients long enough to deliver a portion of them to the distal ileum, where they are not normally present, to stimulate the release of a cascade of metabolic responses called the "ileal brake" phenomenon including the release of satiety hormones glucagon-like peptide-1 (GLP-1), known to control appetite, which slows gastric emptying and small bowel transit, decreases glucagon secretion, increases pancreatic β-cell growth, and improves insulin sensitivity [112, 113] and peptide YY (PYY), known to reduce appetite by further slowing gastric emptying [105]. Systematic reviews indicate a high degree of variability in the effectiveness of different fiber sources to promote satiety and reduce energy intake [114, 115].

Colonic Effects

Microbiota

Fiber intake affects the colonic microbiota ecosystem which may be a factor in influencing the lean and obese human phenotypes related to the effects of healthy fiber-rich dietary patterns vs. low-fiber Western-style diets [116, 117]. One randomized trial found that the consumption of 21 g polydextrose or soluble corn fiber in the form of three cereal bars/day for 3 weeks changed the gut microbiota of overweight subjects by shifting the colonic *Bacteroidetes* to *Firmicutes* ratio to one that was more typical of lean individuals, independent of caloric restriction [117].

Metabolizable Energy

Compared to low-fiber foods, fiber-rich foods tend to decrease the efficiency of macronutrient bioavailability, especially that of dietary fat, leading to higher fecal macronutrient excretion [116]. The consumption of >25 g fiber/day can lead to the excretion of 3–4% of macronutrient energy in the feces, which is equivalent to 80 kcal in a 2000-kcal diet [119–121].

Satiety and Energy Metabolism

SCFAs are involved in the crosstalk existing between microbes and human appetite and energy regulation [122–128]. Fiber fermentation produces SCFAs of which 95% consist of acetate, propionate, and butyrate in a molar ratio of 60:20:20. It has been estimated that as much as 70% of the fiber from mixed diets is fermentable depending on physical properties [104, 105]. SCFAs

can contribute to energy homeostasis and satiety by affecting multiple cellular metabolic pathways and receptor-mediated mechanisms [122–126]. Butyrate reduces systemic inflammation, improves insulin sensitivity, and possibly increases energy expenditure [127]. In obese subjects, propionate appears to increase the release of postprandial plasma PYY and GLP-1 from colonic cells to help control energy intake. In cultured human colonic cells, propionate was shown to stimulate the release of GLP-1 and PYY along with reducing energy intake [128]. A 24-week study indicated that colonic generated propionate entering the circulatory system helped to reduce body weight gain and significantly reduce intra-abdominal fat accretion and intrahepatocellular lipid content in overweight adults with nonalcoholic fatty liver disease [128].

Conclusions

Overweight and obesity are complex multifactorial conditions leading to chronic positive energy balance, primarily related to excessive calorie intake and low energy expenditure, but genetic, environmental, and emotional factors also play a role. During the last several decades, there has been an increased exposure to higher energy-dense and lower fiber-containing foods and increasingly sedentary lifestyles, which have led to net habitual positive energy balances and weight gain in Western populations. For overweight or obese individuals who successfully lose weight, as many as 80% typically drift back to their original weight or more because after weight loss there are an array of metabolic regulatory processes at work to promote weight regain, so it is difficult to maintain weight loss. Consequently, maintaining a healthy weight is a daily effort, but healthy fiber-rich dietary patterns can help to promote satiety and reduce overall dietary energy density to assist in weight control. Fiber intake is inversely associated with obesity risk, and populations with higher fiber diets tend to be leaner than those with low fiber diets. The human gastrointestinal and energy metabolism regulatory systems evolved on pre-agriculture high fiber diets. Prospective cohort studies suggest that increased total fiber intake by ≥12 g/day to >25 g fiber/day, especially as a replacement for refined low fiber food, can prevent weight gain by 3.5–5.5 kg each decade. RCTs show that adequate fiber intake ≥28 g fiber/day from fiber-rich diets can significantly reduce body weight and waist circumference compared to low fiber Western diets (≤20 g fiber/day). Fiber-rich diets are usually more effective at promoting weight loss than are fiber supplements. RCTs show that healthy fiber-rich dietary patterns such as the MedDiet, DASH, New Nordic, and vegetarian diets do not result in weight gain and high adherence to these diets can support weight loss and lower waist circumference compared to control diets such as low fat or Western diets in overweight or obese individuals. Biological mechanisms associated with adequate fiber intake, healthy dietary patterns, and body weight regulation include effects on lowering diet energy density directly or by displacing higher energy-dense processed foods, promoting postprandial satiety, reducing metabolizable energy, and triggering other colonic microbiota or metabolic factors.

Appendix 1. Fifty High-Fiber Foods Ranked by Amount of Fiber per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat-cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (Garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report. Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part D. Chapter 1: Food and nutrient intakes and trends. 2015; 97–8; Table D1.8

USDA National Nutrient Database for Standard Reference, Release 27. http://www.ars.usda.gov/nutrientdata. Accessed 17 February 2015

Appendix 2. Comparison of Common Dietary Patterns per 2000 kcal (Approximated Values)[a]

Components	Western dietary pattern (USA)	USDA base pattern	DASH diet pattern	Healthy Mediterranean pattern	Healthy vegetarian pattern (lacto-ovo based)	Vegan pattern
Emphasizes	Refined grains, low-fiber foods, red meats, sweets and solid fats	Vegetables, fruit, whole grain, and low-fat milk	Potassium-rich vegetables, fruits and low-fat milk products	Whole grains, vegetables, fruit, dairy products, olive oil, and moderate wine	Vegetables, fruit, whole grains, legumes, nuts, seeds, milk products, and soy foods	Plant foods: vegetables, fruits, whole grains, nuts, seeds, and soy foods
Includes	Processed meats, sugar sweetened beverages, and fast foods	Enriched grains, lean meat, fish, nuts, seeds, and vegetable oils	Whole grain, poultry, fish, nuts, and seeds	Fish, nuts, seeds, and pulses	Eggs, non-dairy milk alternatives, and vegetable oils	Non-dairy milk alternatives
Limits	Fruits and vegetables, whole grains	Solid fats and added sugars	Red meats, sweets, and sugar-sweetened beverages	Red meats, refined grains, and sweets	No red or white meats, or fish; limited sweets	No animal products
Estimated nutrients/components						
Carbohydrates (% total kcal)	51	51	55	50	54	57
Protein (% total kcal)	16	17	18	16	14	13

Appendix 2 (continued)

Components	Western dietary pattern (USA)	USDA base pattern	DASH diet pattern	Healthy Mediterranean pattern	Healthy vegetarian pattern (lacto-ovo based)	Vegan pattern
Total fat (% total kcal)	33	32	27	34	32	30
Saturated fat (% total kcal)	11	8	6	8	8	7
Unsat. fat (% total kcal)	22	25	21	24	26	25
Fiber (g)	16	31	29+	31	35+	40+
Potassium (mg)	2800	3350	4400	3350	3300	3650
Vegetable oils (g)	19	27	25	27	19–27	18–27
Solid fats (g)	31	18	–	17	21	16
Sodium (mg)	3600	1790	1100	1690	1400	1225
Added sugar (g)	79 (20 tsp)	32 (8 tsp)	12 (3 tsp)	32 (8 tsp)	32 (8 tsp)	32 (8 tsp)
Plant food groups						
Fruit (cup)	≤1.0	2.0	2.5	2.5	2.0	2.0
Vegetables (cup)	≤1.5	2.5	2.1	2.5	2.5	2.5
Whole grains (oz.)	0.6	3.0	4.0	3.0	3.0	3.0
Legumes (oz.)	–	1.5	0.5	1.5	3.0	3.0+
Nuts/seeds (oz.)	0.5	0.6	1.0	0.6	1.0	2.0
Soy products (oz.)	0.0	0.5	–	–	1.1	1.5

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report of the 2015Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Appendix E-3.7: Developing Vegetarian and Mediterranean-style Food Patterns. 2015; 1–9

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Chapter 10
Fiber-Rich Whole Plant Foods in Weight Regulation

Keywords Whole plant foods • Weight maintenance • Weight loss • Body composition • Whole grains • Fruit • Vegetables • Pulses • Nuts

Key Points

- The worldwide overweight and obesity pandemic is among the greatest public health challenges of our time with over 2 billion people now overweight or obese globally. Even a small daily positive energy balance of 50 kcals/day, by increased energy intake, lower fiber diets, and/or reduced activity, can lead to an annual weight gain of 0.4–0.9 kg/year.
- Diets rich in whole or minimally processed plant foods (whole plant foods), especially lower energy density and fiber-rich healthier varieties, are associated with a lower risk of weight, body fat, and waist circumference (WC) gain and obesity compared to energy-dense, low fiber Western diets.
- Within the whole plant foods category, specific foods have been shown to be more effective for weight control than others. Cohort studies show ≥3 daily whole-grain servings, especially with at least 10 g of cereal fiber, can significantly reduce body weight and WC compared to < one half a serving of whole grains/day. Randomized controlled trials (RCTs) show that whole grains can help reduce body fat and contribute to net daily energy negative balance by increasing metabolic rate and fecal metabolizable energy excretion.
- Prospective cohort studies indicate that whole or minimally processed fruits and vegetables, especially healthier varieties, are associated with a lower risk of weight, WC, or body fat gain and obesity, whereas higher energy-dense, lower fiber fruits and vegetables may promote weight gain.
- RCTs show that daily consumption of healthy fruits and vegetables (lower in energy density and rich in fiber), dietary pulses, and nuts do not promote weight gain and can lead to modest weight loss and increased weight loss in hypocaloric diets.
- Higher fiber whole plant foods can promote better weight management by helping to suppress appetite, improve glycemic control, reduce dietary energy density and available metabolizable energy, and promote colonic microbiota health.

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Introduction

Although overweight and obesity have affected humans throughout history they were the exception and not the norm [1]. The earliest recognition of obesity health risks and anti-obesity recommendations on diet, exercise, and lifestyle were formulated by the Greek physician Hippocrates. The overweight and obesity status of the human population largely remained an exception until the 1970s, when increasing urbanization, sedentary jobs, and the availability of processed foods produced a sharp rise in overweight and obesity in both children and adults. The worldwide overweight and obesity pandemic is among the greatest public health challenges of our time with over two billion people now overweight or obese globally [2–4]. Obesity or excessive abdominal adiposity in adulthood and childhood is a growing risk factor for major chronic diseases [5–9]. These conditions are associated with increased health-care costs and reduced workforce productivity and an estimated >300,000 premature adult deaths each year in the USA [10, 11]. A small daily positive energy balance of 50 kcal/day, by increased energy intake, lower-fiber diets, and/or reduced activity, can lead to an annual weight gain of 0.4–0.9 kg/year [12–16]. Further, a higher habitual intake of 200 kcal/day above energy balance in overweight or obese women may increase weight gain by as much as 9 kg/year [17]. People tend to eat similar amounts or volumes of food on a day-to-day basis regardless of the food energy density, so the common advice of just eating less of all foods may not be the optimal approach for weight management [18–22]. A systematic review found that higher-energy-dense, lower-fiber dietary patterns may predispose children to later increased risk of being overweight or obese as adults [23]. For overweight or obese individuals who successfully lose weight, as many as 80% typically drift back to their original weight or more [24]. This is because after weight loss there is an array of metabolic regulatory processes causing a cascade of hunger signals aimed to stimulate weight regain [25–27]. One study showed that weight-loss maintainers for ≥5 years reported consuming a diet with a significantly lower energy density (1.4 kcal/g) than the weight regain individuals (1.8 kcal/g) [28]. The primary diet difference was that the weight maintainers consumed more fiber-rich foods such as vegetables (4.9 servings/day) and whole-grain products (2.2 servings/day) compared to less than one daily serving of vegetables and whole grains for the weight regainers. Successful long-term weight-loss maintenance is associated with six key strategies to help counteract weight regain metabolic processes: (1) engaging in physical activity, (2) eating a low-energy-dense and high-fiber diet, (3) consuming breakfast, (4) self-monitoring weight on a regular basis, (5) limiting consumption of higher-energy-dense foods, and (6) catching dietary missteps before they become a habit [15, 29–31]. A 2011 prospective investigation involving three separate cohorts that included 120,877 US women and men found that specific foods are independently associated with long-term weight change, with important implications for strategies for obesity prevention (Fig. 10.1) [32]. The objective of this chapter is to review the effects of specific whole or minimally processed plant foods (whole plant foods) on weight and body composition regulation.

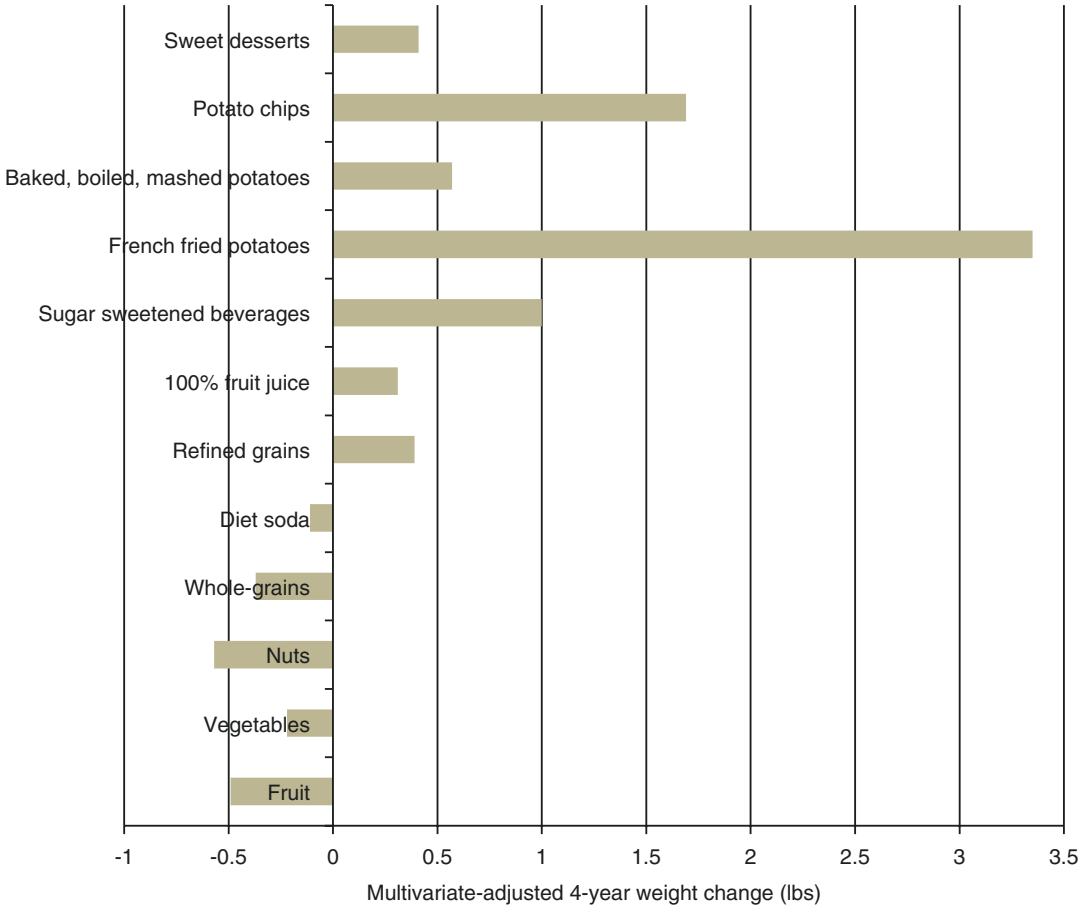

Fig. 10.1 Effect of specific 'whole or processed plant food' per daily serving on weight change from 3 large US Cohorts of 120,877 from men and women [32]

Whole Plant Foods

Although whole plant foods are more generally associated with lower energy density, reduced obesity, and chronic disease risk than highly processed plant foods [33], they vary widely in nutrient and phytochemical composition, energy density, and physical properties so specific foods vary in their effectiveness in weight regulation (Appendix 1) [34–42]. The MyPlate visual educational tool was developed to encourage Americans to increase their intake of whole and minimally processed fruits and vegetables and whole grains, which promote better weight control and other health benefits such as reduced chronic disease risk [43].

Whole-Grain Foods

Background

Whole-grain products including brown rice, oatmeal, popcorn, whole wheat, or rye bread and crackers and fiber-rich breakfast cereal contain the whole intact kernel with variable levels of fiber, vitamins, minerals, and phytochemicals [44–48] (Appendix 1). In contrast, refined-grains including white rice and white bread, pastry, donuts, and low-fiber breakfast cereals are mainly comprised of the starchy endosperm with most of the fiber, vitamins, minerals, and phytonutrients removed during processing. The US dietary guidelines recommend ≥3 servings of whole grains/day and ≤3 servings of refined grains/day to promote health and wellness associated with reduced risk of various chronic diseases [44, 49]. However, only about 1% of Americans follow the recommendation for whole-grain intake as the average American's intake is <1 ounce whole grains/day, and 70% exceed the recommended intake for refined grains [44, 49]. Substituting whole-grains for refined grains can have a favorable effect on energy-balance metrics [50]. A 2017 randomized controlled trial (RCT) (81 men and postmenopausal women; 60% men; age range 40 to 65 years; mean BMI 35; 207 g whole grains (40 g fiber/day) vs. refined grain based diet (21 g fiber/day); 6 weeks) found that the whole grain diet contributed to a 92 kcal/day high net energy loss compared to the refined grain diet. These findings support the effects of whole grains on negative energy balance by increasing metabolic rate and fecal energy excretion to help reduce adiposity.

Prospective Cohort Studies

Observational studies consistently show that higher intakes of whole grains, but not refined grains, are associated with lower BMI and/or reduced obesity risk [51]. A systematic review and five prospective cohort studies on weight and body composition are summarized in Table 10.1 [52–57]. A 2008 systematic review of cohort studies (15 studies; 119,829 participants) found that whole-grain intake resulted in a mean reduced BMI by 0.6 units, waist circumference by 2.7 cm, and waist/hip ratio by 0.023 per 3 servings/day compared to <0.5 serving/day [52]. This analysis also showed that the daily consumption of three servings of whole grains increased total fiber by 9 g/day and reduced total fat by 11 g/day in the diet. Prospective studies consistently show an inverse association between whole-grain (rich in cereal fiber) intake and body weight [53–57]. A European Prospective Investigation into Cancer and Nutrition (EPIC) study (89,432 participants; mean age 53 years; 6.5 years of follow-up), whole grains providing 10 g of daily cereal fiber significantly reduced both weight and waist circumference (WC) [53]. The Physicians' Health Study (17,881 men; mean age 53 years; 8 and 13 years of follow-up) showed an inverse association between breakfast cereal intake and weight gain with a significant 22% lower risk of ≥10 kg weight gain compared with the lowest consumers [54]. The Health Professionals Follow-Up Study (27,082 men; mean age 52 years; 8 years of follow-up) found that each daily 40 g increase in whole grains reduced weight gain by 0.5 kg with bran being approximately twice as effective as whole grain [55]. A 2003 Nurses' Health Study (74,091 women; mean age 50 years; 12 years of follow-up) showed that women consuming 2.3 daily servings of whole grains weighed 0.9 kg less than those consuming 0.7 servings, whereas women with similar refined-grain intake gained 1.2 kg [56]. In the Minneapolis Public School study (240 students; mean age 13 years; 2 years), students who consumed >1.5 whole-grain servings daily reduced BMI by 7% compared to those students consuming <0.5 servings [57].

Table 10.1 Summary of whole-grain (WG) prospective cohort studies on weight and body composition regulation

Objective	Study details	Results
Systematic review		
Harland and Garton Review evidence relating to the intake of WG and healthy body weight [52]	15 cohort studies; 119,829 primarily European and American adults	WG significantly reduced BMI by 0.6 units, waist circumference (WC) by 2.7 cm, and waist/hip ratio by 0.023 in individuals consuming 3 servings/day compared to <0.5 servings/day. Higher intake of WG led to increased fiber intake by 9 g/day and lowered total fat by 11 g/day and saturated fat by 3.9 g/day
Prospective cohort studies		
Du et al. Investigate the association of total fiber, cereal fiber, and fruit and vegetable fiber with changes in weight and WC. (European Prospective Investigation into Cancer and Nutrition [EPIC]) [53]	89,432 participants, mean age 53 years; followed for an average of 6.5 years (multivariate adjusted)	A 10 g/day higher cereal fiber intake was associated with annual mean weight reduction by 0.77 g and lower waist circumference by 0.10 cm.
Bazzano et al. Assess the association between WG and refined-grain breakfast cereal intakes and risk of overweight and weight gain (USA, the Physicians' Health Study) [54]	17,881 men; mean age 53 years; mean BMI 24; ≥1 WG servings/day vs. rarely consume; 8 and 13 year follow-ups (multivariate adjusted)	Over 8 and 13 years of follow-up, men who consumed any type of breakfast cereal consistently weighed less than those who rarely consumed breakfast cereals (p-trend = 0.01). Those who consumed ≥1 serving/day of breakfast cereals were 22% less likely after 8 years and 12% less likely after 13 years to become overweight compared with men who rarely or never consumed breakfast cereals
Koh-Banerjee et al. Ascertain the associations between changes in quantitative estimates of WG intake and 8-year weight gain among men (USA, Health Professionals Follow-Up Study) [55]	27,082 men; mean age 52 years; mean BMI 25; 27 g WG /day vs. 11 g WG /day; 8 years of follow-up (multivariate adjusted)	WG intake was significantly inversely associated with long-term weight gain. A dose-response relationship was observed that for every 40 g/day increased intake of WG foods, there was a significantly reduced weight gain of 0.5 kg. Bran that was added to the diet or obtained from fortified grain foods further reduced the risk of weight gain for every 20 g/day increase in intake by 0.36 kg.
Liu et al. Examine the associations between the intakes of dietary fiber and WG or refined-grain products and weight gain over time (USA, Nurses' Health Study) [56]	74,091 women; mean age 50 years; mean BMI 25; median intake of 2.3 WG servings/1000 kcal vs. 0.07 WG servings/1000 kcal; 12 years of follow-up (multivariate adjusted)	Women in the highest quintile of WG intake weighed 0.9 kg less than women in the lowest quintile of intake, whereas women in the highest quintile of refined-grain intake weighed 1.2 kg more than women in the lowest quintile of intake. Women in the highest quintile of fiber intake had a 49% lower risk of major weight gain than women in the lowest quintile
Steffen et al. Investigate the association between WG intake and BMI in adolescents (USA, Minneapolis Public School students study) [57]	240 students; mean age 13 years; ≥1.5 WG vs. < 0.5 WG servings/day; 2 years of follow-up (multivariate adjusted)	The students consuming higher WG had significantly lower BMI by 1 unit compared to the students with lower WG intake. Also, the students with higher WG intake had significantly greater insulin sensitivity

Randomized Controlled Trials (RCTs)

RCTs of whole-grain intake on weight and body composition are summarized in Table 10.2 [58–68]. A comprehensive meta-analysis (26 RCTs; 2,060 participants; 18–150 g whole grains; 2–16 weeks) showed that overall increased whole-grain intake had insignificant effects on body weight by 0.06 kg, waist circumference (WC) by 0.10 cm, and a significant reduction of body fat by 0.48% compared with control diets [58]. A subgroup analysis found that brown and black rice significantly decreased body weight by 1.1 kg and body fat by 1.20%, oats significantly decreased

Table 10.2 Summary of whole-grain (WG) RCTs on weight and body composition regulation

Objective	Study design	Results
Systematic review and meta-analysis		
Pol et al. Assess the effects of WG foods compared with non-WG foods on changes in body weight, percentage of body fat, and waist circumference by using a meta-analytic approach [58]	26 RCTs; 2,060 participants; daily WG dose ranged from 18 to 150 g; duration ranged from 2 to 16 weeks with the majority of studies lasting 4–6 weeks	WG intake had insignificant effects on body weight by 0.06 kg and waist circumference by −0.10 cm, and a small but significant lowering effect on the percentage of body fat by 0.48% compared with that for a non-WG control. Whole wheat cereal lowered body fat more than a control by 0.71% ($p = 0.08$). A subgroup analysis for individual grains showed that only WG rice decreased body weight by 1.1 kg and percentage of body fat by 1.20% compared with the white rice control. WG oats decreased waist circumference by 1.2 cm more than the control
RCTs		
Ad libitum energy intake		
Ampatzoglou et al. Assess the impact of increasing WG on overall dietary intake, body weight, blood pressure, blood lipids, blood glucose, microbiota, and gastrointestinal symptoms in healthy, middle-aged adults (UK crossover RCT) [59]	33 subjects; 12 males and 21 females; mean age 48 years; mean BMI 28; mean 28 g vs. 168 g WG/day; 6 weeks; 4 weeks of washout; adherence was achieved by specific dietary advice and provision of a range of cereal food products	During the WG intervention, there was a significant increase in plasma alkylresorcinols and total fiber intake, without any effect on energy or other macronutrients. Although there were no effects on studied variables, there were trends toward increased 24-h fecal weight ($p = 0.08$) and reduction in body weight ($p = 0.10$) and BMI ($p = 0.08$) during the high WG intervention compared with the low WG period
Shimabukuro et al. Evaluate the effects of brown rice and white rice on abdominal fat distribution and metabolic parameters (Japan BRAVO study crossover RCT) [60]	27 male subjects with the metabolic syndrome; mean age 41 years; mean BMI 28; switch from brown to white rice and white to brown rice; 8 weeks on each rice for total of 16 weeks each group; no washout	In the brown rice to white rice group, body weight, BMI, and waist circumference were decreased by the end of the 8-week brown rice diet period and returned to baseline values by the end of the white rice diet period
		In the white rice to brown rice group, body weight, BMI, and waist circumference were comparable with the baseline values by the end of the 8-week white rice diet period, but waist circumference was lower at the end of the 8-week brown rice diet period
		Intra-abdominal visceral fat (%) was significantly lower after 8 weeks of brown rice consumption than after a comparable period of white rice (Fig. 10.2)
Brownlee et al. Evaluate the effect of substituting WG foods in the diet of habitual refined-grain consumers on markers of CVD risk and weight measures (UK parallel RCT) [61]	316 participants; mean aged 46 years; mean BMI 30; diets: control <30 g WG/day for 16 weeks, 60 g WG/day for 16 weeks, and 60 g WG/day for 8 weeks followed by 120 g WG/day for 8 weeks	An increase in WG consumption for a 16-week period did not significantly affect any biomarkers of cardiovascular health including weight or body fat percentage. Most of WG interventions increased fiber intake by 6 g/day with one increasing fiber to 11 g/day

Table 10.2 (continued)

Objective	Study design	Results
Restricted energy intake		
Harris Jackson et al. Investigate the effect of consuming WG to replace refined grains in the diets of individuals with metabolic syndrome or at risk for metabolic syndrome (USA parallel RCT) [62]	50 subjects; mean age 46 years; mean BMI 33; controlled weight-loss diet containing 163–301 g WG/day vs. 0 g WG/day; 12 weeks	Replacing refined grains with WG within a weight-loss diet did not significantly improve weight, BMI, or abdominal visceral adipose tissue loss. However, the WG diet significantly reduced the prevalence of prediabetes by 90% compared with 13% for the refined-grain diets. WG diets were more effective at normalizing blood glucose levels and reducing the risk of individuals with prediabetes progressing to type 2 diabetes
Kristensen et al. Study the effect of replacing refined wheat with WG wheat on body weight and composition (EU parallel RCT) [63]	79 postmenopausal women; mean age 68 years; mean BMI 30; energy-restricted diet (by 300 kcal/day) with 105 g whole wheat grains daily or refined wheat foods; 12 weeks	Body weight decreased significantly from baseline in refined wheat group by 2.7 kg and WG wheat group by 3.6 kg with no significance between the groups ($p = 0.11$). The reduction in body fat percentage was significantly greater in the WG group (Fig. 10.3). Serum total and LDL cholesterol significantly increased by 5% in the refined wheat group but did not change in the WG group ($p = 0.02$)
Maki et al. Investigate the effect of ready-to-eat (RTE) oat WG cereal containing viscous fiber, as part of a dietary program for weight loss (USA parallel RCT) [64]	144 subjects; mean age 49 years; mean BMI 32; 78% female; 2 portions/day of whole-grain RTE oat whole-grain cereal (3 g/day oat β-glucan) or energy-matched low-fiber foods (control), reduced energy diet by 500 kcal/day;12 weeks	Both groups lost weight in the WG oat cereal group by 2.2 kg vs. the control by 1.7 kg ($p = 0.325$). Waist circumference decreased significantly more with WG oat cereal by 3.3 cm compared with 1.9 cm for the control ($p = 0.012$) (Fig. 10.4)
Katcher et al. Determine whether including WG foods in a hypocaloric (reduced by 500 kcal/day) diet enhances weight loss and improves CVD risk factors (USA parallel RCT) [65]	50 metabolic syndrome adults; 25 males and 25 females; mean age 46 years; mean BMI 36; 5 WG servings/day vs. < 0.25 servings in the refined-grain group; all participants were given the same dietary advice in other respects for weight loss; 12 weeks	Body weight, waist circumference (WC), and body fat percentage decreased significantly in both groups, but there was a significantly greater decrease in body fat percentage in the abdominal region in the WG group than in the refined-grain group. C-reactive protein (CRP) decreased 38% in the WG group independent of weight loss compared to no change in the refined-grain group. Total, LDL, and HDL cholesterol decreased in both diet groups Total fiber and magnesium intakes increased in the WG compared to the refined-grain group
Kim et al. Assess the effect of type of rice consumed on weight control when consumed with an energy-restricted diet (Korea parallel RCT) [66]	40 overweight Korean women; 20–35 years of age; energy-restricted diets containing either white rice or mixture of brown rice and black rice; 6 weeks	The subjects showed a significant reduction in weight by 1.38 kg and body fat by 1.2% with the brown and black rice supplemented diets than the white rice group
Melanson et al. Investigate the effects of exercise plus hypocaloric WG diet on weight loss (USA parallel RCT) [67]	134 adults; mean age 42 years; mean BMI 31; hypocaloric diet with and without WG breakfast cereals; 23 vs. 17 g fiber/day; 24 weeks	Weight loss was insignificantly different for the WG breakfast cereal diet (4.7 kg) and hypocaloric comparison diet (5.0 kg)
Saltzman et al. Evaluate the effects of WG oats on weight loss and body composition (USA parallel RCT) [68]	41 normal weight, overweight and obese participants; age 18–76 years; hypocaloric (−895 kcal/day); low-fiber diet (13 g fiber/day) vs. 45 g rolled oats (17 g fiber/1000 kcal); 6 weeks	In a hypocaloric diet, there was no significant difference in weight loss (4.4 vs. 4.3 kg) or total fat mass loss (2.6 vs. 3.0 kg) between a high fiber diet containing rolled oats and a low-fiber diet

Fig. 10.2 Effect of brown vs. white rice on mean intra-abdominal visceral fat in Japanese men with metabolic syndrome after 8 weeks ($p < 0.018$) [60]

waist circumference by 1.2 cm, and whole wheat cereal lowered body fat by 0.71% ($p = 0.08$) compared to control diets.

Several RCTs on increased whole grain in ad libitum diets show mixed outcomes on weight and body composition [59–61]. A crossover RCT (33 adults; mean age 48 years; mean BMI 28; 168 g vs. 28 g daily whole grains; 6 weeks) detected a slight trend toward lower body weight for whole grains [59], whereas a parallel RCT (316 subjects; mean age 46 years; mean BMI 30; <30 g, 60 g, and 120 g whole grains; 8–16 weeks) did not find a significant effect on body weight or fat (%) [61]. However, a Japanese crossover RCT (27 males; mean BMI 26; brown vs. white rice; 8 weeks) found that the brown rice diet decreased body weight, BMI, and WC compared to the white rice diet period [60]. Also, the intra-abdominal visceral fat (%) was significantly lower after 8 weeks of brown rice consumption than after a comparable period of white rice (Fig. 10.2).

Seven RCTs evaluated the additive effect of adding whole-grains to energy restricted diets on body weight and composition [62–68]. Three RCTs found that adding whole grains to a hypocaloric diet did not significantly improve weight reduction [62, 67, 68]. However, a 2014 UK RCT (50 subjects; mean age 46 years; mean BMI 33; 163–301 g vs. 0 g whole grains/day; 12 weeks) showed that although a whole grain energy restricted diet did not significantly improve body weight or composition, it did significantly reduce the risk of pre diabetes by 90% compared to 13% for the refined grain energy restricted diet [62]. A 2012 Danish RCT in postmenopausal women (79 women; mean age 68 years; mean BMI 30; energy-restricted diet (by 300 kcal/day) with 105 g whole wheat grain daily or refined wheat foods; 12 weeks) found that body weight decreased significantly from baseline in the refined wheat group by 2.7 kg and in the whole-grain wheat group by 3.6 kg with no significance between the groups ($p = 0.11$) [63]. However, the whole-grain group had a significantly lower body fat (%) (Fig. 10.3). A 2010 US oat breakfast cereal RCT (144 subjects; mean age 49 years; mean BMI 32; 78% female; 2 portions/day of whole-grain ready-to-eat (RTE) oat cereal (3 g/day oat β-glucan) or energy-matched low-fiber foods (control), as part of a reduced energy diet by 500 kcal/day; 12 weeks) found that WC decreased significantly more with oat cereal by 3.3 cm compared with 1.9 cm for the control ($p = 0.012$) (Fig. 10.4) [64]. A 2008 US RCT in individuals with metabolic syndrome (50 adults; mean age 46; mean BMI 36; 5 whole-grain servings vs. <0.25 servings; 12 weeks) reported a significant

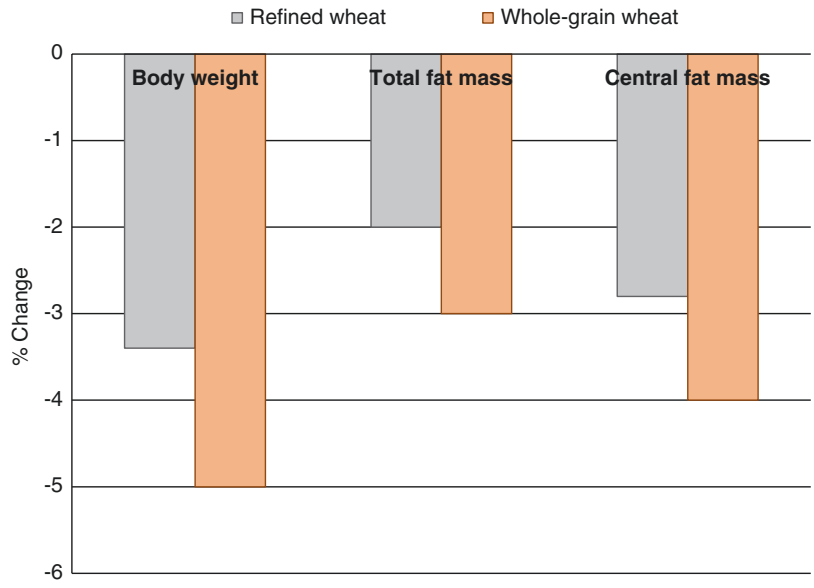

Fig. 10.3 Effect of whole grain in an energy-restricted dietary intervention on change in body weight, total fat mass, and central fat mass in postmenopausal women after 12 weeks (total fat mass $p < 0.05$) [63]

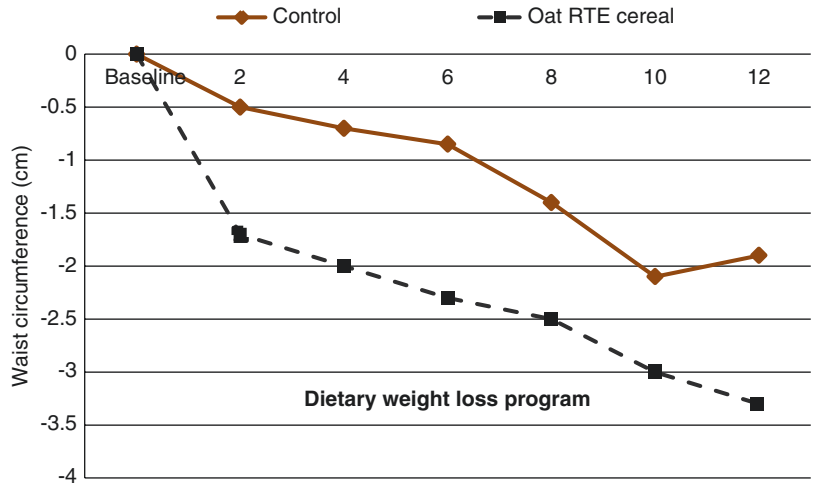

Fig. 10.4 Effect of whole-grain ready-to-eat (RTE) oat cereal on waist circumference in obese adults in a dietary weight-loss program for 12 weeks ($p = 0.012$) [64]

reduction in abdominal fat (%) and CRP in the whole-grain vs. refined-grain group [65]. A 2008 Korean rice-based hypocaloric diet [40 women; age 20–35 years; 6 weeks] found that consuming brown and black rice significantly reduced body weight by 1.4 kg and body fat by 1.2% vs. white rice [66].

Fruit and Vegetables

Background

Fruit and vegetables (F/V) are generally known to be important healthy dietary components and the Dietary Guidelines for Americans (Myplate.gov) recommends making one-half of a meal's plate fruit and vegetables [43, 69, 70]. F/V include a diverse group of plant foods that vary widely in content of energy, fiber, available carbohydrates, nutrients, and phytonutrients as shown in Appendix 1. Adequate intake of F/V (≥400 g/day) makes important contributions to health because of their unique concentrations of antioxidant vitamins and phytochemicals, especially vitamins C and A, and carotenoids and flavonoids; minerals (especially electrolytes high in potassium and magnesium and low in sodium); and fiber [69–74]. A potential benefit of a diet rich in fruit and non-starchy vegetables is their low energy density which may help in preventing weight gain due to their water, fiber, and bulk volume which contribute to satiation compared to the typical low fruit and vegetable diets associated with the Western lifestyle. Globally, F/V consumption is only a small fraction of the recommended levels [75]. In the USA, >85% of the population fall short of meeting the daily F/V intake recommendation [43].

Systematic Reviews and Meta-Analyses

Overall, meta-analyses and systematic reviews of prospective studies and RCTs show that increased intake of whole or minimally processed F/V reduces risk of increased weight gain, waist circumference (WC), and/or adiposity (Table 10.3) [76–79]. Increasing F/V intake as a weight-loss strategy has produced conflicting results mainly associated with the inclusion or exclusion of 100% fruit juice, raising the possibility that these divergent findings may be the result of the lower satiation signals when consuming F/V as juice compared to their whole, unprocessed form [43, 77, 78]. A meta-analysis of prospective studies (17 cohorts; 563,277 participants; 9 months to 20 years) found that each daily 100 g fruit (or slightly over 1 serving) reduced annual weight by 14 g and that fruit intake was inversely associated with WC [76]. This analysis also demonstrated significantly reduced risk of adiposity for total F/Vs by 9% (highest vs. lowest intake) [76]. A meta-analysis of whole or minimally processed F/Vs without 100% fruit juice (eight RCTs; 1,026 participants; mean 14.7 weeks) showed a significant reduction in body weight by 0.68 kg compared to isocaloric lower F/V intake in diets [78]. A systemic review of energy-restricted diets (12 intervention trials and 11 longitudinal studies) demonstrated in intervention trials that higher intake of F/Vs was associated with modest weight loss in overweight and obese adults but not in children and longitudinal studies showed significantly less weight gain in longer-term studies [79].

Table 10.3 Summary of fruit and vegetable (F/V) prospective cohort studies and RCTs on weight and body composition regulation

Objective	Study design	Results
Systematic review and meta-analysis		
Schwingshackl et al. Perform a systematic review and meta-analysis of prospective cohort studies on F/V consumption in relation to changes in anthropometric measures [76]	17 cohort studies; 563,277 participants; 9 months–20 years	Higher intake of fruits was associated with reduced annual weight by 13.7 g/100 g intake (slightly over 1 serving). No significant changes were observed for combined F/Vs or vegetable intake. Increased intake of fruits was associated with a reduction in waist circumference by 0.04 cm/year. Comparing the highest vs. lowest intake, reduced risk of adiposity was observed for combined F/V by 9%, fruit by 17%, and vegetables by 17%
Kaiser et al. Synthesize the best available evidence on the effectiveness of the general recommendation to eat more F/V for weight loss or the prevention of weight gain [77]	7 RCTs; 1,103 participants; primary or secondary outcome of body weight; minimally processed F/V including juices; >8 weeks	Increased F/V intake including 100% juice insignificantly increased body weight by 0.04%
Mytton et al. Quantify the relationship between changes in F/Vs excluding juice intake, energy intake, and body weight [78]	Eight RCTs; 1,026 participants, minimally processed F/Vs excluding juice; mean 14.7 weeks duration	High F/V intake significantly reduced body weight by 0.68 kg vs. lower F/V intake, despite no difference in daily energy intake ($p = 0.07$). Increased F/V intake, in the absence of specific advice to decrease consumption of other foods, appears unlikely to lead to weight gain in the short term and may have a role in weight maintenance or loss
Ledoux et al. Assess the relationship between F/V intake and adiposity [79]	12 intervention trials (including 1 with children) and 11 longitudinal studies (including 4 with children)	In energy-restricted intervention trials, higher intake of F/V was weakly associated with weight loss among overweight or obese adults, but not children. In longitudinal studies, high F/V intake was associated with less or slower weight gain over lengthy time intervals among adults, but to a lesser degree among children
Prospective or longitudinal cohort studies		
Shefferly et al. Evaluate the relationship between 100% juice intake and weight status in preschool children (USA, Early Childhood Longitudinal Study, Birth Cohort) [80]	8,950 children; examined at ages 2, 4, and 5 years (multivariate adjusted)	Regular 100% juice consumption between ages 2 and 4 years increased the odds of becoming overweight by 30%. However, significant weight was not observed at age 5 years
Bertoia et al. Examine the effect of increased F/V intake and weight change over time, including subtypes and individual F/V (USA, the Nurses' Health Study I and II and the Health Professionals Follow-Up Study) [81]	133,468 men and women; mean age men 47 years; mean age women 49 and 36 years; between 1986 and 2010 multiple 4-year weight measurement cycles; 16 to >24 years of follow-up (multivariate adjusted)	Increased intake of fruits was associated with 4-year weight loss per daily serving for total fruits by 0.53 lb, berries by 1.11 lb, and apples/pears by 1.24 lb (Fig. 10.5). Increased intake of several vegetables was also associated with weight loss per daily serving for total vegetables by 0.25 lb, tofu/soy by 2.47 lb, and cauliflower by1.37 lb (Fig. 10.6). In contrast, increased intake of starchy vegetables, including corn, peas, and potatoes, was associated with weight gain (Fig. 10.7). Vegetables having both higher fiber and lower glycemic load were more strongly associated with weight loss compared with lower-fiber, higher-glycemic-load vegetables

(continued)

Table 10.3 (continued)

Objective	Study design	Results
Rautiainen et al. Investigate whether intake of F/V and total fiber is associated with weight change and the risk of becoming overweight and obese (USA, Women's Health Study) [82]	18,146 women; mean baseline age 54 years; mean baseline BMI 22; mean follow-up of 15.9 years; 8,125 women became overweight or obese (multivariate adjusted)	Vegetable intake was associated with greater weight gain (p-trend = 0.02), and fruit intake had a 13% lower risk of becoming overweight or obese (higher vs. lower intake; multivariate adjusted). Overall, greater intake of fruit but not vegetables by middle-aged and older women with a normal BMI is associated with lower risk of becoming overweight or obese
Vergnaud et al. Assess the association between the baseline consumption of F/V and weight change (EU, European Prospective Investigation into Cancer and Nutrition (EPIC) study) [83]	373,803 participants; mean age 52 years; mean BMI 26; country-specific validated questionnaires; per 100 g F/V/day and weight change (g/year); mean follow-up of 5 years	Baseline F/V intake was associated with weight loss in men and women who quit smoking during follow-up. There was a weak association between vegetable intake and weight loss in women who were overweight and were former smokers and weak associations between fruit intake and weight loss in women who were >50 years of age, were of normal weight, or were never smokers
Representative RCTs		
Tapsell et al. Assess the effects of higher vegetable consumption on weight loss (Australia, single-blind parallel RCT) [84]	120 adults; mean BMI 30; mean age 49 years; two 20% energy deficit groups with healthy diet advice to consume vegetables each day. The test group was asked to consume ≥5 servings of low-energy-dense vegetables each day, but the control vegetable group consumed half the portions (0.5 vs. 1.0 cup cooked or 1 vs. 2 cups of raw, respectively); 12 months	Both groups significantly reduced intake of high-energy-dense vegetables and increased portions of low-energy-dense vegetable as instructed. The higher percentage energy from vegetables was positively associated with weight loss and sustainability (Fig. 10.8). Weight loss was sustained for 12 months by both groups, but the higher vegetable group reported significantly greater hunger satisfaction
Christensen et al. Investigate the effects of fruit intake in people with type 2 diabetes, HbA1c, body weight, waist circumference (Denmark, parallel RCT) [85]	63 subjects with type 2 diabetes; mean age 58 years; mean BMI 32; 78% male; diet >2 servings vs. <2 serving fruit daily, difference in fruit intake 172 g; 12 weeks	Higher fruit intake reduced body weight by 0.8 kg (p = 0.19) and WC by 1.3 cm (p = 0.36) compared to lower fruit intake
Dow et al. Evaluate the effect of red grapefruit on body weight, blood pressure, and blood lipids (USA. parallel RCT) [86]	74 adults; mean BMI 32; 1/2 red grapefruit 3 times daily vs. control diet; 6 weeks	Red grapefruit was associated with modest weight loss by 0.6 kg, significantly reduced waist circumference by 2.45 cm and significantly improved systolic blood pressure by 3.2 mm Hg and reduced LDL-C by 18.7 mg/dL
Peterson et al. Evaluate the effect of the consumption of dried California Mission figs (*Ficus carica* "Mission") on serum lipid levels and body weight (USA, crossover RCT) [87]	102 adults; mean age 55 years; 69% females; dried California Mission figs (120 g/day) added to their usual diet vs. their usual diet; 5 weeks	Blood lipids and lipoproteins remained unchanged with the addition of figs. Body weight insignificantly increased by 0.4 kg (p = 0.08)
Basu et al. Examine the effects of blueberries on features of metabolic syndrome and body weight (USA, parallel RCT) [88]	48 subjects; mean age 50 years; mean BMI 38; freeze dried blueberries equivalent to 350 g blueberries/day vs. control; 8 weeks	Blueberry supplementation did not significantly affect body weight or waist circumference ($p > 0.05$)

Table 10.3 (continued)

Objective	Study design	Results
Whybrow et al. Examine the effects of incorporating F/Vs into the diets on body weight (Scotland, parallel RCT) [89]	34 males and 28 females; mean age 43 years; mean BMI 24; supplements of 0, 300 or 600 g F/V daily, isocaloric diets; 8 weeks	There was no evidence of a significant change in body weight for the control by 0.48 kg, for the 300 g F/Vs by −0.29 kg, and for the 600 g F/Vs by −0.14 kg ($p = 0.24$)
De Oliveira et al. Investigate effect of fruit intake on body weight change (Brazil, parallel RCT) [90]	49 women; mean age 44 years; mean weight 79 kg; dietary supplements: apples or pears vs. oat cookies three times daily; 12 weeks	Compared to baseline, the fruit group significantly lost 1.22 kg, whereas the oat cookie group had a nonsignificant weight loss of 0.88 kg. The difference between the two groups was statistically significant ($p = 0.004$)

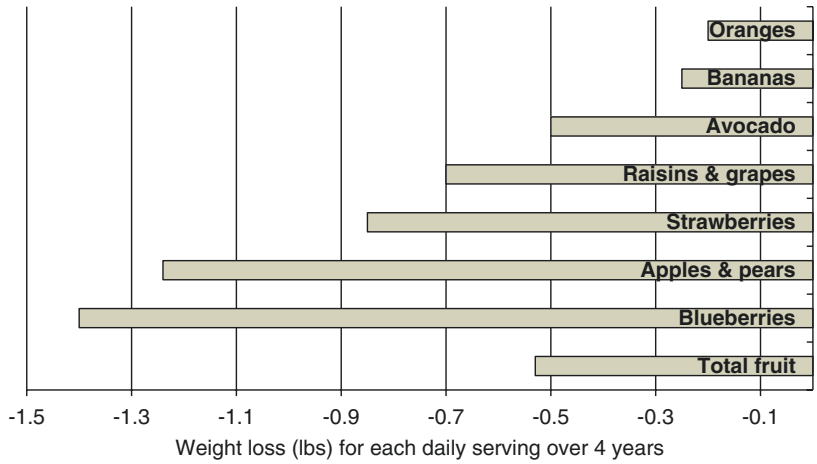

Fig. 10.5 Association between a daily serving of fruits on weight change over 4 years from three US large prospective studies in men and women (multivariate adjusted) [81]

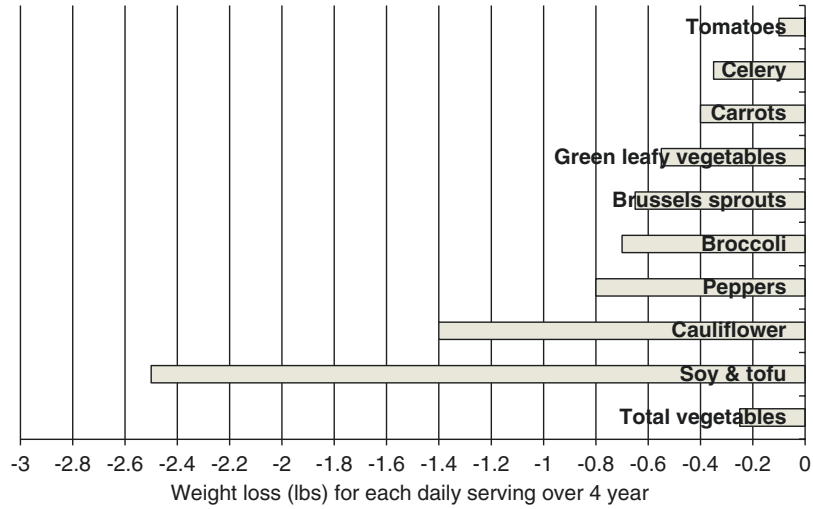

Fig. 10.6 Association between a daily serving of vegetables on weight change over 4 years from three US large prospective studies in men and women (multivariate adjusted) [81]

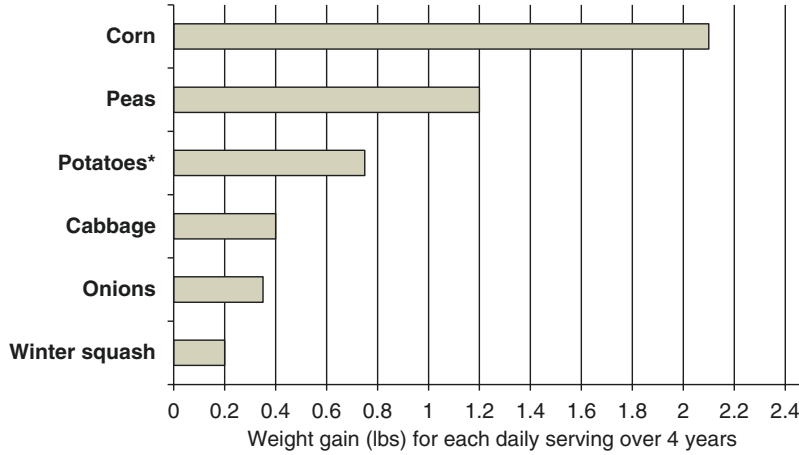

Fig. 10.7 Association between a daily serving of starchy or higher-energy-dense vegetables on weight gain over 4 years from three US large prospective studies in men and women, multivariate adjusted [81]. *Includes baked, boiled, mashed white potatoes, sweet potatoes, and yams and excludes French fries and potato chips

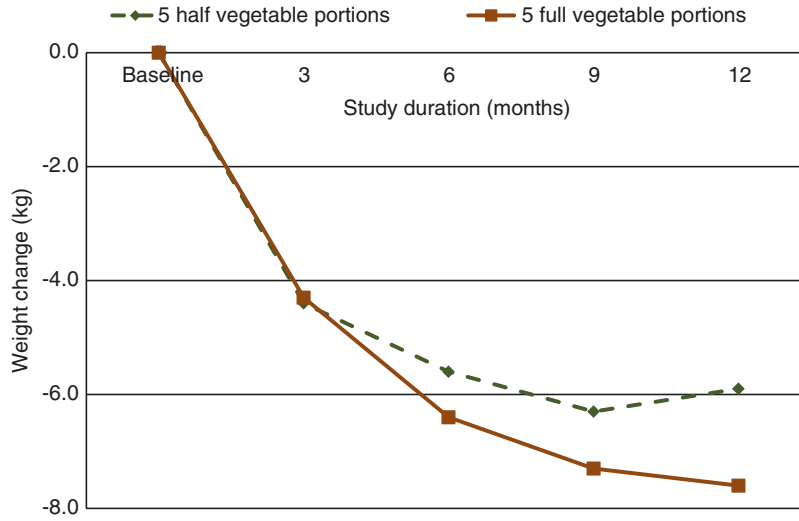

Fig. 10.8 Effect of vegetables added to a 20% reduced energy diet on weight loss in 120 obese adults over 12 months ($p = 0.024$) [84]

Prospective Cohort Studies

Table 10.3 provides a summary of F/Vs Cohort studies and weight regulation [80–83]. Several prospective studies showed that specific types of F/Vs vary in their effect on body weight. Pooled data from three US prospective studies (133,468 men and women; follow-up 16 years to over 24 years) observed highly variable effects of specific F/Vs on weight change, after adjustment for covariates [81]. Increased intake of fruits was associated with 4-year weight loss per daily serving for total fruits by 0.53 lb, berries by 1.11 lb, and apples/pears by 1.24 lb (Fig. 10.5). One serving of some vegetables was also associated with 4-year weight loss for total vegetables by 0.25 lb, tofu/soy by 2.47 lb, and cauliflower by 1.37 lb (Fig. 10.6). In contrast, increased intake of starchy vegetables, including corn,

peas, and potatoes, was associated with 4-year weight gain (Fig. 10.7). Vegetables having both higher fiber and lower glycemic load were more strongly associated with weight loss compared with lower-fiber, higher-glycemic-load vegetables. The Women's Health Study (18,146 women; mean baseline age 54 years; 15.9 years of follow-up) found that greater intake of fruit but not vegetables, by middle-aged and older women with a normal BMI was associated with lower risk of becoming overweight or obese [82]. The EPIC study (373,803 participants; mean age 52 years; mean follow-up of 5 years) found that F/V intake was associated with weight loss in men and in women who quit smoking during the follow-up period [83]. There was a weak association between fruit intake and weight loss in women >50 years, normal weight, or never smokers. A longitudinal study in preschool children (8,950 children; examined at age 2, 4, and 5 years) reported that regular consumption of 100% juice between ages 2 and 4 years was associated with a significant 30% increased risk of being overweight, but the statistical significance was lost at age 5 years [80].

Randomized Controlled Trials (RCTs)

Seven representative RCTs related to increased F/V intake and change in body weight and waist circumference (WC) are summarized in Table 10.3. A long-term reduced energy weight-loss RCT (120 subjects; mean age 49 years; mean BMI 30; 12 months) demonstrated that increased whole or minimally processed low-energy-dense vegetable intake significantly lowered body weight (Fig. 10.8) [84]. Other RCTs on specific fruit showed that increased apples, pears, red grapefruit, and blueberries significantly lowered body weight and/or waist circumference [86, 88, 90], whereas figs were associated with an insignificant increase in body weight [87]. Two other RCTs showed that increasing total F/V intake did not significantly affect body weight and/or WC [85, 89].

Protein Foods

Protein-rich whole or minimally processed plant foods have been considered potentially protective against long-term weight gain and obesity [91]. A pooled analysis of three large US prospective cohorts (120,784 men and women including the Nurses' Health Studies and the Health Professionals Follow-Up Study; protein intake and weight changes in 4-year cycles; 16–24 years follow-up) showed that protein foods had different effects on 4-year weight gain, with significant weight gain for red meats, chicken with skin, and regular cheese by 0.13–1.17 kg per daily serving; no association for milk, legumes, peanuts, or eggs; and significant weight loss for yogurt, peanut butter, walnuts, other nuts, chicken without skin, low-fat cheese, and seafood by 0.14 to 0.71 kg per daily serving [92]. The effect of dietary pulses and tree nuts on body weight and composition will be evaluated in more detail.

Dietary Pulses

Background

Dietary pulses (e.g., pinto beans, split peas, lentils, chickpeas) and soybeans are rich in fiber and protein with relatively low glycemic response properties [93]. A serving of legumes is half a cup or 90–100 g of cooked legumes, which contains 5–10 g of fiber, 7–8 g of protein, and <5% of energy as

fat, with the exception of chickpeas and soybeans which have 15% and 47% energy from fat, respectively. Pulses promote satiety by adding bulk and high levels of fiber (e.g., resistant starch) and protein, especially as a replacement for meat products [38]. An NHANES cross-sectional study found that bean consumers had significantly lower body weight and a 22% lower risk of being obese than non-consumers [94]. However, pulse consumption has been in decline with the global shift to Western-style diets [95]. For example, between the 1960s and 1990s, legume intake decreased by 40% in India and by 24% in Mexico. Legumes are infrequently consumed by North Americans and northern Europeans, with <8% of Americans consuming pulses daily.

Randomized Controlled Trials (RCTs)

Dietary pulses have a modest weight-loss effect [96]. A meta-analysis (21 RCTs median intake 1 serving (132 g)/day; 940 participants; median 6 weeks) showed a significant weight reduction by 0.34 kg for diets containing dietary pulses compared with pulse free control diets [96]. This modest weight loss with dietary pulse intake was demonstrated in both energy-restricted diets and in diets intended for weight maintenance. Six trials (509 participants) reported that dietary pulse consumption did not significantly reduce WC (−0.37 cm), but a trend was shown in six trials (340 participants) that supported lower body fat (−0.34%; $p = 0.07$). These findings are generalizable to overweight and obese populations suggesting that one daily serving of dietary pulses does not lead to weight gain and may support modest weight loss.

Total and Specific Nuts

Background

Nuts (e.g., almonds, pistachios, walnuts, hazelnuts, pecans, peanuts) are nutrient-dense sources of fiber, protein, unsaturated fat, vitamins (e.g., B vitamins and vitamin E), minerals (e.g., potassium and magnesium), phytosterols, and polyphenols [35, 97]. Although nuts have a relatively high energy density (about 6 kcal/g) due primarily to a high unsaturated fat content and low water content, human studies have shown that nuts have a lower metabolizable energy than predicted from the Atwater energy tables because of the incomplete absorption of nut fat and other macronutrients [98, 99]. Human studies consistently report that the regular consumption of tree nuts, as a replacement for less healthful foods, can help prevent weight gain [100, 101]. Mechanistic studies indicate that nuts weight control effects are largely attributable to their high satiety and low metabolizable energy (poor bioaccessibility leading to inefficient energy absorption) properties [102]. Compensatory dietary responses account for 55–75% of the energy provided by nuts. Limited data suggest that routine nut consumption is associated with elevated resting energy expenditure and thermogenic effects.

Prospective Cohort Studies

Two prospective studies consistently show that increased nut consumption is protective against weight gain and obesity [103, 104]. The Spanish Seguimiento Universidad de Navarra (SUN) project (8865 men and women; mean age 38 years; mean BMI 23; 28 months of follow-up) demonstrated that people who consumed nuts ≥2 times weekly had a 40% lower multivariate risk for weight gain compared with non-nut consumers who gained an average of 0.4 kg more weight [103]. The Nurses'

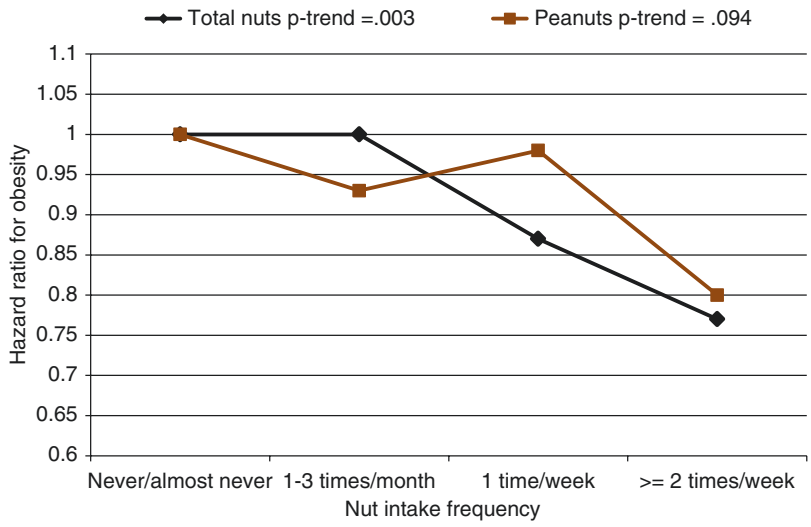

Fig. 10.9 Effect of nut intake frequency on obesity risk in healthy middle-aged women over 8 years (multivariate adjusted) [104]

Health Study II (51,188 women in the Nurses' Health Study II; mean age 36 years; mean BMI 24; 8 years of follow-up) found that women consuming nuts ≥2 times/week had a significant 33% lower risk of obesity and gained 0.51 kg less weight compared to non-nut consumers after 8 years of follow-up [104]. The different effects of total nut and peanut intake on obesity risk are illustrated in Fig. 10.9.

Randomized Controlled Trials (RCTs)

RCTs consistently show that diets supplemented with nuts do not increase body weight, body mass index, or waist circumference (WC) compared with control diets [105–114].

Meta-Analysis

A systematic review and meta-analysis (33 RCTs; 75% almonds and walnuts; 1,866 subjects; 2–152 weeks) found that increased nut intake resulted in an insignificant decreased mean body weight by 0.47 kg, BMI by 0.40, and WC by 1.25 cm [105]. Although the decreases in weight and body composition are relatively small, the results alleviate any concerns that eating nuts may promote obesity in general or when eaten as a cardioprotective food. As almonds and walnuts represent 75% of the weight management RCTs in the meta-analysis, the following highlights some key almond and walnut trials.

Almonds

RCTs have consistently shown that almonds added to the habitual diet do not increase body weight or when incorporated into a hypocaloric diet promote significant additional weight loss [106–111]. Two crossover RCTs demonstrate that habitual diets supplemented with 2 servings (or 320–344 kcal) of

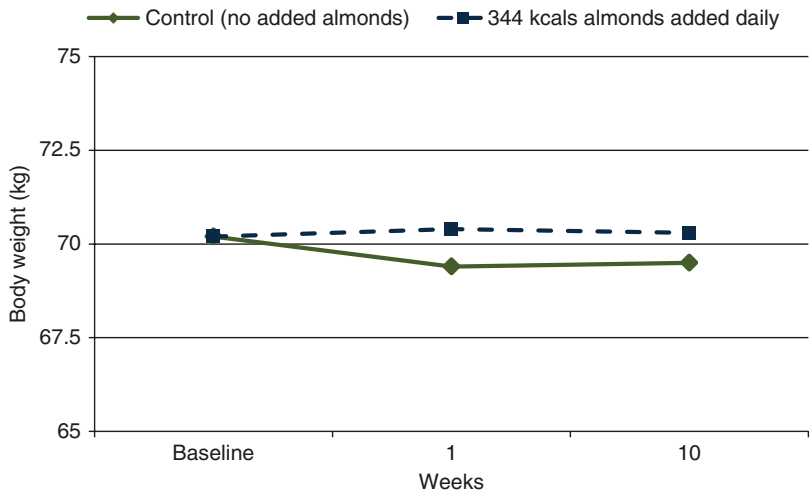

Fig. 10.10 Effect of adding 2 servings (344 kcal) of almonds daily to the usual diet for 10 weeks [107]

almonds daily, compared to nut-free control diets, for 10 weeks to 6 months, did not increase body weight (Fig. 10.10) [106, 107]. A 2013 RCT (137 subjects; 43 g almonds daily; 4 weeks) showed that almonds lowered postprandial glycemia and suppressed hunger and desire to eat sensations, especially when consumed as a snack [108]. A long-term weight-loss RCT (123 subjects; mean age 47 years; mean BMI 34; about 90% women; hypocaloric diet with 56 g almonds as snacks daily vs. nut-free snacks; 18 months) found that there was no significant difference in 18 months of weight loss between the two diets with the almond group losing 3.7 kg vs. the unsupplemented group losing 5.9 kg [109]. Two shorter-term weight-loss RCTs (65–108 subjects; 50–84 almonds/daily vs. nut-free diets or diet rich in complex carbohydrates; 3–6 months) found significantly lower body weight and BMI with almond consumption compared to control diets [110, 111].

Walnuts

Like almonds, walnuts have similar types and numbers of weight-loss RCTs showing that, adding them to the habitual diet does not significantly cause weight gain [112–114]. A 2005 crossover RCT (90 subjects; mean age 54 years; mean BMI 26; habitual diet plus added walnuts 12% energy or 28–56 g or no added walnuts; 6 months) demonstrated that the walnut group consumed a net mean increase of 133 kcal/day compared to the control group, resulting in an insignificant weight gain of 0.4 kg vs. the 3.1 kg theoretically calculated weight gain that had been projected over this time period [112]. A 2012 crossover RCT (46 subjects; mean age 57 years; mean BMI 33; 28 women and 18 men; 56 g walnuts or 350 kcal/day added to the habitual diet vs. no walnuts added to the habitual diet; 8 weeks) found that the walnut-free diet had small but significant

reductions in BMI by 0.4 units and body weight by 1 kg compared to the walnut-added diet. The BMI and weight increases in the walnut group were much less than expected based on the added energy intake [113]. A 2016 weight-loss RCT (245 women; mean age 50 years; mean BMI 33; 42 g walnuts/day; 6 months), found that a walnut supplemented diet reduced body weight by 7 kg and BMI by 2.6 kg/m^2, which was similar to reductions shown for low-fat and low carbohydrate diets without walnuts [114].

Conclusions

The worldwide overweight and obesity pandemic is among the greatest public health challenges of our time with over 2 billion people now overweight or obese globally. Even a small daily positive energy balance of 50 kcals/day, by increased energy intake, lower fiber diets, and/or reduced activity, can lead to an annual weight gain of 0.4–0.9 kg/year. Further, a higher habitual intake of 200 kcal/day above energy balance in overweight or obese women may increase weight gain by as much as 9 kg/year. Diets rich in whole or minimally processed plant foods (whole plant foods), especially lower energy density and fiber-rich healthier varieties, are associated with a lower risk of weight, body fat, and waist circumference (WC) gain and obesity compared to energy-dense, low fiber Western diets. Within the whole plant foods category, specific foods have been shown to be more effective for weight control than others. Cohort studies show $\geq$3 daily whole-grain servings, especially with at least 10 g of cereal fiber, can significantly reduce body weight and WC compared to < one half a serving of whole grains/day. RCTs show that whole grains can help reduce body fat and contribute to net daily energy negative balance by increasing metabolic rate and fecal metabolizable energy excretion. Prospective cohort studies indicate that whole or minimally processed fruits and vegetables, especially healthier varieties, are associated with a lower risk of weight, WC, or body fat gain and obesity, whereas higher energy-dense, lower fiber fruits and vegetables may promote weight gain. RCTs show that daily consumption of healthy fruits and vegetables (lower in energy density and rich in fiber), dietary pulses, and nuts do not promote weight gain and can lead to modest weight loss and increased weight loss in hypocaloric diets. Higher fiber whole plant foods can promote better weight management by helping to suppress appetite, improve glycemic control, reduce dietary energy density and available metabolizable energy, and promote colonic microbiota health.

Appendix 1. Estimated Range of Energy, Fiber, Nutrient, and Phytochemical Composition of Whole Plant Foods/100 g Edible Portion[a,b]

Components	Whole grains	Fresh fruit	Dried fruit	Vegetables	Legumes	Nuts/seeds
Nutrients/phytochemicals	Wheat, oats brown rice, whole-grain bread, cereal, pasta, rolls, and crackers	Apples, pears, bananas, grapes, oranges, blueberries, strawberries, and avocados	Dates, dried figs, apricots, cranberries, raisins, and prunes	Potatoes, spinach, carrots, peppers, lettuce, green beans, cabbage, onions, cucumber, cauliflower, mushrooms, and broccoli	Lentils, chickpeas, split peas, black beans, pinto beans, and soybeans	Almonds, Brazil nuts, cashews, hazelnuts, macadamias, pecans, walnuts, peanuts, sunflower seeds, and flaxseed
Energy (kcal)	110–350	30–170	240–310	10–115	85–170	520–700
Protein (g)	2.5–16	0.5–2.0	0.1–3.4	0.2–5.0	5.0–17	7.8–24
Available carbohydrate (g)	23–77	1.0–25	64–82	0.2–25	10–27	12–33
Fiber (g)	3.5–18	2.0–7.0	5.7–10	1.2–9.5	5.0–11	3.0–27
Total fat (g)	0.9–6.5	0.0–15	0.4–1.4	0.2–1.5	0.2–9.0	46–76
SFA[a] (g)	0.2–1.0	0.0–2.1	0.0	0.0–0.1	0.1–1.3	4.0–12
MUFA[a] (g)	0.2–2.0	0.0–9.8	0.0–0.2	0.1–1.0	0.1–2.0	9.0–60
PUFA[a] (g)	0.3–2.5	0.0–1.8	0.0–0.7	0.0.0.4	0.1–5.0	1.5–47
Folate (μg)	4.0–44	<5.0–61	2–20	8.0–160	50–210	10–230
Tocopherols (mg)	0.1–3.0	0.1–1.0	0.1–4.5	0.0–1.7	0.0–1.0	1.0–35
Potassium (mg)	40–720	60–500	40–1160	100–680	200–520	360–1050
Calcium (mg)	7.0–50	3.0–25	10–160	5.0–200	20–100	20–265
Magnesium (mg)	40–160	3.0–30	5.0–70	3.0–80	40–90	120–400
Phytosterols (mg)	30–90	1.0–83	N/A	1.0–54	110–120	70–215
Polyphenols (mg)	70–100	50–800	N/A	24–1250	120–6500	130–1820
Carotenoids (μg)	N/A	25–6600	0.6–2160	10–20,000	50–600	0.0–1200

[a]SFA (saturated fat), MUFA (monounsaturated fat), and PUFA (polyunsaturated fat)

[b]U.S. Department of Agriculture, Agriculture Research Service, Nutrient Data Laboratory. 2014. USDA National Nutrient Database for Standard Reference, Release 27. http://www.ars.usda.gov/nutrientdata. Accessed 17 February 2015.

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Chapter 11
Fiber in Type 2 Diabetes Prevention and Management

Keywords Diabetes • Prediabetes • Insulin resistance • Insulin sensitivity • Glycemic control • Visceral fat • Systemic inflammation • Short-chain fatty acids • Dietary fiber • Cereal fiber • Whole oats • Psyllium

Key points

- The prevalence of prediabetes and diabetes has increased globally in parallel with the rising levels of obesity in adults and children, a phenomenon sometimes called diabesity. If this global trend continues, by 2030 an estimated one billion people are expected to have prediabetes and diabetes.
- As much as 90% of diabetes risk management is attributed to modifiable risk factors such as diet and physical activity and their effect on increased risk of overweight and obesity.
- Prospective cohort studies consistently show that increased intake of total fiber and cereal fiber and lower glycemic index and glycemic load diets is effective in reducing diabetes risk.
- Meta-analyses of randomized controlled trials (RCTs) including people with prediabetes and diabetes consistently show that increased fiber intake from diets and supplements significantly lowers fasting blood glucose (FBG) and glycosylated hemoglobin (HbA1c) levels compared to control diets.
- Whole oat products such as oatmeal and psyllium, a gel-forming, low fermentable fiber supplement, have been shown clinically to be among the most effective fiber sources in lowering FBG and HbA1c in diabetic and prediabetic individuals compared to placebo.
- The primary mechanisms related to adequate fiber intake and diabetes prevention and management are (1) reducing the risk of obesity and visceral fat accumulation, (2) promoting and maintaining a healthy microbiota ecosystem, (3) attenuating elevated systemic inflammation, and (4) controlling postprandial and fasting glycemic responses and protecting against insulin resistance.

Introduction

Type 2 diabetes (diabetes) is characterized by elevated blood glucose levels due to cellular insulin resistance and the progressive incapability of the pancreas to compensate for the insulin resistance with insulin secretion [1]. Currently in the USA, approximately 10% of the population is living with diabetes [1–3]. Estimates from the International Diabetes Federation forecast a major increase in people with diabetes globally from 382 million in 2013 to 592 million in 2035 [2]. The prevalence of prediabetes among US adults increased significantly from 30.2% in 1999–2002 to 36.5% in 2007–2010 [3]. The prevalence of prediabetes and diabetes has increased globally in parallel with the rising

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levels of obesity in adults and children, a phenomenon sometimes called diabesity [4–6]. If this global trend continues, by 2030 about one billion people are expected to be prediabetic and diabetic. Diabetes is the sixth leading cause of death in the USA, and it contributes significantly to increased risk of macrovascular complications often manifested as coronary heart disease, atherosclerosis, and amputations and microvascular diseases in the eyes, kidneys, and nerves [7–10].

Diabetes is a disease that is preventable through the practice of a healthy lifestyle, including the consumption of a healthy, fiber-rich dietary pattern, weight loss/management, and physical activity [6–13]. Evidence backed up by epidemiology studies strongly suggests overweight or obesity and associated nonalcoholic fatty liver disease to be the most important risk factors in the development of diabetes [6, 14]. When adjusted for BMI, studies revealed significant and independent associations of low-fiber, low-quality diets and sedentary behaviors to diabetes [12]. The best healthy lifestyle factors associated with diabetes prevention and management consist of: (1) fiber-rich diets primarily from whole grains, fruits and vegetables, pulses, nuts, and seeds to achieve a daily fiber intake of about 30 g or more/day; (2) limited intake of red meat, sugar-sweetened beverages, high-fat dairy, and refined grains; and (3) controlled energy intake (plus physical activity on most days of the week) to limit the risk of gaining body weight [6, 11–15]. Fiber properties, such as low energy density, fermentability, and viscosity, and other plant phytochemical components are thought to be important parameters influencing improved weight control and microbiota health associated with lower risk of diabetes and mortality [16–19]. However, the mean intake of total fiber in the USA is only about 17 g/day, which is only about half the adequate intake of 14 g total fiber per 1000 kcal or 25 g for adult women and 38 g for adult men. Only 5% of the US population consume adequate daily fiber levels [17]. The objective of this chapter is to review the role of fiber on diabetes prevention, risk factors, and management.

Dietary Fiber and Type 2 Diabetes (Diabetes)

Background

In the 1970s, the fiber diabetes hypothesis, which associated the change from high-fiber, low-glycemic diets (traditional diets) to low-fiber, high-glycemic diets (Western diets) as a primary controllable cause for diabetes, was postulated by the early fiber and chronic disease pioneers Drs. Burkitt and Trowell [20, 21]. Their hypothesis was based on a number of convergent lines of evidence. During their time as physicians at different African hospitals during the 1950s and 1960s, Drs. Burkitt, Trowell, Cleave, and Walker observed spikes in diabetes rates as rural Africans moved to the large cities and replaced their traditional (high-fiber) diets with Western (low-fiber) diets. They uncovered health statistics from England and Wales showing a 50% reduction in diabetes death rates when high-fiber whole-grain flour was mandated during World War II to replace refined flour. A third important piece of the evidence was clinical research by Drs. Jenkins and Anderson demonstrating the direct effects of fiber on postprandial blood glycemic and insulinemic responses. Fiber-rich, whole, and minimally processed foods contain other non-fiber diabetes-protective nutrients and phytochemicals such as magnesium, unsaturated fats, carotenoids, tocopherols, and phenolic acids, which can work synergistically to help prevent and manage diabetes when consumed at high enough levels [22]. The fiber content of whole (and minimally processed) plant foods is listed in Appendix 1.

Prospective Cohort Studies

A summary of cohort study meta-analyses and representative individual prospective studies on the effect of fiber and diabetes prevention are summarized in Table 11.1 [23–32].

Table 11.1 Summary of prospective cohort studies and related analyses in fiber and type 2 diabetes (diabetes) prevention

Objective	Study details	Results
Meta-analyses and pooled data		
Kuijsten et al. Evaluate the association between intake of dietary fiber and diabetes (European Prospective Investigation into Cancer and Nutrition [EPIC]-InterAct study plus meta-analysis) [23]	19 cohorts; 617,968 participants; 41,066; cases of type 2 diabetes; 5–16 year follow-up (multivariate adjusted)	Diabetes risk was reduced per 10 g/day increase for total fiber by 9%, for cereal fiber by 25%, for vegetable fiber by 7%, and for fruit fiber by 5% (Fig. 11.1)
Yao et al. Conduct a meta-analysis of prospective studies evaluating the associations of total fiber intake and fiber subtypes on the risk of diabetes [24]	17 cohort articles; 488,293 subjects and 19,033 diabetes cases; 4–14 year follow-up (multivariate adjusted)	The diabetes risk was reduced for total fiber by 19%, for cereal fiber by 23%, for fruit fiber by 6%, and insoluble fiber by 25%. A nonlinear inverse relationship was found for total fiber intake and diabetes risk (Fig. 11.2). The risk of diabetes was decreased by 6% for each 2 g/day increment in cereal fiber intake (Fig. 11.3)
Bhupathiraju et al. Assess the effects of glycemic index, glycemic load, and risk of diabetes (USA—Nurses' Health Study I and II and Health Professionals Follow-Up Study and meta-analysis) [25]	**Pooled analysis**. 205,157 men and women; 15,027 diabetes cases; 4-year cycle **Meta-analysis**. 24 cohort articles, 4–14-year follow-up, 31,088 diabetes cases (multivariate adjusted)	A high glycemic index diet had a 33% higher diabetes risk than low glycemic index diet. The combination diet that was high in glycemic index and low in cereal fiber had >50% higher risk of diabetes (Fig. 11.4). In a meta-analysis, higher glycemic index increased diabetes risk by19% vs. lowest index, and glycemic load had a similar effect
Representative prospective cohort studies and related analyses		
AlEssa et al. Examine the associations of carbohydrate quality measures (e.g., carbohydrate intake; starch intake; glycemic index; glycemic load; total, cereal, fruit, and vegetable fiber intakes; and different combinations) with plasma adiponectin, C-reactive protein [CRP], and glycated hemoglobin [HbA1c] (US Nurses' Health Study, cross-sectional analysis) [26]	2,458 diabetes-free women, age 58 years, mean BMI 26 (multivariate adjusted)	Diets with higher fiber intake and lower starch-to-fiber-intake ratio were significantly associated with higher concentrations of adiponectin and lower concentrations of HbA1c, but only cereal fiber intake was associated, inversely, with CRP concentrations. Total fiber and cereal fiber intake were positively associated with adiponectin; cereal fiber intake was positively associated with adiponectin; fruit fiber intake was negatively associated with HbA1c concentrations; higher starch-to-total-fiber-intake ratio was associated with lower adiponectin and higher HbA1c. All values were significant
Pastorino et al. Examine the relationship between a high-fat, high-glycemic index, low-fiber dietary pattern across adult life and diabetes risk using reduced rank regression (UK) [27]	5,362 individuals; 2,547 males and 2815 females; born in March 1,946 in England, Scotland, and Wales; 5-day diet diaries were available at age 36, 43, and 53 for 1,180 study members; diabetes incidence was 106 from 53 to 60–64 years (multivariate adjusted)	Diets with high-fat, high-glycemic-index, and low-fiber intakes were prospectively associated with diabetes risk among women, and this association was independent of energy intake, BMI, and waist circumference. Women in the highest quintile of the low-fiber dietary pattern at age 43 had an increased risk of diabetes by 445%
Kuijsten et al. Evaluate the association between intake of dietary fiber and diabetes (EU EPIC study) [23]	26,088 participants; 11,559 participants with diabetes; mean age 52 years; mean BMI 26; high fiber >26.4 g/day and low fiber <18.9 g/day; 10.8 years of follow-up (multivariate adjusted)	Total fiber intake was significantly associated with a lower risk of diabetes by 18% after adjusting for lifestyle and diet (high- vs. low-fiber intake), but it was attenuated to 9% after further adjusting for BMI and no longer statistically significant. Similar inverse associations were observed for the intake of cereal fiber and vegetable fiber. The effect of fiber on diabetes risk may be partially explained by body weight

(continued)

Table 11.1 (continued)

Objective	Study details	Results
Feldman et al. Quantify the association between changes in lifestyle on diabetes risk (Vasterbotten Intervention; Sweden) [18]	35,680 participants; baseline age 30–50 years; 53% women; 10 years of follow-up; 1,184 diabetes cases (multivariate adjusted)	There was a reduced diabetes risk associated with increased fiber intake by 21% for each 3 g/1,000 kcal
Qiao et al. Examine the association of dietary quality and risk of incident diabetes overall and by race/ethnicity among postmenopausal women (USA—Women's Health Initiative) [28]	154,493 postmenopausal women; mean age 63 years; mean BMI 28; mean follow-up of 7.6 years; 10,285 diabetes cases (multivariate adjusted)	Women consuming >13.1 g total fiber vs. ≤13.1 g fiber/day had a 2% lower diabetes risk after multivariate adjustment including BMI. The mean total fiber intake was 15.9 g/day
Hopping et al. Examine the influence of fiber, magnesium, and glycemic load on diabetes (USA—Hawaii component of the Multiethnic Cohort) [29]	75,512 Caucasian, Japanese American, and Native Hawaiian participants; aged 45–75 years; 14 years of follow-up; 8,587 diabetes cases	Comparing extreme quintiles, total fiber intake was significantly associated with reduced diabetes risk among all men by 25% (p-trend < 0.001) and women by 5% (p-trend = 0.05). High intake of cereal fiber reduced diabetes risk significantly by 10% in men and women. High-vegetable-fiber intake lowered risk by 22% in all men but not women. Magnesium intake reduced risk in men by 23% and in women by 16%. Magnesium was strongly correlated with fiber ($r = 0.83$; $p < 0.001$), which may explain some of the protective effect of fiber
Schulze et al. Examine associations between fiber and magnesium intake and risk of diabetes (Germany—EPIC-Potsdam) [30]	9,702 men and 15,365 women; mean age 48 years; mean BMI 26; 7 years of follow-up; 844 diabetes cases	This study found no multivariate-adjusted association between fruit and vegetable fiber and diabetes risk but showed cereal fiber significantly reduced diabetes risk by 28% and soluble fiber reduced multivariate diabetes risk by 17% (9.6 vs. 5.3 g/day) and insoluble fiber by 7% (18.4 vs. 10.3 g/day)
Schulze et al. Prospectively examine the association between glycemic index, glycemic load, and fiber and the risk of diabetes in young women (USA—Nurses' Health Study II) [31]	91,249 women; mean age 37 years; mean BMI 25; 8 years of follow-up; 741 diabetes cases	The quality of carbohydrates consumed is important in preventing diabetes risk in women, after adjustment for age, BMI, family history of diabetes, and other potential confounders. Glycemic index was significantly associated with an increased risk of diabetes by 59% (high vs. low). In contrast, there was a significantly lowered diabetes risk for cereal fiber by 36% and fruit fiber by 21% (Fig. 11.5)
Salmeron et al. Examine prospectively the relationship between glycemic diets, low-fiber intake, and risk of diabetes (USA Health Professional Follow-up Study) [32]	42,759 men; age 40–75 years; 6 years of follow-up; 523 diabetes cases	Glycemic index was associated with an increased risk of diabetes by 37% (high vs. low) after multivariate adjustment. Cereal fiber was inversely associated with diabetes risk by 30% (>8.1 g/day vs. <3.2 g/day). The combination of a high glycemic load and a low-cereal-fiber intake further increased diabetes risk by 117% when compared with a low-glycemic-load and high-cereal-fiber intake

Meta-analyses

Three meta-analyses consistently show that increased intake of total fiber and fiber subtypes and lower-glycemic-index and lower-glycemic-load diets are effective in reducing diabetes risk [23–25]. A 2015 EPIC InterAct Consortium meta-analysis (19 cohort studies; 617,968 participants) found that increasing fiber by 10 g/day reduced diabetes risk, especially with cereal fiber, after multivariate adjustments including BMI (Fig. 11.1) [23]. A 2014 dose-response meta-analysis (17 cohort studies; 488,293 participants) found a nonlinear incverse association between total fiber intake and lower diabetes risk (Fig. 11.2) and a significant inverse linear response for cereal fiber and lower diabetes risk (Fig. 11.3) [24]. In both of these meta-analyses, fruit and vegetable fiber had an insignificant effect on diabetes risk, and there were not enough studies to get an accurate assessment of the effects of insoluble and soluble fiber [23, 24]. Pooled data from the Nurses' Health Study and Health Professionals Follow-Up Study (205,157 participants; 4-year assessment cycles) and a meta-analysis (24 cohort studies; 31,088 diabetes cases) found that higher-glycemic-index and higher-glycemic-load diets significantly

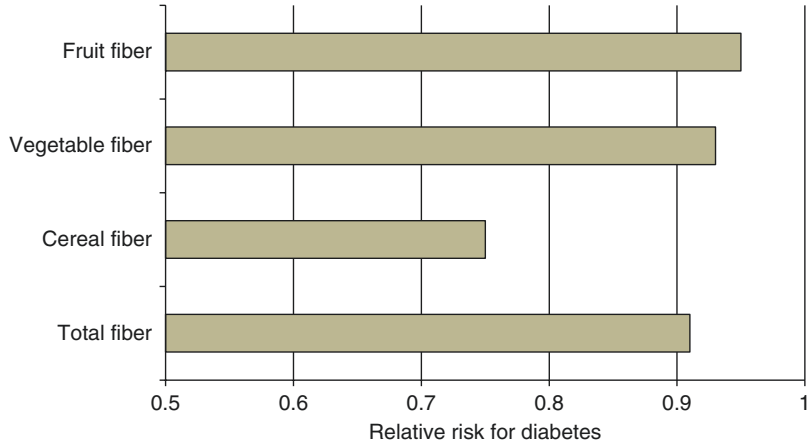

Fig. 11.1 Mean effect of the type of fiber on type 2 diabetes (diabetes) risk from meta-analysis of 19 prospective studies after multivariate adjustment including BMI [23]

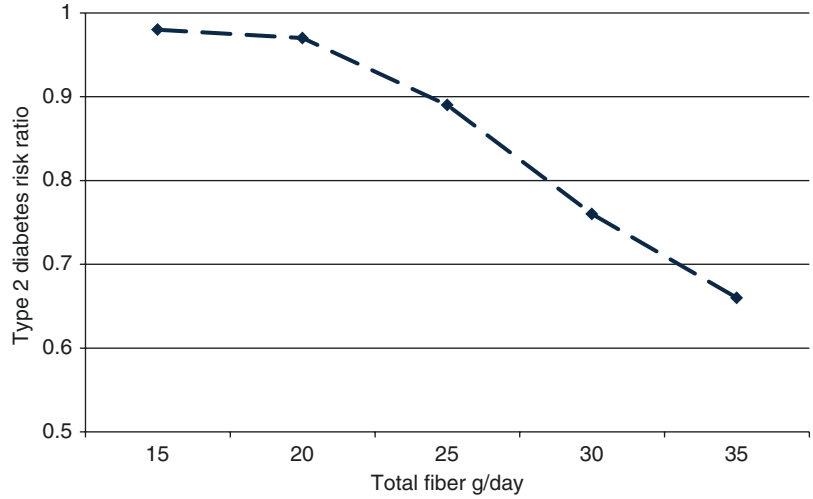

Fig. 11.2 Effect of total fiber intake and risk of type 2 diabetes from a dose-response analysis of 17 prospective studies (p for nonlinearity <0.01) [24]

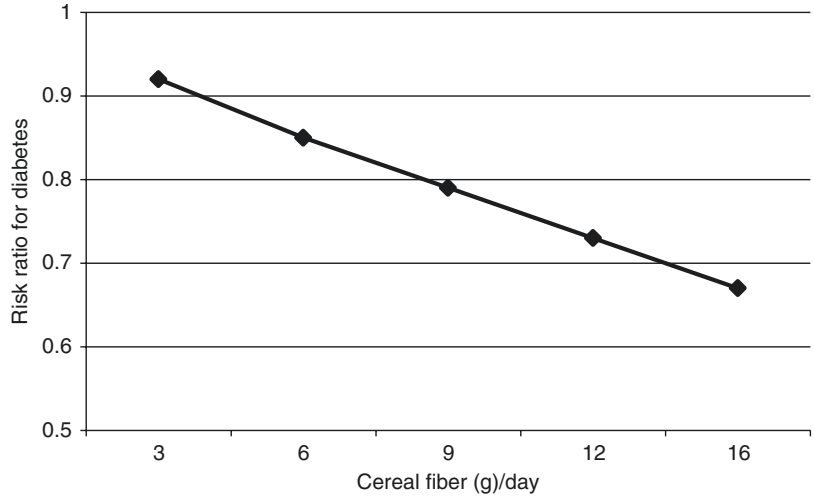

Fig. 11.3 Effect of cereal fiber intake and risk of type 2 diabetes (diabetes) from a dose-response analysis of meta-analysis of 17 prospective studies (p for nonlinearity = 0.721) [24]

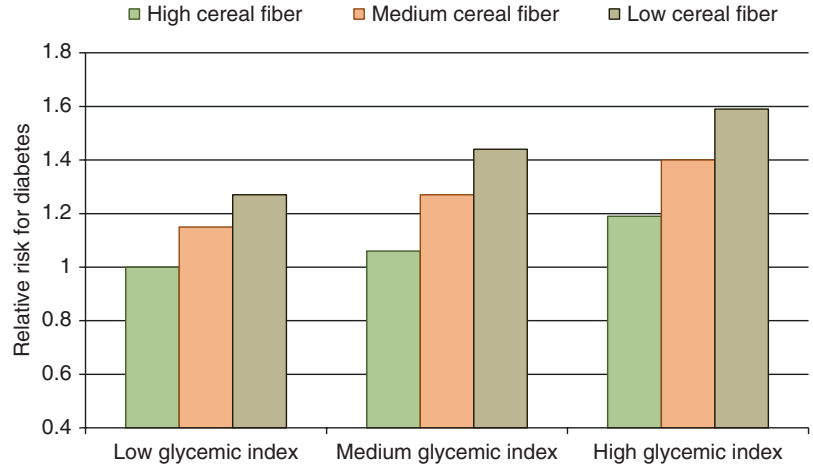

Fig. 11.4 Effect on combinations of cereal fiber and glycemic index on type 2 diabetes (diabetes) risk from pooled Nurses' Health Studies and Health Professional Follow-Up Study data [25]

increased diabetes risk by about 19%, and the combination of high-glycemic-index and low-cereal-fiber diet increased diabetes risk by 59% in men and women (Fig. 11.4) [25].

Cohort Studies and Related Analyses

Cohort studies consistently support the inverse association between fiber intake, especially cereal fiber in a low-glycemic diet, and diabetes risk [26–32]. The Nurses' Health Study (91,249 women; mean age 37 years; 8-year follow-up) found that diets higher in cereal and fruit fiber lowered the risk of diabetes compared to effects of diets with higher glycemic index foods (Fig. 11.5) [31], and similar outcomes were also observed in the Health Professionals Follow-Up Study [32]. A cross-sectional analysis of the Nurses' Health Study (2,458 diabetes-free women; mean age 58 years;

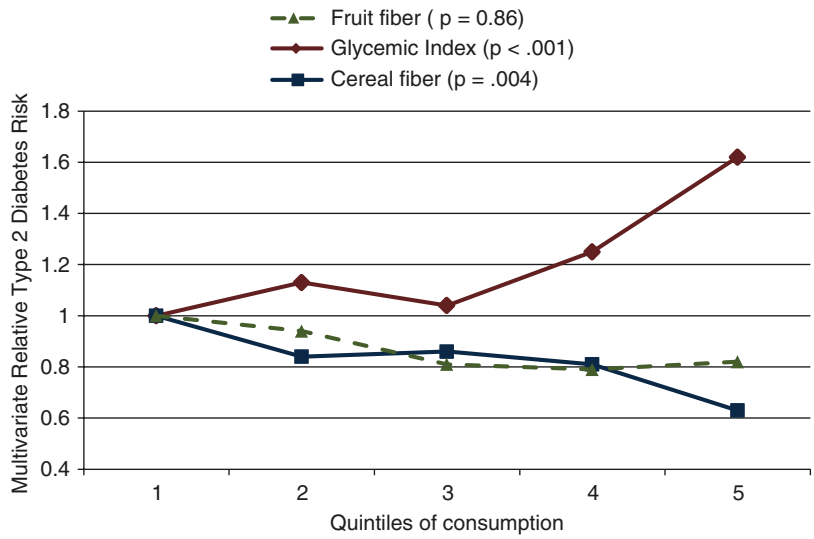

Fig. 11.5 Effect of glycemic index and type of total fiber intake on diabetes risk in women [31]

BMI 26) showed that diets higher in fiber intake and lower in starch-to-fiber ratio were associated with significantly higher concentrations of adiponectin and lower concentrations of hemoglobin A1c (HbA1c), but only cereal fiber intake was associated, inversely, with C-reactive protein (CRP) levels [26]. Total fiber and cereal fiber intake were positively associated with adiponectin. A prospective study of individuals born in 1946 reported that women with diets high in fat and glycemic index and diets low in fiber foods had increased diabetes risk in middle age by over 400% [27]. Postmenopausal women with a low-fiber intake had a 2% overall reduced diabetes risk if they consumed ≥13.1 g fiber compared to <13.1 g fiber [28]. A Hawaii prospective study (75,512 multiethnic Hawaiians; 8,587 diabetes cases; 14 years of follow-up) observed that higher total fiber intake was significantly associated with reduced diabetes risk among all men by 25% (p-trend < 0.001) and women by 5% (p-trend = 0.05). Higher intake of cereal fiber significantly reduced diabetes risk by 10% in both men and women, and higher intake of vegetable fiber was associated with lowered risk in men by 22% but not in women [29]. This study also showed that magnesium was strongly correlated with fiber ($r = 0.83$; $p < 0.001$), diabetes protection which indicates a synergistic relationship as fiber and magnesium are often found in the same whole or minimally processed plant foods. The EPIC-Potsdam study (9,702 men and 15,365 women; mean age 48 years; mean BMI 26; 7 year follow-up; 844 cases of diabetes) found no association between fruit and vegetable fiber and diabetes risk but showed that high cereal fiber significantly reduced diabetes risk by 28% and soluble fiber was twice as effective in reducing diabetes risk as insoluble fiber [30]. Overall these prospective studies show that low-fiber intake, especially with high-glycemic-index or high-glycemic-load diets, appear to be important factors in the etiology of diabetes [23–33]. A 2017 cohort study (35,680 participants; 30–50 years at baseline; 53% women; 10 year follow-up) found a 21% reduced diabetes risk per each increase in fiber intake by 3 g/1,000 kcals [18].

Randomized Controlled Trials (RCTs)

A summary of cohort study meta-analyses and representative RCTs on the effect of fiber on diabetes management and prevention is summarized in Table 11.2 [34–47].

Table 11.2 Summary of RCTs on fiber intake and/or related lifestyle changes on glycemic control in prediabetic or type 2 diabetic (diabetes) individuals

Objective	Study design	Results
Systematic reviews and meta-analyses		
Gibb et al. Assess the effects of psyllium on glycosylated hemoglobin (HbA1c) and fasting blood glucose (FBG) in patients who were being treated for diabetes and in people at risk of developing diabetes [34]	35 RCTs; 25 RCTs in healthy or prediabetic subjects, 2,670 participants; 10 RCTs in diabetic patients, 517 participants; multi-meta-analyses; 3.3–23 g/day; postprandial, 2–26 weeks	**Diabetic patients**. Four multi-week studies found psyllium (approx. 10–15 g/day) significantly reduced mean FBG by 37 mg/dL and HbA1c by 1% compared with the control. Six postprandial studies found that psyllium significantly reduced mean blood glucose by 29 mg/dL and reduced mean peak insulin levels by 0.19 units ($p = 0.23$) **Healthy and prediabetes subjects**. 14 psyllium trials showed reduction of the mean FBG by1.6 mg/dL, which showed a trend that approached significance ($p = 0.075$) vs. control/placebo 11 postprandial studies showed significantly reduced mean peak glucose for psyllium by 12.4 mg/dL and insulin by 127 pmol/L compared with the control **Overall**. There was a significant baseline FBG treatment interaction, indicating that the effect of psyllium was most pronounced in diabetic patients with higher FBG levels
Silva et al. Assess the effect of fiber from foods and supplements on HbA1c and FBG in patients with diabetes [35]	13 RCTs; 605 diabetes patients; 4 trials with high-fiber diets up to 42.5 g/day; 9 trial supplements containing soluble fiber (3.5–15 g/day) including guar, psyllium, β-glucan, and cellulose; 8–24 weeks	HbA1c and FBG values were significantly decreased by 0.55% and 10 mg/dL in patients consuming fiber intakes ranging from 37.4 to 42.6 g/day (considering a 2000 kcal/day diet) or with 3.5 to 15 g/day of fiber supplements vs. control/placebo
Post et al. Determine the effect of fiber from foods and supplements on HbA1c and FBG in patients with diabetes [36]	15 RCTs; 400 participants for FBG and 324 for HbA1c; mean ages ranged from 52 to 69 years; mean BMI ranged from 23 to 33; mean increased fiber intake was 18 g/day (4–40 g/day); 3–12 weeks	A mean intake of 18 g fiber from foods or supplements results in significantly reduced values of HbA1c by 0.26% and FBG by15 mg/dL vs. placebo
Wolfram and Ismail-Beigi Explore the efficacy of different types of diets containing various amounts of fiber in the management of diabetes risk [37]	14 RCTs; 540 subjects; insoluble and soluble fiber from food sources; 1 day–6 months	Increased consumption of vegetables, whole grains, and soluble and insoluble fiber is associated with improved glucose metabolism in both diabetic and prediabetic individuals. High fiber plant based diets improved insulin sensitivity, glucose homeostasis, blood lipids and lipoproteins, and body weight compared with western diets
Representative RCTs		
Prediabetes or metabolic syndrome (Diabetes risk)		
Weinhold et al. Evaluate the efficacy of a worksite lifestyle intervention among employees with prediabetes (USA; parallel RCT) [38]	69 subjects with prediabetes; mean age 51 years; 80% female; mean BMI 35; lifestyle intervention vs. usual care; dietary intake measured by food frequency questionnaire; physical activity by accelerometers; 16 weeks	Mean weight loss for the lifestyle intervention was 5.5% compared to 0.4% for the control group ($p < 0.001$). Mean reductions in FBG were greater in the intervention by 8.6 mg/dL than in the control by 3.7 mg/dL ($p = 0.02$). The lifestyle intervention reduced the total energy and the percentage of energy from all fat intake and increased the intake of total fiber (all $p < 0.01$) (Fig. 11.6)

Table 11.2 (continued)

Objective	Study design	Results
Weickert et al. Compare the effects of isoenergetic high-cereal-fiber and high-protein diets and a diet with moderate increases in both cereal fibers and protein on insulin sensitivity (Germany; parallel RCT) [39]	111 subjects; mean age 55 years; mean BMI 31; 60% female; high cereal fiber diet vs. high protein diet; 6 weeks	Insulin sensitivity was 25% higher after 6 weeks of the high-cereal-fiber diet than after 6 weeks of the high-protein diet ($p = 0.008$)
Cicero et al. Evaluate the long-term effects of AHA Step 2 diet supplemented with psyllium and guar gum on metabolic syndrome components (Italy; parallel RCT) [40]	141 subjects; mean age 58 years; mean BMI 28; AHA Step 2 diet plus psyllium or guar gum 3.5 g 3× daily or no added fiber; 6 months	Long-term supplementation with moderately high dosages of psyllium and guar gum improved most metabolic syndrome factors when consumed with a healthy diet. Both soluble fibers significantly improved BMI, fasting blood glucose and insulin, HOMA index, HbA1c, and LDL-C after 6 months compared to baseline and base AHA Step 2 diet (Fig. 11.7)
Kim et al. Investigate the effects of breakfast cereal with varying amounts of β-glucan on acute glycemic response (USA; crossover RCT) [41]	17 normoglycemic women; BMI ≥ 30 at increased risk for insulin resistance; blood glucose and insulin response measures were obtained at baseline and 30, 60, 120, and 180 min after consuming breakfast cereal with 0, 2.5, 5.0, 7.5, and 10 g β-glucan	10 g β-glucan significantly reduced peak glucose response at 30 min and delayed the rate of glucose response. The peak and area under the curve of insulin responses were significantly affected by β-glucan in an inverse linear relationship. Intake of 10 g of β-glucan improved insulin responses in obese women at risk for insulin resistance
Weickert et al. Evaluate whether intake of purified insoluble oat fiber may improve whole-body insulin sensitivity (Germany; single-blind, crossover RCT) [42]	17 women; mean age 53 years; mean BMI 30; white bread enriched with insoluble fiber 31 g/day vs. white bread; 3 days; 7-day washout	The high-fiber-enriched bread significantly improved insulin sensitivity by 8% (6.85 vs. 6.06 mg/min kg) and increased insulin action by 12% compared to the control white bread
Diabetes		
Nowotny et al. Investigate the effect of reduced energy diet composition for diabetes management (Germany; parallel RCT) [43]	59 diabetic patients treated with hypoglycemic meds; mean age 54 years; mean BMI 35; 54% female; reduced energy diet by a mean of 330 kcal; low-risk diet high in cereal fiber (30 g/day), coffee, and free of red meat; high-risk diet low in cereal fiber (10 g/day), no coffee, and high in red meat intake; 8 weeks	In diabetic subjects, reduced energy diets had similar reductions in body weight, waist circumference, liver fat, and whole-body insulin resistance independent of the cereal fiber level. However, the high-cereal-fiber diet significantly lowered inflammatory markers such as IL-18 and histidine vs. the high-risk diet, which may have long-term benefits for diabetes health
Cugnet-Anceau et al. Analyze the effects of the enrichment of a normal diet with β-glucan in free-living diabetic subjects for 2 months, using a palatable soup (French; parallel, double blinded RCT) [44]	53 diabetic subjects; mean age 62 years; mean BMI 30; mean HA1c 7.4%; 3.5 g β-glucan added to soup vs. control soup daily; 2 months	The 3.5 g β-glucan-supplemented soup was below the threshold to significantly reduce any blood lipids or lipoproteins, FBG, or HA1c compared to the control soup

(continued)

Table 11.2 (continued)

Objective	Study design	Results
Jenkins et al. Investigate the effects of high-cereal-fiber and low-glycemic index diets on glycemic control and cardiovascular risk factors in patients with type 2 diabetes (Canada; parallel RCT) [45]	210 patients with diabetes treated with antihyperglycemic medications; mean age 61 years; mean BMI 31; 64% female; high-cereal-fiber diet, whole grain breads, breakfast cereal, pasta, brown rice (15.7 g fiber/1000 kcal) vs. low-glycemic index diet, whole grain breads, breakfast cereal, pasta, brown rice, nuts, beans, lentils (18.7 g fiber/1000 kcal); 6 months	The low-glycemic index diet resulted in moderately lower HbA1c levels by 0.32% ($p < 0.001$) and FBG by 4.4 mg/dL ($p = 0.02$) compared with the high-cereal-fiber diet. The low-glycemic index diet also increased HDL-C by1.7 mg/dL, and the cereal-fiber diet decreased HDL-C level by 0.2 mg/dL ($p = 0.005$). Low-glycemic-index diets may be useful as part of the strategy to improve glycemic control in patients with diabetes taking antihyperglycemic medications
Jenkins et al. Assess the effect of wheat bran on glycemic control and CHD risk factors in type 2 diabetes (Canada; crossover RCT) [46]	23 subjects with diabetes;16 men and 7 postmenopausal women; mean age 63 years; mean BMI 27; 19 g/day additional cereal fiber as breads and breakfast cereals vs. control low-fiber 4 g/day additional cereal fiber as breads and breakfast cereals; 3 months; 2-month washout	No differences were seen in body weight, fasting blood glucose, HbA1c, serum lipids, apolipoproteins, or blood pressure
Chandalia et al. Investigate the effect of fiber intake on glycemic control in patients with diabetes (USA; crossover RCT) [47]	13 diabetic patients, 12 males, 1 female; mean age 61 years; mean BMI 32; healthy diets: (1) high-fiber diet with 25 g insoluble and 25 g soluble fiber vs. (2) moderate-fiber diet with 16 g insoluble fiber and 8 g soluble fiber as recommended by the American Diabetes Association; 6 weeks; 7-day washout	Notable significant results include lower 24-h area under the curve for both glucose and insulin levels for the high-fiber diet. In participants on the high-fiber diet, plasma glucose was lower by 10%, and insulin was lower by 12%. Plasma total cholesterol ($p = 0.02$), triglycerides ($p = 0.02$), and very-low-density lipoprotein cholesterol ($p = 0.01$) were also lower in participants on the high-fiber diet

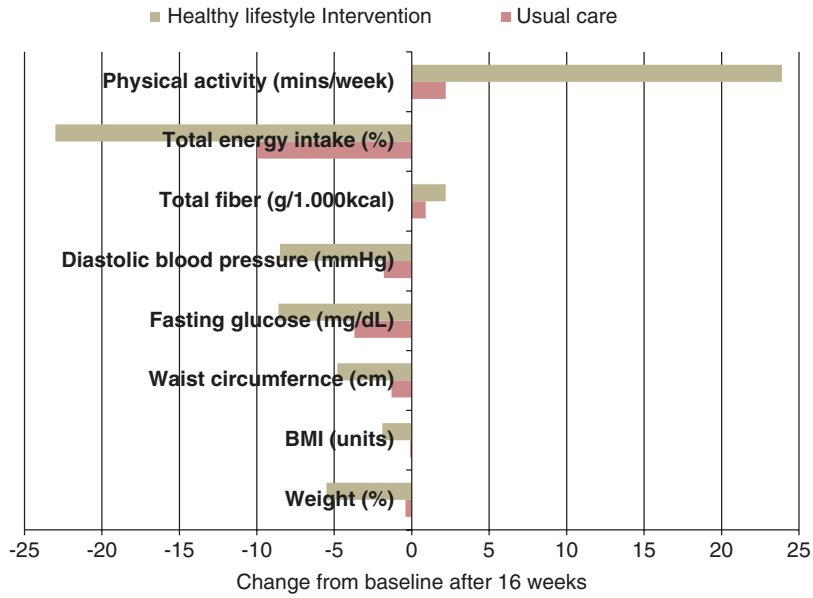

Fig. 11.6 Effect of a 16-week lifestyle intervention ($n = 35$) or usual care ($n = 34$) in prediabetic adults (mean age 51 years) (all change $p \leq 0.02$) [38]

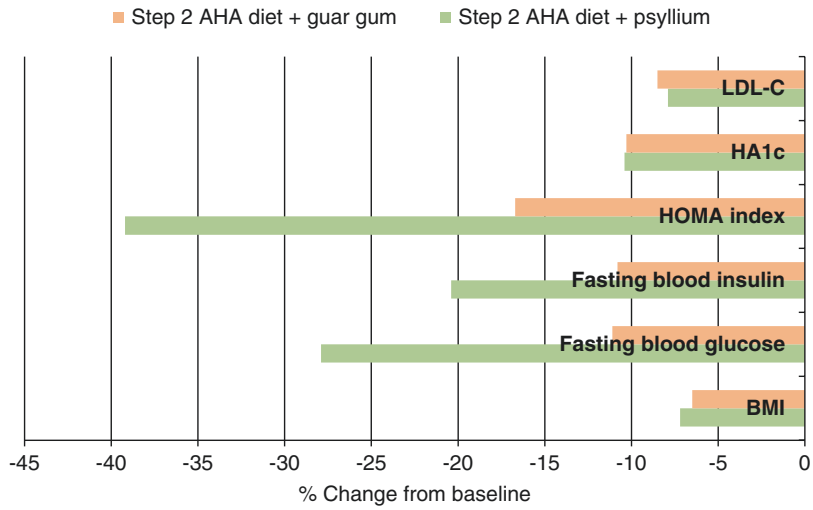

Fig. 11.7 Effect of American Heart Association (AHA) Step 2 diets supplemented with psyllium or guar gum in 114 metabolic syndrome subjects over 6 months (both fiber sources $p < 0.01$) [40]

Systematic Review and Meta-analyses

Four systematic reviews and meta-analyses of RCTs including people with prediabetes, metabolic syndrome, and diabetes consistently support an important role for fiber from both high-fiber diets and supplements in controlling and reducing fasting blood glucose (FBG) and glycosylated hemoglobin (HbA1c) levels [34–37]. Two meta-analyses of RCTs in patients with diabetes estimate that fiber-rich diets increased by a mean of 18 g fiber/day, and fiber supplements such as 3–15 g of guar, psyllium, or β-glucan have modest but significant beneficial effects on glycemic control by reducing mean FBG levels by 10–15 mg/dL and HbA1c by 0.26–0.55 mg/dL compared to control or placebo over 3–24 weeks [35, 36]. Clearly, fiber-rich diets and supplements are effective in aiding in the management of diabetes. A 2011 systematic review showed that increased consumption of vegetables, whole grains, and soluble and insoluble fiber was associated with improved glucose metabolism in both diabetic and prediabetic individuals [37]. Diabetes-protective improvements in insulin sensitivity, glucose homeostasis, blood lipids and lipoproteins, and body weight were more evident following a plant-based diet compared with Western diets. A 2015 meta-analysis of psyllium RCTs (35 RCTs; 3,187 participants; prediabetic and diabetic subjects; 3.3–23 g/day; 2–26 weeks) found that psyllium had no effect on the FBG in euglycemic (normal) individuals, a modest effect on prediabetic subjects and the greatest lowering effect in diabetic subjects [34]. In diabetic subjects, psyllium significantly lowered mean FBG by 37 mg/dL and mean HbA1c by 1% compared to placebo and in healthy or prediabetic individuals mean FBG was lowered by 1.6 mg/dL ($p = 0.075$) [34].

Randomized Controlled Trials

Prediabetes and Metabolic Syndrome (Diabetes Risk)

RCTs consistently show that fiber-rich diets and supplements can reduce the risk of transitioning from prediabetes or metabolic syndrome to diabetes, especially in combination with healthy lifestyle habits and diets [38–42]. A 2015 USA worksite diabetes prevention program RCT (69 prediabetes subjects; mean age 51 years; 80% female; mean BMI 35; 16 weeks) demonstrated that a healthy lifestyle with

reduced total energy, low fat, and increased fiber intake reduced the risk of advancing from prediabetes to diabetes by increasing weight loss and improving glycemic control compared to usual care or Western lifestyle (Fig. 11.6) [38]. A 2010 Italian RCT (141 subjects with metabolic syndrome; mean age 58 years; mean BMI 28; American Heart Association (AHA) diet plus psyllium or guar vs. no soluble fiber supplement; 6 months) showed that added soluble fiber significantly reduced BMI, and improved glycemic control, and lipoprotein profiles compared to the standard AHA diet without added supplemental soluble fiber (Fig. 11.7) [40]. Several RCTs found that high intake of cereal fiber >31 g/day significantly improved insulin sensitivity compared to refined low-cereal-fiber or high-protein diets [39, 43]. A dose-response RTC on oat β-glucan and postprandial glycemic response found that 10 g β-glucan significantly delayed glucose response and lowered insulin levels in obese women at increased risk for diabetes [41].

Diabetes Management

The effect of fiber on diabetes management depends on the type and amount of fiber and the glycemic properties and energy level of the diets [43–47]. Several RCTs with low levels of β-glucan (3.5 g/day in soup) or cereal fiber (19 g/day from bread and breakfast cereal) were inadequate to improve glycemic control in diabetic patients [44, 46]. A crossover RCT (13 diabetic subjects; mean age 61 years; mean BMI 32; healthy high-fiber diet with 25 g insoluble fiber and 25 g soluble fiber vs. American Diabetes Association diet with 16 g insoluble fiber and 8 g soluble fiber; 6 weeks) found that the higher-fiber diet significantly reduced FBG and fasting insulin and blood lipid and lipoprotein levels, but there was insufficient study duration to obtain accurate HbA1c values [47]. A 2008 Canadian RCT (210 diabetes patients treated with hypoglycemic medication; mean age 61 years; mean BMI 31; 64% female; high-cereal-fiber diet with 15.7 g fiber /1000 kcal vs. a low-glycemic diet including whole grain cereal foods plus nuts, beans, and lentils 18.7 g fiber/1000 kcal) showed that the combined effects of low-glycemic-index and high-fiber diets significantly reduced HbA1c and FBG and increased HDL-C compared to the high-cereal-fiber diet alone [45]. A 2015 German RCT (59 diabetes patients with hypoglycemic meds; mean age 54 years; mean BMI 35; reduced energy diet by a mean of 330 kcal/day with 30 g cereal fiber, ad libitum coffee, and no red meat vs. 10 g cereal fiber, no coffee and red meat allowed; 8 weeks) reported that reduced-energy diets had similar reductions in body weight, waist circumference, liver fat, and whole-body insulin resistance irrespective of the dietary composition in overt type 2 diabetes. However, the 30 g cereal fiber diet with coffee and no red meat significantly lowered inflammatory markers such as IL-18 and histidine vs. the 10 g cereal fiber diet with no coffee and red meat, which may have long-term benefits for diabetes health.

Dietary Fiber and Diabetes Mechanisms

As much as 90% of diabetes risk and management is attributed to modifiable risk factors such as diet and physical activity and their effects on overweight and obesity risk [48]. Lifestyle intervention with calorie restriction, fiber-rich diets, and exercise to promote weight loss, as shown in the US Diabetes Prevention Program and other international programs, significantly reduced the risk of conversion to diabetes in high-risk patients with impaired glucose tolerance by 58% [11–13]. The mechanisms for the effect primary of adequate fiber intake on diabetes prevention and management are reducing the risk of obesity and visceral fat accumulation; attenuating systemic inflammation; promoting and maintaining a healthy microbiota ecosystem; and controling postprandial and fasting glycemic response (Fig. 11.8).

Adequate Dietary Fiber Intake

Properties
- lower energy density
- Higher volume/bulk

Mouth:
- longer chewing time
- slower eating rate

Stomach:
- increases distension
- delays emptying rate (w/ bulking/viscosity)
- increases satiety/satiation

Small intestine:
- decreases postprandial glycemic response
- delays hunger

Pancreas:
- lowers insulin response
- maintains β-cell function

Large intestine:
- promotes fermentation to SCFAs
- increases healthy microbiota
- enhances satiety peptides
- increases anti-diabetes peptides (e.g. GLP-1)
- strengthens colon barrier for less endotoxin leakage

Body weight and fat:
- lowers obesity risk
- lowers risk of visceral/ectopic fat
- lowers level of systemic inflammation

Circulation:
- promotes insulin sensitivity
- lowers HbA1c and fasting blood glucose
- lowers systemic inflammation

Reduced diabetes risk and improved management

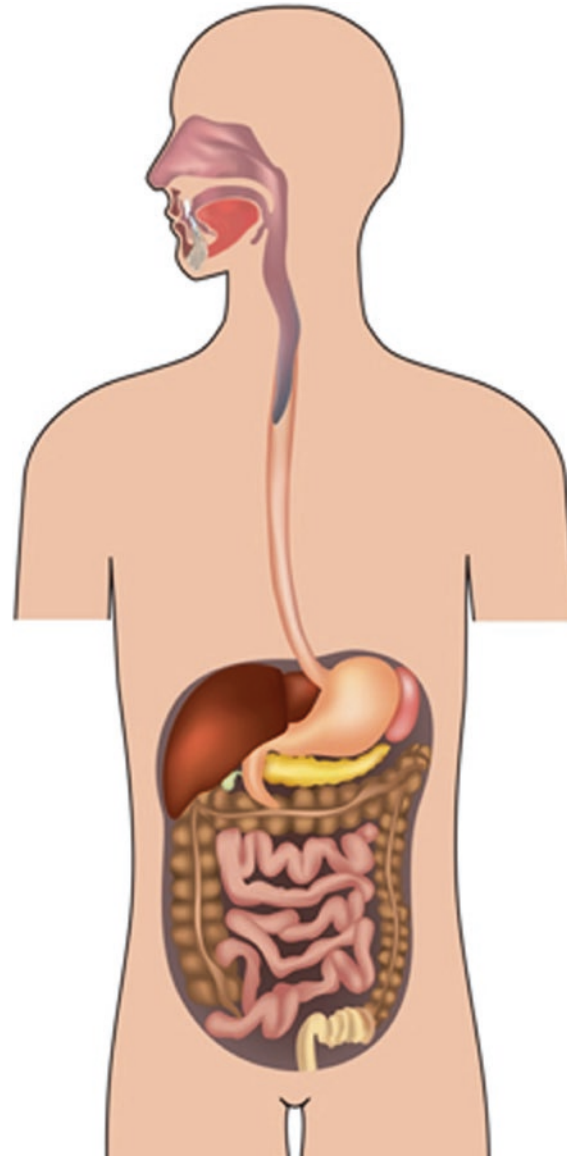

Fig. 11.8 Potential dietary fiber mechanisms for type 2 diabetes (diabetes) prevention and management

Obesity and Visceral Fat

Positive energy balance and excessive adiposity, especially abdominal fat, are primary risk factors for diabetes, with higher BMI being the strongest risk factor for diabetes, especially in Asian populations [5]. Prospective cohort studies consistently find that high BMI, waist circumference, and waist/hip ratio increase diabetes risk by about 90% per standard deviation [49]. Also, weight gain starting in young adulthood is an important independent predictor of diabetes risk [50]. There is an established association between visceral and ectopic body fat and insulin resistance [51–54]. This leads to hypertriglyceridemia, ectopic fat deposition (including hepatic steatosis), and insulin resistance in muscle, liver, and pancreatic tissues due to elevated systemic

inflammatory cytokines associated with insulin receptor dysfunction, resulting in progressively increasing insulin resistance and diabetes risk.

Fiber-rich foods have lower dietary energy density both directly and by displacing higher energy-dense foods, lowering macronutrient bioavailability and leading to increased excretion [55]. In general, fiber is 2 kcal/g or less compared to 4 kcal/g for sugar and digestible starch, because fiber digestion bypasses the small bowel to be anaerobically fermented by large bowel microflora to short-chain fatty acids (SCFAs) and the gases carbon dioxide, hydrogen, and methane or remains as indigestible fiber [56–58]. The consumption of >25 g fiber/day can reduce macronutrient energy availability by 3–4%, which is equivalent to about 100 kcal/day [59, 60]. This relationship appears to be dose dependent. One study found that for each additional 5 g/day of fiber consumed, there was 36 kcal/day increase in fecal energy content [61]. Fiber may help to delay hunger, increase satiety by slowing the rate of gastric emptying, and promote appetite control and fat oxidation by signaling a variety of gastrointestinal hormonal pathways including orexigenic ghrelin and anorexigenic and metabolic stimulating peptide YY, cholecystokinin (CCK), and glucagon-like peptide-1 (GLP-1) [62–65]. Potential variables include fiber type and level, physical characteristics of the fiber source consumed, or timing of intake (before or during a meal), which can promote satiation by increasing gastric distention and altering intestinal satiety hormones to suppress food intake [66, 67]. Whole fiber-rich foods tend to be more effective in appetite, energy intake, and weight control than processed whole foods (e.g., apple sauce or juice), supplements, or energy-dense foods enriched with added isolated fiber sources [68–79].

Prospective studies and RCTs support the role of adequate fiber intake to reduce the risk of obesity and excessive central obesity and visceral fat accumulation [80–92]. A systematic review of prospective and clinical studies concluded that fiber intake was inversely associated with the risk of gaining body weight and waist circumference [80]. Obese individuals tend to have lower fiber intake than those who are normal weight or overweight [81]. In women, high-fiber diets are more effective at preventing weight gain than low-fiber diets, and a daily increase of 10 g fiber/1000 kcal was shown to reduce body weight by about 2 kg and fat by 2% over 20 months, after adjusting for energy intake [82, 83]. A 10 g higher-fiber intake was associated with a 1.9-cm-smaller waist circumference, reduced BMI by 0.8 units, and improved insulin sensitivity [84, 85]. Several prospective studies suggest that increasing fiber intake by10–12 g/day can significantly reduce weight gain, visceral fat accumulation, and waist circumference [86–88]. In a number of RCTs, ad libitum fiber-rich diets containing about 30 g fiber/day or more have consistently been shown to prevent weight gain and provide sustained weight loss compared with fiber diets of <20 g/day [89–92].

Systemic Inflammation

Chronic inflammation is a major risk factor underlying the development of insulin resistance with aging [93]. Chronic inflammation impairs normal lipid accumulation, adipose tissue function, and mitochondrial function and causes endoplasmic reticulum stress, which leads to insulin resistance [93]. A meta-analysis (14 RCTs; in overweight and obese subjects; 3–18 g increased fiber/day vs. control diets;3–16 weeks) showed that intervention with fiber-rich food or fiber supplements significantly reduced CRP by 0.47 mg/L, where the total fiber intake was 8 g/day higher in the intervention group than in the control group [94]. This analysis also reported that in subjects with CRP ≥ 3 mg/L, increased fiber reduced CRP levels by 0.72 mg/L (p = 0.060). Analyses of US NHANES' cross-sectional data found that of the macronutrients only fiber was inversely associated with elevated plasma CRP levels [95], and individuals consuming >22.5 g/day of fiber had a 34% lower risk of having elevated CRP compared to those consuming 8 g/day of fiber [18]. The Nurses' Health Study found CRP to be inversely associated with healthier, fiber-rich diets and positively associated with

low-fiber Western diets [96]. Weight loss, healthy diets, and increased fiber intake are known to increase adiponectin levels, which appears to be related to improved insulin sensitivity [97].

Microbiota Dysfunction

The link between the colonic microbiota and diabetes is becoming well established as studies show the direct involvement of microbiota in the triad of obesity, insulin signaling dysfunction, and low-grade inflammation, which are the primary factors in diabetes progression [98–100]. *Proteobacteria* have been shown to be significantly higher in people with diabetes compared to healthy persons and positively correlated with plasma glucose [101]. Two other studies also showed that diabetic subjects were characterized by a reduction in the number of *Clostridiales* bacteria (*Roseburia* species and *Faecalibacterium prausnitzii*), which produce the SCFA butyrate [102, 103]. Potential mechanisms associated with the effects of microbiota dysbiosis on insulin resistance are increased systemic inflammation associated with the colonic permeability of lipopolysaccharide (LPS) from gram-negative bacteria pathobionts, low incretin secretion and fecal butyrate production, macrophage influx into the visceral fat tissue, and activation of hepatic Kupffer macrophage cells [104, 105].

Dietary fiber is critical in attenuating the obesity, systemic inflammation, and insulin resistance triad by its fermentation to SCFAs [104–106]. Particularly butyrate and propionate are important mediators associated with food intake, insulin sensitivity, and insulin resistance through gut peptides such as GLP-1 and systemic inflammation [64, 65, 104–110]. In the colon, butyrate is the preferred energy source for colon cells. Butyrate promotes the assembly of tight endothelial junctions to reduce leakage of intestinal endotoxic bacterial LPS into the circulation which helps alleviate systemic inflammation and risk of developing insulin resistance. For visceral fat, propionate has been shown in human adipose tissue obtained from overweight adults, to reduce visceral fat inflammation by down-regulating the proinflammatory cytokine TNF-α [110]. In a RCT, the consumption of 21 g polydextrose or soluble corn fiber in the form of 3 cereal bars/day for 3 weeks changed the gut microbiota of overweight subjects by shifting the colonic *Bacteroidetes*-to-*Firmicutes* ratio to one that was more typical of lean individuals, independent of caloric restriction [111]. A growing number of intervention trials support the beneficial role of fiber-rich diets and fiber supplements in promoting a healthy microbiota ecosystem and diabetes prevention and management [112–118].

Glycemic Control

Glycemic metabolic control is a major cornerstone of diabetes management as achieving HbA1c goals decreases the risk for microvascular complications and may also reduce cardiovascular disease (CVD) risk [15]. The monitoring of carbohydrate intake, whether by carbohydrate counting or experience-based estimation, remains a key strategy in achieving glycemic control. For glycemic control and good health, carbohydrate intake from fiber-rich vegetables, fruits, whole grains, legumes, and dairy products should be advised over intake from other carbohydrate sources, especially those that contain high levels of added sugars. Substituting low-glycemic load foods for higher-glycemic load foods may modestly improve glycemic control. However, the literature regarding glycemic index and glycemic load in individuals with diabetes is complex, and it is often difficult to discern the independent effect of fiber compared with that of glycemic index on glycemic control or other outcomes. People with diabetes should consume at least the amount of fiber recommended for the general public (14 g fiber/1000 kcal or 25 g/day for women and 38 g/day for men). Fructose as “free fructose” such

as in whole and minimally processed fruit tends to result in better glycemic control compared with isocaloric intake of highly processed sucrose or starchy food and beverages. A meta-analysis (12 RCTs; 612 diabetic subjects; ≥4 weeks) showed a significant decrease of HbA1c with low-GI diet by 0.4% compared to a control diet [119]. This level of HbA1c decrease is clinically significant, comparable to the decrease achieved through medications, and significant in reducing microvascular complications [120, 121].

In a population-based study of 1,114 middle-aged and elderly men and women, intake of fiber was positively associated with insulin sensitivity, independent of both physical fitness and waist circumference [122]. When fiber, either insoluble or soluble fiber, is consumed at about 30 g fiber or more/day, especially with about 10–12 g fiber per meal, there tends to be enough critical mass of fiber to physically increase stomach and/or small intestinal bulk or viscosity to delay the digestion and absorption of available carbohydrates and acutely reduce postprandial glycemic and insulinemic response rates, which can, along with healthy dietary patterns, potentially enhance insulin sensitivity [41, 123–127]. Consumption of soluble fiber supplements reduces postprandial glucose and insulin responses after low-glycemic carbohydrate-rich meals, which is explained by the viscous and/or gel-forming properties of soluble fiber, which slow gastric emptying and macronutrient absorption from the gut [128]. When recommending a fiber supplement for diabetes prevention or management, only a soluble low-fermenting, gel-forming fiber such as psyllium has been clinically proven [34, 128]. A meta-analysis on psyllium RCTs (35 RCTs; 3,187 participants; prediabetic and diabetic subjects; 3.3–23 g/day; 2–26 weeks) found in diabetic subjects that psyllium significantly lowered mean FBG by 37 mg/dL and mean HbA1c by 1% compared to placebo and in healthy or prediabetic individuals mean FBG was lowered by 1.6 mg/dL ($p = 0.075$) [34]. Other fiber sources that may be effective are partially hydrolyzed guar gum and β-glucan from oats or barley [128]. The potential mechanisms of action for insoluble fiber include speeding intestinal transit time and increasing insulin sensitivity and for soluble fiber delaying postprandial glucose response and gastric emptying rate [129].

Highlighted Fiber-Rich Food for Diabetes Prevention and Management: Whole Oats

Whole oat products such as oatmeal are one of the most effective fiber-rich food sources for improving glycemic control and blood lipids profiles for reducing diabetes risk and managing diabetes health effects [130–132]. The predominant effect of oats on diabetes risk and management are attributed to the bioactivity of β-glucan. β-glucan increases intestinal viscosity, decreases the absorption of carbohydrates and lipids, and reduces food intake to control hyperglycemia, lower lipid, and reduce weight. Also, β-glucan plays a role in promoting colonic microbiota health by increasing the production of SCFAs, increasing microflora diversity, and driving the release of bioactive compounds, which may lower the risk of obesity and associated disorders. A 2016 meta-analysis (18 RCTs; 1024 subjects; oat product dose ranged from 20 to 136 g/day and β-glucan 3 to 10 g/day) found that oat products intake resulted in a greater decrease in fasting glucose and insulin ($p < 0.05$) and glycosylated hemoglobin (HbA1c) ($p < 0.001$), compared with control products, in hyperlipidaemic and overweight subjects, especially people with diabetes [130]. A 2015 systematic review and meta-analysis (14 RCTs; 608 diabetic subjects) showed that oats intake significantly reduced the concentrations of HbA1c by 0.42%, fasting glucose by 0.39, total cholesterol by 0.49 mmol/L, and LDL-cholesterol by 0.29 mmol/L in diabetic patients compared to control products [131]. Oatmeal significantly reduced the acute postprandial glucose and insulin responses compared with the control meal. A 2016 RCT (298 overweight diabetic patients; mean age 59 years; 30-day centralized intervention; 1-year free-living follow-up; usual care group received no intervention; the healthy diet group received a healthy low-fat and high-fiber diet; and healthy diet with the same amount of cereals replaced by 50 and 100 g oats) found that

after the 30-day intervention, compared to the healthy diet, the 50 g-oats (2.7 β-glucan) group significantly lowered postprandial blood glucose by 1.04 mmol/L and total cholesterol by 0.24 mmol/L and the 100 g-oats (5.3 β-glucan) group significantly lowered postprandial blood glucose by 1.48 mmol/L, HOMA-IR by 1.77 mU mol/L^2, total cholesterol by 0.33 mmol/L, and LDL-cholesterol by 0.22 mmol/L [132]. In the 1-year follow-up, significantly greater effects in reducing weight by 0.89 kg, HbA1c by 0.64%, and triglycerides by 0.70 mmol/L were observed in the 100 g-oats group. In this RCT, short- and long-term whole oats intake had significant effects on controlling hyperglycemia, lowering blood lipids and reducing weight, which provides support evidence for recommending oats as a good whole grain selection for overweight diabetic patients. These studies suggest a potential option to help reduce the global progression of prediabetes and diabetes.

Conclusions

The prevalence of prediabetes and diabetes has increased globally in parallel with the rising levels of obesity in adults and children, a phenomenon sometimes called diabesity. Estimates from the International Diabetes Federation forecasts a major increase in people with diabetes globally from 382 million in 2013 to 592 million in 2035. If this global trend continues, by 2030 about one billion people are expected to have prediabetes and diabetes. As much as 90% of diabetes risk management is attributed to modifiable risk factors such as diet and physical activity and their effect on increased risk of overweight and obesity. Prospective cohort studies consistently show that increased intake of total fiber and cereal fiber and lower glycemic index and glycemic load diets is effective in reducing diabetes risk. Meta-analyses of RCTs including people with prediabetes and diabetes consistently show that increased fiber intake from diets and supplements significantly lowers fasting blood glucose and HbA1c levels compared to control diets. Whole oat products such as oatmeal and psyllium, a gel-forming, low fermentable fiber supplement, have been shown clinically to be among the most effective fibers sources in lowering fasting blood glucose and HbA1c in individuals with diabetes and prediabetes compared to placebo. The primary mechanisms related to adequate fiber intake and diabetes prevention and management are (1) reducing the risk of obesity and visceral fat accumulation, (2) promoting and maintaining a healthy microbiota ecosystem, (3) attenuating elevated systemic inflammation, and (4) controlling postprandial and fasting glycemic responses and protecting against insulin resistance.

Appendix 1. Fifty High-Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cups (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from being frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture Part B. Section 2: Total Diet. 2010; Table B2.4
Dietary Guidelines Advisory Committee. Scientific Report of the 2015 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. 2015; 97, 98; Table D1.8
USDA National Nutrient Database for Standard Reference, Release 27 http://www.ars.usda.gov/nutrientdata. Accessed 17 February 2015

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Chapter 12
Fiber in Healthy Aging

Keywords Dietary fiber • Healthy aging • All-cause mortality • Disease-specific mortality • Cardiovascular disease • Type 2 diabetes • Metabolic syndrome • Colorectal cancer • Obesity • Inflammation • Frailty

Key Points

- People are now living longer than at any other time in history, but many people are aging poorly with decreased healthy life expectancy. For most people, the aging process is not genetically predetermined as the rate at which people age can be modified by diet, exercise, personal habits, and psychosocial factors. Healthy aging is marked by good mental health and social engagement, lack of physical disability, and the absence of premature chronic disease or death.
- Within the normal aging process, dietary quality is a major determinant of suboptimal aging or healthy aging. Dietary fiber is the most significant shortfall macronutrient in Western diets, which is a major public health concern because its deficiency is associated with increased chronic disease risk, suboptimal aging, obesity, microbiota dysbiosis, and increased morbidity. Adequate fiber intake is among the most important dietary components supporting healthy aging.
- Dose-response meta-analyses estimate that increasing total fiber intake by 10 g/day increments significantly reduces mortality risk for all-cause by 10–11%, coronary heart disease (CHD) by11–20%, total cardiovascular disease (CVD) by 9%, and cancer by 6–9%.
- Adequate fiber intake (14 g/1,000 kcal) is associated with healthy aging through its effects on lowering the risk of, for example, cardiovascular diseases, stroke, weight gain, metabolic syndrome, type 2 diabetes, certain cancers, colonic microbiota dysfunction, frailty, and periodontitis.
- A 2016 prospective study (adults ≥ 49 years; 10 years of follow-up) suggests that higher fiber intake improved the odds of healthy aging by 80% compared to low fiber intake.

Introduction

People are now living longer than at any other time in history,but most people are aging poorly with decreased healthy life expectancy [1, 2]. This decrease in healthy life expectancy is associated with the global adoption of the Western lifestyle, especially since the 1980s, which is primarily responsible for pandemic rates of obesity, metabolic syndrome, type 2 diabetes, non-alcoholic fatty liver disease, and other related health conditions in both adults and children [3–6]. US adults have shorter and less healthy lives than populations in 32 other high-income countries [7]. As a result, population longevity

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forecasts suggest a stagnation or decline in life expectancy over the next 25 years [4–8]. For most people, the aging process is not genetically predetermined as the rate at which people age can be modified by diet, exercise, personal habits, and psychosocial factors [1–4, 9]. Within the normal aging process, there is suboptimal aging, in which extrinsic factors accelerate the aging process, or healthy or successful aging, in which extrinsic factors slow the aging process.

Dietary fiber (fiber) is the most significant shortfall macronutrient in Western diets, which is a major public health concern because its deficiency is associated with increased chronic disease risk, suboptimal aging, obesity, microbiota dysbiosis, and increased morbidity and mortality [10–18]. Specifically, only about 5–10% of the US population consume adequate daily fiber [15]. The mean intake of fiber in the United States is about 16 g/day (18 g for males and 15 g for women), which is about half of the adequate daily intake of 14 g fiber/1000 kcal (approximately 25 g for women and 38 g for men) [16, 19]. Fiber-rich foods and diets tend to be lower in energy density and higher in nutrient quality (e.g., lower in saturated and trans-fatty acids, sodium, and added sugars and richer in essential nutrients or phytochemicals such as potassium and antioxidants (e.g., vitamin C and E, carotenoids, and polyphenols). The consumption of adequate amounts of fiber from a variety of plant foods is associated with reduced risk of developing several chronic diseases or conditions, including cardiovascular disease, type 2 diabetes, metabolic syndrome, colorectal cancer, obesity, and premature mortality [15–24]. The number of mechanisms by which fiber promotes healthy aging is unparalleled by any other nutrient or food component due to its importance in: maintaining a healthy and diverse colonic microbiota, promotes colonic, cardiometabolic, and immunity health; improving serum lipid profiles and glycemic control; promoting satiety and reducing food intake; reducing risk of weight gain; and attenuating systemic inflammation [13–33]. Also, there is emerging evidence that adequate fiber intake may help to promote healthy aging by reducing epigenetic DNA methylation and slowing the rate of telomere shortening [34–37]. The fiber level of 50 top fiber-rich foods is listed in Appendix 1. The objective of this chapter is to review the effects of fiber intake on successful (healthy) aging.

Healthy Aging

Healthy aging is marked by the absence of chronic disease or related premature death, lack of physical disability, good social engagement, and good mental health [9]. Adequate fiber intake has been consistently shown to support healthy aging [38–53]. Elevated systemic inflammation markers such as C-reactive protein (CRP) have an important role in unhealthy aging (inflammaging) [49–51]. A meta-analysis (14 randomized controlled trials (RCTs)) found that in overweight and obese adults the increased fiber intake by ≥ 8g/day above the usual intake significantly reduced CRP compared to low fiber Western diets [52].

Mortality Risk

Prospective cohort studies consistently show that increased fiber intake is positively associated with lower all-cause and disease-specific mortality risk (Table 12.1) [38–47]. Five meta-analyses estimate that increasing total fiber intake by 10 g/day increments significantly reduces mortality risk for all causes by 10–11%, coronary heart disease (CHD) by11–20%, total cardiovascular disease (CVD) by 9%, and cancer by 6–9% [38–42]. A meta-analysis (seven cohort studies; 62,314 deaths among 908,135 participants) found that the pooled adjusted total mortality was reduced for the highest category of total fiber intake compared to the lowest by 23% [42]. Several dose-response meta-analyses showed that there is an adjusted reduced mortality risk for total and disease specific by 6–11% per 10 g/day increment of total fiber intake (Fig.12.1) [39, 42]. A meta-analysis (25 cohort studies; 1,752,848 individuals; average follow-up of 12.4 years) showed that individuals in the highest vs. lowest fiber intake had mortality rates lowered by 23% for CVD, by 17% for cancer, and by 23% for

Table 12.1 Summary of prospective cohort studies on the effect of fiber on all-cause and disease-specific mortality

Objective	Study Details	Results
Systematic reviews and meta-analyses		
Hajishafiee et al. Assess the relation between cereal fiber intake and cause-specific mortality [38]	14 cohort studies; 1,688,794 participants; 6–40 years of follow-up; 48,052 all-cause deaths, 16,882 CVD deaths, 19,489 cancer deaths, and 1,092 inflammatory diseases deaths (multivariate adjusted)	The highest vs. the lowest category of cereal fiber intake reduced mortality risk for all causes by 19%, CVD by 18%, and cancer by 15%
Kim and Je Assess the association between fiber intake and mortality from CVD and all cancers [39]	15 prospective cohort studies; 1,409,014 subjects, follow-up of 6–18 years (multivariate adjusted)	The dose-response meta-analyses found that a 10 g/day increment in fiber intake was inversely associated with reduced mortality risk from CVD by 9%, from CHD by 11%, and from all cancers by 6%. For highest vs lowest fiber intake mortality risk was reduced for CVD by 23%, for CHD by 24%, and for all cancer by 14% (Fig.12.1)
Liu et al. Investigate fiber consumption and all-cause mortality and cause-specific mortality [40]	25 prospective cohort studies; 1,752,848 individuals; average follow-up 12.4 years (1–40 years) (multivariate adjusted)	For highest vs. lowest fiber intake, mortality risk was lower by 23% for CVD, by 17% for cancer, and by 23% for all-cause mortality (Fig.12.2). For each 10 g/day increase in fiber intake, the mean mortality risk was reduced for all causes by 11%, for CHD by 20%, ischemic heart disease by 34%, and for cancer by 9%
Yang et al. Quantify the effect of fiber intake on all-cause mortality [41]	17 prospective cohort studies up to May 2014; 982,411 individuals and 67,260 deaths (multivariate adjusted)	Higher-fiber intake was associated with reduced all-cause mortality risk as follows: (1) When comparing highest vs lowest fiber intake, there was a significant reduction in all-cause mortality by 16%. For each 10 g/day increase in fiber intake, all-cause mortality risk was reduced by 10%
Kim et al. Evaluate the effect of fiber intake on total mortality [42]	Seven prospective cohort studies; 908,135 persons; 62,314 deaths; mean follow-up of 17.6 years (7.7–40 years); highest vs. lowest fiber intake was 27 g vs. 15 g/day (multivariate adjusted)	Highest vs. lowest fiber intake reduced total mortality risk by 23%. For each 10 g/day of fiber intake, total mortality risk was reduced by 11%. Per fiber source, cereal and vegetable fiber were significantly associated with lower total mortality, while fruit fiber showed no association
Prospective cohort studies		
Chan and Lee Examine the associations of total dietary fiber intake and water-insoluble and water-soluble fibers with cancer and all-cause mortality (US; NHANES Survey III) [43]	15,740 adults; mean age 44.5 years; 47% male; total fiber intake approx.<8.1–>22.5 g/day; average follow-up of 13.7 years (multivariate adjusted)	Fiber showed protective benefits for mortality risk. Total fiber reduced adjusted risk of total mortality by 13% and cancer mortality by 23%. Insoluble fiber reduced adjusted risk of cancer mortality by 14% and colorectal-rectal cancer mortality by 58%

(continued)

Table 12.1 (continued)

Objective	Study Details	Results
Buil-Cosiales et al. Evaluate the association of fiber intake and whole-grain, fruit, and vegetable consumption with all-cause mortality in a Mediterranean cohort of elderly adults at high cardiovascular disease (CVD) risk (Spain Prevencion con Dieta Mediterranea (PREDIMED) study) [44]	This prospective study of 7,216 adults; 55–75 years; high CVD risk; mean of 5.9 years of follow-up; 425 deaths; compared highest vs. lowest fiber intake (35 g vs. 17 g/day) (multivariate adjusted)	Fiber was associated with mortality risk as follows: (1) Increased fiber intake significantly reduced all-cause mortality by 37%. (2) Increased fiber intake was associated with reduced CVD risk by 54% (p-trend = 0.059)
Chuang et al. Assess the relationship between fiber intake and mortality inadults (EU; European Prospective Investigation into Cancer and Nutrition (EPIC)) [45]	452,717 adults;aged 25–70 years; mean follow-up of 12.7 years, 23,582 deaths; comparison of highest vs. lowest fiber intake (28.5 g vs. 16.4 g/day) (multivariate adjusted)	Increased fiber intake was associated with total and disease-specific mortality as follows: (1) Increased fiber intake significantly reduced total mortality risk by 24%.(2) There was a 10% total mortality risk reduction per 10 g fiber/day. (3) Higher-fiber intake was associated with significantly lower smoking-related cancers and circulatory, respiratory, digestive, and inflammatory disease deaths in both men and women
Park et al. Investigate fiber intake in relation to total and cause-specific mortality in a large prospective cohort of men and women (US; The National Institutes of Health-AARP Diet and Health Study) [46]	567,169 adults; aged 50–71 years; mean 9 years of follow-up; 31,500 deaths; highest and lowest daily fiber intake (29 g vs.13 g for men) and (26 g vs. 11 g for women) (multivariate adjusted)	A fiber-rich diet from whole plant foods lowered premature death rates as follows: (1) For total mortality, higher-fiber intake significantly reduced risk by 22% and 10 g/day of fiber intake reduced risk in men by12% and in women by 15%. (2) Higher-fiber intake significantly lowered risk of death from cardiovascular, infectious, and respiratory diseases by 24–56% in men and 34–59% in women. (3) Fiber was inversely associated with cancer death in men, but not in women
Streppel et al. Study the effect of fiber intake on coronary heart disease (CHD) and all-cause mortality in men (the Netherlands; The Zutphen Study) [47]	1,373men born between 1900 and 1920; examined repeatedly between1960 and 2000; 1,130 deaths with 348 from CHD (multivariate adjusted)	Every additional 10 g fiber intake/day reduced CHD mortality by17% and all-cause mortality by 29%. The effect of fiber intake on all-cause mortality varied by age with a decrease at age 50 years by 9% and at age 80 by only 1%

all-cause mortality (Fig.12.2) [40]. A meta-analysis (14 cohort studies; 1,688,794 participants; followed for 6–40 years) found that cereal fiber lowered mortality risk for allcauses by 19%, CVD by 18%, and cancer by 15% (highest to lowest intake) [38]. Five prospective studies consistently report a significant association between fiber intake and lower mortality risk [43–47]. A 2012 EPIC cohort study observed that increasing fiber intake in men and women has a similar 20% lowering of total mortality risk at between 20 and 28.5 g fiber/day, but at ≥28.5 g/day there was a 30% lower mortality risk for men and no change in risk reduction for women, which may be reflective that fewer women in the study were consuming fiber ≥28.5 g/day [45]. A 2011 US National Institutes of Health (NIH) and AARP Diet and Health prospective study found that an increase in fiber intake by 10 g/day reduced premature death risk in men by12% and in women by 15% [46]. Several prospective studies report that the consumption between 25 and 35 g/day of fiber significantly lowers all-cause mortality

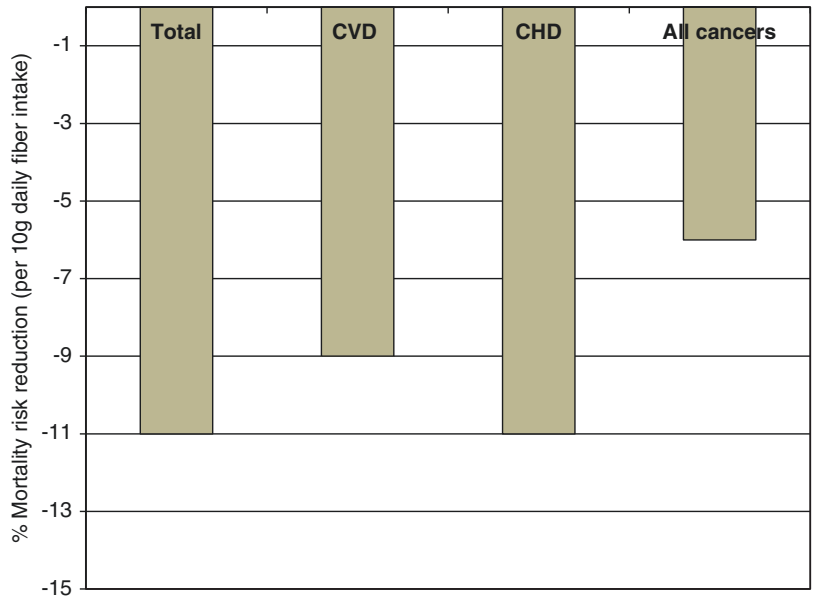

Fig. 12.1 Effect of total fiber intake level on adjusted total, cardiovascular disease (CVD), coronary heart disease (CHD), and all-cancer mortality risk from several meta-analyses of prospective cohort studies [39, 42]

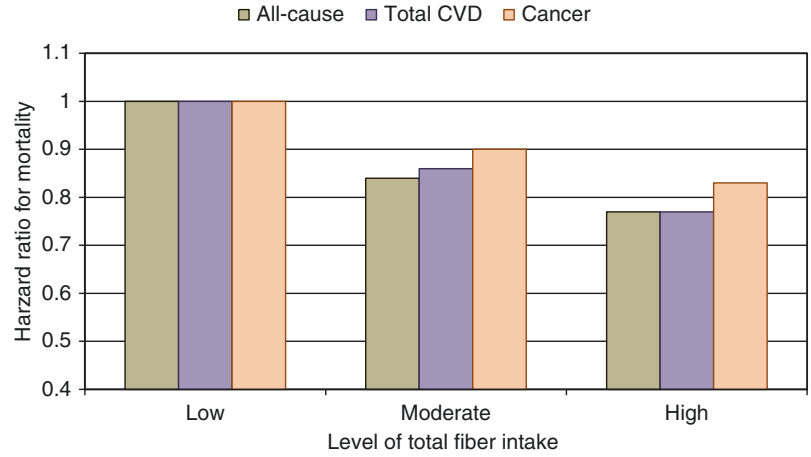

Fig. 12.2 Effect of increasing fiber intake on mortality risk in men and women from meta-analysis of cohort studies (multivariate adjusted) [40]

risk by16–43% compared to lower-fiber diets (11–24 g/day) [39–45]. Finally, the Zutphen Study found that the association between fiber intake and all-cause mortality risk was weakened with increasing age, such that every additional 10 g of fiber intake at age 50 years lowered risk by 29%, but at age $\geq$ 80 years, the risk reduction was only 1% [47]. The 2014 World Cancer Research Fund (WCRF) and the American Institute of Cancer Research (AICR) continuous update report concluded that there was limited suggestive evidence that adequate fiber intake is inversely related to all-cause and breast cancer mortality [48].

Successful Aging Studies

Adequate fiber intake is associated with successful aging and lower fiber intake has been associated with increased risk of frailty in the elderly [53–56]. A 2016 Australian prospective study on successful aging (1,609 adults; aged ≥49 years who were free of cancer, coronary artery disease, and stroke; followed for 10 years) found that 15.5% of the participants had aged successfully [53]. The participants in the highest quartile of total fiber intake had 80% greater odds of aging successfully compared to those in the lowest fiber intake. In contrast, those who were consistently below the median of fiber intake had significantly lower odds of successful aging by about 40%. In elderly adults, the frailty phenotype is associated with long-stay care facilities and/or standardized diets that are low in fiber and food variety, which can subsequently reduce microbiota diversity and increase dysbiosis associated with inflammaging-related frailty [54, 55]. A cross-sectional study (371 elderly subjects; mean age 78 years; four group, community-dwelling, outpatient day hospitals, in short-term rehabilitation care (<6 weeks), or in long-term care facilities) observed that elderly from either the community or long-term care facilities consuming unhealthy diets (e.g., low in fiber and high in sugars and animal fats) had low microbiota diversity and increased signs of biological aging and frailty [54]. Additionally, elderly in long-term care facilities had a gradual change in their core community-based microbiota composition over approximately18 months to a new core elderly type microbiota composition associated with dysbiosis and frailty. In another cross-sectional study (178 elderly adults; mean age 78 years; stratified by their current living situation; community-dwelling; outpatients; short-term hospitalized subjects; long-term care residents) observed that elderly in long-term care facilities had significantly poorer frailty test scores compared to elderly living in a residential community [55]. The long-term care elderly consumed less diverse and lower-fiber diets and experienced microbiota dysbiosis (higher proportion of *Bacteroidetes* and lower fecal short-chain fatty acids (SCFAs)) and accelerated frailty. The residential community-living elderly consumed more diverse and higher-fiber diets and had healthier microbiota (higher diversity index with a higher proportion of *Firmicutes*/*Lachnospiraceae* and high levels of fecal SCFAs and lower rates of frailty). In a Chinese study, age and high-fiber diets were associated with changes in the colonic microbiota of centenarians, suggesting that a high-fiber diet has a role in establishing a new structurally balanced microbiota architecture that may benefit the health of centenarians [56].

Cardiovascular Disease (CVD)

CVD is a major cause of mortality representing 31% of worldwide total deaths [57]. A meta- analysis of 22 cohort studies found an inverse association between fiber intake and cardiovascular disease incidence with a significant 9% lower risk for each 7 g intake of fiber/day [58]. A Cochrane systematic review found that increased fiber intake reduced CVD risk factors, blood lipids,and blood pressure [59]. For blood lipids (23 RCTs; 1,513 participants), a wide variety of fibers were shown to significantly reduce mean blood lipid levels for total cholesterol by 8.9 mg/dL, LDL cholesterol by 5.4 mg/dL, and HDL cholesterol by 1.2 mg/dL, but triglyceride levels remained unchanged. For blood pressure (ten trials; 661 participants randomized), the review reported a significant mean lower effect on diastolic blood pressure by 1.8 mm Hg. However, the reduction in systolic blood pressure by 1.9 mmHg did not reach the level of statistical significance [59]. The PREvención con DIeta MEDiterránea (PREDIMED) trial (7,216 elderly men and women at high CVD risk; up to 7 years of follow-up)

found an inverse association between fiber and CVD risk with a 27% lower risk for daily intake of 33 g fiber vs 19 g fiber (p = 0.08; multivariate adjusted) [60].

Coronary Heart Disease (CHD)

Of the CVD deaths, CHD, including overall coronary artery diseases, accounts for about 57% of deaths in men and 52% of deaths in women [58]. While CHD death rates have declined over the years, the number of deaths remains high and is expected to increase with the global aging of populations.A dose-response meta-analysis of prospective studies estimated that for each 10 g/day increment of total fiber, there was an 8% decreased risk of all coronary events and risk of CHD death by 24% [61]. A number of intervention trials have consistently demonstrated that intakes of ≥26–30 g total fiber/day from wholefoods including whole-grain foods (especially oats and barley), fruits, vegetables, legumes, nuts, or ≥3–12 g isolated soluble, viscous fiber supplements/day (including oat/barley β-glucan, psyllium, guar, or pectin) can lower LDL-C by 4–8% [62–65]. A large randomized trial of Finnish men (21,930 men; aged 50–69 years; 35 g vs. 16 g total fiber/day; followed for 6 years) reported significantly adjusted CHD death risk reduction by 32% (Fig.12.3) and lower adjusted CHD event risk by 16% (Fig.12.4) for high- vs. low-fiber intake [66]. Fiber-rich foods and isolated viscous soluble fibers qualify for CHD prevention health claim regulations in the United States, EU, and many other countries and for lifestyle treatment guidelines for managing hypercholesterolemia [67–69]. Additionally, two observational studies suggest that fiber intake is inversely associated with atherosclerosis and carotid intima-media thickness (IMT) with significant effects in individuals consuming ≥35 g fiber/day or high intake of soluble viscous fiber vs. those consuming <25 g fiber/day in multivariate-adjusted models, with the higher-fiber diets significantly lowering CRP levels as a possible mechanism of action [70, 71].

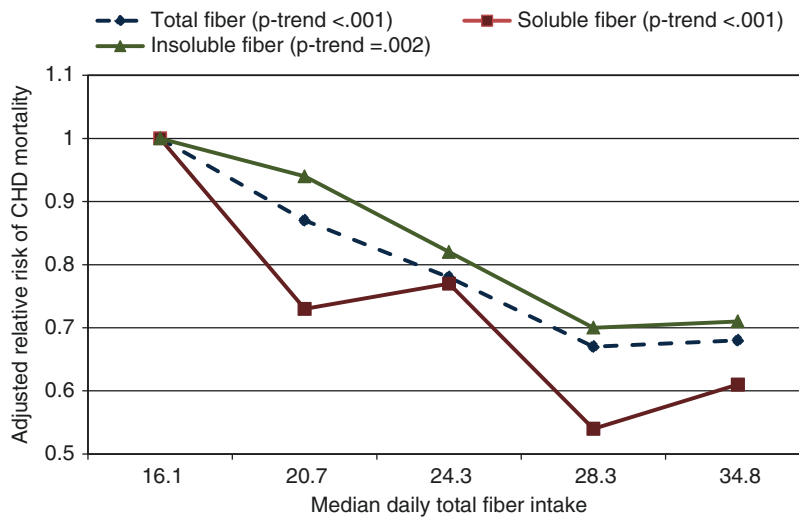

Fig. 12.3 Effect of total, soluble, and insoluble fiber intake on risk of coronary heart disease (CHD) death in 21,930 middle-aged men followed for 6.1 years (multivariate adjusted) [66]

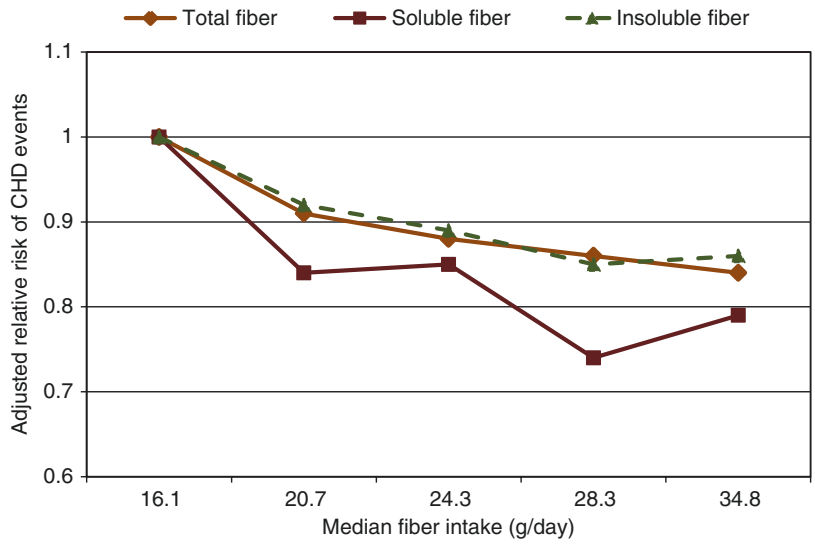

Fig. 12.4 Effect of total, soluble, and insoluble fiber intake on risk of coronary heart disease (CHD) events in 21,930 middle-aged men followed for 6.1 years (all significant p-trend<0.07; multivariate adjusted) [66]

Hypertension

Worldwide, 40% of the adult population have some degree of elevated blood pressure with an estimated one billion people having hypertension, which accounts for 13% of total deaths, and this is expected to increase with the aging of global populations [58, 72]. Several meta-analyses and a review of RCTs report increased fiber intake by 6–11.5 g/day has only modest pooled mean blood pressure-lowering effects (systolic by 0.9–1.2 mm Hg and diastolic by 0.7–1.7 mm Hg) in the general population [23, 73, 74]. Overall, increased fiber intake is more effective in lowering blood pressure in older (>40 years) and in hypertensive populations than in younger and normotensive ones. Specific studies with hypertensive subjects found that increased fiber intake significantly reduced systolic and diastolic blood pressure by 6 mm Hg and 4.2 mm Hg, respectively, which suggests a potential adjunctive role for fiber in managing hypertension. Of the fiber sources, β-glucan was found to be the most effective blood pressure-lowering fiber source with 4 g/day lowering pooled mean systolic and diastolic blood pressure by 2.9 mm Hg and1.5 mm Hg, respectively [73]. The INTERMAP population study (4,680 men and women; age 40–59 years; from Japan, China, the United Kingdom, and the United States) observed significant modest reductions in systolic blood pressure for higher-fiber intake by 1.7 mm Hg and insoluble fiber by1.8 mm Hg, independent of other nutrients [75].

Stroke

Worldwide stroke and related cerebrovascular diseases account for 11% of total deaths, and this number is expected to increase with the aging of the worldwide population [58]. Meta-analyses of prospective studies consistently find an inverse dose-response relationship between fiber intake and stroke risk [76–79]. One meta-analysis of six prospective studies, including about 315,000 subjects with about 9,000 stroke cases, reported a 12% reduction in stroke risk for each 10 g fiber/day [76]. Another meta-analysis projected a 17% lower stroke risk for the highest vs. lowest fiber intakes [77].

Overweight and Obesity

In a meta-analysis (53 cohort studies; 9,976,077 participants;738,144 deaths) overweight and obesity is associated with increased risk of all-cause mortality with the lowest risk observed at BMI 23–24 among never smokers [80]. All-cause mortality risk increases by 18% for a five unit increment in BMI among never smokers. Obesity represents a state of accelerated aging as adipose cells are not inert fat storage depots of excessive energy intake, but part of an active endocrine organ that produces adipokine cell signaling messengers, such as leptin, adiponectin, IL-6, and TNF-α, which can influence systemic and tissue function, including peripheral insulin resistance, ectopic lipid deposition, and inflammation [81–85]. Excessive fat mass associated with obesity increases hyperlipidemia, hyperglycemia, and hyperinsulinemia, which leads to inflammaging and oxidative stress in various body systems and organs including the circulatory and muscle systems, liver, kidney, and brain. This metabolic stress can lead to cellular and systemic dysregulation associated with increased risk of developing insulin resistance, β-cell failure, reduced insulin production, type 2 diabetes, atherosclerosis, tumorigenesis, or neurodegenerative disorders such as Alzheimer's disease.

Populations with higher-fiber diets tend to be leaner than those with low-fiber diets [15–18, 28, 30, 86]. A systematic review of 43 prospective cohort, case-control, and randomized trials found moderately strong evidence that fiber-rich foods have a protective role against weight gain and increased waist size [87]. One comprehensive review of intervention studies estimated that increasing fiber intake by14 g fiber/day, with ad libitum energy intake, was associated with a mean 10% decrease in energy intake and a reduction of weight by 1.9 kg after 4 months [88]. A weight loss RCT with metabolic syndrome subjects found that dietary guidance to increase fiber intake to ≥30 g/day was as effective as the energy-restricted diet program intervention based on the American Heart Association dietary guidelines in promoting clinically meaningful weight loss over 1 year [89]. In general,RCTs with ad libitum fiber-rich diets in the range of ≥30 g fiber/day consistently prevent weight gain and/or promote weight loss compared with lower-fiber diets of <20 g/day [90–95].

Metabolic Syndrome

Metabolic syndrome occurs in 20–40% of the worldwide adult population and 70–90% of young obese children [96]. It is a major and worldwide escalating public health challenge that is a result of urbanization, surplus energy intake, increasing obesity, and sedentary life habits. Its symptoms include abdominal obesity, atherogenic dyslipidemia (elevated triglycerides, elevated apolipoprotein B, and reduced HDL cholesterol), elevated blood pressure, elevated glucose levels, and proinflammatory and pro-thrombotic states. Metabolic syndrome is associated with a twofold increase in risk of CVD, CVD mortality, and stroke and a 1.5-fold increase in risk of all-cause mortality over 5–10 years compared to healthy control subjects [97]. Individuals with metabolic syndrome tend to have lower-fiber intake [98]. Several intervention studies show that high adherence to fiber-rich healthy dietary patterns, especially with weight loss, are effective in reducing metabolic syndrome risk [89, 90]. Viscous soluble fibers, such as psyllium, have favorable effects on satiety and body weight control, fasting lipids and glycemic control, and blood pressure, which may have a useful role in the prevention and management of metabolic syndrome [93, 99].

Type 2 Diabetes (Diabetes)

The prevalence of prediabetes and diabetes has increased globally in parallel with the rising levels of obesity in adults and children [100, 101]. In the United States, adults ≥65 years have more than double the rate of diabetes of the general population, which accelerates the aging process related to

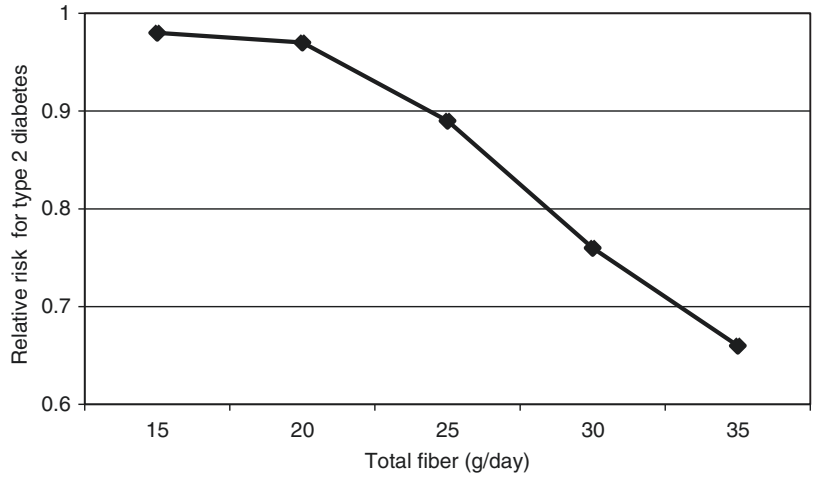

Fig. 12.5 Meta-analysis of 17 prospective cohort studies on total fiber intake and type 2 diabetes risk (p for nonlinearity <0.01) [24]

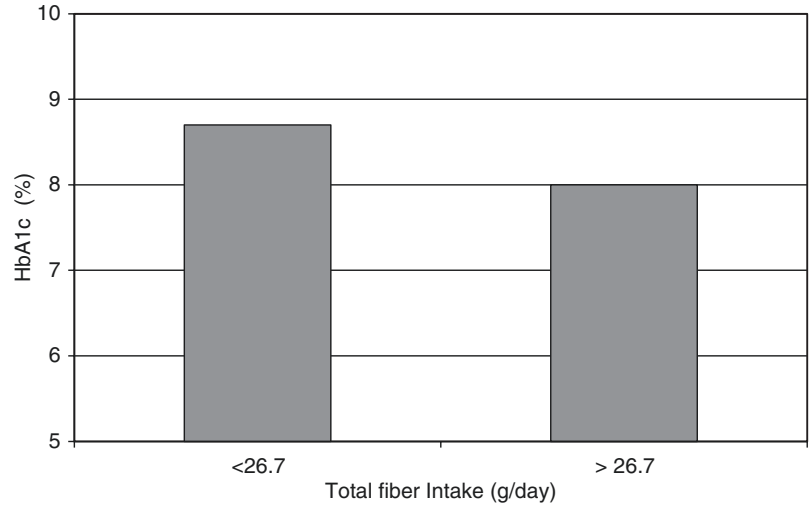

Fig. 12.6 Effect of fiber intake on glycated hemoglobin (HbA1c) in type 2 diabetes Mexican patients ($p = 0.011$) [105]

renal dysfunction, cardiovascular disease, stroke, impaired wound healing, infection, depression, and cognitive decline [102]. A dose-response meta-analysis of 17 prospective studies found a nonlinear inverse association between fiber intake and diabetes risk with a linear inverse effect occurring at ≥25 g fiber/day (Fig.12.5) [24]. Several large clinical trials support a role for high fiber in reducing diabetes risk [103, 104]. The Chinese Da Qing Diabetes Study found that healthy diets rich in whole-grain cereal and vegetable fiber significantly lowered diabetes risk by 31% compared to lower-fiber diets without exercise or weight control guidance over 6 years [103]. A Finnish Diabetes Prevention trial, including a comprehensive lifestyle program with 15 g fiber/1000 kcal, exercise, and 5% weight loss, reported a 58% lower-diabetes risk over a 3-year period [104]. A cross-sectional study (395 Mexican diabetic patients), showed that fiber intake was inversely associated with HbA1c levels (Fig.12.6), triglycerides, body weight, and waist size while improving HDL-C levels [105]. This study confirms the benefits of increasing fiber intake while lowering calorie consumption as an appropriate strategy to reduce body weight and promote blood glucose control in individuals with diabetes.

A double-blind, crossover RCT (40 women; mean age 48 years; mean BMI 30; high-amylose maize resistant starch (RS2) added to cookies at 15 and 30 g daily vs. control cookies; 4 weeks; 4 weeks of washout), found that the daily intake of 30 g/day of fiber in the form of resistant starch significantly improved insulin sensitivity by 16% in women with insulin resistance (prediabetes) [106].

Cognitive Function

A limited number of studies suggest that increased fiber intake has the capacity to reduce age-related cognitive decline [107, 108]. In a large-scale French longitudinal study (4,809 elderly women; born between 1925 and 1930; questionnaire on lifestyle and recent cognitive change; validated dietary data), it was found that soluble fiber intake had the most significant contribution to a reduction in age-related cognitive impairment [107]. A double-blind, placebo controlled, crossover RCT (47 adults, 60% female; mean age 23 years; 5 g oligofructose-enriched inulin vs. maltodextrin in decaffeinated coffee or tea at breakfast; 4-h postprandial assessment) showed that oligofructose-inulin significantly improved subjective well-being, mood, and cognitive score [108]. Specifically, the participants felt happier and less hungry and had improved cognitive performance and mood scores. The most consistent effects were greater accuracy on a recognition memory task and improved recall performance (immediate and delayed) on episodic memory tasks after oligofructose-inulin intake than after the placebo.

Cancer

Fiber was first hypothesized to reduce the risk of cancer, especially colorectal cancer, in the early 1970s by Dr. Burkitt, who observed lower rates of colorectal cancer among Africans who consumed a traditional diet high in fiber compared to those with an urban Western diet [109]. Over the last decade, it has become increasingly clear that colonic microbiota influence cancer initiation and progression, depending on the bacteria composition, as pathogenic bacteria have oncogenic promotional properties, and commensal and symbiotic microbiota have tumor-suppressive properties [110]. Adequate fiber intake stimulates bacterial fermentation in the colon to yield SCFAs such as butyrate, which promotes an acidic colonic pH to control pathogenic bacteria growth and promotes histone deacetylase (HDAC) inhibitor to suppress the viability and growth of colorectal cancer cells. Additionally, obesity and diabetes are associated with increased cancer incidence and mortality [111]. As previously summarized in this chapter, adequate fiber intake can potentially contribute to reduced risk of obesity and diabetes by reducing the risk of weight gain, dyslipidemia, and systemic and tissue inflammation (inflammaging) and improving insulin sensitivity and colonic microbiota diversity and ecosystem health. These metabolic changes may contribute directly or indirectly to reduced cancer progression. Fiber-related weight loss may protect against cancer development, and related improvements in insulin sensitivity may also prove to be helpful in reducing cancer progression. Inadequate fiber intake has been implicated in the increased incidence of several cancers [112]. The four most common cancer sassociated with low-fiber intake are summarized as follows:

Colorectal Adenoma and Cancer

Globally rates of colorectal cancer, which accounts for 10% of all cancers, has doubled since the 1970s, and incidence is strongly associated with the Western lifestyle [113, 114]. The World Cancer Research Fund and American Institute for Cancer Research (WCRF and AICR) continuous update report on colorectal cancer concluded that there was “convincing” evidence that increased fiber intake was protective against the risk of colorectal cancer [114], which is supported by several meta-analyses

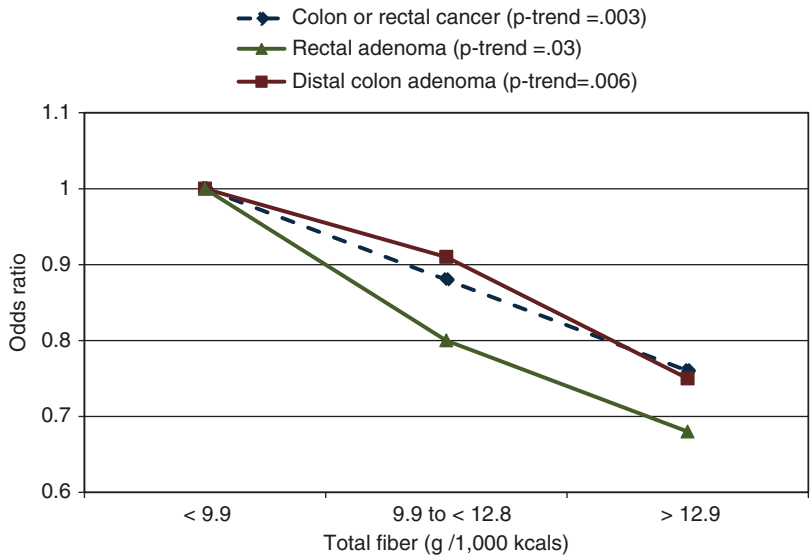

Fig. 12.7 Effect of increasing fiber intake and incidence of colorectal adenoma risk in 57,774 subjects with a mean age of 63 years screened over 3–5 years from the prostate, lung, colorectal, and ovarian cancer screening trial [116]

[25, 116]. A large US prospective study found evidence that high-fiber intakes are associated with a reduced risk of colorectal adenoma and cancer, indicating that fiber may act early in the adenoma-carcinoma sequence and reduce the risk of adenomas and cancer (Fig.12.7) **[**116**]**. In an EPIC study, total fiber was inversely associated with colorectal cancer with a 13% reduction per 10 g/day increase in fiber, after multivariate adjustments [117].

Breast Cancer

The relationship between fiber intake and breast cancer is complex. The WCRF and AICR continuous updates conclude that there is limited human evidence that fiber reduces breast cancer risk or survival [48]. There is however some suggestive human evidences that increasing fiber intake may decrease the risk of all-cause mortality when consumed before or 12 months after breast cancer diagnosis [48]. Two meta-analyses of prospective studies similarly report a significant dose-response for total fiber intake and breast cancer risk reduction by 5–7% per 10 g fiber intake [118, 119]. A meta-analysis assessment of fiber type showed that soluble fiber reduced breast cancer risk by 9% compared to 5% for insoluble fiber [118]. In an EPIC prospective study (334,849 women; median age 50 years; median follow-up of 11.5 years), it was shown that fiber from non-starchy vegetables was inversely associated with breast cancer risk, with a 10% reduced risk observed for the highest vegetable fiber intake, but the effect was stronger for estrogen receptor-negative and progesterone receptor-negative tumors with a 26% lower cancer risk than for estrogen receptor-positive and progesterone receptor-positive tumors with a lower cancer risk by 8% [120]. In the Women's Healthy Eating and Living Trial, a subgroup analysis of women at baseline with hot flashes observed that those in the higher-fiber group had significantly lower breast cancer recurrence compared to the lower-fiber controls [121]. The Nurses' Health Study II (90,534 premenopausal women who completed a dietary questionnaire in 1991; mean age 37 years; 20 years of

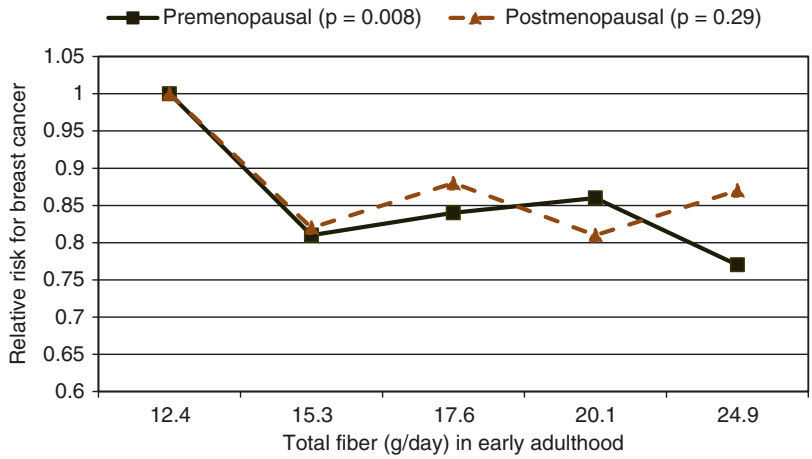

Fig. 12.8 Effect of increasing fiber intake in early adulthood on breast cancer risk in women with a mean age of 37 years followed for 20 years in the Nurses' Health Study II [122]

follow-up; 2,833 invasive breast cancer cases) showed that higher-fiber intake during adolescence and early adulthood significantly reduced breast cancer risk by 19% and that youth may be a particularly important stage in life for affecting breast cancer risk (Fig.12.8) [122]. Several proposed mechanisms for fiber's protective effect include the sequestration of estrogen in the digestive system and reduction of β-glucuronidase activity in the colon resulting in increased estrogen excretion in the feces [15].

Prostate Cancer

The 2014 WCRF and AICR continuous update report concluded that there is no or limited evidence that increased fiber intake is directly protective against the risk of prostate cancer [123]. However, a 2105 Physicians' Health Study observed that a low-fiber, Western dietary pattern was associated with higher prostate cancer-specific and all-cause mortality and a high-fiber prudent (healthy) dietary pattern was associated with lower all-cause mortality [124]. A 2015 meta-analysis (12 case-control and 5 cohort studies; 8,000 men) found that increased fiber intake insignificantly reduced prostate cancer risk by11% (highest vs. lowest fiber intake) [125].

Digestive and Renal Cancer

Meta-analyses support an inverse relationship between fiber intake and digestive and renal cancer risk [126–128]. For gastric cancer, a meta-analysis (21 observational studies; 580,064 subjects) found a significant inverse dose-response relationship with a lower risk by 44% per 10 g fiber intake [126]. For cancer of the esophagus, a meta-analysis (15 observational studies; 16,885 subjects) reported dose-response effects with 31% lower risk per 10 g/day increment of fiber intake [127]. For renal cell carcinoma, a meta-analysis (seven observational studies) reported adequate fiber intake was associated with a 16% reduction in risk compared to a low-fiber intake [128].

Colonic Health

Bowel Regularity

The frequency of constipation increases with aging, as it affects approximately 26% of men and 34% of women over 65 years of age compared to about 2% of younger adults [129, 130]. Age-related constipation has been associated with a number of common aging conditions such as diabetes, sedentarism, depression, and poly-pharmaceutical use [129]. Increasing fiber intake to ≥25 g/day from fiber-rich foods or fiber supplementation taken before a meal is recommended to promote bowel regularity by increasing colon motility due to the increased stool volume associated with higher-fiber intake along with bound water and microbiota. Since excessive fiber intake may cause bloating, flatulence, and abdominal discomfort, increasing fiber intake should be done gradually over time along with drinking the recommended levels of water (eight glasses or 2 L/day) [130]. In a randomized trial, low-fermentable wheat bran and psyllium husk fiber were shown to decrease transit time and increase daily stool regularity as well as promote healthier stool weights and structure compared to low-fiber controls [131]. Wheat bran had a greater effect on transit time than psyllium, whereas psyllium had a greater effect on stool water content (softer stools) and higher stool weight than wheat bran. Additionally, 50% of the subjects reported hard stools in the low-fiber group compared to <10% of the subjects in the fiber-supplemented groups. Also, bran particle size has a major effect on stool volume with coarse bran being two and one half times more effective in increasing stool volume than fine bran when consumed at the same dose [15, 16, 132, 133]. The results of a meta-analysis of 65 studies found that wheat bran improves bowel function by increasing the pooled mean total stool weight by 3.7 g/g of intact wheat bran with a transit time decrease of 45 min/g of intact wheat bran when initial transit time was greater than 48 h [134]. One cohort study suggests that chronic constipation in postmenopausal women may increase CVD risk [135].

Diverticular Disease

Diverticular disease has a spectrum of stages ranging from asymptomatic to uncomplicated symptoms to complicated and severe life-threatening conditions, which increase with age [136]. In Westernized countries the diverticulosis prevalence is about 13% for persons under 50 years of age, 30% for persons 50–70 years of age, 50% for persons 70–85 years of age, and 66% for persons older than 85 years. The best estimate is that 60% of the risk is associated with modifiable factors such as Western lifestyle, chronic and excessive nonsteroidal anti-inflammatory drug usage,and smoking. Four prospective studies suggest that fiber-rich diets, mainly from cereal and fruit or vegetarian diets, and low consumption of red or processed meat decrease risk of diverticular disease and its complications [137–140]. Six RCTs suggest that fiber-rich diets, wheat bran, or methylcellulose can improve symptoms and/or bowel function [141–148]. Fiber-related mechanisms associated with reduced diverticular disease risk are related to improved digestive health including improved laxation, a more diverse and healthier microbiota ecosystem contributing higher fecal concentration of butyrate and symbiotic bacteria, and improved body weight regulation [15].

Periodontitis

Periodontitis is a set of inflammatory diseases affecting the tissues that surround and support the teeth, which leads to the progressive loss of the alveolar bone around the teeth and, if left untreated, can lead to the loosening and subsequent loss of teeth [149, 150]. Periodontitis is one of the most common-chronic infections and affects up to 50% of the adult population, especially during aging in adults with diabetes or elevated systemic inflammation. The increased inflammation associated with periodontitis may contribute to elevated risk of CHD and age-related cognitive decline [151]. A pilot intervention trial found that adults eating higher-fiber meals for 8 weeks had significantly reduced periodontal disease markers and levels of CRP compared to adults consuming the usual Western diet [152]. Two Department of Veterans Affairs longitudinal studies observed the benefits of fiber-rich foods in reducing periodontal disease risk as follows: (1) in men (age ≥ 65 years; mean 15-year follow-up), each serving of fiber-rich foods, especially fruit, was associated with lower risk of alveolar bone loss by 24% and tooth loss by 28% [153], and (2) in men (age 47–90 years; 20-year follow-up),higher adherence to the fiber-rich Dietary Approaches to Stop Hypertension (DASH) diet reduced root caries by 30% vs. low adherence to the DASH diet [154].

Conclusions

People are now living longer than at any other time in history, but many people are aging poorly with decreased healthy life expectancy. For most people, the aging process is not genetically predetermined as the rate at which people age can be modified by diet, exercise, personal habits, and psychosocial factors. Healthy aging is marked by good mental health and social engagement, lack of physical disability, and the absence of premature chronic disease or death. Within the normal aging process, dietary quality is a major determinant of suboptimal aging or healthy aging. Dietary fiber is the most significant shortfall macronutrient in Western diets, which is a major public health concern because its deficiency is associated with increased chronic disease risk, suboptimal aging, obesity, microbiota dysbiosis, and increased morbidity. Adequate fiber intake is among the most important dietary components supporting healthy aging. Dose-response meta-analyses estimate that increasing total fiber intake by 10 g/day increments significantly reduces mortality risk for all cause by 10–11%, CHD by11–20%, total CVD by 9%, and cancer by 6–9%. Adequate fiber intake (14 g/1000 kcal) is associated with healthy aging through its effects on lowering the risk of, for example, cardiovascular diseases, stroke, weight gain, metabolic syndrome, type 2 diabetes, certain cancers, colonic microbiota dysfunction, frailty, and periodontitis. A 2016 prospective study (adults ≥ 49 years; 10 years of follow-up) suggests that higher-fiber intake improved the odds of healthy aging by 80% compared to low fiber intake.

Appendix 1. Fifty High-Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat-cereal	1/3–3/4 cup (30 g)	9–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–11/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds, whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, airpopped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific report of the 2015Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part D. Chapter 1: Food and nutrient intakes, and health: current status and trends. 2015: 97–8; Table D1.8

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Chapter 13
Fiber and Coronary Heart Disease

Keywords Dietary fiber • Coronary heart disease • Mortality • Total cholesterol • Low-density lipoproteins • High-density lipoproteins • Triglycerides • C-Reactive protein • Cereal fiber • β-Glucan • Psyllium • Pectin

Key Points

- Although there have been some decreasing trends in overall coronary heart disease (CHD) mortality rate over the last several decades due to the use of cholesterol-lowering drugs and surgical procedures, CHD is still a leading cause of death globally and its prevalence is expected to increase as the global population ages. CHD affects both men and women, usually developing after the fifth decade of life in men and the sixth decade of life in women. The role of elevated lipids, lipoproteins, and inflammation as risk factors for CHD is well established.
- Adopting a fiber-rich dietary pattern with healthy vegetable oils and low in saturated and *trans*-fatty acids; incorporating bioactive foods and supplements such as soluble fiber, antioxidants, and plant sterols and stanols; exercising regularly; and maintaining a healthy weight are key to managing risk and preventing CHD.
- The importance of increasing fiber intake to reduce CHD risk is supported by strong scientific evidence from numerous prospective cohort studies and randomized controlled trials (RCT). Increased fiber intake from fiber-rich diets with whole (minimally processed) plant foods or dietary supplements containing viscous soluble fibers such as β-glucan or psyllium are known to have strong RCT evidence for lowering elevated blood lipids to normal healthy levels and reducing CHD risk.
- Dose-response meta-analyses consistently show that adequate fiber intake significantly reduces CHD risk by 8–14% and CHD mortality by 23–30%.
- Two primary fiber CHD-protective mechanisms are (1) lowering fasting lipid and lipoprotein profiles and (2) attenuating elevated systemic inflammation risk by controlling body weight and abdominal and visceral fat gain and maintaining a healthy colonic microbiota ecosystem.

Introduction

The role of elevated lipids, lipoproteins, and inflammation as risk factors for coronary heart disease (CHD) is well established [1–12]. Although there have been some decreasing trends in overall CHD mortality rate over the last several decades due to the use of cholesterol-lowering drugs and surgical procedures, CHD is still a leading cause of death globally, and its prevalence is expected to increase as

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the global population ages [1–5, 12]. CHD affects both men and women, often developing after the fifth decade of life in men and the sixth decade of life in women. Between 2015 and 2030, annual US costs related to CHD and related cardiovascular diseases are forecasted to increase from $84.8 billion to $202 billion. Atherosclerosis, the cause of CHD, is a complex pathological process that takes place in the walls of blood vessels and develops over many years via an inflammatory process affecting medium- and large-sized blood vessels throughout the cardiovascular system [1, 5, 6]. In this process when the endothelium lining of blood vessels is exposed to raised levels of total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) and certain other substances, such as free radicals, the endothelium becomes permeable to lymphocytes and monocytes, which can migrate into the deep layers of the wall of the blood vessel. When this occurs, LDL-C particles are attracted to the site of migration and are engulfed by the monocytes, which are then transformed into macrophages (foam cells). Subsequently, smooth muscle cells migrate to the site from deeper layers of the vessel wall and can form a fibrous cap consisting of smooth muscle and collagen. At the same time, the macrophages involved in the original reaction begin to die, resulting in the formation of a necrotic core covered by the fibrous cap. These atheromatous plaques enlarge as cells and lipids accumulate in them, and the plaque begins to migrate into the vessel lumen increasing the risk of rupture, blood clot formation, or thrombus. If the thrombus is large enough and a coronary blood vessel or a cerebral blood vessel is blocked, this results in a heart attack.

Although advances in medical science and technology have led to novel treatments such as lipid-lowering drugs and surgical procedures which have a vital role in reducing CHD mortality, lifestyle changes remain the cornerstone of management and prevention of CHD and are warranted in primary and secondary prevention settings [7–12]. Lifestyle changes recommended for those with high cholesterol levels include adopting a diet low in saturated and *trans* fatty acids; incorporating bioactive foods and supplements, such as dietary fiber (fiber), antioxidants, and plant sterols and stanols into the diet; exercising regularly; not smoking; and maintaining a healthy weight [9–12]. For primary CHD prevention, the benefits achievable through diet and lifestyle are likely to be similar or better than those due to drug treatment because of their more comprehensive health effects on CHD and other chronic diseases [8]. These lifestyle factors can affect CHD risk through a number of intermediary biological mechanisms including reducing fasting lipid profiles; circulating inflammation, abdominal and visceral fat, and blood pressure; and increasing microbiota diversity and health and insulin sensitivity [8–10]. The Health Professionals Follow-Up Study (51,529 US health professionals; mean age 53 years; followed for 8 years) found that Western dietary patterns (higher in saturated fat and sodium, high-glycemic refined carbohydrates, and low in fiber, nutrients, and phytochemicals) significantly increased CHD risk, independent of other lifestyle variables, compared to healthy dietary patterns (lower in saturated fat and sodium, low in high-glycemic refined carbohydrates, and higher in fiber, nutrients, and phytochemicals) (Fig. 13.1) [11]. A 2016 cross-sectional

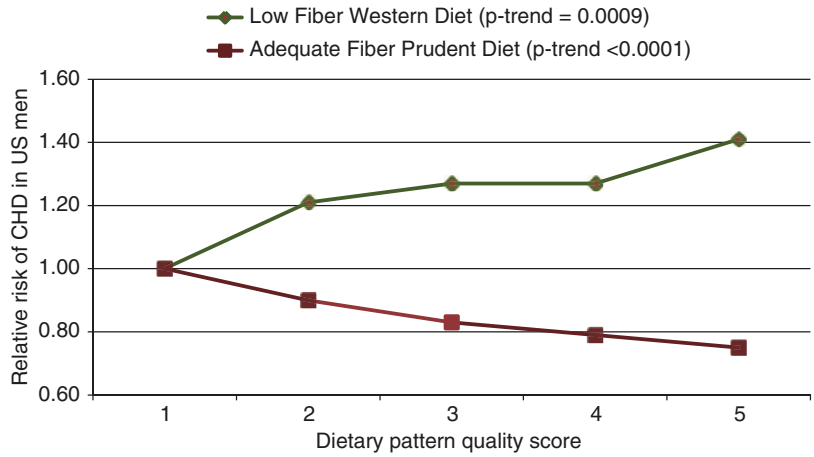

Fig. 13.1 Effect of dietary patterns scores (including low vs. adequate fiber content) and risk of coronary heart disease (CHD) in men (mean baseline age 53 years) followed for 8 years from Health Professionals Follow-Up Study [11]

study (300 patients with coronary artery disease (CAD): mean age 61 years) observed that patients with the most severe CAD consumed higher intakes of refined carbohydrates and the saturated fat palmitic acid, and a low intake of fiber, protein, potassium, magnesium, B-vitamins, and vitamin C [12]. The objective of this chapter is to review the effects of fiber on CDH risk with a focus on circulatory lipids and inflammatory biomarkers.

Fiber and Coronary Heart Disease Risk

Overview

There is strong scientific evidence that adequate fiber intake from foods and/or dietary supplementation with viscous, soluble fiber has an important role in helping to reduce CHD risk, especially in individuals with elevated cholesterol [12–16]. CHD risk factors such as elevated fasting lipids and systemic inflammation can be attenuated by adequate intake of fiber (14 g/1000 kcals or approximately 25 g/day for women and 38 g/day for men) [12–17]. Potential mechanisms associated with fiber and reduced CHD risk are summarized in Table 13.1 [13–40]. Common food sources of soluble, viscous fiber are summarized in Table 13.2 [21, 22]. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention double-blind, placebo-controlled trial (22,000 men; mean age 57 years; 6 years duration; 1,400 nonfatal myocardial infraction (MI) and CHD deaths) observed significant reductions in major coronary events and deaths with adequate intake of total, soluble, and insoluble fiber (Fig. 13.2) [41]. For dietary fiber (35 g/day vs. 16 g/day), there was a significant reduced coronary

Table 13.1 Potential fiber-related biological mechanisms associated with reducing coronary heart disease (CHD) risk [13–40]

Target	Increase	Decrease
Food intake	Chewing	Energy density (2 kcal/g)
	Eating time	Hunger
Body weight	Weight maintenance or loss	Weight gain and obesity
Stomach	Satiety signals	Gastric emptying rate
		Lipid emulsification
		Lipolysis
Liver	Lipoprotein uptake	Lipogenesis
	Bile acid synthesis and secretion	
Small intestine	Satiety signals	Dietary fat absorption
Peripheral tissue	Insulin sensitivity	Ectopic fat
		Insulin resistance
Circulatory system	Short-chain fatty acids	Blood pressure
		Postprandial lipids and glucose
		Fasting lipids and lipoproteins (e.g., TC, LDL-C, and TG)
		Inflammatory markers (e.g., CRP)
		Oxidized LDL-C
		Intima-media thickness
Large intestine	Fermentation	Bile-acid reabsorption
	Short-chain fatty acids	Inflammatory activity
	Symbiotic microbiota	Lipopolysaccharide absorption
	Satiety signals	
Fecal excretion	Bile acids	Metabolizable energy
	Dietary fat	

TC total cholesterol, *LDL-C* LDL-cholesterol, *TG* triglycerides, and *CRP* C-reactive protein

Table 13.2 Short list of estimated soluble and total fiber from common food sources [21, 22]

Food source	Soluble fiber (g)	Total fiber (g)
Cereal grains		
Oatmeal (1 cup cooked)	2	4.0
All-Bran Original (1/2 cup)	0	10
All-Bran (R) Bran Buds (R) cereal with wheat bran and psyllium seed husk (1/3 cup)	3	13
Cheerios 100% whole grain oats cereal® (3/4 cup)	1	3.0
Fiber One (R) cereal (1/2 cup)	1	14
Shredded Wheat (R) cereal (1 cup)	1	6.0
Ground psyllium seeds (1 Tbsp.)	5	6.0
Fruit		
Apple (medium)	1.0	3.5
Pear (medium)	1.5	5.0
Banana (medium)	1	3.0
Blackberries (1 cup)	2	7.5
Orange (medium)	2	3.0
Avocado (1/2 fruit)	1.5	4.5
Prunes (1/4 cup)	1.5	3.0
Vegetables (1 cup cooked)		
Broccoli	3.0	7.0
Carrots	2.5	6.0
Okra	2.0	5.0
Legumes (1/2 cup cooked)		
Black beans	2.5	8.0
Navy beans	2.2	8.0
Pinto beans	1.5	6.0
Lentils	1.0	8.0
Chickpeas (garbanzo)	1.0	6.0

incidence by 16% and death by 32%, after adjusting for CHD risk factors. Cereal fiber was more effective than vegetable or fruit fibers.

Global health and regulatory authorities have widely accepted the beneficial effects of fiber on reducing CHD risk [22–30]. The National Cholesterol Education Program (Adult Treatment Panel III) Therapeutic Lifestyle Changes guidance for hypercholesterolemic patients includes soluble, viscous fiber-rich foods (e.g., 30 g oatmeal/day) or supplements (e.g., 5–10 g/day oat β-glucan or psyllium) as an option to reduce LDL-C levels and CHD risk, along with other lifestyle modifications such as lower intake of saturated fats (<7% of energy) and cholesterol (<200 mg/day), weight reduction (e.g., adjusting energy intake to prevent weight gain), and increased regular physical activity (e.g., expending ≥ 200 kcal/day) [22]. The consumption of 5–10 g β-glucan or psyllium is expected on average to lower LDL-C by 5%. Along with the Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA), most global food regulatory authorities have established a cause and effect relationship between increased intake of various dietary and supplemental soluble, viscous fibers in conjunction with diets that are low in saturated fat and cholesterol and CHD risk reduction for the general population [23–30]. The qualifying FDA and EFSA requirements for making the soluble, viscous fiber claims range from 3 to 10 g/day (e.g., ≥3 g/day for beta-glucan from oats or barley, ≥6 g/day for pectin, ≥7 g/day for psyllium seed husk, and ≥10 g/day for guar gum).

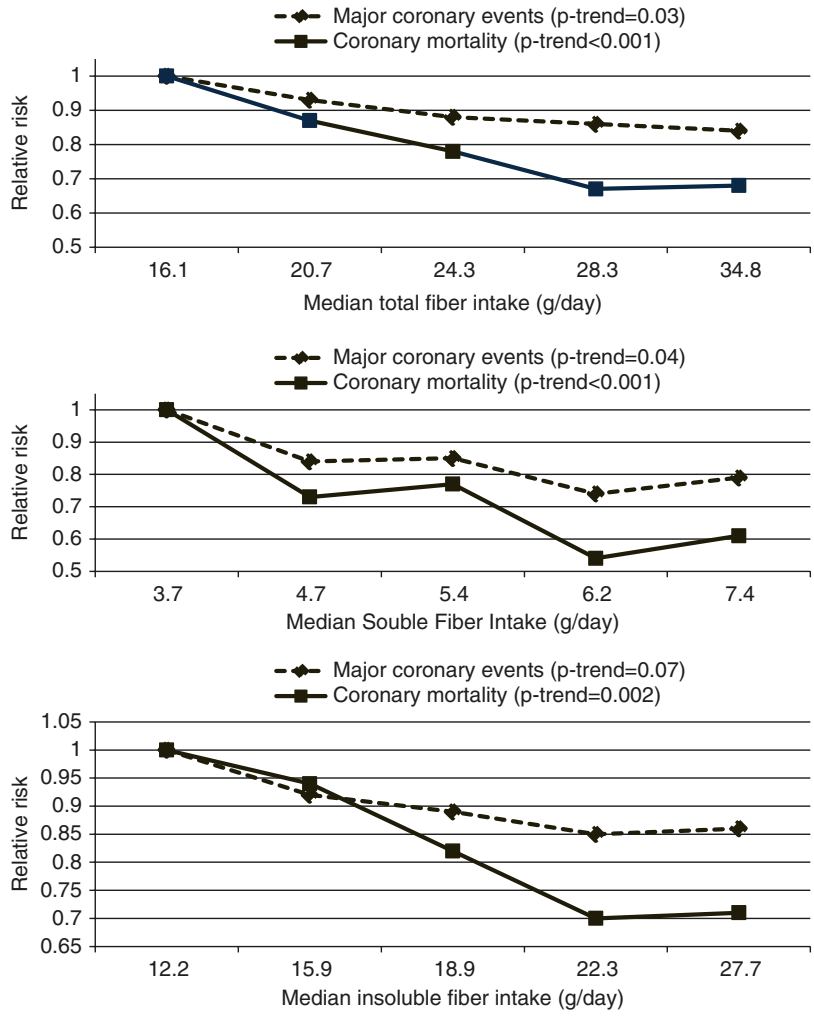

Fig. 13.2 Effects of total, soluble, and insoluble fiber intake on coronary heart disease (CHD) risk in Finnish men (age 50–69 years) followed for 6.1 years from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study [41]

Randomized Controlled Trials (RCTs)

Fasting Blood Lipids

Generally, RCTs support the CHD protective role of fiber, especially soluble viscous fiber, in decreasing elevated fasting TC and LDL-C without significantly changing high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) levels (Table 13.3) [42–59]. The effect of fiber on lowering elevated lipids and lipoproteins depends on the fiber's physical properties with high viscosity being the most important factor [20, 53]. The Cochrane systematic review (17 RCTs; 1067 participants; wide range of fiber sources) concluded that there was a significant beneficial effect to increased fiber intake on mean lowering of TC by 8.9 mg/dL and LDL-C levels by 5.4 mg/dL, but not TG levels by 0.0 mg/dL or HDL-C levels by −1.2 mg/dL [42]. Seven meta-analyses of RCTs clearly demonstrated the significant TC and LDL-C lowering effects of the viscous, soluble fibers β-glucans and psyllium in supplement and food forms, especially in individuals with elevated blood lipids [44–50]. For β-glucan

Table 13.3 Summary of RCTs on increased intake of fiber-rich diets, isolated fiber ingredients and supplements, and blood lipids and lipoproteins

Objective	Study details	Results
Systematic reviews and meta-analyses—all types of fiber sources		
Hartley et al. Determine the effectiveness of increased fiber intake on primary CVD prevention (Cochrane systematic review) [42]	17 RCTs; 1,067 participants randomized; most studies had a duration ≤ 12 weeks; wide variety of fiber sources—foods and supplements	Increased fiber intake significantly reduced total cholesterol (TC) levels by 8.9 mg/dL and LDL-cholesterol (LDL-C) levels by 5.4 mg/dL but there was no reduction in triglycerides (TG). There was a significant lowering of HDL-cholesterol (HDL-C) by 1.2 mg/dL
Brown et al. Evaluate the effect on blood lipids of pectin, oat bran, guar gum, and psyllium [43]	25 RCTs; 1,600 subjects from normo- and hypercholesterolemic healthy and diabetic populations; age range 26–61 years; 2–10 g soluble fiber/day	These soluble fibers were associated with small but significant decreases in TC by 1.7 mg/dL and LDL-C by 2.2 mg/dL. The effects on plasma lipids of soluble fiber from oat, psyllium, or pectin were not significantly different. TG and HDL-C were not significantly influenced by soluble fiber
β-glucan (oat/barley bran)		
Systematic reviews and meta-analyses		
Zhu et al. Evaluate the pooled clinical trial effects of beta-glucan from oat and barley on fasting lipid levels in subjects [44]	17 RCTs; 916 hyperlipidemic subjects including 14 parallel and three crossover RCTs; β-glucan dose ranged from 2.8 to 10.3 g/day (mean 5.5 g/day); 4–12 weeks	β-glucan significantly lowered TC by 10 mg/dL and LDL-C by 8 mg/dL with no significant differences in HDL-C and TG vs. control diets independent of baseline TC or LDL-C, age (< or ≥50 years), duration (< or ≥8 weeks), barley-derived β-glucan, or oat-derived β-glucan at > or ≤5 g day, or small or large subject number
Whitehead et al. Evaluate the pooled clinical trial effects of oat beta-glucan/day on fasting lipid levels [45]	28 RCTs; 2,700 subjects; age range 25–63 years; healthy (n = 12), hyperlipidemic (n = 13), and diabetic (n = 3) subjects; average β-glucan intake from food and supplements was 5.5 g/day (3–12 g/day); average 6 weeks (2–12 weeks)	Diets containing ≥3 g oat bran β-glucan/day reduced serum TC and LDL-C relative to control by 9.5 and 11.5 mg/dL, respectively, with no significant effects on HDL-C or TG. LDL-C lowering was significantly greater with higher baseline LDL-C
Thies et al. Evaluate clinical trial effects of oats or oat bran on fasting lipids and CHD risk [46]	64 RCTs; oat bran, ready-to-eat oat cereals, and oatmeal	Compared to control diets, oat diets (≥50 g oat products/day) reduced TC by 3–6% and LDL-C by 4–8%, which could translate into a 6–18% decrease in CHD risk. The form of oats consumed did not affect the outcome
Ripsin et al. Evaluate the pooled clinical trial effects of oat beta-glucan on fasting lipid levels [47]	10 RCTs; 1,000 normo- and hypercholesterolemic subjects; age 20–73 years; mean oat β-glucan intake 3.7 g/day from food and supplement sources (1–8 g/day); mean study duration was 5.5 weeks	Oat β-glucan sources reduced TC by 1.5 mg/dL vs. a wheat control. Larger reductions were seen in subjects with higher baseline blood TC levels, especially when the dose was ≥3 g β-glucan/day

Table 13.3 (continued)

Objective	Study details	Results
Psyllium		
Systematic review and meta-analyses		
Wei et al. Evaluate the effects of psyllium for a potential dose-response relationship with fasting lipids [48]	21 RCTs; 1,030 subjects; including 687 mild and moderate hypercholesterolemic individuals; mean psyllium intake 10.2 g/day from enriched foods and supplements (3–20 g/day); 2–26 weeks	Compared with placebo, the intake of 10.2 g psyllium/d lowered serum TC by l4.5 mg/dL and LDL-C by 10.5 mg/dL. There was a significant inverse dose-response relationship between psyllium and LDL-C with 5, 10, and 15 g psyllium/day reducing LDL-C by 5.6, 9.0, and 12.5%, respectively
Anderson et al. Evaluate the effects of psyllium and low-fat diets on fasting lipids [49]	8 RCTs; 656 hypercholesterolemic adults; 10 g psyllium/day or cellulose (placebo)-supplemented low-fat diets; 8 weeks	Compared to the cellulose placebo group, the psyllium group had significantly lowered TC by 4% and LDL-C by7%, and there was no effect on HDL-C or TG levels
Olsen et al. Estimate the clinical trial effects of psyllium- enriched cereal products on fasting lipids [50]	12 RCTs; hypercholesterolemic subjects with TC ranging from 200 to 300 mg/dL; psyllium-enriched cereal products with 10 g psyllium/day; AHA Step 1 and 2 or low-fat diets; 8–26 weeks	Compared to control cereals, psyllium-enriched cereals lowered TC by 12 mg/dL (5%) and LDL-C by 13.5 mg/dL (9%). HDL-C levels were unaffected in subjects eating psyllium cereal. Psyllium effects on blood lipids were independent of sex, age, or menopausal status
Viscous, soluble fiber RCTs		
Brouns et al. Evaluate the effects of sources and types of pectin on LDL-C lowering (The Netherlands; crossover RCT) [51]	7–8 subjects per trial arm; 6–15 g/day of different pectins in mildly hypercholesterolemic subjects; 3–4 weeks	The most effective pectin sources for LDL lowering were citrus pectin DE-70 and apple pectin DE-70. Compared to cellulose, these pectin sources at 15 g/day lowered LDL-C by 7–10% and at 6 g/day reduced LDL-C by 6–7%
Pal et al. Study the effects of fiber-rich healthy diets or psyllium-supplemented diets on fasting lipids (Australia; parallel RCT) [52]	72 overweight and obese adults; randomized to (1) control (Western) diet + placebo (20 g fiber/day), (2) Western diet + psyllium (55 g fiber), (3) healthy diet + placebo (32 g fiber), or (4) healthy diet + psyllium (59 g fiber); psyllium supplement or placebo (12 g) drink was consumed three times daily 5–10 min before each meal; 12 weeks	Fiber-rich healthy diets and psyllium-supplemented diets significantly lowered TC levels by 15–21% and LDL-C levels by 26–30% compared with the lower-fiber control diet after 6 and 12 weeks (Fig. 13.2). Also, HDL-C, TG, and body weight and composition were improved in subjects on the healthy diet and psyllium-supplemented diets
Vuksan et al. Assess the role of fiber viscosity rather than quantity in predicting cholesterol-lowering effect in healthy individuals (Canada; crossover RCT) [53]	23 healthy subjects; mean age 35 years; 12 males and 11 females; mean LDL-C 110 mg/dL; three-arm experiment including low-viscosity wheat bran, medium-viscosity psyllium, and a high-viscosity viscous fiber blend in fiber-rich cereal added to the typical diet; 3 weeks; 2 weeks of washout	The magnitude of LDL-C reduction showed a significant positive association with the fiber's viscosity. Despite the smaller quantity consumed, the high-viscosity fiber lowered LDL-C to a greater extent than lower-viscosity fibers

(continued)

Table 13.3 (continued)

Objective	Study details	Results
Chen et al. Examine the effect of dietary fiber intake on serum lipids among persons without hypercholesterolemia (USA; parallel RCT) [54]	110 participants, mean age 48 years; 60% female; mean serum cholesterol level approx. 200 mg/dL; 8 g/day of water-soluble fiber from oat bran or a control in foods; 3 months	The mean net changes in total, HDL-C, and LDL-C were −2.4 mg/dL ($p = 0.56$), −1.7 mg/dL ($p = 0.26$), and −1.3 mg/dL ($p = 0.71$), respectively. This trial does not support the hypothesis that water-soluble fiber intake from oat bran reduces total and LDL cholesterol in individuals with relatively normal serum cholesterol levels
Kris-Etherton et al. Evaluate whether an intervention of foods high in soluble fiber from psyllium and/or oats plus a telephone-based, personalized behavior change support service improves serum lipids and elicits cholesterol-managing lifestyle changes vs. usual care (USA; parallel RCT) [55]	150 moderately hypercholesterolemic men and women; age range from 25 to 70 years; four servings/day of high-fiber foods and each subject had weekly telephone conversations with a personal coach who offered support and guidance in making lifestyle changes consistent with the National Cholesterol Education Program's (NCEP) cholesterol-lowering guidelines. The usual care group received a handout describing the NCEP Step 1 diet; 7 weeks	In the intervention group, blood lipids decreased for TC by 5.6%, for LDL-C by 7.1%, for LDL-C/HDL-C ratio by 5.6%, and TG by 14.2% significantly lower than usual care. The intervention group also reported an increase in their knowledge, ability, and confidence to make cholesterol-managing diet and exercise changes, greater decrease in energy intake from saturated fat by1.6%, increase in soluble fiber intake by 7.3%, and increase in exercise vs. the usual care group (all $p < 05$)
Non-viscous whole grains RCTs		
Giacco et al. Evaluate circulatory CVD and diabetes biomarkers in response to a diet with whole grains compared with a diet containing the same amount of refined cereal foods (Kuopio-Finland/ Naples, Italy; parallel RCT) [56]	146 adults with metabolic syndrome; both genders; LDL-C approx. 130 mg/dL; age range 40–65 years; participants were assigned to a diet based on wheat and rye whole grain (total fiber 33 g) or on refined cereal products (total fiber 20 g); 12 weeks	At the end of the study, insulin sensitivity indices, blood lipids, and inflammatory markers did not change significantly in the whole grain and control groups as compared with baseline, and no differences between the two groups were observed
Ross et al. Compare the effects of a whole-grain-rich diet with a matched refined-grain diet on plasma biomarkers (Switzerland; crossover RCT) [57]	17 healthy, normal cholesterolemia subjects; 11 females and 6 males; mean age 34 years; mean BMI 23; 150 g whole-grain or refined-grain-based foods; 2 weeks; 5 weeks of washout during crossover	Whole-grain diets tended to decrease plasma TC and LDL-C ($p = 0.09$), but did not change plasma HDL-C, fasting glucose, CRP, or homocysteine compared with the refined-grain diets
High-fiber diets		
Ma et al. Evaluate the effects of a high-fiber diet vs. the American Heart Association (AHA) weight loss diet on weight loss in obese adults (USA; parallel RCT) [58]	240 obese adults with metabolic syndrome; mean age 52 years; randomized into either a high-fiber diet (~30 g fiber/day) or the AHA diet (~20 g fiber/day) including caloric restriction	High-fiber diets have similar beneficial effects on weight, TC, LDL-C, TG, and CRP as the AHA diet including caloric reduction. Thus, a simplified approach to focus only on increased fiber intake may be an option for reducing weight and CHD risk factors
Esposito et al. Assess the long-term effects of high vs. low-fiber MedDiets on cardiometabolic health in overweight adults (Italy; parallel RCT) [59]	180 men and women with metabolic syndrome; mean age 44 years: a MedDiet (32 g fiber/day; 600 g/day whole-grains, fruits and vegetables, and nuts; low sat fat/olive oil) or a control diet (17 g fiber/ day; 300 g/day whole-grains, fruits and vegetables, and nuts; high sat fat); 2 years	The higher-fiber MedDiet improved TC, HDL-C, TG, CRP, HOMA score, and body weight vs. the lower-fiber control diet. Also, the fiber-rich diet significantly reduced metabolic syndrome risk by 50% compared to the control diet

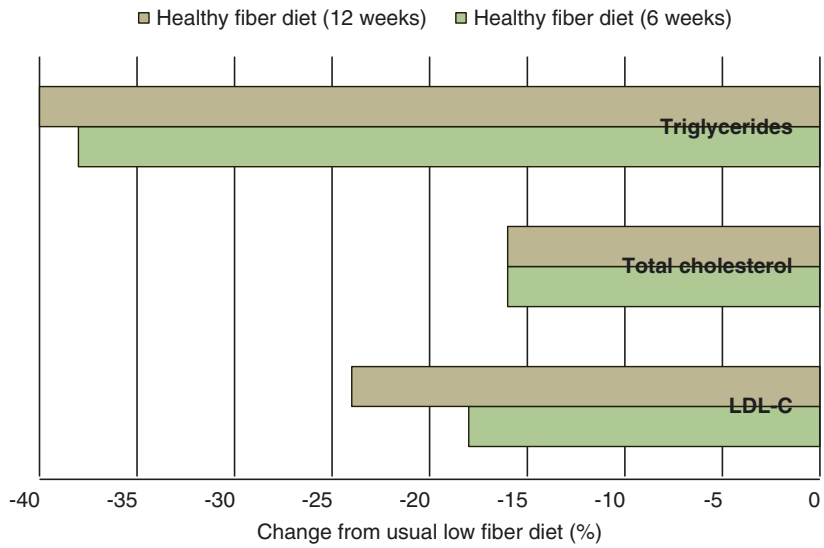

Fig. 13.3 Effect of a healthy fiber-rich diet (32 g fiber/day) vs. low-fiber Western diets (20 g fiber/day) on fasting blood lipid profile in 72 metabolic syndrome subjects with mean age 42 years and BMI 34 (all $p = 0.001$) [52]

meta-analyses, the mean of all subjects showed that the mean consumption of 5.5 g/day can significantly reduce TC by 10 mg/dL and LDL-C by 8–11.5 mg/dL compared to control diets [44, 45]. One RCT found that in subjects without hypercholesterolemia, 8 g/day of oat bran β-glucan insignificantly lowered TC and LDL-C [54]. For the psyllium meta-analyses, the mean of all subjects found that the mean consumption of 10 g/day significantly reduced TC by 14.5 mg/dL and LDL-C by 10.5 mg/dL compared to control diets [48]. There was also an inverse dose-response effect between psyllium intake and LDL-C levels. One RCT demonstrated that higher-viscosity soluble fiber blends can further decrease LDL-C more than psyllium at half the dose [53]. Both citrus and apple pectin at 6 g/day have been shown to reduce LDL-C by about 7% in mildly hypercholesterolemic individuals [51]. Two studies show that consuming primarily insoluble fiber-rich wheat or rye whole grains did not significantly reduce blood lipids more than refined-grain diets [57, 58]. Three large RCTs demonstrated that fiber-rich diets (containing 14 g fiber/1000 kcals) were associated with significant lipid lowering compared to lower-fiber control diets [52, 58, 59]. An Australian RCT (72 healthy overweight and obese adults; healthy fiber rich diets (32 g fiber/day) vs. Western diet (20 g fiber/day); 6–12 weeks) showed that higher-fiber diet significantly lowered blood lipids after 6 weeks (Fig. 13.3) [52].

Systemic Inflammation

The effects of fiber on reducing systemic inflammatory markers (e.g., CRP, IL-6) are more modest and less consistent than for lowering elevated fasting lipids (Table 13.4) [36–38, 60]. A meta-analysis (14 RCTs; 728 subjects; BMI 27–36; mean 12 weeks with a range of 3–16 weeks) found a small but significant mean reduction in CRP by 0.37 mg/L for higher-fiber intake compared to the lower fiber (control) [38]. However, a subgroup analysis determined that significant reduction in CRP only occurred when there was ≥8 g fiber increase above the control group. A systematic review (11 RCTs; 690 overweight or obese subjects; age 38–63 years; 3–16 weeks) found that fiber only significantly lowered CRP when subjects consumed high-fiber or hypocaloric diets [36]. A review article reported that six of seven RCTs reported significantly lowered CRP due to the synergistic effects of fiber, weight loss, and other anti-inflammatory phytochemicals found in many fiber-rich foods [37].

Table 13.4 Summary of RCTs on increased fiber intake and systemic inflammation

Objective	Study details	Results
Meta-analyses and systematic reviews		
Jiao et al. Estimate the effect of fiber intake on CRP in overweight and obese adults [38]	14 RCTs on fiber-rich foods or fiber supplements; 728 overweight/obese adults; 12 weeks (3–16 weeks)	Higher-fiber intake modestly, but significantly reduced CRP by 0.37 mg/L vs. control. A subgroup analysis found that an increase in fiber of >8 g/day significantly reduced CRP by 0.47 mg/L vs. 0.17 mg/L for <8 g/day
Buyken et al. Evaluate the effect of fiber clinical trials on inflammatory markers in overweight and obese adults [36]	11 RCTs on fiber and CRP or IL-6; 690 overweight/obese adults; age range 38–63 years; 3–16 weeks	Fiber lowered CRP in only a few trials where diets were high in fiber (48 g/day) or hypocaloric
North et al. Systematically review the effects of clinical trials for fiber's effects on systemic inflammation [37]	7 RCTs; 550 subjects; 65% women; mean 46 weeks (3–104 weeks); mean fiber intake was 19 g/1000 kcals	Six of these trials reported that fiber-rich diets or added psyllium reduced CRP by 25–54%. These fiber-rich diets also promoted weight loss and included other anti-inflammatory nutrients and phytochemicals, which are synergistic contributors to reduced inflammation
Crossover RCT		
King et al. Study the effects of naturally fiber-rich diets vs. psyllium fiber-supplemented low-fiber diets on systemic inflammatory response [60]	35 subjects (18 lean normotensives and 17 obese hypertensive individuals); aged 18–49 years; 80% women; randomized into a DASH diet with high-fiber or a psyllium fiber-supplemented diet (about 30 g fiber/day) compared to a baseline diet of 12 g fiber/day; 3 weeks; no washout	Compared to baseline, CRP levels were significantly reduced in the high-fiber DASH diet group by 14% and in the psyllium fiber-supplemented diet group by 18%. Body weight, TG, TC, or insulin resistance status did not differ between the groups after 3 weeks

A crossover RCT with both lean and obese adults found that both a high-fiber diet and a psyllium-supplemented diet (30 g fiber/day) significantly reduced CRP by 14–18% compared to a usual diet of 12 g fiber/day after 3 weeks.

Prospective Cohort Studies

Large prospective cohort studies consistently report that increasing fiber intake significantly reduced CHD risk and mortality (Table 13.5) [13, 43, 61–74]. The evidence from five dose-response meta-analyses all support the role of higher-fiber diets (increased by 7–10 g/day) in reducing the risk of CHD events and premature death compared with lower-fiber diets [13, 61–64]. Four dose-response meta-analyses estimate that each 10 g/day increase in fiber intake was associated with a significantly reduced CHD risk by 11–14%, CHD events by 8%, and CHD mortality by 20–27% [13, 61–63]. Another dose-response meta-analysis found that 7 g of total fiber/day was associated with a significant reduction in both CVD and CHD risk by 9% [64]. Cereal, fruit, and vegetable fiber and both insoluble and soluble fiber have been shown to contribute to reducing CHD risk [13, 61–64]. A dose-response meta-analysis curve for total fiber intake and CHD events is shown in

Table 13.5 Summary of prospective cohort studies on increased fiber intake and coronary heart disease (CHD) and mortality risk

Objective	Study details	Results
Systematic reviews and Meta-analyses		
Kim et al. Examine dose-response association between fiber intake and CHD mortality risk [61]	15 prospective cohort studies; 1,409,014 subjects (Multivariate adjusted)	CHD mortality risk was significantly lowered by 24% for the highest vs. lowest category of fiber. In a dose-response analysis, each 10 g/day in fiber intake lowered CHD risk by 11%
Wu et al. Assess the association between fiber intake and risk of CHD and quantitatively estimate their dose-response relationships [62]	18 cohort studies; 672,408 participants (Multivariate adjusted)	A significant dose-response relationship was observed between fiber intake and CHD risk. The highest vs. lowest category of fiber intake reduced CHD risk by 7% for all coronary events and 17% for CHD mortality. Each 10 g/day increment of total fiber was associated with an 8% decrease in risk of all coronary events (Fig. 13.4) and a 24% decrease in mortality risk
Liu et al. Investigate the effects of fiber intake and all-cause mortality and cause-specific mortality [63]	25 cohort studies; 1,752,848 individuals; cohorts were primarily from the USA and EU; follow-up of 12 years (range 1–40 years) (Multivariate adjusted)	For each 10 g/day increase in fiber intake, there was a lower risk of all-cause mortality by 11%, CHD mortality by 20%, and ischemic heart disease mortality by 34%. Also, higher-fiber intake lowered overall CVD and all-cause mortality rates by 23%
Threapleton et al. Evaluate a potential dose-response association for fiber intake on CVD and CHD incident or fatal events [64]	22 cohort studies; 1,751,619; follow-up of 6–22 years (Multivariate adjusted)	A significantly lower risk of 9% was seen for both CVD and CHD with every additional 7 g/day of total fiber consumed. Total, soluble, insoluble, cereal, fruit, and vegetable fiber intake were inversely associated with risk of CHD at 4–7 g/day
Pereira et al. Conduct a pooled analysis of fiber and its subtypes and CHD risk [13]	Ten US and EU prospective cohort studies; 91,058 men and 245,186 women; follow-up of 6–10 years, 5,249 incident total coronary cases and 2,011 coronary deaths (Multivariate adjusted)	The following significant CHD risks were observed: Total fiber: Each 10 g/day lowered incidence risk by 14% and mortality risk by 27%
		Cereal fiber: Each 10 g/day lowered CHD risk by10% and mortality risk by 25%
		Fruit fiber: Each 10 g/day lowered CHD risk by 16% and mortality risk by 30%
		Vegetable fiber: Each 10 g/day insignificantly lowered CHD risk
Prospective cohort studies		
Li et al. Evaluate the effect of fiber intake after myocardial infarction (MI) on secondary MI mortality risk (USA—the Nurses' Health Study and The Health Professionals Follow-Up Study) [65]	Two large prospective cohort studies; 4,000 US MI survivors; median post-MI follow-up of 9 years; 682 total and 336 CVD deaths for women and 451 total and 222 CVD deaths for men (Multivariate adjusted)	Higher post-MI fiber intake was associated with a significantly lower mortality by 25%. The strongest protective effects were from cereal fiber (whole-grain foods), which lowered risk of mortality by 27% (highest to lowest intake)

(continued)

Table 13.5 (continued)

Objective	Study details	Results
Buil-Cosiales et al. Investigate the effect of fiber diets rich in whole grains, fruit, and vegetables on all-cause mortality in a Mediterranean cohort of older adults with high CVD risk (Spain—Prevencion con Dieta Mediterranea [PREDIMED]) [66]	7,216 men and women with high CVD risk; mean age 67 years; mean follow-up of 6 years, 425 participants died, which included 103 CVD deaths (Multivariate adjusted)	Highest fiber (35 g/day) intake lowered CVD mortality risk by 54% vs. those with the lowest fiber intake of 19 g/day (p-trend = 0.059). Also, fruit intake of >210 g/day lowered all-cause mortality risk by 41%, and the highest fruit intake (585 g/day) significantly lowered CVD mortality risk by 56%
Rebello et al. Study the effect of different types and food sources of carbohydrates, on ischemic heart disease (IHD) mortality (Singapore Chinese Health Study) [67]	53,469 Chinese adults; average follow-up of 15 years; 1,660 IHD deaths (Multivariate adjusted)	For IHD mortality, fiber intake was associated with lower risk in men by 6% and in women by 21%. These risk reductions were observed by replacing one daily serving of rice with one serving of fruit, vegetables, or whole-wheat bread
Crowe et al. Evaluate the effect of total fiber and fiber food sources on ischemic heart disease (IHD) mortality (European Prospective Investigation into Cancer and Nutrition-Heart [EPIC] study) [68]	306,331 men and women from 8 European countries; follow-up of 11.5 years; 2,381 IHD deaths (Multivariate adjusted)	IHD mortality risk (multivariate adjusted) was reduced for: 10 g total fiber/day by 15% 5 g cereal fiber/day by 9% 2.5 g fruit fiber/day by 6% 2.5 g vegetable fiber/day by 10%
Eshak et al. Examine the association between fiber intake and CVD and CHD mortality (Japan) [69]	58,730 Japanese men and women; aged 40–79 years; 14 years of follow-up; 1,100 CHD/CVD deaths (Multivariate adjusted)	There was a significant reduction in CHD mortality risk in both men and women for total fiber by 19%, for insoluble fiber by 52%, and for soluble fiber by 29% (highest vs. the lowest quintile of intake)
Streppel et al. Assess the effect of fiber intake on CHD and all-cause mortality (The Netherlands-Zutphen study) [70]	1,373 men (born between 1900 and 1920) examined between 1960 and 2000; 40 years of follow-up; 348 CHD-related deaths occurred (Multivariate adjusted)	Each 10 g fiber/day reduced CHD mortality risk by17%. The effectiveness of fiber intake on all-cause mortality decreased gradually with increasing age between 50 and 80 years. The average daily fiber intake decreased from 33 g/day in 1960 to 21 g/day in 2000
Nettleton et al. (2007). Determine the effect of fiber sources on carotid intima-media thickness (CIMT) (USA—Los Angeles Atherosclerosis Study) [34]	573 subjects; mean age 62 years; 53% men; measured ultrasonographically at baseline and after 18 months (Multivariate adjusted)	CIMT progression declined across fiber intake quintiles (from highest to lowest) with a inverse association for viscous fiber and pectin, marginally significant for total fiber (p = 0.06). The median fiber intake ranged from the highest quintile (25 g/day) to the lowest quintile (13 g/day)
Mozaffarian et al. Examine the effect of fiber intake from fruit, vegetables, and cereal sources on CVD risk in elderly persons (USA—Cardiovascular Health Study) [71]	3,588 men and women, mean age 72 years; mean follow-up of about 9 years; 811 CVD events (Multivariate adjusted)	Fiber was inversely associated with CVD risk (p-trend = 0.02), with 21% lower risk in the highest quintile of fiber intake (29 g/day), compared with the lowest quintile (5 g/day). Of the food sources of fiber, only higher-cereal fiber (>6.3 g/day) intake was associated with lower CVD risk compared to <1.7 g/day. In a post hoc analysis, two slices of dark breads were associated with lower CVD risk by 24%

Table 13.5 (continued)

Objective	Study details	Results
Bazzano et al. Assess the relationship between total fiber and its subcomponents and the risk of CVD and CHD (USA—NHANES I Follow-Up Study) [72]	10,000 adults; mean age 49 years; 38% males; average follow-up of 19 years; 1,843 incidences of CHD and 3,762 cases of CVD (Multivariate adjusted)	A 10 g increase in total fiber significantly reduced CHD and CVD risk by 7%. A 5 g increase in soluble fiber significantly reduced CHD and CVD risk by 5%
Liu et al. Examine the effect of increasing fiber intake on the risk of MI in mid-life women (USA—Women's Health Study) [73]	39,876 women; mean age 54 years; 6 years of follow-up; 177 MI cases (Multivariate adjusted)	Comparing the highest quintile of fiber intake (median: 26 g/day) with the lowest quintile (median: 12.5 g/day), MI risk was reduced by 32%. Inverse associations were observed for both soluble and insoluble fiber and risk of MI
Wolk et al. Measure the association of fiber and different fiber food sources on risk of CHD in women (USA—the Nurses' Health Study) [74]	68,782 women; mean age 50 years; 10-year follow-up; 591 major CHD events (Multivariate adjusted)	For a 10 g/day increase in fiber intake, total CHD events risk was reduced by19%. Among different fiber food sources, only cereal fiber per 5 g/day increase was associated with a significant reduced risk of CHD by 37%

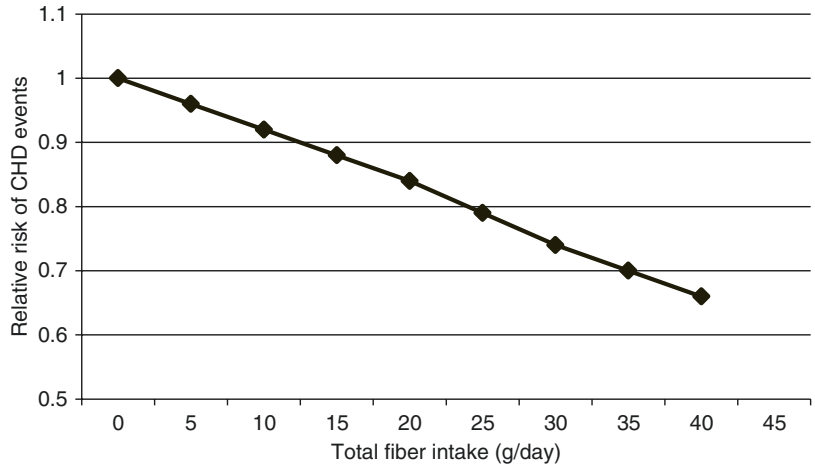

Fig. 13.4 Dose-response relationship between total fiber intake and coronary heart disease (CHD) event risk from a meta-analysis of 18 cohort studies ($p = 0.001$) [62]

Fig. 13.4 [62]. A 2016 meta-analysis suggests that high intake of fiber (mean ~23.2 g/day) significantly reduced CHD mortality by 24%, compared to a low intake of fiber (mean ~12.5 g/day) with no significant differences by gender or geographical region [61]. Eleven prospective studies from the USA, EU, China, and Japan consistently show that increased fiber intake by about ≥10 g/day significantly reduced the risk of CHD, ischemic heart disease (IHD), myocardial infarction (MI) incidence, and CVD/CHD mortality [65–74]. These prospective studies suggest that increased cereal fiber at 5–10 g/day from dark breads and breakfast cereals can reduce CHD risk in mid to later life [65, 68, 70, 71, 74]. An inverse association between soluble, viscous fiber intake and carotid intima-media thickness progression [34], and the effect of fiber on CHD risk was similar in men and women and for geographic regions [13, 61–74].

Conclusions

Although there have been some decreasing trends in overall CHD mortality rate over the last several decades due to the use of cholesterol-lowering drugs and surgical procedures, CHD is still a leading cause of death globally and its prevalence is expected to increase as the global population ages. CHD affects both men and women, often developing after the fifth decade of life in men and the sixth decade of life in women. Between 2015 and 2030, annual US costs related to CHD and related cardiovascular diseases are forecasted to increase from $84.8 billion to $202 billion. The role of elevated lipids, lipoproteins, and inflammation as risk factors for CHD is well established. Adopting a healthy fiber-rich dietary pattern with healthy vegetable oils and low in saturated and *trans*-fatty acids; incorporating bioactive foods and supplements such as soluble fiber, antioxidants, and plant sterols and stanols; exercising regularly; and maintaining a healthy weight are key to managing risk and preventing CHD. The importance of increasing fiber intake to reduce CHD risk is supported by strong scientific evidence from numerous prospective cohort studies and RCTs. Increased fiber intake from fiber-rich diets with a variety of whole foods, food ingredients, or supplements including viscous soluble fibers such as β-glucan or psyllium have strong RCT evidence supporting their effectiveness in lowering elevated blood lipids to normal healthy levels for reduced CHD risk. Dose-response meta-analyses consistently show that a daily increase in fiber intake significantly reduces CHD risk by 8–14% and CHD mortality by 23–30%. Two primary fiber CHD-protective mechanisms are (1) reducing fasting lipid and lipoprotein profiles and (2) attenuating elevated systemic inflammation risk by controlling body weight and abdominal and visceral fat gain and maintaining a healthy colonic microbiota ecosystem.

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Chapter 14
Fiber and Hypertension

Keywords Dietary fiber • Beta-glucan • Blood pressure • Hypertension • Aging • Overweight • Obesity

Key Points

- Increasing global population trends of aging, overweight, and obesity are major factors associated with elevated blood pressure (BP) and hypertension.
- Lifestyle factors such as poor quality dietary patterns, excess energy intake, sedentary lifestyles, alcohol consumption, smoking, and anxiety and stress are important underlying controllable factors in most cases of hypertension.
- Observational studies consistently show that increased fiber intake (by 7–15 g/day above the usual levels) is significantly associated with reduced BP and hypertension risk compared to the low fiber intake in Western diets.
- Meta-analyses of intervention trials show that increased fiber intake is more effective in lowering BP in older (>40 years), overweight/obese, and elevated BP or hypertensive persons than in younger, leaner, and normotensive individuals.
- Viscous, soluble fiber (e.g., β-glucan) sources are generally more effective in lowering BP than insoluble fiber sources (e.g., wheat bran).
- In hypertensive individuals already on drug therapy, lifestyle modifications such as increased fiber intake may adjunctively further lower BP.
- Potential fiber BP-lowering mechanisms include: reducing risk of weight gain and central obesity; improving vascular health by lowering elevated total and LDL cholesterol, and lowering raised systemic inflammation via healthier colonic microbiota; and attenuating risk of insulin resistance.

Introduction

Elevated blood pressure (BP) including prehypertension (systolic BP >120–139 mm Hg or diastolic BP >80–89 mm Hg) and hypertension (systolic BP ≥140 mm Hg or diastolic BP >90 mm Hg) is a common and growing public health problem [1, 2]. Globally, the overall prevalence of elevated BP in adults ≥25 years of age is approximately 40%. By 2025, because of population growth and an aging population, it is projected that about 1.5 billion individuals will have hypertension [2–5]. Increased BP etiology is linked to the renin-angiotensin-aldosterone system (RAAS), a hormonal cascade that functions in the homeostatic control of BP and extracellular fluid volume [6]. Aldosterone causes the tubules of the

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kidneys to increase the reabsorption of sodium and water into the blood while at the same time causing the excretion of potassium, which increases the volume of extracellular fluid leading to elevated BP.

Increasing global population trends—aging and overweight and obesity—are the major factors associated with elevated BP and hypertension [7]. Aging is directly associated with elevated BP risk (Fig. 14.1) [5]. Excess body weight is associated with increased activity of the renin-angiotensin-aldosterone system, insulin resistance, and reduced kidney function associated with salt-sensitive hypertension [7–9]. Rates of hypertension are twice as likely to occur in obese (40%) vs. normal-weight (20%) individuals, with larger waist size being a further multiplier of the risk of hypertension [8]. The relationship between weight change and BP is summarized in Fig. 14.2 [9]. Elevated BP is a major risk factor for stroke, coronary heart disease (CHD), damage to retinal blood vessels, and kidney disease/renal failure [3–6]. The adult risk of cardiovascular disease (CVD) doubles for each 20/10 mm Hg incremental increase above 115/75 mm Hg. Elevated BP is directly associated with the progression of intima-media thickness (IMT) in the common carotid artery (CCA) (mm/year) as summarized in Fig. 14.3 [10].

Lifestyle factors such as poor-quality dietary patterns, excess energy intake, sedentary lifestyle, alcohol consumption, smoking, and anxiety and stress are important underlying controllable factors in most cases of hypertension [1–5, 7–11]. Guidelines for prevention, treatment, and control of elevated BP

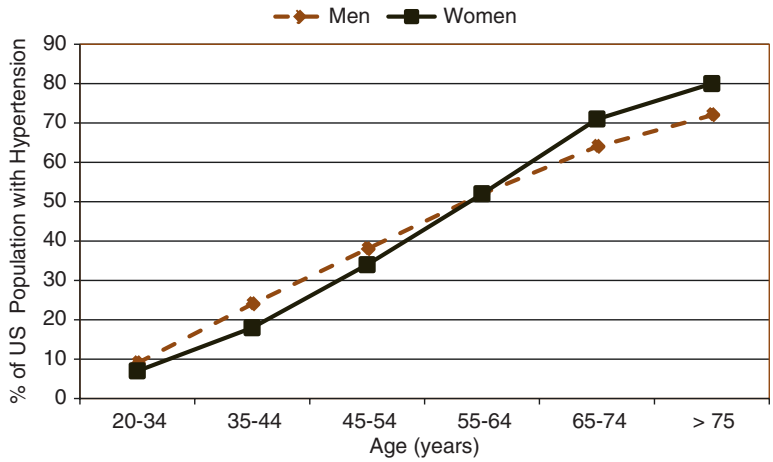

Fig. 14.1 Prevalence of hypertension with increasing age from US NHANES 2007–2010 data [5]

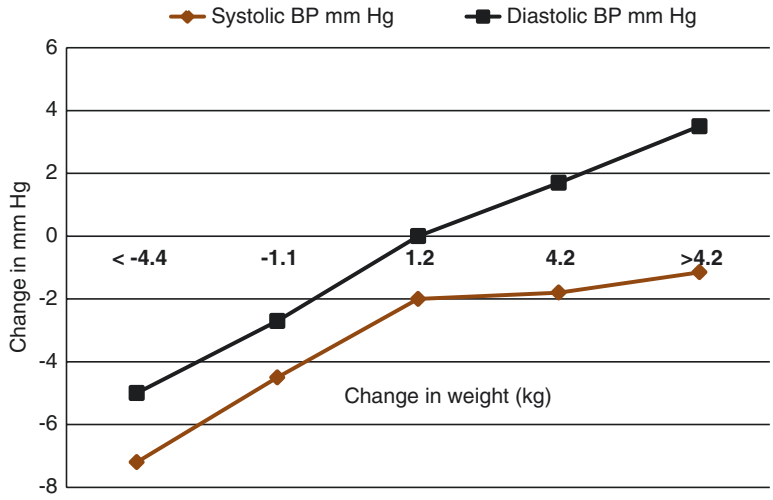

Fig. 14.2 Effect of the level of weight change on systolic blood pressure (BP) and diastolic BP [9]

focus on lifestyle modifications including weight loss and maintenance, reduced salt intake, increased consumption of dietary fiber (fiber) rich diets including whole grains rich in B-glucan, fruits and vegetables, routine participation in physical activity, cessation of smoking, limiting of alcohol consumption, and anxiety and stress control [1–5, 7, 8]. In hypertensive individual's already on drug therapy, lifestyle modifications can further lower BP. Potential nutrients and phytochemicals associated with BP are summarized in Table 14.1 [1–5, 12–27]. Fifty top fiber-rich foods in rank order are provided in Appendix 1.

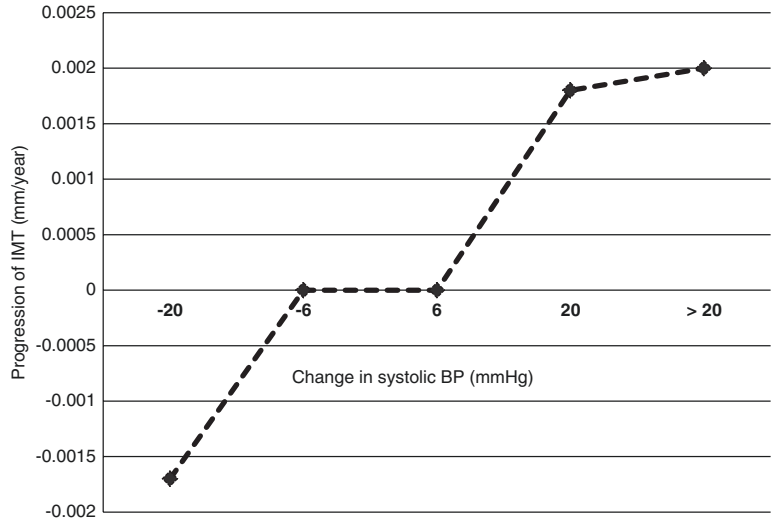

Fig. 14.3 Effect of systolic blood pressure (BP) on intima-media thickness progression in the common carotid artery [10]

Table 14.1 Effects of nutrients and phytochemicals on risk of elevated blood pressure [1–5, 12–26]

Dietary factors	Postulated effects	Strength of evidence
Minerals		
Excessive salt	Increase	+/+
Adequate potassium	Decrease	+/+
Adequate magnesium	Decrease	+/−
Adequate calcium	Decrease	+/−
Fats		
Excessive saturated/trans fat	Increase	+/−
Diet rich in omega-3 polyunsaturated fat	Decrease	+/+
Diet rich in omega-6 polyunsaturated fat	Decrease	+/−
Diet rich in monounsaturated fat	Decrease	+
Carbohydrate		
Excessive refined carbohydrates	Increase	+
Excessive sugar-sweetened beverage intake	Increase	+
Fiber	Decrease	+
Protein		
Dairy	Decrease	+
Plant	Decrease	+
Red meat	Uncertain	+/−
Antioxidant nutrients/phytochemicals		
Vitamin C/E	Uncertain	+/−
Carotenoids	Decrease	+
Polyphenols	Decrease	+

Key to evidence: +/− = limited or equivocal evidence; + = suggestive evidence from observational studies and clinical trials; +/+ = persuasive evidence, primarily from clinical trials

The objective of this chapter is to provide a review of the role of fiber in the prevention and treatment of elevated BP and hypertension.

Effects of Dietary Fiber on Elevated Blood Pressure and Hypertension

Potential Mechanisms

There are fewer cohort studies and randomized controlled trials (RCTs) on the effects of fiber on BP than on blood lipids and lipoproteins, and the mechanisms are not understood at the present time [27]. Potential fiber mechanisms supporting reduced BP and hypertension risk are as follows:

1. Reduces food/dietary energy density and increases satiety and satiation, which reduce the risk of weight gain or obesity.
2. Enhances insulin sensitivity which may improve vascular and endothelial function.
3. Promotes healthier LDL-C and HDL-C profiles for improved endothelial health and a slower rate of arterial plaque buildup.
4. Attenuates elevated systemic inflammation and LDL oxidation.
5. Promotes a healthier microbiota and increased fermentation to short-chain fatty acids (SCFAs), leading to potential improved cardiometabolic health [27–31].

A recent mechanism was discovered which links fiber's effect in favorably altering the composition of colonic microbiota and production of SCFAs to the up-regulation of receptor in the gastrointestinal tract that helps to control BP [32–35]. Fiber's effect on BP depends on the type of fiber (insoluble or soluble); dose of fiber, whether it is from isolated supplemental fiber or high-fiber foods containing other BP-lowering components; and individual phenotypes [16, 36, 37]. In general, soluble fiber has better BP-lowering effects than insoluble fiber, and older, hypertensive and overweight/obese individuals experience greater BP-lowering effects than younger, normotensive, and lean individuals [36, 37].

Observational Studies

Observational studies consistently show that increased fiber intake (by 7–15 g/day above the usual levels) is significantly associated with reduced BP and hypertension risk compared to low-fiber Western diets [38–43]. The Coronary Artery Risk Development in Young Adults (CARDIA) Study (2,909 healthy adults; 18–30 years of age; fiber intake highest <10.5 g/1000 kcal vs. > 5.9 g/1000 kcal; 10 years of follow-up) observed that fiber was associated with significantly lower systolic BP by 2.2 mm Hg and diastolic BP by 2.7 mm Hg in white subjects, but the level of statistical significance was not observed in black subjects [38]. The Health Professionals Follow-Up Study (30,681 men; age range 40–75 years; 4 years of follow-up; 1,248 cases of hypertension) found that men consuming <12 g fiber/day had a 57% increased risk of hypertension compared with an intake of >24 g/day (Fig. 14.4) [39]. Also, fiber, potassium, and magnesium were each significantly associated with lower risk of hypertension when considered individually and after adjustment for age, relative weight, alcohol consumption, and energy intake. The Nurses' Health Study (41,541 US women; age 38–63 years old; 4 years of follow-up; 2,526 cases of hypertension) showed an inverse association of calcium, fiber, potassium, and magnesium with reported BP but not with the incidence of hypertension [40]. These associations remained after adjusting for age, body mass index, alcohol consumption, waist-to-hip ratio, physical activity, smoking, caffeine intake, menopausal status, and the use of hormones. Women consuming ≥25 g fiber/day had lower risk of elevated BP by 109% vs. those consuming <10 g fiber/day (Fig. 14.5) [40]. The INTERMAP population study (4,680 adults from Japan, China, the

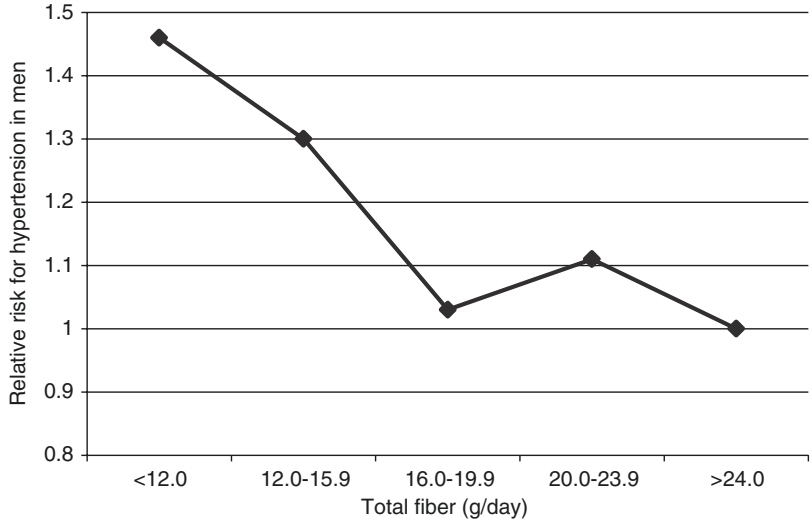

Fig. 14.4 Effect of daily total fiber intake on hypertension risk in US men during 4 years of follow-up from the Health Professionals Follow-Up Study ($p = 0.015$; fully adjusted including magnesium, potassium, and fiber) [39]

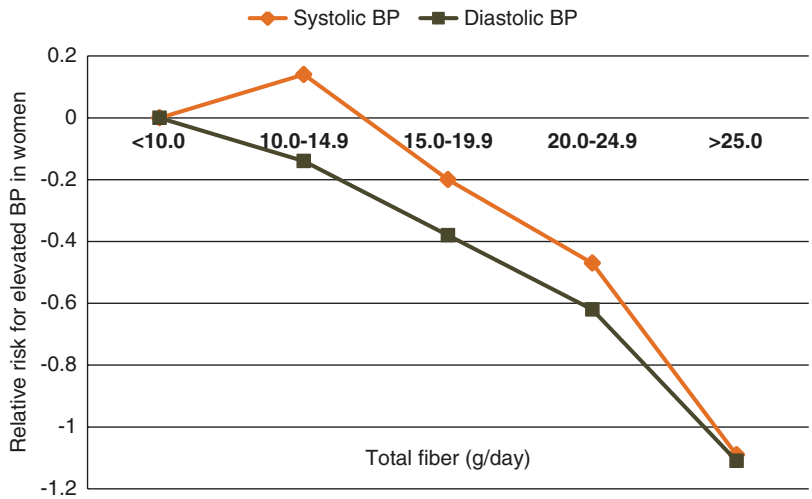

Fig. 14.5 Effect of increasing fiber intake on elevated blood pressure (BP) risk in women after 4 years of follow-up from The Nurses' Health Study [40]

UK, and the USA; aged 40–59 years) found a significant reduction in systolic BP by 1.7 mm Hg for each 7 g fiber/1000 kcal increase, independent of the effects of other nutrients associated with fiber-rich foods such as potassium and magnesium [41]. Further, several studies indicate that fiber intake is inversely associated with preeclampsia (elevated BP) during pregnancy [42, 43].

Randomized Controlled Studies (RCTs)

Table 14.2 summarizes the RCTs on fiber intake from foods or supplements and BP [16, 17, 36, 37, 44–56].

Table 14.2 Summaries of RCTs on increased fiber from foods and supplements on blood pressure (BP)

Objective	Study details	Results
Systematic reviews and meta-analyses		
Hartley et al. Investigate the effectiveness of increased fiber intake for the prevention of CVD including BP lowering (Cochrane systematic review) [44]	Eight published RCTs; 661 participants age ≥ 18 years; high risk of CVD and from the general population; duration ≥12 weeks)	Increased fiber intake modestly but significantly reduced mean systolic BP by 1.9 mm Hg and diastolic BP by 1.8 mm Hg
Evan et al. Assess the clinical effects of fiber rich foods on BP with emphasis on oats [16]	18 RCTs including/5 β-glucan RCTs; 1,333 adults; age range 29–69 years; median increased fiber intake was 6 g/day; ≥ 6 weeks of duration	The pooled mean BP for all fiber sources was insignificantly reduced for systolic BP by 0.9 mm Hg and diastolic BP by 0.7 mm Hg. Diets rich in β-glucans significantly lowered systolic BP by 2.9 mm Hg and diastolic BP by 1.5 mm Hg with a median increase of 4 g /day β-glucans from whole oats or oat bran-enriched foods or oat-based breakfast cereals compared with similar wheat-based test foods
Thies et al. Systematically review the literature describing long-term intervention studies that investigated the effects of oats or oat bran on CVD risk factors including BP (US) [45]	25 RCTs; primarily on oat bran or breakfast cereals vs. low fiber or wheat bran cereal; β-glucan level and design details not provided	Only three RCTs found that oats significantly reduced BP vs. control products. However, a meta-analysis was not undertaken
Streppel et al. Evaluate the clinical effect of fiber supplements on BP [36]	24 RCTs; 1,400 adults; mean age 42 years; mean BMI ≥25; mean BP 133/82 mm Hg; mean fiber intake was 11.5 g/day; 11 soluble fiber RCTs; seven insoluble fiber; six mixed soluble and insoluble fibers RCTs; mean duration of 9 weeks with a range of 2–24 weeks	Increased total fiber intake by an average of 11.5g/day significantly reduced diastolic BP by1.3 mm Hg and insignificantly lowered systolic BP by 1.1 mm Hg. Soluble fiber lowered systolic BP by 1.3 mm Hg and diastolic BP by 0.8 mm Hg. Insoluble fiber lowered systolic BP 0.2 mm Hg and diastolic BP by 0.6 mm Hg. BP reductions were greater in older (>40 years) and in hypertensive populations than in younger and in normotensive ones
Whelton et al. Assess the clinical effect of fiber rich foods and supplement fiber intake on BP [37]	25 RCTs; 1,477 adults; median fiber increase by 10.7 g/day intervention vs. control; five trials with hypertensive patients only; vegetables, fruit, cereal, pectin, and guar gum in the form of foods and supplement pills; 2–26 of weeks duration	Increased fiber intake from all trials significantly reduced diastolic BP by 1.7 mm Hg but insignificantly lowered systolic BP by 1.2 mm Hg. Subgroup analyses found significant BP reductions for durations of ≥8 weeks in systolic BP by 3.1 mm Hg and diastolic BP by 2.6 mm Hg and in hypertensive subjects' lowered systolic BP by 6 mm Hg and diastolic BP 4.2 mm Hg
Viscous soluble fiber		
β-glucan		
Maki et al. To assess the clinical effects of consuming foods containing oat β-glucan on BP (USA—double-blind parallel RCT) [46]	97 overweight/obese hypertensive subjects; mean age 49 years; 56% women; mean systolic BP 130–179 mm Hg/diastolic BP 85–109 mm Hg; foods with 7.7 g oat β-glucan or control foods with 0 g β-glucan; 12 weeks	Obese subjects consuming foods rich in oat β-glucan significantly lowered systolic BP by 8.3 mm Hg and diastolic BP by 3.9 mm Hg vs. the control group. No significant differences in blood pressure responses were observed in the nonobese individuals

Table 14.2 (continued)

Objective	Study details	Results
He et al. Examine the clinical effect of oat beta-glucan on BP (USA—double-blind parallel RCT) [47]	110 adults; age 30–65 years; stage 1 hypertension; foods containing 8 g oat β-glucan or control foods with 0 g β-glucan; 6 and 12 weeks	Oat β-glucan intake significantly reduced systolic BP by 2.0 mm Hg and insignificantly lowered diastolic BP by 1.0 mm Hg
Davy et al. Evaluate the clinical effect of oat beta-glucan on BP (USA; parallel RCT) [48]	36 overweight/obese men; mean age 59 years; elevated BP; addition of 14 g/day of fiber including oat cereal (5.5 g β-glucan) or wheat cereals (no β-glucan); resting and ambulatory BP; 12 weeks	Oat consumption insignificantly lowered systolic and diastolic BP by 1 mm Hg compared to wheat. Also, no significant differences in 24-h, daytime, and nighttime BP observed between oats and wheat in this study. Subjects in both groups significantly increased body weight by 0.8 kg
Pin et al. Investigate whole-grain oat-based cereals and refined grain wheat-based cereals for effects on BP and β-blocker medications (USA; parallel RCT) [49]	88 adults on antihypertensive medications; mean age 48 years; mean BP below 140/88 mm Hg; oatmeal or oat squares (3 g β-glucan) vs. wheat crisps or hot wheat cereal (0 β-glucan); 12 weeks	73% of oat β-glucan participants' vs. 42% in the wheat group either stopped or reduced their β-blocker medications by half. Those in the oats group who did not experience a β-blocker reduction had a significant 6 mm Hg decrease in systolic BP vs. the wheat group
Keenan et al. Assess the effects of β-glucan-rich whole oat cereals on BP when added to a standard American diet (USA; parallel RCT) [50]	18 hypertensive and hyperinsulinemic overweight/obese adults, age 20–70 years; oat cereal group (standardized to 5.5 g β-glucan/day) or to a low-fiber cereal control; 6 weeks	The oat cereal group significantly lowered systolic BP by 7.5 mm Hg and diastolic BP by 5.5 mm Hg compared to the control group. In the oat cereal group, a trend toward greater insulin sensitivity suggested a possible mechanism for BP lowering
Saltzman et al. Investigate the effects of a hypocaloric diet with and without oats on BP (USA; parallel RCT) [51]	43 overweight/obese adults; mean age 45 years; mean baseline BP of 118/71 mm Hg; 8 weeks study two hypocaloric diets, 45 g oats/day or no added oat control; 6 weeks	The hypocaloric oat diet significantly lowered systolic BP by 5 mm Hg and insignificantly decreased diastolic BP by 1 mm Hg vs. the control diet. There was no significant difference in weight loss between the two groups
Psyllium		
Pal et al. Investigate the effects of increased fiber intake from a healthy diet or fiber supplement (psyllium) on BP (Australian; parallel RCT) [52]	72 adults; mean age 42 years; mean BMI 35; BP 113/65 mm Hg; fiber intake from a (1) healthy diet (31 g fiber/day), (2) psyllium fiber supplemented diet (21 g fiber/day), and (3) low-fiber diet; 12 weeks	Subjects consuming the healthy fiber-rich diet had significantly lowered systolic BP by 9% compared with the low-fiber control after 12 weeks. For the psyllium-supplemented diets, there was a significant reduction after 6 weeks but not after 12 weeks vs. the low-fiber group
Cicero et al. Assess the long-term effects of psyllium and guar gum on BP (Italy; open label) [53]	141; subjects mean age 58 years; mean BMI 27; hypertensive >140/90 mm Hg; diets standard AHA Step 1 diet or a Step 1 diet supplemented with 7 g/day psyllium or guar gum (3.5 g to be taken 20 min before the main two meals); 6 months	Long-term supplementation with psyllium fiber significantly reduced both systolic BP by 5.2 mm Hg and diastolic BP by 2.2 mm Hg compared to the non-fiber-supplemented AHA Step 1 diets. The guar gum-supplemented diet did not significantly reduce BP
Burke et al. Investigate the effect of soy protein and psyllium on BP in treated hypertensive individuals (Australia; parallel RCT) [17]	41 treated hypertensive adults; mean age 56 years; mean BP 133/75 mm Hg; diets: soy protein (25% of energy), psyllium (12 g soluble fiber), or combination of soy protein and psyllium vs. low protein and fiber (control); 24-h ambulatory BP; 8 weeks	Protein and psyllium fiber had significant additive effects to lower 24-h and awake systolic BP. Relative to control subjects, the net reduction in 24-h systolic BP was 5.9 mm Hg with psyllium and with protein. Findings were independent of age, gender, and change in weight, alcohol intake, or urinary sodium and potassium

(continued)

Table 14.2 (continued)

Objective	Study details	Results
Insoluble fiber		
Urquiaga et al. Evaluate the clinical effect of red wine grape pomace flour on BP (Chile; parallel RCT) [54]	38 adults with metabolic syndrome; mean age 44 years; mean BMI 29; mean BP 125/80 mm Hg; red wine grape pomace fiber (20 g/day; 10 g of fiber (93% insoluble), 822 mg of polyphenols and an antioxidant capacity of 7,258 ORAC units) vs. control group; 16 weeks	Red wine grape pomace fiber significantly decreased systolic BP by 4.3 mm Hg and diastolic BP by 4.7 mm Hg. There were also significant decreases in fasting glucose and carbonyl groups in plasma proteins and increases in plasma γ-tocopherol and δ-tocopherol. This suggests a potential synergistic interaction between insoluble fiber and antioxidants to increase BP lowering over fiber alone
Kestin et al. Investigate the clinical effects of cereal brans on BP (Australia—double-blind crossover RCT) [55]	24 men; mean BP 125/79 mm Hg; elevated blood lipids; 11.8 g fiber/day from wheat bran vs. baseline diet; 4 weeks; no washout	The baseline BP was unaltered by the addition of wheat bran
Fehily et al. To evaluate the clinical effect of wheat bran-rich food on BP (UK—crossover RCT) [56]	147 men and 54 women; mean age for men 36 years, women 41 years; 73% men; mean baseline BP of 132/80 mm Hg; diet: cereal fiber 19 g/day (wholemeal bread, whole-grain breakfast cereals bran) vs. 6 g/day (avoid wholemeal bread, higher-fiber breakfast cereals, and wheat bran); 4 weeks; no washout	The high-cereal fiber diet had no detectable effect on BP compared to the lower-fiber diet

Meta-analyses and Systematic Reviews

These analyses generally show that increased fiber intake has relatively modest and heterogeneous BP-lowering effects with more significant BP-lowering effects in older (>40 years) and in hypertensive populations than in younger and normotensive populations [16, 36, 37, 44, 45]. A 2016 Cochrane systematic review (8 RCTs; 661 adults with high CVD risk; >12 weeks) found that increased fiber intake overall had a significant mean BP-lowering effect for systolic BP by 1.9 mm Hg and for diastolic BP by 1.8 mm Hg [44]. A 2015 meta-analysis (18 RCTs including/5 β-glucan RCTs; normal BP and mild hypertension participants; age range 29–60 years; median increased fiber by ≥6 g fiber/day; median ≥6 weeks) showed that increased fiber of all types combined was significantly associated with lower diastolic BP, but not systolic BP, with each 1 g increase in fiber-lowering diastolic BP by 0.11 mm Hg [16]. This analysis also found that β-glucans (median increase by 4 g/day) from whole oats or oat bran enriched foods or oat-based breakfast cereals compared with similar wheat-based test foods significantly lowered systolic BP by 2.9 mm Hg and diastolic BP by 1.5 mm Hg for the overall analysis population. A 2014 systematic review of oat products and oat bran found that only 3 of 25 interventions in normal and hypertensive subjets showed that oats significantly lowered BP compared to control products [45]. Two 2005 meta-analyses of several dozen RCTs showed that increased fiber intake (by about 11 g fiber/day) significantly reduced the mean for diastolic BP by 1.3–1.7 mm Hg in all subjects compared to significant clinically and statisically reduced systolic BP by 6 mm Hg and diastolic BP by 4.2 mm Hg in hypertensive subjects [36, 37].

Representative RCTs

RCTs show that soluble viscous fiber is more effective in lowering BP than insoluble fiber such as wheat bran (Table 14.2) [17, 46–56].

Soluble Fiber

β-Glucan. RCTs consistently show increased β-glucan intake significantly lowers BP vs. control diets in hypertensive individuals [46–51]. Four studies in overweight or obese hypertensive individuals found that 3–8 g oat β-glucan/day significantly lowered systolic BP by 2.0–8.3 mm Hg and/or diastolic BP by 3.9–5.5 mm Hg vs. control over 6–12 weeks [46, 47, 49, 50]. In contrast, one RCT with overweight and obese subjects with elevated BP did not show oat cereal with 5.5 g β-glucan to significantly lower BP after 12 weeks, but the subjects increased weight by 0.8 kg during the study [48]. Oat β-glucan was shown to have an adjunctive systolic BP-lowering effect when consumed with β-blocker medications [49], and hypocaloric diets with oat β-glucan were more effective in lowering systolic BP than control diets [51].

Psyllium. Three RCTs indicate that the consumption of 7–21 g/day of psyllium can play a role in significantly lowering BP, especially systolic BP in hypertensive people [17, 52, 53]. An Australian RCT (72 obese adults; mean age 42 years; normal BP; 21 g psyllium/day) showed a significant reduction of systolic BP by 9% after 6 weeks but not after 12 weeks compared to a low-fiber diet control (21 g fiber/day) [52]. In contrast, an RCT (41 hypertensive subjects on BP medication; 12 g psyllium/day; 24-h ambulatory BP) had significantly lower systolic BP by 2.4 mm Hg vs. the low-fiber control [17]. The combination of dietary protein and psyllium fiber had significant additive effects in lowering 24-h and awake systolic BP with a relative net reduction in 24-h systolic BP of 5.9 mm Hg vs. control subjects. For an AHA Step 1 diet, an open-label study (141 overweight, hypertensive adults; mean age 58 years; antihypertensive medications; 6 months of duration) reported that the supplementation of 7 g psyllium fiber/day (3.5 g twice/day) significantly reduced systolic BP by 5.2 mm Hg and diastolic BP by 2.2 mm Hg compared to a standard AHA diet after 6 months [53].

Insoluble Fiber

Foods rich in insoluble fiber typically have less potent effects on BP than soluble fiber sources [54–56]. Fiber-rich diets composed primarily of insoluble fiber cereal brans from wheat and rice bran or whole wheat bread and breakfast cereals had no effect on BP compared to refined low-fiber diets in normotensive to prehypertensive subjects [55, 56]. However, 20 g red wine grape pomace flour/day (10 g insoluble fiber plus 822 mg grape polyphenols with an antioxidant capacity of 7258 ORAC units) was shown to significantly reduce both systolic and diastolic BP by >4 mm Hg each, compared to the low-fiber and low-antioxidant control [56].

Conclusions

Elevated BP including prehypertension is a common and growing public health problem. Globally, the overall prevalence of elevated BP in adults ≥25 years of age is approximately 40%. By 2025, because of population growth and an aging population, it is projected that about 1.5 billion individuals will have hypertension. Increasing global population trends of aging, overweight, and obesity are the major factors associated with elevated BP and hypertension. Lifestyle factors such as poor quality dietary patterns, excess energy intake, sedentary lifestyles, alcohol consumption, smoking, and anxiety and stress are important underlying controllable factors in most cases of hypertension. Observational studies consistently show that increased fiber intake (by 7–15 g/day above the usual levels) is significantly associated with reduced BP and hypertension risk compared to low fiber intake in Western diets. Meta-analyses of intervention trials show that increased fiber intake is more effective in lowering BP in older (>40 years), overweight/obese, and elevated BP or hypertensive persons than in younger, leaner, and normotensive individuals. Viscous, soluble fiber (e.g., β-glucan) sources are generally more effective in lowering BP than insoluble fiber sources (e.g., wheat bran). In hypertensive individuals already on drug therapy, lifestyle modifications such as increased fiber intake may adjunctively further lower BP. Potential fiber BP-lowering mechanisms may include: reducing risk of weight gain and central obesity, improving vascular health by lowering elevated total and LDL cholesterol, and lowering raised systemic inflammation via healthier colonic microbiota; and decreasing visceral fat volume to help attenuate risk of insulin resistance.

Appendix 1. Fifty High-Fiber Whole or Minimally Processed Plant Foods Ranked by Amount of Fiber per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50-60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multigrain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report of the 2015Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Chapter 1: Food and nutrient intakes and health: current status and trends. 2015; 97–8; Table D1.8

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Chapter 15
Fiber-Rich Diets in Chronic Kidney Disease

Keywords Chronic kidney disease • Dietary fiber • Dietary patterns • Hypertension • Inflammation • Microalbuminuria • Obesity • Glomerular filtration rate • Whole foods

Key Points

- Chronic kidney disease is a major global public health problem. Worldwide, an estimated 200 million people have chronic kidney disease with the numbers expected to rise with the increasing aging population as prevalence in individuals over age 60 is approximately 25%. Chronic kidney disease can lead to an increased risk of end-stage renal disease (ESRD), cardiovascular disease, and premature mortality.
- The high adherence to a Western lifestyle is associated with increased renal dysfunction, which can evolve into chronic kidney disease and progress to ESRD.
- Healthy dietary patterns including fiber-rich whole grains and fruits and vegetables have been shown to improve renal function and decrease metabolic acidosis compared to poor quality diets low in fruits and vegetables and high in processed foods and animal products.
- In patients with chronic kidney disease, a 10 g/day increase in total fiber was shown to reduce C-reactive protein by 38% and overall mortality by 17%.
- Several observational studies and intervention trials suggest that the increased consumption of fiber-rich foods and/or fiber supplements is associated with improved renal function and lower risk of chronic kidney disease because of fiber's beneficial effects on microbiota health, attenuation of systemic inflammation, and lessening of the risk of weight gain.
- In older adults, healthy fiber-rich dietary patterns including the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diet were found to help improve renal function and reduce risk of chronic kidney disease or related mortality.

Introduction

Chronic kidney disease (CKD) is recognized as a major global public health problem, but awareness of it is relatively low among the public [1]. Worldwide, an estimated 200 million people have CKD with increased rates expected with the increasing aging population [2, 3]. In the United States, estimates of CKD in the general population range from 8 to 14% with African-Americans having a four-fold excess risk of CKD compared to non-Hispanic white people. Its prevalence in individuals over age 60 is approximately 25% [3–5]. CKD patients experience an increased rate of mortality by 59%

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compared with individuals without CKD. About one million people in the United States are being treated for end-stage renal disease (ESRD), with an estimated cost of over $40 billion/year because of increases in ESRD, renal cancer, cardiovascular disease (CVD), bone disorders, and fractures, especially in older populations [6, 7].

The kidney is a highly vascularized organ, which plays a major role regulating electrolyte concentrations and blood pressure, lipid metabolism, production and utilization of systemic glucose, degradation of hormones, and excretion of waste metabolites [7]. CKD is basically decreased kidney function as indicated by the presence of microalbuminuria or a reduced estimated glomerular filtration rate (eGFR), which is calculated based on the serum creatinine [7, 8]. By eGFR criteria, CKD is diagnosed if eGFR is <60 mL/min/1.73 m^2 for a period of 3 months or greater. Kidney disease is divided into stages, with mild CKD represented by stages 1 and 2 and moderate to severe CKD represented by stages 3–5 [8]. CKD, even in its early stages, can cause hypertension and potentiate the risk for CVD [9]. In the various stages of CKD, there is progressive kidney damage and diminished functionality, which has the risk of leading to ESRD or kidney failure requiring dialysis or a kidney transplant [8].

In Western dietary patterns, diabetes and obesity are important risk factors associated with the increased risk of CKD [10–12]. Western dietary patterns rich in refined carbohydrates, salt, fat, and protein from red meat and low in fiber-rich foods, are generally associated with increased risk of CKD [10–12]. Abdominal obesity is considered a major risk factor for CKD development and progression (Fig. 15.1) [12–20]. An analysis of data from the US NHANES 1999–2010 (6,918 young adults; ages 20–40 years) found that abdominal obesity in young adults, especially in Mexican-Americans, was independently associated with 3.5-fold higher odds of the CKD risk factor albuminuria even with normal blood pressures, normoglycemia, and normal insulin levels [21]. Specifically, increased ectopic fat (fatty kidney) can cause physical compression of the kidney's renal vein and artery that pass through the renal sinus increasing renal interstitial pressure, decreasing sodium excretion, and stimulating inflammation, oxidative stress, and lipotoxicity factors that

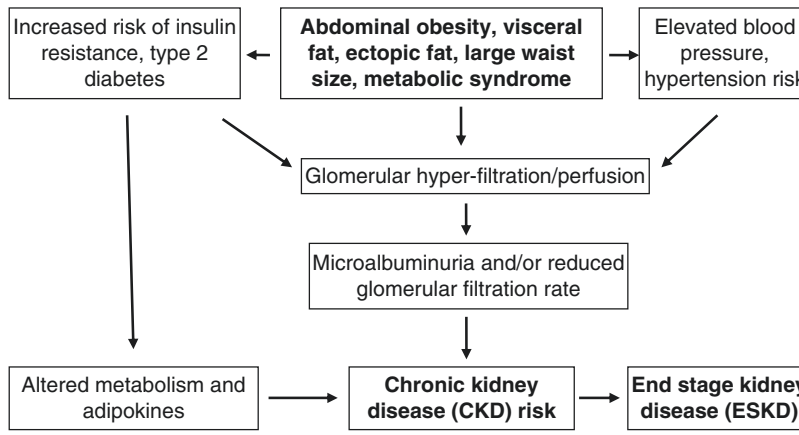

Fig. 15.1 Effect of abdominal obesity-related conditions and chronic kidney disease (CDK) risk [12–20]

may also contribute to renal dysfunction associated with hypertension and CKD. The objective of this chapter are to review the effects of dietary fiber (fiber), whole plant foods, and dietary patterns on CKD risk and management.

Lifestyle and Chronic Kidney Disease (CKD)

The American Heart Association (AHA) Life's Simple 7, which includes: (1) nonsmoking or quit >1 year ago, (2) BMI < 25, (3) blood pressure (BP) <120/80 mm Hg, (4) ≥150 min/week of physical activity, (5) healthy dietary pattern (high in fruits and vegetables, fish, fiber-rich whole grains, (6) low intake of sodium, and (7) avoid on low intake of sugar-sweetened beverages), has been shown to reduce CKD risk [22]. The Atherosclerosis Risk in Communities (ARIC) cohort study (14,832 participants; mean age 54 years; 55% female; 26% blacks; BMI range 23–31; median 22 year follow-up; 2,743 CKD cases) showed a significant inverse association between the adherence to Life's Simple **7** goals and incident CKD (Fig. 15.2) [22]. The Chronic Renal Insufficiency Cohort (CRIC) Study (3,006 persons with mild-to-moderate CKD; mean age 58 years; 48% female; 47% non-Hispanic white, 45% diabetes; median follow-up of 4 years; 726 CKD progression events, 353 atherosclerotic events, and 437 deaths) found that greater adherence to all components of a healthy lifestyle was associated with 68% reduced risk for adverse outcomes, including progression of CKD, atherosclerotic events, and all-cause mortality [18].

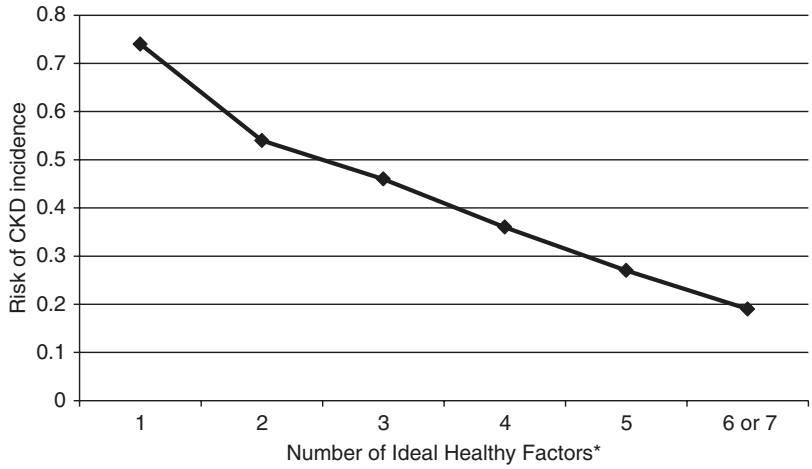

Fig. 15.2 Dose-response relationship between number of ideal Life's Simple 7 health factors and chronic kidney disease (CKD) incidence (p-trend < 0.001; multivariate adjusted) [22]. *(*1*) nonsmoking or quit >1 year ago, (*2*) BMI < 25, (*3*) blood pressure (BP) <120/80 mmHg, (*4*) ≥150 min/week of physical activity, and (*5*) healthy dietary pattern (high in fruits and vegetables, fish, fiber-rich whole grains; (*6*) lower in sodium; and (*7*) limit sugar-sweetened beverages)

Fiber and Chronic Kidney Disease (CKD)

Fiber Randomized Controlled Trials (RCTs)

Adequate fiber intake may improve CKD by attenuating elevated microinflammatory levels and proteolytic fermentation metabolites [23]. A systematic review and meta-analysis (14 RCTs;143 CKD patients; median age 52 years; fiber supplemented/high-fiber diets vs. non-supplemented/low-fiber diets; median fiber 27 g/day; median protein 60 g/day; median follow-up 4.5 weeks) found that fiber supplementation significantly reduced serum urea by 1.8 mmol/L and serum creatinine by 22.8 mmol/L [24].

Fiber Mechanisms

Inflammation

Several observational studies demonstrated that increased fiber intake may be especially effective at reducing systemic inflammation in CKD patients and lowering mortality risk [25, 26]. A National Health and Nutrition Examination Survey (NHANES III) (14,533 adults; mean age 45 years; 48% males; prevalence of CKD 5.8%) found that for each 10 g/day increase in total fiber intake, the odds of elevated serum C-reactive protein (CRP) levels were decreased in individuals without CKD by 11% and with CKD by 38% [25]. Also, total fiber intake was not significantly associated with overall mortality in those without CKD but was inversely related to mortality in those with kidney disease. In CKD patients, each 10 g/day increase in intake was associated with reduced overall mortality risk for total fiber by 17%, for insoluble fiber by 23%, and soluble fiber by 33%. The Uppsala Longitudinal Study of Adult Men (1,110 community-dwelling elderly men from Sweden; mean age 71 years; mean BMI 26; median 10-year follow-up; 300 deaths, 138 cardiovascular disease, 111 cancer, 19 infections, 33 other causes) showed that high-fiber intake was associated with significantly better kidney function (Fig. 15.3), lower odds of having CRP >3 mg/L, and reduced risk of mortality [26]. High-fiber intake was more strongly associated with survival in individuals with kidney dysfunction than in those without CKD. Total fiber was independently and directly associated with significantly improved eGFR (adjusted difference, 2.6 mL/min/1.73 m^2) per

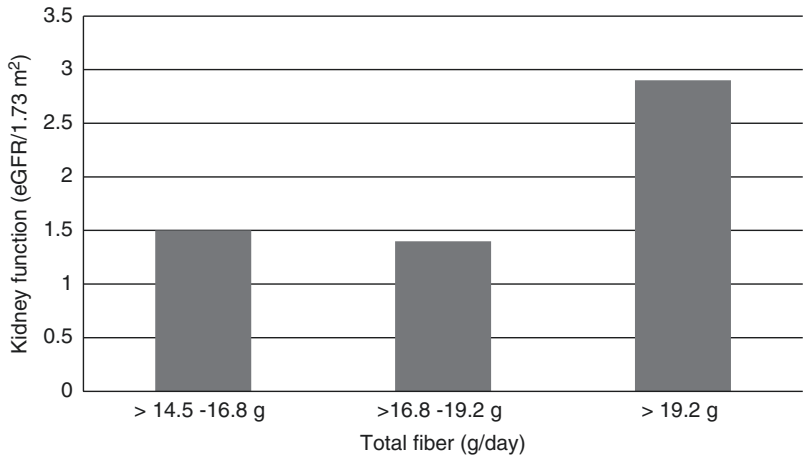

Fig. 15.3 Effect of fiber intake/day in elderly men with chronic kidney disease on kidney function as estimated glomerular filtration rate (eGFR) multivariate adjusted $p = 0.02$ [26]

10 g/day higher intake. Meta-analysis (14 RCTs) showed that increased fiber intake by 8 g/day from supplements or fiber-rich foods compared with control significantly reduced CRP levels by about 0.5 mg/L and for those individuals with elevated CRP the reduction was 0.72 mg/dL ($p = 0.06$) [27]. Lowering CRP has been associated with reduced incidence and complication of CKD as elevated CRP has been associated with impaired eGFR in hypertensive adults with a mean age of 60 years [26, 28]. A 2017 Chinese longitudinal cohort study (157 CKD patients; mean age 48 yrs; 47% male; 18 months of follow-up) found that fiber intake (≥ 25 g/day) was protective against eGFR decline and reduced pro-inflammatory factors compared to lower fiber intake (<25 g/day) [29].

Colonic Microbiota

There is increasing clinical evidence that individuals at risk or patients with CKD have distinctly dysbiotic colonic microbiota, which can activate a cascade of metabolic abnormalities, including uremic toxin production, inflammation, and immunosuppression, that ultimately leads to CKD or promotes progressive kidney failure and cardiovascular disease [30]. The human colonic microbiota contains >100 trillion microbial cells, which act essentially as an organ to influence human nutrition, metabolism, physiology, and immune function [30]. As the colonic microbiota is intimately influenced by diet, the discovery of the kidney-colonic axis has created new nutritional CKD therapeutic opportunities involving the microbiota and fiber, prebiotics, probiotics, and symbiotics. The changes in colonic microbiota of patients with CKD lead to disturbance of this symbiotic relationship and may contribute to the progression of CKD. Protein fermentation by colonic microbiota generates numerous toxic metabolites, including p-cresol and indoxyl sulfate which may lead to a disruption of colonic barrier function in CKD patients. This may allow translocation of endotoxin and bacterial metabolites into the systemic circulation, which contributes to uremic toxicity, inflammation, progression of CKD, and associated cardiovascular disease. Increased fiber intake appears to help to reestablish intestinal symbiosis, neutralize bacterial endotoxins, and inhibits the absorption of colonic-derived uremic toxins such as p-cresol and indoxyl sulfate [30, 31]. A 2015 single-blind RCT (six males and seven females; mean age 65 years; eGFR <50 mL/min/1.73 m^2) showed that increasing fiber intake from 17 g to 27 g/day significantly reduced circulating p-cresol by 20% [31]. A 2015 cross-sectional analysis (40 CKD patients; mean age 69; 60% male; 45% diabetic; mean estimated eGFR of 24 mL/min/1.73 m^2), found that total fiber intake was significantly associated with lower free and total serum p-cresol sulfate but not indoxyl sulfate [32]. Similarly, the Uppsala Longitudinal Study in Adult Men (390 CKD men; mean age 70 years; media follow-up 9.1 years) showed that excess dietary protein relative to fiber intake was significantly associated with increased incidence of CVD events in men with CKD [33].

Whole Plant Foods

Whole Grains

The National Kidney Foundation, the American Kidney Fund, the National Institute of Diabetes and Digestive and Kidney Diseases, and the US Department of Health and Human Services have recommended limiting or the exclusion of whole grains as part of the renal diet because of the potential risk of excessive phosphorus intake [34]. However, the phosphorus content in whole grains is covalently bound to organic molecules (primarily phytate) and requires the enzyme phytase to be released to become available for absorption. While some phytase is contained in some raw whole grains (corn, oats, and millet have little to no phytase activity), the enzyme is decreased in milling, food preparation, and over time. Also, since the enzyme required for the release of phosphorus from phytate is not present in the

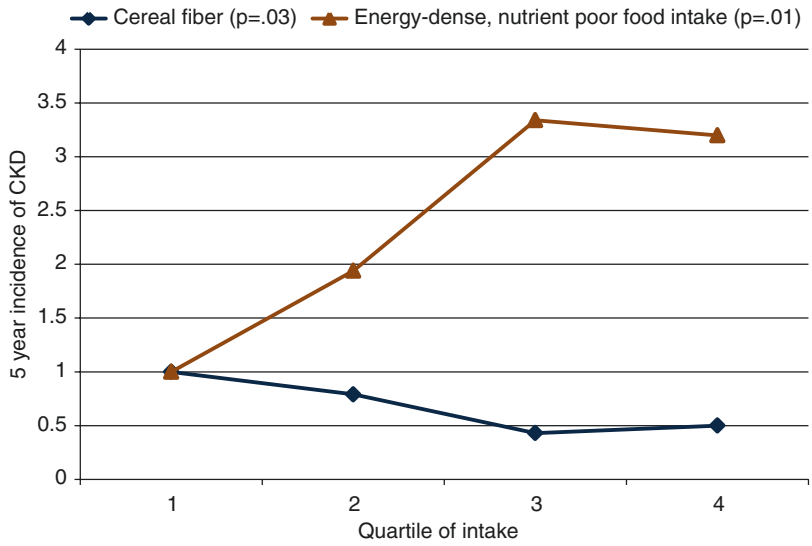

Fig. 15.4 Effect of a cereal fiber-rich diet vs. poor-quality diet on 5-year incidence of chronic kidney disease (CKD) in adults ≥50 years of age (multivariate adjusted) [35]

human intestinal lumen when ingesting cooked food, the bioavailability of phosphorus from whole grains is low. The Australian Blue Mountains Eye Study (2,600 participants; aged ≥ 50 years; 19.4% had moderate CKD and 80.6% did not have CKD; 5-year follow-up) found that fiber from cereal (predominantly from rolled oats and whole meal/whole grain breads) significantly lowered adjusted incidence of CKD by 50% and energy dense, nutrient-poor foods (Western diets) significantly increased CKD risk by 220% (Fig. 15.4) [35]. Consequently, it has been proposed that modest consumption of whole grains by CKD patients may provide benefits to help protect against CKD and other chronic diseases [34, 35].

Fruits and Vegetables

High adherence to a Western-type diet which is deficient in fruits and vegetables high in red and processed meats can lead to the accumulation of non-metabolizable anions and metabolic acidosis, which increases progressively with aging due to the physiological decline in kidney function [36]. In response to this state of diet-derived metabolic acidosis, the kidney implements compensating mechanisms aimed to restore the acid-base balance, such as the removal of the non-metabolizable anions, the conservation of citrate, and the enhancement of kidney ammonia genesis. These changes even if present to a minor degree may be an important variable in predicting increased calcium excretion and lead to metabolic abnormalities including hypertension, diabetes, and chronic kidney failure [36]. Two RCTs in stage 3 or 4 CKD patients suggest that increased fruit and vegetable intake or oral bicarbonate are equally effective in reducing urine angiotensinogen and in preserving glomerular filtration rate [37, 38]. Also, added fruits and vegetables were associated with reduced systolic blood pressure in CKD patients.

Dietary Patterns

Western diets have resulted in increased intake of animal protein, refined carbohydrates, and phosphate- and sodium-based preservatives and higher risk of abdominal obesity and systemic inflammation associated with CKD risk, and progression to end-stage renal disease (ESRD) [39, 40]. Healthy

dietary patterns consisting of mostly whole plant foods and lower in processed foods and meats have been shown to improve renal function, reduce CKD risk, and delay progression and mortality risk in older adults at increased risk of CKD. Table 15.1 provides a summary of eight prospective studies, one meta-analysis of RCTs, and one large RCT of the MedDiet vs. low-fat diets [40–48].

Table 15.1 Summary of prospective cohort studies and RCT on dietary patterns on the progression of chronic kidney disease (CKD) and mortality

Objective	Study details	Results
Prospective cohort studies		
Smyth et al. Investigate the effect of diet quality on renal outcomes (USA NIH-AARP Diet and Health Study [41]	544,635 participants; age 51–70 years; diets: Alternate Healthy Eating Index (AHEI), Healthy Eating Index (HEI), Mediterranean diet (MedDiet) score, Dietary Approach to Stop Hypertension (DASH) scores; 14.3-year follow-up; 4,848 deaths from renal cause or initiated dialysis (multivariate adjusted)	All the healthy dietary patterns were associated with significantly improved renal function by 18–29%. Greater than 3.6 g sodium/day was associated with a 17% increased risk of renal dysfunction, and adequate potassium was associated with a 17% reduced risk of renal dysfunction
Banerjee et al. Examine (DAL) the association between dietary acid load and progression to end-stage renal disease (ESRD) (USA National Health and Nutrition Examination Survey III) [42]	1,486 adults with CKD; age 20 years; ESRD monitored over a median 14.2 years of follow-up; 311 (20.9%) participants developed ESRD (multivariate adjusted)	Higher levels of dietary acid load were associated with increased risk of ESRD by 204% for the highest tertile and 81% for the middle tertile compared with the lowest tertile. The risk of ESRD associated with DAL tertiles significantly increased as estimated glomerular filtration rate (eGFR) as decreased. Among participants with albuminuria, high dietary acid load was strongly associated with ESRD risk
Foster et al. Determine the association of lifestyle characteristics with estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 and rapid eGFR decline in older adults (USA Framingham Offspring Study) [43]	1,802 participants; mean age 59 years, 54.8% women; measures of diet quality, physical activity, alcohol intake, current smoking status; 6.6-year follow-up; 9.5% of participants developed incident eGFR < 60 (multivariate adjusted)	Higher diet quality was associated with a significant 37% reduced odds of renal dysfunction. Higher diet quality was associated with 31% lower risk of rapid eGFR decline. No associations were observed with physical activity, smoking status, or alcohol intake with incident eGFR < 60 or rapid eGFR decline
Gutierrez et al. Examine relationships between dietary patterns and health outcomes in persons with CKD (USA Reasons for Geographic and Racial Differences in Stroke (REGARDS) study) [44]	3,972 participants with CKD; mean age 69 years; five empirically derived dietary patterns identified via factor analysis: convenience (Chinese and Mexican foods, pizza, other mixed dishes), plant based (fruits, vegetables), sweets/fats (sugary foods), Southern (fried foods, organ meats, sweetened beverages), and alcohol/salads (alcohol, green leafy vegetables, salad dressing); 6 years of follow-up; 816 deaths and 141 ESRD events (multivariate adjusted)	Higher plant-based pattern scores were associated with lower risk of mortality by 23%, whereas higher Southern pattern scores were associated with greater risk of mortality by 51% (highest vs. lowest quartiles). There were no associations of dietary patterns with incident ESRD

(continued)

Table 15.1 (continued)

Objective	Study details	Results
Chang et al. Investigate the effect of the DASH diet on risk of coronary heart disease and CKD (USA Coronary Artery Risk Development in Young Adults [CARDIA] Study) [45]	2,354 African-American and white participants; mean age 35 years; 47% male; DASH vs. Western diets; 15-year follow-up; 3.3% developed incident microalbuminuria (multivariate adjusted)	Poor diet quality and obesity were significantly associated with about a 100% increased risk of microalbuminuria. Also, compared to individuals with no unhealthy lifestyle-related factors (poor diet quality, current smoking, and obesity), increased odds of incident microalbuminuria were 31%, 173%, and 534% higher for presence of 1, 2, and 3 unhealthy lifestyle-related factors
Huang et al. Test the hypothesis that adherence to MedDiet may better preserve kidney function (Sweden, Uppsala Longitudinal Study of Adult Men cohort) [46]	1,110 men; mean age 70 years; MedDiet Score; follow-up of 9.9 years; 168 deaths (multivariate adjusted)	Adherence to a MedDiet was associated with lower odds of CKD or mortality in elderly men. Compared with low adherents, medium and high adherents had significantly lower risk of CKD by 23% and 42%, respectively. Among those individuals with CKD, phosphate intake and net endogenous acid production were progressively lower across increasing MedDiet adherence groups. Compared with low adherents, medium and high adherents had lower mortality risk by 23 to 25%
Lin et al. Evaluate the effect of healthier eating patterns vs. the Western dietary pattern (USA subgroup analysis from the Nurses' Health Study) [47]	3,121 women; mean age 67 years; 97% Caucasian, 54% hypertension, and 23% diabetes; microalbuminuria or eGFR decline; 11-year follow-up (multivariate adjusted)	The Western pattern score was directly associated with higher microalbuminuria by 117% and rapid eGFR decline of $\geq$3 mL/min/1.73 m^2 per year by 77% (high vs. low quartile). The DASH score had decreased risk for rapid eGFR decline by 45%, but had no association with microalbuminuria (high vs. low quartile; multivariate adjusted; Fig. 15.5). The general healthy dietary pattern was not associated with microalbuminuria or eGFR decline
RCTs		
Oyabu et al. Clarify the effect of low-carbohydrate diet (LCD) on renal function in overweight and obese individuals without CKD (meta-analysis) [40]	9 RCTs; 1,687 participants; 46% male; four studies in diabetic patients; 861 were fed LCD and 826 were fed the control diet; carbohydrate consumption 4–45% of total energy intake; 6–24 months (multivariate adjusted)	The increase in eGFR in the LCD group was greater than that in the control group in overweight and obese individuals without CKD. The mean change in eGFR in the LCD group was greater than that in the control diet by 0.13 mL/min/1.73m^2
Díaz-López et al. Investigate the effects of MedDiets on kidney function (Spain, PREDIMED [Prevención con Dieta Mediterránea] Study) [48]	785 participants; 55% women; mean age 67 years; diets: a MedDiet supplemented with extra virgin olive oil or mixed nuts or a control low-fat diet; 1 year (multivariate adjusted)	The three dietary approaches were associated with improved kidney function, with similar average increases in eGFR (Fig. 15.6), but no changes in urinary albumin-creatinine ratio. Both the MedDiet and low-fat diet are equally beneficial in elderly individuals at high cardiovascular risk

Renal Function and CKD Risk

Six prospective cohort studies and two RCT analyses provide consistent evidence that healthy dietary patterns are associated with improved renal function and Western diets are associated with progressively poorer renal function [40–43, 45, 47, 48]. All variations of higher-quality or healthy dietary patterns based on minimizing meat, salt, added sugar, and heavily processed foods while emphasizing phytochemical-rich whole plant foods have generally similar significant effects on improving renal function by 19–31% [41–43, 45, 48]. In contrast, Western dietary patterns are associated with increased CKD risk and poor renal function [42, 45, 47]. Dietary patterns with greater than 3.6 g sodium/day were associated with a 17% increased risk of renal dysfunction, and adequate potassium was associated with a 17% reduced risk of renal dysfunction [41]. Higher Alternate Healthy Eating Index (AHEI), Healthy Eating Index (HEI), Mediterranean diet (MedDiet) score, and Dietary Approaches to Stop Hypertension (DASH) scores improved renal function by 18–29% compared to lower adherence [41]. The CARDIA Study found in young US adults with a mean age of 35 years that poor diet quality and obesity was associated with a significant 100% increased risk of microalbuminuria, a risk factor for CKD, over a 15-year follow-up [45]. The Nurses' Health Study in women with a mean age of 67 years found that those with high adherence to the Western diet had a 117% increased risk of microalbuminuria, whereas those who followed healthy diets especially the DASH diet had no association with microalbuminuria after an 11-year follow-up (Fig. 15.5) [47]. Also, in this study women with high Western diet scores had a significantly increased risk of rapid eGFR decline of ≥3 mL/min/1.73 m^2 per year by 77% compared to a significant reduced risk of eGFR decline by 45% in women with the highest DASH scores or no eGFR decline with a generally healthy diet. A PREDIMED [Prevención con Dieta Mediterránea] RCT sub-study found in older adults (mean age 67 years) with high CVD risk that healthy MedDiets and low-fat diets were equally effective for improving kidney function, with similar average increases in eGFR (Fig. 15.6), but no changes in urinary albumin-creatinine ratio noted after full adjustment after 1 year [48]. The Framingham Offspring Study (1,802 participants; mean age 59 years; 6.6-year follow-up) showed that higher diet quality was associated with a significant 37% reduced odds of renal dysfunction and a 31% lower risk of rapid eGFR decline [43]. The US National Health and Nutrition Examination Survey

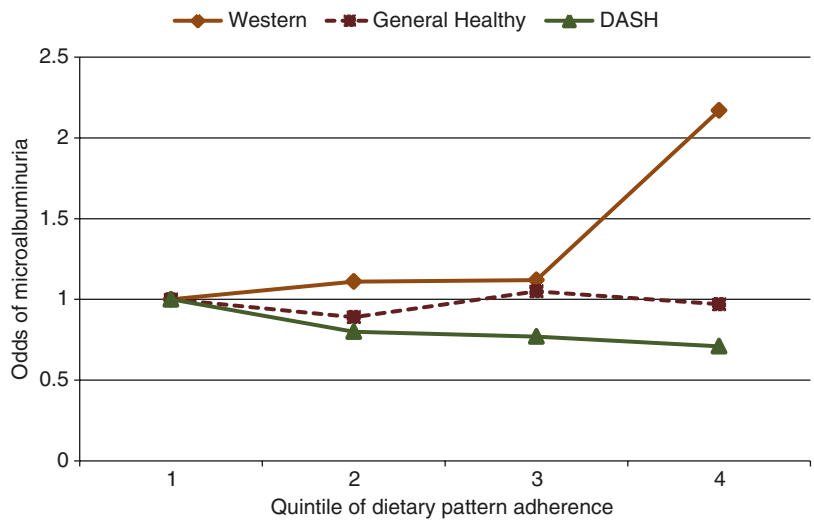

Fig. 15.5 Effect of dietary pattern adherence on microalbuminuria risk in older women (mean age 67 at baseline) after 11 years (p-trend = 0.01; fully adjusted) [47]

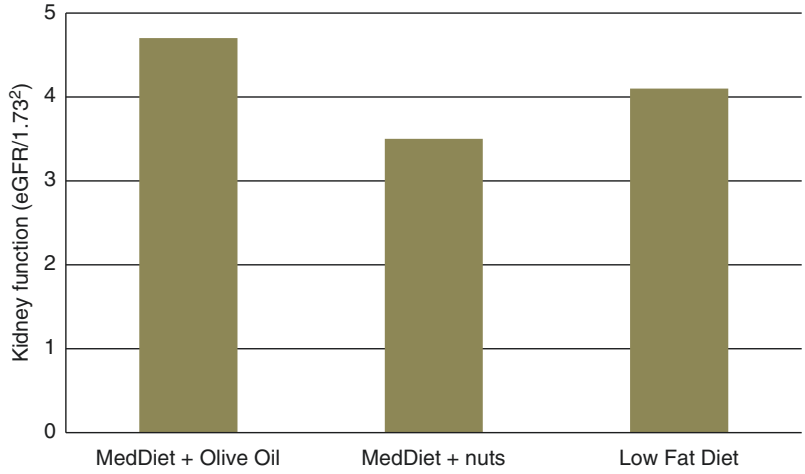

Fig. 15.6 Effect of Mediterranean diet (MedDiet) and low-fat diet on kidney function in elderly participants at high CVD risk after 1 year ($p < 0.001$ vs. baseline for each; $p = 0.9$ for difference among groups) [48]

III (1,486 CKD patients; 14.2-year follow-up) found that high dietary acid load (DAL) typical of the Western dietary pattern increased the risk of end-stage renal disease by 204% for the highest tertile and 81% for the middle tertile of DAL [42]. A meta-analysis (nine RCTs; 1,687 overweight or obese non-CKD subjects) showed that low-carbohydrate dietary patterns improved glomerular renal function vs. typical or higher carbohydrate dietary patterns [40].

Mortality

Two prospective studies show the importance of diet quality in reducing mortality rates in CKD patients in their later 60s followed over a period of 6–11 years [44, 46]. Higher adherence to a plant-based healthy diet or a Mediterranean diet significantly reduced premature mortality by about 25%, whereas adherence to Western diets such as the Southern pattern in the US increased mortality by 51%.

Nutritional Guidelines

A modified version of the DASH diet is available for persons with later stages of CKD with a protein intake of 0.6–0.8 g/kg of body weight/day, as well as a lower phosphorus (0.8–1.0 g/day) and potassium (2–4 g/day) intake [39, 49]. Protein intake may be restricted to 0.6 g/kg of ideal body weight per day when eGFR decreases to <60 mL/min/1.73 m^2. High-protein diets should be avoided in persons with established CKD who are not receiving dialysis. Adequate fiber intake should be encouraged for CKD patients. No specific levels of fiber intake are suggested, but the adequate intake level of 14 g/1000 kcal should be a good target intake level, which is typical of most healthy diets [23–27, 39]. Increasing fruit and vegetable intake may help to avoid metabolic acidosis and reduce urine albumin and slow loss of renal function [36–39]. Fifty top fiber-rich foods in rank order are provided in Appendix 1.

Conclusions

CKD is recognized as a major global public health problem. Worldwide, an estimated 200 million people have CKD with the numbers expected to rise with the increasing aging population as prevalence in individuals over age 60 is approximately 25%. CKD can lead to an increased risk of end-stage renal disease (ESRD), cardiovascular disease, and premature mortality. A Western lifestyle is associated with increased renal dysfunction, which can evolve into CKD and progression to ESRD. Healthy dietary patterns including fiber-rich whole grains and fruits and vegetables have been shown to improve renal function and decrease metabolic acidosis compared to poor quality diets low in fruits and vegetables and high in processed foods and animal products. In patients with CKD, a 10 g/day increase in total fiber was shown to reduce CRP by 38% and overall mortality by 17%. Several observational studies and intervention trials suggest that the increased consumption of fiber-rich foods and/or fiber supplements is associated with improved renal function and lower risk of CKD because of fiber's beneficial effects on microbiota health, attenuation of systemic inflammation, and lowering of the risk of weight gain. In older adults, including the MedDiet and DASH diet were healthy fiber-rich dietary patterns found to help improve renal function and reduce risk of CKD or related mortality.

Appendix 1. Fifty High-Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High-fiber bran ready-to-eat-cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50-60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (Garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds, whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multi-grain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report of the 2015 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Chapter 1: Food and nutrient intakes and health: current status and trends. 2015;97–8; Table D1.8

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Chapter 16
Fiber and Stroke Risk

Keywords Dietary fiber • Ischemic stroke • Hemorrhagic stroke • Mortality • Soluble fiber • Insoluble fiber • Blood pressure • Obesity • Systemic inflammation • Glycemic control

Key Points

- Over 70% of stroke risk is attributable to behavioral factors such as poor diet, low physical activity, and smoking and their association with metabolic risk factors including elevated systolic blood pressure, BMI, fasting plasma glucose, total and LDL cholesterol, and systemic inflammation.
- Nutrients and phytochemicals associated with reduced stroke risk are dietary fiber, potassium, magnesium, calcium, cysteine, flavonoids, carotenoids (e.g., lycopene, lutein), dairy protein and other components, and long-chain omega-3 fatty acids.
- Prospective studies consistently show that fiber intake is inversely associated with stroke risk with approximately 12% lower stroke risk per 10 g/day total fiber intake with cereal fiber being generally the most effective fiber source.
- Adequate fiber intake has an important role in stroke protection by reducing major risk factors such as hypertension, overweight and obesity, pre- and type 2 diabetes, dyslipidemia, and systemic inflammation. However, fiber is typically the most significant shortfall healthy macronutrient in Western diets with an average intake of about half the recommended level.

Introduction

Stroke is a major cause of disability and death worldwide. It changes the lives not only of the stroke victims but also of their families as many stroke victims become dependent in their activities of daily living due to significant stroke related cognitive and physical effects [1–6]. Stroke is the brain equivalent of a heart attack and the leading cause of neurological functional impairment by a vascular cause [3–6]. Of all strokes, 87% are ischemic [4]. Globally, stroke and related cerebrovascular diseases are the second most common cause of death, accounting for 6.2 million deaths [2]. Forecasts project a >20% increase in stroke prevalence between 2012 and 2030, because of increasing aging populations. Stroke is uncommon in people under 40 years. Women have an increased lifetime incidence of stroke compared to men, largely due to an increase in stroke risk in older postmenopausal women. Each year, 800,000 people experience a new or recurrent stroke with women accounting for 60% of strokes.

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Strokes are caused by a disruption of the blood supply to the brain due to either blockage (ischemic stroke) or rupture of a blood vessel (hemorrhagic stroke) [3]. An irregular heartbeat is a major risk factor for blood clot formation in the heart and the clot may then travel through the blood vessels to the brain and cause a stroke. Ruptured blood vessels can occur in the presence of an aneurysm, for example, or due to damage from uncontrolled high BP. Stroke was historically called "apoplexy," because of the sudden neurologic impairment it causes. A previous stroke significantly increases risk of further episodes. Stroke carries a high risk of death and survivors can experience loss of vision and/or speech, paralysis, and confusion. The risk of death depends on the type of stroke [3]. There are three major stroke types: (1) transient ischemic attack (TIA), in which symptoms tend to resolve within 24 h; (2) stroke caused by carotid stenosis (narrowing of the artery in the neck that supplies blood to the brain); and (3) a rupture of a cerebral blood vessel. Even where advanced technology and facilities are available, 60% of those who suffer this type of stroke die or become dependent.

Globally, 90.5% of the stroke burden is attributable to modifiable risk factors, including 74.2% due to behavioral factors of smoking, poor diet, and low physical activity and their association with metabolic factors including high systolic blood pressure (BP), high BMI, high fasting plasma glucose, high total cholesterol, and low glomerular filtration rate [2, 7]. Weight reduction, healthy diets, regular physical activity, smoking cessation, and low-to-moderate alcohol consumption may reduce stroke risk ≥50% [5–12]. Diet and lifestyle randomized controlled trials (RCTs) on stroke outcomes are limited because of the long-term follow-up required to conduct these studies [5, 6]. Examples of nutrients and phytochemicals associated with reduced stroke risk are dietary fiber (fiber), potassium, magnesium, calcium, cysteine, flavonoids, carotenoids (e.g., lycopene, lutein), plant protein, and long chain omega-3 fatty acids (in women) [13–23]. Adequate fiber intake is an important indicator of a healthy dietary pattern because it has an important role in promoting healthy body weight, cardiometabolic, and microbiota health [24–30]. However, fiber is typically the most significant shortfall healthy "macronutrient' in Western diets with an average intake of about half the recommended level [28–30]. Fifty top fiber-rich foods in rank order are provided in the Appendix 1 [31–34]. The objective of this chapter is to review the effects of fiber in stroke risk.

Fiber and Stroke Risk

Prospective studies generally show that fiber intake is inversely associated with stroke risk (Table 16.1) [19, 36–44]. Meta-analyses of prospective cohort studies and a review article support an inverse association between intake of fiber and stroke risk with an overall by stroke reduction by 17% (high vs. low intake), and meta-analyses of RCTs show that fiber supplementation has a weak to modest lowering effect on blood pressure [35, 38]. A sub-analysis of the effect of fiber intake on stroke risk by fiber sources, gender, and stroke type is summarized in Fig. 16.1. Two dose response meta-analyses of prospective studies (ranging from 6 to 11 studies 325,000 subjects) showed similar significant inverse association between fiber intake and stroke risk [36, 37]. One meta-analysis found a 12% lower stroke risk per 10 g/day total fiber with a greater effect for women than for men [36]. The other meta-analyses found that total fiber intake significantly reduced stroke risk by 7% per 7 g/day and soluble fiber insignificantly reduced stroke risk by 6% per 4 g/day but there were too few studies to analyze the relationship between insoluble fiber or fiber from cereals, fruit, or vegetables and stroke risk [37]. A Swedish study (66,677 subjects; mean age 60 years; mean 10.3 year follow-up) demonstrated that increased daily total fiber by about 25 g/day reduced multivariate stroke risk by 10% and stroke risk was reduced for higher intake of fruit fiber by 15%, vegetable fiber by 10%, and cereal fiber by 6% [40]. A high stroke risk population based study (1347 adults; mean age 61 years; mean BMI 27; mean BP 153/88 mmHg; 66%; hypercholestorlemic; 12 years of follow-up) showed that high fiber

Table 16.1 Summaries of prospective cohort studies on fiber intake and stroke risk

Objective	Study details	Results
Systematic reviews and meta-analyses		
Chen et al. Assess the relationship between fiber intake and stroke risk in men and women [36]	Six prospective cohort studies; 314,864 subjects; 8,920 stroke cases, mean follow-up of 8–18 years (multivariate adjusted)	Total fiber intake reduced the mean stroke risk by 13% (highest vs. lowest intake), which was higher in women than men. The risk reduction for ischemic stroke was 17% and hemorrhagic stroke was 14%. A dose-response analysis suggested a 12% lower stroke risk per 10 g fiber/day
Threapleton et al. Investigate the global effects of fiber on stroke risk [37]	Eight prospective cohort studies from the United States, northern Europe, Australia, and Japan; mean follow-up of 8–19 years; 2,781 incident events, 95 fatal strokes (multivariate adjusted)	Total fiber intake was inversely associated with risk of hemorrhagic and ischemic stroke, with some evidence of heterogeneity between studies The stroke risk per 7 g total fiber/day was significantly reduced by 7%. Soluble fiber intake, per 4 g/day, insignificantly lowered stroke risk by 6% with evidence of low heterogeneity between studies. There were few studies reporting stroke risk in relation to insoluble fiber or fiber from cereals, fruits, or vegetables
Zhang et al. Evaluate the association between fiber intake and stroke risk [38]	11 prospective studies; 325,627 participants (multivariate adjusted)	Total fiber intake reduced mean stroke risk by 17% (highest vs. lowest intake). Increased fiber intake was inversely associated with stroke risk in a dose-response manner. There was a trend for an inverse association between higher fiber consumption and stroke mortality
Prospective cohort studies		
Threapleton et al. Investigate the effect of fiber on risk of ischemic and hemorrhagic stroke in women (UK Women's Cohort Study) [39]	27,373 women; mean age 52 years; followed for 14.4 years; 135 hemorrhagic and 185 ischemic stroke cases (multivariate adjusted)	Greater intake of total, soluble, insoluble, and cereal fiber and higher fiber dense foods were associated with significantly lower risk of total stroke. For total fiber, 6 g/day reduced total stroke risk by 11%. In non-hypertensive women, higher fiber intake was associated with lower ischemic stroke risk. In healthy weight women greater cereal intake was associated with lower ischemic stroke risk
Larsson et al. Evaluate the association between intake of total fiber and fiber sources and stroke incidence in healthy Swedish adults (Swedish; Mammography Cohort and the Cohort of Swedish Men) [40]	69,677 adults; mean age 60 years; mean BMI 25; mean fiber intake 25.6 g/day for women and 23.4 g/day for men; mean 10.3 years of follow-up; 3,680 incident cases of stroke (multivariate adjusted)	High intakes of total fiber and fiber from fruits and vegetables but not from cereals were inversely associated with risk of stroke. Total stroke risk was reduced by 10% for total fiber, 15% for fruit fiber, 10% for vegetable fiber, and 6% for cereal fiber. The associations did not differ significantly by sex or intakes of vitamin C, folate, β-carotene, magnesium, and potassium or processed or unprocessed red meat, dairy products, coffee, or tea intake

(continued)

Table 16.1 (continued)

Objective	Study details	Results
Casiglia et al. Clarify whether high fiber intake has an impact on incidence and risk of stroke at a population level (Italy) [41]	1,347 adults; mean age 61 years; mean BMI 27 kg/m^2; mean BP 153/88 mm Hg; 66%; hypercholestorlemic;12 years of follow-up) evaluated the effect of fiber intake on stroke risk (multivariate adjusted)	In a high stroke risk population, >25 g/day soluble fiber intake or >47 g/day insoluble fiber significantly reduced stroke risk by 50%
Larsson et al. Determine the effect of fiber on stroke risk in male smokers (Sweden) [42]	26,556 Finnish male smokers; mean age 57 years; mean BMI 26 kg/m^2; mean BP 142/87 mm Hg; mean total cholesterol 240 mg/dL; 60% physically active; 13.6 years follow-up; 3281 total stroke cases (multivariate adjusted)	These findings do not support the hypothesis that a high intake of dietary fiber is independently inversely associated with the risk of stroke. However, high consumption of fruits, vegetables, and cereals may reduce the risk of stroke. Vegetable fiber intake, as well as fruit and vegetable consumption, were significantly inversely associated with risk of cerebral infarction. Vegetable consumption was inversely related to risk of subarachnoid hemorrhage and cereal consumption to risk of intracerebral hemorrhage
Oh et al. Study the effect of carbohydrate quality on stroke risk in women (USA Nurses' Health Study) [43]	78,779 US women; mean age 48 years; mean BMI 24; 18 years of follow-up; 1,020 stroke incident cases (multivariate adjusted)	Total fiber was associated with borderline significant reduction in total stroke risk by 17% ($p = 0.07$) and ischemic stroke by 22% ($p = 0.09$) (Fig. 16.2). Cereal fiber intake was inversely associated with significant risk decreases for total stroke by 34% and hemorrhagic stroke by 49%
Bazzano et al. Evaluate the effect of increasing fiber intake on stroke risk (USA, The NHANES 1 Epidemiologic Follow-up Study) [44]	9,776 adults; mean age 50 years; mean BMI 26; mean BP 135/83 mm Hg; mean total cholesterol 220 mg/dL; mean fiber intake ranged from 5.9 to 20.7 g/day; mean 19 years follow-up; 928 stroke cases (multivariate adjusted)	A higher intake of fiber, especially soluble fiber, reduced CHD events by 15% (5.9 g/day vs. 0.9 g/day). Total fiber had an insignificant effect on stroke risk reduction for incidence by 5% and for mortality by 1%. However, the median fiber intake for the highest quartile was below the adequate intake level
Ascherio et al. Investigate the association of fiber, potassium, and related nutrients with risk of stroke in men (USA Health Professionals Follow-up Study) [19]	43,738 US men; age range 40–75 years; median fiber intake varied from 12.4 to 28.9 g/day; 8 years follow-up; 328 stroke incident cases (multivariate adjusted)	Total fiber significantly reduced stroke risk by 30% (highest vs. lowest intake). Of the sources of fiber only cereal fiber was inversely associated with risk of stroke. The inverse association was stronger in hypertensive than normotensive men

consumption of >25 g soluble fiber or >47 g insoluble fiber may significantly reduce stroke incidence by 50% [41]. The Nurses' Health Study (78,779 women; mean age 48 years; 18 years of follow-up; 1,020 stroke incident cases) observed that high carbohydrate intake and high glycemic load increased stroke risk among women whose BMI was ≥25 and higher total fiber and cereal fiber reduced total stroke risk in women regardless of BMI level (Fig. 16.2) [43]. The Health Professionals Follow-up Study (43,738 US men; age range 40–75 years; 8 years of follow-up; 328 stroke incident cases) reported that total fiber lowered stroke risk by 30% (highest vs. lowest intake) with cereal fiber being the only fiber source significantly inversely associated with stroke risk [19].

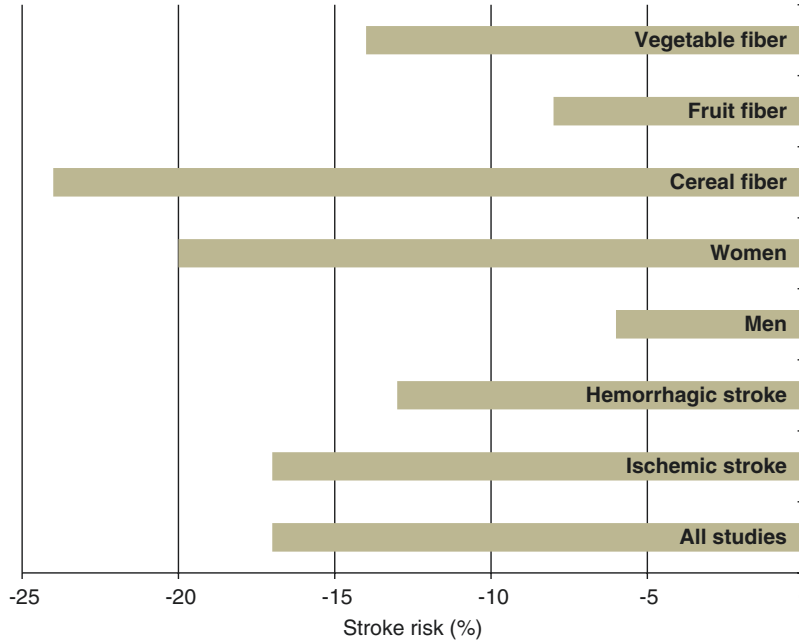

Fig. 16.1 Effect of dietary fiber intake (highest vs. lowest intake) on stroke risk subgroups from a meta-analysis 11 prospective studies [35, 38]

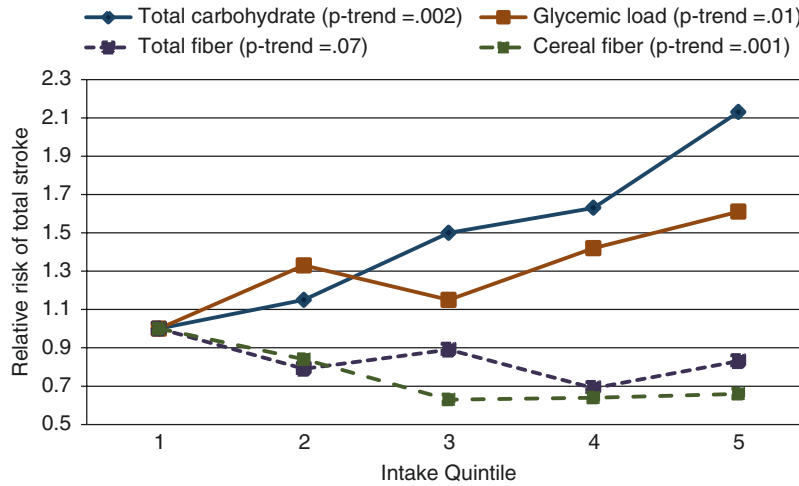

Fig. 16.2 Effect of carbohydrates and fiber intake on stroke risk in US women [43]

Fiber Mechanisms and Comorbities

Fiber-related mechanisms potentially contributing to stroke protection by reducing the major comorbities such as hypertension, overweight and obesity, pre- and type 2 diabetes, and coronary heart disease and thier risk factors at the systemic metabolic process and cellular levels [5, 45] (Table 16.2).

Table 16.2 Potential fiber mechanisms associated with lower stroke risk factors [19, 23, 28, 32, 35–86]

Target	Increase	Decrease
Food intake	Chewing	Energy density
	Eating time	Hunger
Body weight	Weight maintenance or loss	Weight gain and obesity risk
Stomach	Satiety signals	Gastric emptying rate
		Lipid emulsification
		Lipolysis
Liver	Lipoprotein uptake	Lipogenesis
	Bile acid synthesis and secretion	
Small intestine	Satiety signals	Dietary fat absorption
Peripheral tissue	Insulin sensitivity	Ectopic fat
Circulatory system	Short-chain fatty acids	Blood pressure
		Postprandial lipids and glucose
		Fasting lipids and lipoproteins (e.g., TC, LDL-C, and TG)
		Inflammatory markers (e.g., CRP)
		Oxidized LDL-C
		Intima-media thickness
Large intestine	Fermentation	Bile acid reabsorption
	Short-chain fatty acids	Inflammatory activity
	Prebiotic microbiota	Lipopolysaccharide absorption
	Satiety signals	
Fecal excretion	Bile acids	Metabolizable energy
	Dietary fat	

TC total cholesterol, *LDL-C* LDL-cholesterol, *TG* triglycerides, and *CRP* C-reactive protein

Hypertension

Hypertension is observed in 75% of patients with acute ischemic stroke and in 80% of patients with acute intracerebral hemorrhages and is independently associated with poor functional outcome [5–7]. Specifically, lifestyle factors that are causally related to elevated BP include excessive salt intake, low potassium intake, excessive weight, high alcohol consumption, a low fiber dietary pattern, elevated cholesterol, use of tobacco, physical inactivity, and type 2 diabetes [3–5]. In a meta-analysis (six trials; 71,000 prehypertensive participants), those randomized to diet or drug antihypertensive treatment had a significant 22% lower stroke risk compared with those taking placebo [46]. In RCTs, antihypertensive therapies that reduce systolic BP by 10 mm Hg are associated with an average 41% reduction in stroke risk [47]. Meta-analyses of RCTs have found that increased fiber intake is significantly inversely associated with BP among older individuals (>40 years) with higher BMI and hypertension [48–50]. Soluble fibers such as β-glucan and psyllium tend to be more effective in lowering BP than insoluble fibers.

Overweight and Obesity

Obesity is an accelerator of chronic diseases and is associated with increased mortality and morbidity including, stroke, hypertension, coronary heart disease, disability, type 2 diabetes, osteoarthritis, and certain types of cancer [3–6]. Growing evidence supports a positive relationship between stroke and overweight and obesity, independent of age, lifestyle, or other cardiovascular risk factors. Excess adipose tissue, especially ectopic fat, is an active secretory organ with adipocyte-derived hormones and cytokines actively associated with dysregulation of many biological processes leading to increased

stroke risk [51]. A meta-analysis (25 prospective studies; 2,274,961 participants from Asia, Europe, and the United States; follow-up ≥4 years; >30,000 stroke incident cases) found an increased ischemic stroke risk for overweight individuals by 22% and for obese individuals by 64% [11]. Populations with fiber-rich diets tend to be leaner than those with low fiber diets [52]. Fiber-rich diets help to protect against weight gain by delaying hunger and increasing satiety and reducing energy intake by displacing energy-dense foods that contribute to weight gain [53–55]. A systematic review of 43 observational studies and RCTs found moderately strong evidence that fiber-rich foods have a protective role against weight gain and increased waist size [56]. Generally, RCTs of *ad libitum* fiber-rich diets (≥30 g fiber/day) show them to prevent weight gain and/or promote modest weight loss compared to RCTs with diets containing <20 g fiber/day [57–61].

Pre- and Type 2 Diabetes

Diabetes is an independent risk factor for stroke with diabetic individuals having more than double the risk for stroke compared to the general population [5]. The Chinese Diabetes and Stroke Surveillance System study (327,268 diabetic and 307,984 stroke patients) found the relationship between stroke and type 2 diabetes to be strong, especially in females, with the incidence of stroke among patients with diabetes up to threefold higher than in the general population [62]. People with prediabetes, an intermediate metabolic state between normal glucose metabolism and diabetes, have a ten times increased risk of developing diabetes compared to those with a normal glucose metabolism. An average of 37% (range 29–53%) of the nondiabetic patients with a recent ischemic stroke or TIA were prediabetic [63]. A meta-analysis (ten RCTs; 23,152 participants; average 3.75 years duration) showed that drug and lifestyle approaches to prevent diabetes reduced fatal and nonfatal stroke by 24% with lifestyle approaches being significantly superior to drug treatment [64]. Prospective studies suggest that high intake of fiber diets are associated with a lower risk of insulin resistance [65–68]. A dose-response meta-analysis (17 prospective cohort; 488,293 participants; 19,033 diabetes cases) found a reduced risk of type 2 diabetes for intake of total fiber by 19%, cereal fiber by 23%, fruit fiber by 6%, and insoluble fiber by 25% (highest vs. lowest intake) [69]. A nonlinear relationship was found for total fiber intake and risk of type 2 diabetes (Fig. 16.3) [69]. Fiber mechanisms associated with reduced diabetes risk include (1) displacing higher glycemic carbohydrates from the diet; (2)

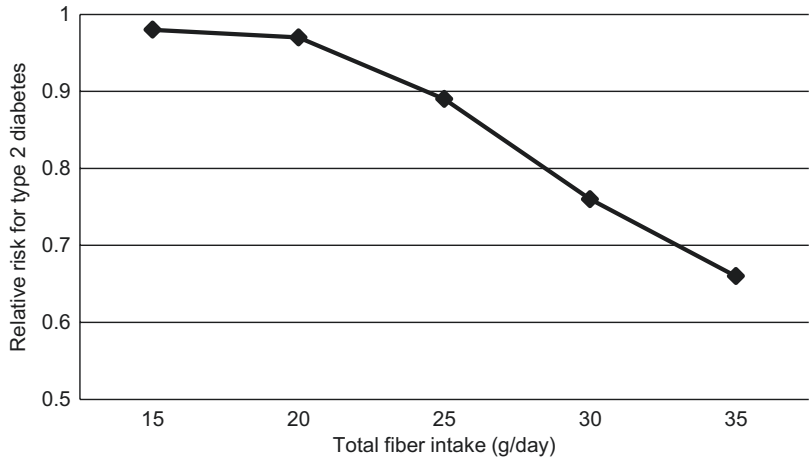

Fig. 16.3 Effect of fiber intake on type 2 diabetes risk from a dose-response meta-analysis of prospective studies (p for nonlinearity < 0.01); diabetes is a major independent stroke risk factor [69]

promoting satiety by slowing the eating rate, digestion, and absorption; (3) stimulating metabolic responses in the gastrointestinal tract such as the release of glucagon-like peptide-1 to improve insulin sensitivity; and (4) promoting a healthy colonic microbiota thereby increasing the amount of short chain fatty acids such as butyrate, which is associated with reduced systemic inflammation and improved insulin sensitivity [28, 70–72].

Coronary Heart Disease

Coronary heart disease (CHD) and its primary risk factors including dyslipidemia and elevated systemic inflammation increase stroke risk [5].

Dyslipidemia

Dyslipidemia is a major adverse factor for CHD and stroke risk and significantly influenced by the level of dietary fiber intake. A 2016 Geographic and Racial Differences in Stroke (REGARDS) study (23,867 participants; 1031 strokes; mean follow-up 7.5 years), observed that elevated total LDL-C and non-HDL-C were significantly associated with ischemic stroke risk in a disease free population at baseline [73]. The Asia Pacific Cohort Studies Collaboration (29 cohorts; 352,033 participants; mean age 47 years; 42% female; 2.7–24 years follow-up) found that each 1 mmol higher total cholesterol level was associated with 35% increased risk of CHD, 25% increased ischemic stroke risk, and 20% increased risk of fatal hemorrhagic stroke [74]. A meta-analysis on the efficacy of cholesterol-lowering interventions on total, fatal, or nonfatal stroke (78 RCTs; 266,973 patients; mean age of 61 years; 61% males; 3.5 years duration) showed that each 1% reduction in total cholesterol predicted a 0.8% relative stroke risk reduction [75]. Prospective cohort studies and RCTs, especially with viscous soluble fiber sources, consistently show that fiber reduces CHD risk. Four dose-response meta-analyses found that each 10 g/day increase in fiber intake was associated with a significantly reduced CHD risk by 11–14%, CHD events by 8%, and CHD mortality by 20–27% [76–79]. Five meta-analyses and a systematic review of RCTs report that soluble, viscous fiber-rich foods (e.g., oat and barley food products) and supplements (e.g., β-glucans, psyllium, pectin, and guar gum) significantly reduced total and LDL-cholesterol levels without adversely affecting HDL-C and TG levels to help maintain normal fasting lipid levels compared to lower fiber diets [80–84].

Systemic Inflammation

Elevated systemic C-reactive protein (CRP) levels are independently associated with increased ischemic stroke risk [85–87] and attenuated with increased fiber intake [88–90]. A meta-analysis (12 prospective studies; 66,560 adults; 3,091 stroke incident cases) showed that elevated CRP increased ischemic stroke by 46% vs. lowest levels with the risk higher in men than for women [85]. Another meta-analysis (54 cohort studies; 160,309 participants without a history of vascular disease; mean age 60 years; 48% females; 27,769 fatal or nonfatal disease outcomes; median 5.8 years of follow-up) found per 1-standard deviation higher log of CRP concentration 23% increased risk for CHD and a 32% elevated risk for ischemic stroke (multivariate adjusted models including fibrinogen) [87]. A meta-analysis (14 RCTs; 728 adults; mean BMI ranged from 27 to 36; median CRP 4.0 mg/L; duration ranged from 3 to 16 weeks with 60% lasting 12 weeks) found that the increased consumption of fiber or fiber-rich foods produced a modest but significant mean reduction of 0.4 mg/L in circulating

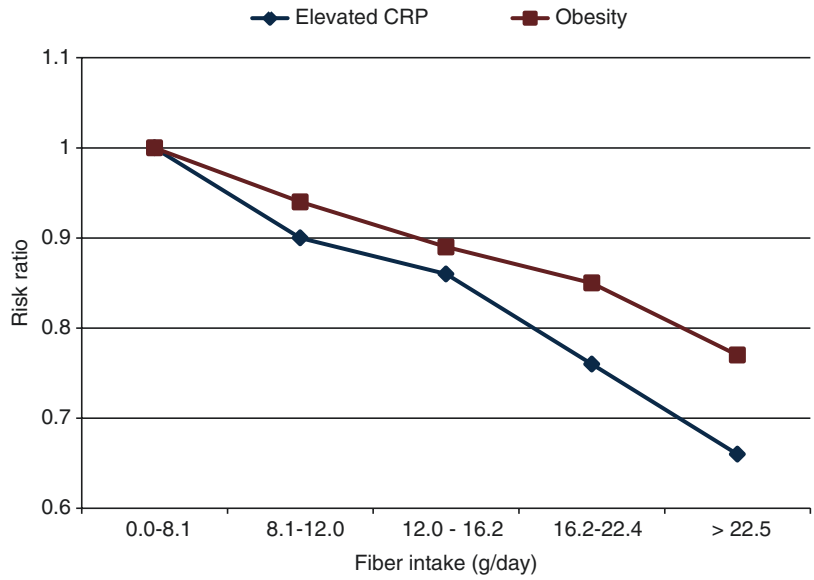

Fig. 16.4 The relationship between fiber intake and elevated CRP and obesity in adults aged 20+ years in US National Health and Nutrition Examination Study (NHANES) 1999–2010 [90]

CRP, especially with an increased fiber intake of 8 g/day above the control group [88]. In a systematic review of seven RCTs, six found statistically significant 25–54% reductions in CRP concentrations with increased intake of fiber-rich foods such as fruits, vegetables, whole-grain bread and cereals, beans, and/or nuts, when accompanied by weight loss and modified intake of fatty acids [89]. Increased fiber can lower elevated CRP in part by reducing obesity risk as shown in Fig. 16.4 [90].

Conclusions

Stroke is a major cause of disability and death worldwide as it is the brain equivalent of a heart attack and a leading cause of neurological functional impairment. Globally, stroke and related cerebrovascular diseases are the second most common cause of death, accounting for 6.2 million deaths annually. Forecasts project a >20% increase in stroke prevalence between 2012 and 2030, because of increasing aging populations. Over 70% of stroke risk is attributable to behavioral factors such as poor diet, low physical activity, and smoking and their association with metabolic risk factors including elevated systolic blood pressure, BMI, fasting plasma glucose, total and LDL cholesterol, and systemic inflammation. Nutrients and phytochemicals associated with reduced stroke risk are dietary fiber, potassium, magnesium, calcium, cysteine, flavonoids, carotenoids (e.g., lycopene, lutein), dairy protein and other components, and long-chain omega-3 fatty acids. Prospective studies consistently show that fiber intake is inversely associated with stroke risk with approximately 12% lower stroke risk per 10 g/day total fiber intake with cereal fiber being generally the most effective fiber source. Adequate fiber intake has an important role in stroke protection by reducing major risk factors such as hypertension, overweight and obesity, pre- and type 2 diabetes, dyslipidemia, and systemic inflammation. However, fiber is typically the most significant shortfall healthy macronutrient in Western diets with an average intake of about half the recommended level.

Appendix 1. Fifty High Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (Garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multi-grain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report of the 2015Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Chapter 1: Food and nutrient intakes and health: Current status and trends. 2015; 97–8; Table D1.8

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Chapter 17
Fiber and Colorectal Cancer

Keywords Colorectal cancer • Colon cancer • Rectal cancer • Adenomas • Total fiber • Wheat bran fiber • Fruit fiber • Vegetable fiber • Legume fiber • Microbiota • Short-chain fatty acids • Butyrate

Key Points

- Dietary factors have an important influence on colorectal cancer (CRC) and colorectal adenoma (CRA) risk. Examples of known or suspected dietary-related CRC or CRA risk factors are higher intake of alcohol and red meat; lower intakes of dietary fiber, calcium, and folate; and elevated BMI.
- The 1970s fiber hypothesis stimulated a surge of observational and intervention studies, but the early findings were inconsistent due to differences in the type and amount of fiber consumed, study populations (e.g., US vs European), length of follow-up time, poor dietary compliance, and tumor site heterogeneity. Despite these early inconsistencies, there is now convincing evidence that higher intake of fiber-rich foods reduces CRC risk and that low fiber intake is associated with an increased risk of CRC.
- Dose-response meta-analyses found that each daily 10 g increase in total or cereal fiber reduced CRC risk by 10% (in prospective studies) and reduced CRA risk by 9% and 30% for total fiber and cereal fiber, respectively (primarily in case-control studies).
- Two large US-based randomized controlled trials (RCTs), the Wheat Bran Fiber Trial and the Polyp Prevention Trial, indicated that increased intake of fiber-rich foods did not significantly lower the risk of CRA recurrence, but there were several trial limitations including relatively poor dietary compliance and short duration (2–4 years). However, a pooled analysis of these two trials found that increased intake of dietary fiber significantly reduced the risk of CRA recurrence in men by 19%, and a reanalysis of the US Polyp Prevention Trial found that subjects with the highest fiber intake had a significantly 32% lower risk of CRAs compared with low fiber controls.
- CRC-protective mechanisms depend on the fiber's properties: (1) soluble fermentable fiber lowers colonic pH, inhibiting pathogenic bacteria and increasing butyrogenic bacteria to promote healthy colonic mucosal cells, reduces colon inflammation, and inhibits cancer cell proliferation and facilitates apoptosis; and (2) insoluble fiber dilutes or inactivates potential carcinogens by bulking stools and binding carcinogens to reduce their exposure to the colon and rectum. Also, fiber-rich foods tend to be lower in energy density compared to more processed foods for better weight control, and they are major contributors of potential cancer-protective nutrients such as folate, antioxidant nutrients such as vitamins C and E, and phytochemicals such as phenolics and carotenoids.

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Introduction

Colorectal cancer (CRC) rates have doubled since the 1970s, and incidence is strongly associated with the Western lifestyle and aging populations [1–4]. In 2015, there were 1.7 million cases of CRC globally, which caused 832,000 deaths [1]. By 2035, 2.4 million new cases of colorectal cancer are projected to be diagnosed. Although, in recent years, there has been an increasing number of tumors diagnosed, there is a decreased mortality rate because of more appropriate and available information, earlier diagnosis, and improvements in treatment. In economically developed countries, CRC ranked third for cancer incidence and second for cancer deaths with the odds of developing CRC before age 79 years 1 in 14 men and 1 in 23 women [1]. In lower socioeconomically developed countries, the odds of developing CRC before age 79 years are 1 in 94 men and 1 in 112 women with CRC ranking as the eighth most common cancer and the sixth leading cause for cancer mortality.

The development of CRC is characterized by a progressive "adenoma-carcinoma sequence," where the normal colonic epithelium acquires genetic and epigenetic mutations in specific oncogenes or tumor suppressor genes, which leads to a hyperproliferative mucosa [4–6]. This condition may result in to the conversion of mucus-forming glands to benign adenomas, which may change into adenocarcinomas with the potential for metastasis over an average of 10 years. CRC biology is complex arising from many different causes. As with most cancers, CRC risk increases with age. CRC diagnoses are sporadic in the younger age groups with similar incidence rates between males and females up to the age of 45 years; however, after age 45, there is a steeper increase in incidence for males, especially after 70 years of age. Individuals with a history of ulcerative colitis and Crohn's disease are associated with high risk of developing CRC.

Preventative measures, including dietary and lifestyle modifications, are important approaches to help reduce the global CRC risk [7, 8]. A recent meta-analysis of 43 studies showed CRC risk was associated with a number of lifestyle factors including smoking, alcohol, body fatness, diet, physical activity, medication, and/or hormone replacement therapy (Fig. 17.1) [7]. Specifically, factors found to potentially promote CRC risk included tobacco smoking and higher body mass index (BMI) and alcohol, dietary fat, or red meat intake, and factors found to potentially protect against CRC risk included use of over-the-counter drugs such as nonsteroidal anti-inflammatory drugs (NSAIDS) or aspirin, diet and lifestyle

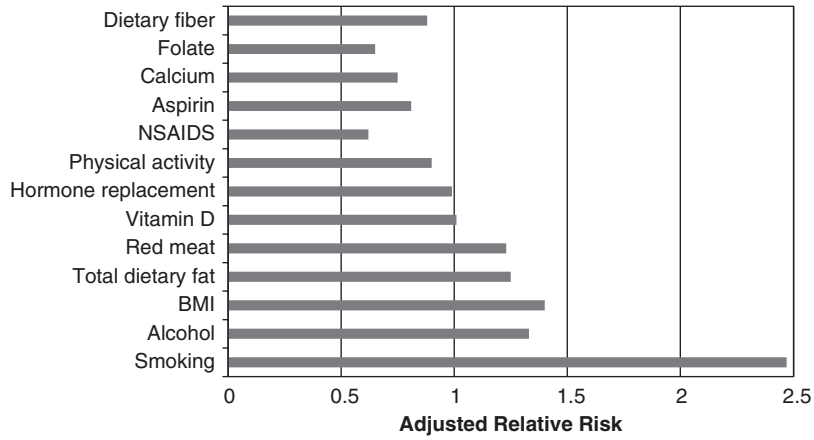

Fig. 17.1 Effect of lifestyle risk factors on colorectal cancer risk from a meta-analysis of 43 observational studies through March 2016 [7]

factors such as higher folate, calcium, and dietary fiber (fiber) intake and physical activity. In the 1980s, Doll and Peto estimated that 35% of cancer-related deaths and 90% of stomach cancer- and CRC-related deaths could be attributed to dietary factors [8, 9]. Over the past several decades, numerous observational studies and randomized clinical trials (RCTs) have been conducted to identify potential dietary contributors to CRC risk [7–9]. However, data from these studies have often shown inconsistent or only modest associations or outcomes. This is not surprising given the complex CRC pathogenesis with the interactions of diet, lifestyle, genetic, epigenetic, and microbiota determinants of risk and individual anatomic, histologic, and molecular variability associated with the prolonged latency period required for CRC carcinogenesis [7, 8]. Since fiber has been one of the most widely studied dietary components related to CRC risk, the objective of this chapter is to review the biological mechanisms, observational studies, and RCTs on the CRC protective effects of fiber.

Fiber and Colorectal Cancer Risk

Overview

In the 1970s, Dr. Burkitt hypothesized that high fiber intake protects against CRC based on observations of the low CRC incidence among Africans who consumed a high-fiber diet [10]. Subsequently, fiber is one of the most-studied CRC dietary protective components because of its diverse impact on healthy colorectal function including reducing transit time, diluting and binding potential carcinogens, stimulating a healthy colonic microbiota ecosystem, and promoting a healthier diet, with lower energy and higher nutrient/phytochemical density compared to the Western diet [8–11]. However, human studies on fiber and CRC, especially the early prospective cohort studies and RCTs, produced inconsistent outcomes, because of differences in fiber type and level of intake, study populations (US vs European), length of follow-up time, overadjustment for folate, poor dietary compliance, and tumor site heterogeneity or long-term delays required for colorectal adenoma recurrence [8, 12–29]. In recent years, the inverse association between high fiber intake and CRC risk has become increasingly stronger [8, 12, 14, 15, 20, 23, 30].

Biological Mechanisms

Overview

Chronic consumption of Western diets low in fiber and high in red or processed meat can lead to colonic dysbiosis associated with lower saccharolytic fermentation and less production of short-chain fatty acids (SCFAs), such as butyrate, and higher proteolytic fermentation and excess primary bile acid secretion and their conversion to pro-carcinogenic secondary bile acids, which exposes the colonic mucosa to increased carcinogenic risk [31–39]. Fiber has been the most-studied dietary component as regards to colorectal carcinoma mechanisms. Fiber CRC prevention mechanisms vary with the source of fiber and its metabolites and physical and functional properties [11, 31–34]. Fermentable fibers, mostly soluble, promote a healthy microbiota ecosystem, including increased butyrate-producing bacteria and reduced pathogenic bacteria. Increased colonic butyrate supports colorectal mucosal cellular health and inhibits tumor formation. Limited fermentable fiber, mostly insoluble, may speed up colonic transit to decrease the colonic epithelium exposure time to carcinogens and increase stool bulk to bind or dilute

concentration of carcinogens. Also, fiber-rich foods can contribute significant levels of bioactive nutrients such as folate, calcium, and vitamin D and phytochemicals such as phenolics, carotenoids, and lignans, which may have CRC protective effects [8, 11]. There are a number of mechanisms that are associated with fiber's protective effects against CRC risk, which are further reviewed as follows:

Colonic pH

In the distal colon, a primary site of CRC, the pH ranges from about 7.0 (lower-fiber diets) to 5.5 (higher-fiber diets) [31]. Fermentable fiber can lower colonic pH to help prevent colonic pathogenic infection and reduce carcinogens formation. Colonic fiber fermentation produces short chain fatty acids (SCFAs) including acetate, propionate, and butyrate which have acid dissociation constants of approximately 4.8, which can decrease colonic pH. Both in vitro and human studies show that higher-fiber diets lower colonic pH into the range of 5.5, which is significantly correlated with lower total pathogenic bacterial counts including *Escherichia coli* and *Enterobacteriaceae* species [31, 37, 38]. Specific fermentable fiber sources such as prebiotic oligosaccharides can stimulate the growth of beneficial probiotic bacteria and competitively prevent pathogen colonization by blocking their binding to mucosal surface receptor sites in the colonic lumen [31, 38]. Also, increased butyrate levels and resulting decrease in pH can decrease the formation of colonic carcinogenic metabolites [31]. A reduced colonic pH can repress protease activity and thus impair protein fermentation, decreasing the production of and further hindering the absorption of ammonia, a potential carcinogenic product of protein fermentation. Additionally, at a pH of 6 or below, bile acids become highly protonated and insoluble which inhibits their uptake by colonocytes. Importantly, colonic acidification may reduce the activity of bacterial enzymes, including 7α-dehydroxylase, which is involved in the formation of secondary bile acids, and other bacterial enzymes (e.g., nitroreductases, azoreductases, β-glucosidases, and β-glucuronidases) known to convert relatively harmless compounds to reactive toxic metabolites.

Healthy Colonic Mucosal Barrier and Epithelium

The colonic mucosal barrier is one of the body's primary defense mechanisms as it acts both as a barrier that protects the colonic epithelium against chemical and biological hazards and directs immunoregulatory signals to prevent infections [31, 33, 40–43]. The intake of fermentable fiber and the resulting formation of butyrate supports the maintenance of the integrity of the mucosal and epithelial layers which strengthens the colonic protective barrier. Butyrate is the preferred energy source for colon epithelial cells and is associated with higher colonic blood flow, epithelial cell proliferation, cell differentiation, and anti-inflammatory effects that modulate barrier protection. Other physicochemical properties of fiber that may support barrier protection include the following: (1) insoluble fiber (e.g., wheat and rice bran) or minimally fermented, soluble, viscous fiber (e.g., psyllium) reduces the transit time and dilutes luminal contents, which decreases the contact of the epithelial cells with potentially harmful or carcinogenic compounds or metabolites [31, 44, 45], and (2) blood cholesterol-lowering fibers, such as β-glucans and psyllium, can play a direct role in binding conjugated bile salts and removing compounds potentially harmful to colon epithelial cells [31, 46].

Anticarcinogenic Activity

Butyrate is a potent fiber fermentation protective metabolite with a unique role in both maintaining normal colonic mucosa structure and function and in preventing CRC (Fig. 17.2) [31–35]. Clostridia clusters XIVa and IV of the genus *Firmicutes* and *Faecalibacterium prausnitzii* are the predominant

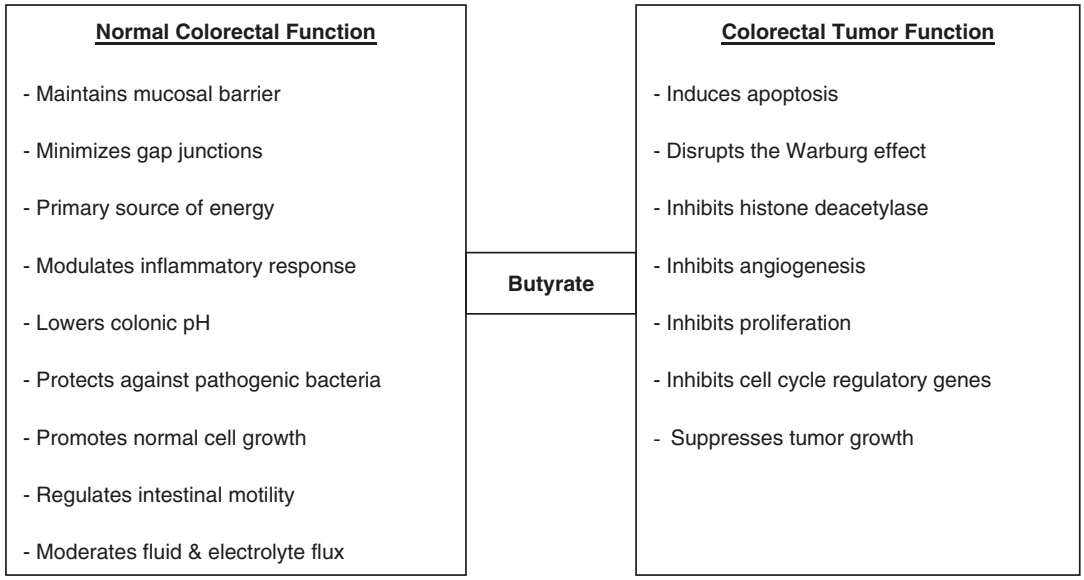

Fig. 17.2 Effects of butyrate on normal colonic and colorectal tumor cells [31–35]

bacteria sources of butyrate. Multiple potential mechanisms have been postulated for butyrate's protective action against colorectal tumorigenesis including (1) antiproliferative activity by activation of the apoptosis cascade via the Warburg effect, arresting the growth of tumors by histone deacetylase (HDAC) inhibitor, and (2) anti-inflammatory properties which are mediated by suppressing the activation of nuclear factor-kB, a transcription factor controlling the expression of genes encoding pro-inflammatory responses and inflammatory mediators like tumor necrosis factor-α (TNF-α) and nitric oxide.

Warburg Effect

Increased intake of fiber helps to protect against colorectal carcinoma by increasing colonic butyrate levels via the promotion of butyrate-producing bacteria in the microbiome, which act as HDAC inhibitors, blocking proliferation and promoting apoptosis of colon cancer cells [47, 48]. It has been hypothesized that butyrate's tumor-suppressive role in colorectal carcinoma is related to the metabolic differences exhibited by normal and cancerous colonocytes. Butyrate represents the primary source of energy in normal colonic epithelial cells. However, colorectal carcinoma cells, like most cancer cells, have a primary requirement for glycolysis or glucose for energy metabolism and intermediate metabolic pathway demands, a phenomenon known as the Warburg effect. This makes butyrate a poor energy source for colorectal carcinoma cells since they cannot effectively catabolized butyrate, which consequently accumulates in the colonic cancer cell and acts as an HDAC inhibitor to impair tumor growth.

Anti-inflammatory Activity

Colorectal Microbiota. The ability of increased fiber intake to specifically increase beneficial colonic microbiota at the expense of pathogenic bacteria is an important process that suppresses intestinal inflammation and carcinogenesis. A 2015 meta-analysis (31 observational and

experimental studies) found an association between colorectal carcinogenesis and microbial dysbiosis, where an overabundance of detrimental bacteria surpasses the number of beneficial bacteria [39]. In patients with CRC, some bacteria are consistently increased (such as *Fusobacteria*, *Alistipes*, *Porphyromonadaceae*, *Coriobacteriaceae*, *Staphylococcaceae*, *Akkermansia* spp. *Enterococcus faecalis*, and *Methanobacteriales*), while beneficial bacteria are diminished (including butyrate-producing *Eubacterium rectale* and *Faecalibacterium prausnitzii*, *Bifidobacterium*, *Lactobacillus*, *Ruminococcus*, *Faecalibacterium* spp., *Roseburia*, and *Treponema*) when compared with healthy volunteers [33, 34].

The metabolism of fiber in the colon plays an important role in counteracting a wide variety of cytokines and other pro-inflammatory mediators which contribute to pathways of inflammation-associated carcinogenesis [31, 33, 49, 50]. Free fatty acid receptor 2 (Ffar2), a receptor for fiber SCFA metabolites, is downregulated in human colon cancers compared to matched adjacent healthy tissue [51]. Fiber appears to suppress colon carcinogenesis and inflammation in a Ffar2-dependent manner through fiber-mediated promotion of beneficial microbiota, *Bifidobacterium* species (spp), and suppression of *Helicobacter hepaticus* and *Prevotellaceae.* Butyrate from butyrogenic bacteria induces T-cell apoptosis to down-regulate a source of inflammation and suppression of IFN-γ-mediated inflammation in colonic epithelial cells. Further, butyrate exhibits strong anti-inflammatory properties in colonic epithelial cells by reducing the lipopolysaccharide (LPS) endotoxins and cytokine-stimulated production of pro-inflammatory mediators such as TNF-α and IL-6 while increasing the release of the anti-inflammatory cytokine IL-10. High fiber intake has been shown to protect against colorectal cancer among individuals with genetically determined low IL10 activity [52]. Individuals with a low IL-10 polymorphism consuming <17.0 g of fiber/day have a significantly higher CRC risk compared to if they consume ≥17 g of fiber/day. Microbiota dysbiosis contributes to neoplastic dysfunction of the colonic epithelium by stimulating a state of chronic inflammation mediated by signaling pathways such as induction of toll-like receptors, upregulation of cyclooxygenase-2 (COX-2), and activation of mitogen-activated protein kinases (MAPK) that promote epithelial proliferation and genetic mutations. Also, microbiota dysbiosis can impede multiple other mechanisms including biotransformation of dietary procarcinogens, production of reactive oxygen and nitrogen species, and genotoxins. Further, individuals with inadequate intake of cancer-protective factors such as folate and biotin or microbiota deficient in healthy probiotic bacteria such as *Bifidobacterium*, which synthesize these vitamins, may lack optimal DNA synthesis and repair processes [31].

Visceral Adipose Tissue (VAT). In linear dose-response meta-analysis, each 25 cm^2 increase in VAT area significantly increases the risk of colonic adenomas, after adjustment for BMI, waist circumference, and subcutaneous adipose tissue, by 13% [53]. Across the studies, VAT was more strongly associated with advanced colonic adenomas than nonadvanced adenomas. Central and visceral obesity has been associated with CRC via its activation of the innate immune response, in which cytokine/adipokine secretion by macrophage infiltrated adipocytes [54]. This interplay contributes to the systemic chronic low-grade inflammation associated CRC tumor development. A pro-inflammatory adipokine profile might serve as a prognostic factor in colorectal cancer risk. Fiber is associated with the attenuation of adipocyte-secreted hormones, the most relevant of

which to colorectal tumorigenesis are adiponectin, leptin, resistin, and ghrelin. All these molecules are known to be involved in cell growth and proliferation, as well as tumor angiogenesis, and it has been demonstrated that their expression changes from normal colonic mucosa to adenoma and adenocarcinoma, suggesting their involvement in multistep colorectal carcinogenesis. Finally, fiber has been shown to be associated with better weight maintenance, reduced risk of central obesity, lower dietary pattern energy density, and metabolizable energy, with the potential to help attenuate the inflammatory activity associated with excessive ectopic or visceral body fat [55–58].

Fiber and Colorectal Cancer (CRC) Risk: Human Studies

Overview

Despite considerable mechanistic evidence supporting fiber's CRC preventative activity, the early large cohort studies and RCTs were equivocal on the protective role of fiber on colorectal adenomas and carcinomas [8]. This led to many healthcare professionals questioning the fiber and colorectal cancer hypothesis. There are several explanations for this discrepancy in the association between fiber and CRC risk including (1) other dietary and lifestyle factors, such as level of intake of folate, calcium, or red and processed meats and BMI or physical activity, (2) the sources of and level of fiber intake (e.g., cereals as the major sources in European cohorts and fruits and vegetables in American cohorts), (3) measurement errors in assessing fiber intake, and (4) a variety of other reasons including differences in study populations, dietary compliance, definition of fiber, length of follow-up time, sex effects, and concerns regarding colorectal adenoma recurrence as a CRC biomarker [8]. More recent systematic reviews and pooled or meta-analyses, and studies and re-analyses of past studies have tilted the scientific evidence to support a protective role for fiber in lowering CRC risk. Given fibers' CRC protective biological mechanisms, association with other improved health and wellness benefits, absence of any adverse consequences, and low intake by Western populations, it is reasonable to recommend the consumption of a high-fiber diet as part of a healthy lifestyle for CRC risk management [8, 12, 30]. Fifty leading fiber-rich foods in rank order are provided in Appendix 1.

Supportive Observational Studies

There are many prospective cohort, case-control, and cross-sectional studies that provide evidence that fiber plays a modest but significant role in helping to reduce the risk of CRC, especially at the distal colon, after adjusting for many dietary and other lifestyle factors. Twenty-five of these observational studies are reported in Table 17.1 [12, 14, 15, 17, 20, 23, 26, 36, 52, 59–76].

Table 17.1 Summaries of observational studies generally supporting protective associations between fiber colorectal cancer (CRC) and adenoma (multivariate adjusted) risk

Objective	Study details	Results
Systematic reviews and meta- or pooled analyses		
Ben et al. Conduct a meta-analysis primarily of case-control studies to analyze the association between fiber intake and risk of colorectal adenoma (CRA) [59]	20 studies (16 case-control studies and 4 cohort studies from the USA, EU, and Asia); approx. 150,000 subjects and 10,948 subjects with CRA; food frequency questionnaires (FFQs)	This meta-analysis supports the hypothesis that high-fiber intake, especially fruit and cereal fiber, reduces CRA risk. The pooled analysis found a significant inverse CRA risk effect per 10 g/day of total fiber by 9%, fruit fiber by 21%, and cereal fiber by 30%. These effects were similar for both early and advanced CRA
Aune et al. Assess the association between fiber intake and CRC risk from prospective cohort studies (World Cancer Research Fund/ American Institute for Cancer Research Continuous Update Report) [12, 15]	25 prospective studies from the USA, EU, and Asia; 19 were included in the dose-response analyses; 14,514 CRC cases among 1,985,552 subjects; ranges of fiber intake: total fiber (6.3–21.4 g/day), fruit fiber (1.8–15.5 g/day), vegetable fiber (1.9–16.8 g/day), cereal fiber (3.0–16.9 g/day), and legume fiber (1.3–3.8 g/day)	This meta-analysis showed that a 10 g/day increase in total and cereal fiber intake was associated with a 10% lower CRC risk. Fruit, vegetable, and legume fiber were suggestive for CRC risk reduction but not confirmed. Moderate but significant inverse associations were shown for both total and cereal fiber and colorectal cancer with a significant reduction in colon cancer but not rectal cancer
Howe et al. Examine the effects of fiber, vitamin C, and beta-carotene intakes on CRC risk [60]	13 case-control studies; 5287 case subjects with colorectal cancer and 10,470 control subjects	This pooled analysis suggests that increased total fiber intake reduced CRC risk by 47% (highest vs lowest quintiles of intake; p-trend <0.001). The findings showed similar inverse associations for both colon and rectal cancers
Prospective cohort and related studies		
Navarro et al. Evaluate the self-reported individual and combinations of fiber (insoluble, soluble, and pectin) on CRC risk in postmenopausal women (Women's Health Initiative; USA) [61]	134,017 postmenopausal women; mean age at baseline approx. 65 years; mean BMI 28; mean 11.7-year follow-up; 1952 CRC cases; mean baseline intake 16 g total fiber/day and approx.12 g insoluble fiber	This study showed a modest trend toward lower CRC risk with a higher intake of total fiber by 10% and insoluble fiber by 13% (p-trend = 0.09 and 0.08 respectively). These results suggest a modest protective effect of higher fiber intake on CRC risk
Park S-Y et al. Examine the sex-specific association of fiber with CRC and its interaction with menopausal hormone therapy (MHT) (Multiethnic Cohort Study; USA) [62]	187,674 participants; 52% females; mean age approx. 60 years and BMI 27 at baseline; 4692 CRC cases identified during a mean follow-up period of 16 years; mean fiber intake ranged from 6.7 to 18.6 g/1000 kcal	This study found an inverse association between total fiber intake and CRC risk in both men and women (Fig. 17.3a–c). In postmenopausal women, increased fiber intake was associated with a lower CRC risk in those who had never used MHT but did not appear to further decrease the risk in those who had used MHT. These findings suggest that fiber and MHT may share overlapping mechanisms in protecting against CRC
Vulcan et al. Assess associations between fiber intake, fiber sources, and incidental CRC and sub-analysis related to sex, tumor location, and metastasis classification (Malmö Diet and Cancer Study; Sweden) [63]	27,931 individuals; 60% women; approx. Mean baseline age 60 years; 728 incident CRC cases; mean follow-up of 15.4 years; dietary data from modified diet history method; mean total fiber intake approx. 20 g/day	This study observed that total fiber intake was inversely associated with CRC risk (p-trend = 0.026), especially colon cancer risk in women (p-trend = 0.013). High fiber intake, especially from fruits and berries, appears to be most effective in preventing tumor development in the colon cancer in women (p-trend = 0.022)

Table 17.1 (continued)

Objective	Study details	Results
Kunzmann et al. Prospectively evaluate the association between fiber intake and the risk of incident and recurrent colorectal adenoma and incident colorectal cancer (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; USA) [14]	57,774 participants; mean age approx. 62 years; mean BMI approx. 27; flexible sigmoidoscopy at baseline and 3 or 5 years after; incident adenoma n = 16,980 and recurrent adenoma n = 1,667; fiber intake was measured by using a self-reported FFQ; the median dietary intake of fiber was 23.3 g/day, and the median energy intake was 1,911.5 kcal/day	This study found that higher fiber intake, especially from cereal and fruit fiber, was associated with reduced risks of colorectal adenoma and distal colon cancer. Highest vs lowest tertile of total fiber intake was associated with a significantly reduced distal colorectal adenoma risk by 24% (p-trend = 0.003) and distal colon cancer by 38% (p-trend = 0.03). However, there was an insignificant 15% reduced CRC risk (p-trend = 0.10)
Murphy et al. Examine whether the previously observed inverse association for fiber and CRC risk persisted after longer follow-up; evaluate association by cancer subsite and fiber food source; and scrutinize the fiber-CRC relationship for possible interactions by age, sex, lifestyles, anthropometric, and other dietary variables (European Prospective Investigation into Cancer and Nutrition [EPIC] Study; EU) [20]	521,448 participants; mean age approx. 52 years; 66% women; mean follow-up of 11 years vs previous 4.5 years; 2.6-fold increased number of CRC cases 1,721 vs 4,517; standardized computer-based single 24-h dietary recalls were collected from 36,900 study participants at baseline; fiber intake ranged from <16.4 to >28.5 g/day	This study consistently showed inverse associations between the intake of total fiber and foods rich in fiber and CRC risk. Total fiber was inversely associated with colorectal cancer per 10 g/day increase with lower CRC and colon cancer risk by13% and 12%, respectively. Similar linear inverse associations were observed for colon and rectal cancers. Fibers from cereals, and fruit and vegetables were similarly associated with reduced colon cancer but for rectal cancer, the inverse association was only evident for cereal fiber. Fig. 17.4a–c summarizes the effect of the highest vs lowest quintile of total, cereal, and total fruit and vegetable fiber CRC, and colon and rectal cancer risk
Hansen et al. Examine associations between intake of fiber and fiber source on colon and rectal cancer risk (HELGA cohort; Scandinavian) [64]	108,081 cohort members; mean age mid-50 years and BMI approx. 26 at baseline; 1,168 incident cases (691 colon and 477 rectal cancer), diagnosed during a median of 11.3 years follow-up	This study observed that the intake of total fiber and of cereal fiber were inversely associated with risk of colon cancer in men. Total fiber per 10 g/day reduced risk of colon cancer by 26% and cereal fiber per 2 g/day by 6%. For women, the intake of 2 g/day cereal fiber was insignificantly associated with lower risk of colon cancer by 3%. No associations were seen for rectal cancer in either men or women
Tantamango et al. Evaluate the association between fiber intake and colonic polyps (The Adventist Health Study: Colon Polyps; USA) [65]	2,818 men and women who had undergone colonoscopy; mean baseline age approx. 72 years; 441 incident cases of colon polyps; 26 years of follow-up	In this study of a high vegetarian population, those consuming low amounts of fiber, especially vegetable fiber had a higher risk of developing colon polyps. Total fiber intake was inversely associated with the risk of colon polyps with a significant 29% lower risk (p = 0.04). Fiber from vegetables including legumes was the most effective with a significantly reduced risk of colonic polyps by 37% (p = 0.01)
Schatzkin et al. Investigate associations of total fiber and specific sources of fiber, and CRC risk (National Institutes of Health–AARP Diet and Health Study; USA) [66]	291,988 men and 197,623 women; mean baseline age approx. 60 years; diet was assessed with a self-administered FFQ at baseline; 2,974 incident CRC cases; 5-year of follow-up	In this large study, cereal fiber was associated with a modest but significantly lower CRC risk by 14% (p-trend = 0.01). However, higher total fiber intake was associated with an insignificant 1% reduced CRC risk

(continued)

Table 17.1 (continued)

Objective	Study details	Results
Wakai et al. Assess the association of total and specific fiber sources and colorectal cancer risk in an at-risk population (Japan Collaborative Cohort Study) [17]	43,115 men and women aged 40–79 years completed a questionnaire on dietary and other factors; total fiber intake estimated using a FFQ; mean follow-up of 7.6 years; 443 colorectal cancer cases recorded	This study supports the potential protective effects for higher total fiber intake in lowering CRC risk, especially for colon cancer. In both men and women, increasing total fiber reduced CRC risk by 27% (p-trend = 0.028) and colon cancer risk by 42% (p-trend = 0.002). No differences appeared in strength of associations between water-soluble and insoluble fiber and CRC risk. Of fiber food sources, bean fiber intake most effectively reduced colon cancer risk by 33% ($p = 0.037$)
Nomura et al. Evaluate the association between total fiber intake and CRC risk (The Multiethnic Cohort Study; USA) [67]	85,903 men and 105,108 women; mean age approx. 60 years; mean 7.3-year follow-up; 1,138 men and 972 women were subsequently diagnosed with CRC; mean total fiber intake 22 g/day	In this study, total fiber was inversely associated with CRC risk in men but not in women because of factors such as replacement hormone usage. Fiber was inversely associated with CRC risk in men with a reduction by 51% ($p < 0.0001$) and women by 25% ($p = 0.002$). After further adjustment for lifestyle and dietary factors, the inverse association remained significant in men with a reduction of 38% ($p = 0.002$) but not in women by 12% ($p = 0.245$)
Lin et al. Examine the association between dietary intakes of fruit, vegetables, and total fiber and CRC risk in a large cohort (Women's Health Study; USA) [68]	39,876 healthy women; aged ≥45 years at baseline, self-reported information on dietary intakes and other risk factors for CRC were included in the analyses; average follow-up of 10 years; 223 women were diagnosed with CRC	This study suggests that legume fiber may reduce CRC risk (highest versus lowest quintile). Although increased total fiber intake insignificantly reduced CRC risk by 25% (p-trend 0.12), higher intake of legume fiber significantly lowered CRC risk by 40% (p-trend = 0.02)
Bingham et al. Assess the association between dietary fiber intake and incidence of colorectal cancer (EPIC; EU) [23]	519,978 individuals; mean baseline age approx. 51 years; fiber intake for women 12.6–31.9 g/day, and for men 12.8–35.6 g/day); non-food supplement fiber sources were not studied; 4.5 years of follow-up; 1,065 incident colorectal cancer cases with 706 tumors located in the colon (287 right side, 286 left side, 133 overlapping or unspecified) and 359 in the rectum	In this study, total fiber intake was inversely associated with CRC and colon cancer incidence by 25% and 28%, respectively (highest vs lowest quintile of intake; $p = 0.006$). The protective effects were highest for the left side of the colon, and least for the rectum. Subsequently, a more detailed analysis of total fiber intake, showed that doubling total fiber intake from low to high reduced CRC risk by 42%. Also, cereal fiber had a borderline significant trend for lower CRC risk by 22% ($p = 0.06$)
Jansen et al. Investigate fiber and plant foods intake effects on CRC mortality in men (The Seven Country Study) [69]	12,763 men; aged 40–59; 25-year follow-up; baseline nutrient intakes were based on chemical analyses of the average diets per cohort	This study found that high-fiber intake was associated with reduced 25 year CRC mortality risk by 33% in men. Each 10 g/day fiber intake was inversely associated with CRC mortality with an energy-adjusted risk reduction of 11%
Platz et al. Evaluate the effect of specific sources of fiber and components on colon polyps (The Health Professionals Follow-Up Study USA) [26]	In a subset of 52,000 men in the HPFS, 16,448 men free of cancer underwent endoscopy; mean age 59 years; mean BMI 25; 690 cases of adenomatous polyps of the distal colon or rectum (531 distal colon and 159 rectum)	This study showed that increased fruit and soluble fiber intake was protective against distal colon adenoma risk. Higher fruit fiber and soluble fiber intake significantly reduced risk by 19% (p-trend 0.03; median, 8.4 g/day vs 1.3 g/day) and by 31% (9.4 vs 3.4 g/day; p-trend = 0.007), respectively. However, increased total fiber had a modest 12% lower risk trend (32 g vs 12 g/day; p-trend = 0.1)

Table 17.1 (continued)

Objective	Study details	Results
Case-control studies		
Song et al. Examine the effect of fiber intake on the risk of colorectal cancer, stratified by tumor site (China) [70]	265 cases and 252 controls residing in Qingdao; mean age 59 years; 58% male; FFQ that included 121 food items	This study suggests a CRC protective role of total fiber, especially vegetable fiber. Control subjects consumed more vegetables and total fiber than CRC patients ($p < 0.05$). Higher total and vegetable fiber intake reduced CRC risk by 56%, colon cancer risk by 60% and rectal cancer risk by 48%. Both, insoluble and soluble fiber protected against colon cancer
Zhong et al. Assess the effect of higher intake of total fiber and fiber fraction on the risk of CRC (China) [71]	613 colorectal cancer cases and 613 controls by age and gender; mean age 56 years; face-to-face FFQ interviews	This study shows that high intake of total fiber, particularly derived from cereal, vegetables, and fruit, was inversely associated with CRC risk in Chinese adults. The risk was reduced for total fiber by 62%, cereal fiber by 52%, vegetable fiber by 55%, and fruit fiber by 59%, respectively ($p < 0.01$; highest vs lowest intake)
Fu et al. Evaluate the hypothesis that fiber intake may modify colorectal cancer risk by offsetting the detrimental effect of cigarette smoking (Tennessee Colorectal Polyp Study; USA) [72]	1,315 adenomatous polyps cases and 3,184 controls by age and gender; mean age 58 years; self-administrated FFQs	This study suggests that higher-fiber intake attenuates the effects of cigarette smoking on the risk of colorectal polyps, especially high-risk polyps, a well-established precursor of CRC. Higher fiber intake was associated with reduced risk of colorectal polyps, which was found to be stronger among cigarette smokers (p-trend = 0.006) than non-smokers (p-trend = 0.21). Among cigarette smokers who smoked ≥23 years, there was a 38% lower risk of high-risk polyps with higher fiber intake (p-trend = 0.004)
Galas et al. Investigate the effect of calcium and fiber intake on CRC risk (Poland) [73]	703 histologically confirmed colon and rectal incident cases and 853 hospital-based controls; mean age mid-50 years; semi-quantitative FFQ	There was a decreased CRC risk for increased calcium intake at every level of total fiber intake with the greatest risk reduction of 77% for the highest level of calcium and total fiber intake ($p = 0.01$). The effect was limited to colon cancer as there was no significant effect on rectal cancer
Ou et al. Examine the relationship between fiber intake and microbiota ecosystem health on CRC risk (USA) [74]	12 healthy African-Americans aged 50–65 years and12 age- and sex-matched native Africans; microbiomes were analyzed with 16S ribosomal RNA gene pyrosequencing together with quantitative polymerase chain reaction of the major fermentative; butyrate-producing, and bile acid-deconjugating bacteria	This study supports the effect of increased intake of a traditional fiber-rich diet vs Western low-fiber diets on the establishment of healthier colonic fecal microbiota ecosystems with higher levels of butyrate-producing bacteria, lower levels of pathogenic bacteria, higher fecal SCFAs and reduced fecal secondary bile acids concentrations, which are characteristic of reduced CRC risk

(continued)

Table 17.1 (continued)

Objective	Study details	Results
Andersen et al. Assess the effect of dietary factors on IL-10 polymorphisms and CRC risk (Danish Diet, Cancer, and Health Study; Denmark) [52]	57,053 subjects in a nested case-control study; including 378 CRC cases and 775 randomly selected control participants; northern Caucasians, mean age 57 years	This study of a Northern Caucasians suggests interaction between IL-10 and total fiber intake and CRC risk. Among those eating <17.0 g of fiber/day, carriers of the low IL-10 variant allele had a statistically significantly higher CRC risk compared non-carriers (p-value for interaction = 0.01)
Dahm et al. Examine the association between fiber intake assessment methodology and CRC risk (UK) [75]	A prospective case-control study nested within seven UK cohort studies; 579 case patients who developed incident colorectal cancer and 1,996 matched control subjects; standardized dietary data obtained from 4- to 7-day food diaries and food frequency questionnaire (FFQ)	This study suggests that fiber density estimates (high vs low quintiles) from food diaries showed a significant inverse association for CRC risk by 34% whereas the same analysis conducted using fiber data obtained by FFQs found an insignificant reduced CRC risk by 12%. Consequently, fiber intake methodological differences may account for the inconsistent associations between fiber intake and CRC risk in some previous studies
Heilbrun et al. Investigate the effects of diet on CRC risk in men with special reference to fiber and fat intake (nested case-control study; USA) [76]	8,006 American Japanese men; 16-year follow-up; 162 CRC cases and 361 controls were identified; dietary data were collected from a personal interview	There was a negative association between total fiber intake and colon cancer risk among men with low-fat-intake (<61 g/d) (p = 0.042). In this subgroup of low-fat-intake men consuming <7.5 g fiber/day, there was an increased colon cancer risk by 1.3-fold compared to those consuming >14.8 g fiber/day
Cross-sectional study		
Chen et al. Evaluate the association between fiber intake and fecal microbiota and advanced colorectal adenoma (A-CRA) and CRC (China) [36]	344 A-CRA patients and 344 healthy controls; mean baseline age 60 years; 50% female; fiber intake was assessed by FFQ; fecal short-chain fatty acids (SCFAs) and fecal microbiota bacteria were measured	This study showed that A-CRA subjects consumed lower total fiber than healthy subjects. Consequently, A-CRA subjects had significantly lower fecal *Clostridium*, *Roseburia*, and *Eubacterium* spp. and significantly higher fecal *Enterococcus* and *Streptococcus* spp. whereas healthy subjects had significantly higher fecal butyrate and butyrate-producing bacteria ($p < 0.05$ for all), which are biomarkers associated with lower CRC risk

Prospective Cohort Studies

Table 17.1 summarizes two of systematic reviews and meta-analyses of cohort studies [12, 15] and 14 cohort studies [14, 17, 20, 23, 26, 61–69] supporting fiber's protective role against CRC.

Meta-analyses

In 2011, the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) Continuous Update Project Report provided the research evidence to change from probable to convincing their consensus on the effect of fiber-rich foods in lowering CRC risk based on an updated meta-analysis of cohort studies [12]. The WCRF and AICR Continuous Update Project meta-analysis (25 cohort studies; 19 cohort studies used for dose-response analysis; 1,985,552 participants) found a modest, statistically significant fiber dose-response with 10% CRC risk reduction for every 10 g of total and cereal fiber consumed daily [15]. Fruit and vegetable fibers were associated with modest 7% and 2% CRC risk reductions, respectively, but these were not statistically significant.

Specific Cohort Studies

All seven cohort studies published since the 2011 WCRF/AICR Continuous Update Project Report have shown that total fiber and/or specific fiber subtypes have a protective role in lowering CRC risk (Table 17.1) [14, 20, 61–65]. A 2016 analysis of the Women's Health Initiative (134,017 postmenopausal women; mean age at baseline 65 years; mean BMI 28; mean 11.7-year follow-up; 1952 CRC cases) found a modest trend for reduced CRC risk with increased intake of total fiber by 10% and insoluble fiber by 13% (multivariate adjusted p-trend = 0.09 and 0.08) [61]. Also, a 2016 update of the US Multiethnic Cohort Study (187,674 participants; 52% women; mean baseline age 60 years; 4,692 cases; mean 16-year follow-up) showed an inverse association between total fiber intake and CRC risk in both women and men (Fig. 17.3a–c) [62]. This study revealed that increased total fiber intake did not lower CRC risk further among women who had ever used menopausal hormone therapy (MHT) which suggests that fiber and MHT may share overlapping mechanisms in protecting against CRC. The 2015 updated Swedish Malmo Diet and Cancer Study (27,931 participants; 60% women; mean baseline age 60 years; 728 incident CRC cases; mean follow-up of 15.4 years) observed an inverse association between total fiber intake and CRC risk (p-trend = 0.026), especially with a lower risk of colon cancer only in women (p-trend = 0.013) [63]. Fiber from fruits and berries was the most effective fiber source in reducing colon cancer risk in women (p-trend = 0.022). Another 2015 prospective evaluation of the US Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (57,774 participants; mean age 62 years; mean BMI 27; flexible sigmoidoscopy at baseline and 3 or 5 years after) reported that higher total fiber intake significantly reduced the risk of distal colorectal adenoma by 24% (p-trend = 0.003) and distal colon cancer by 38% (p-trend = 0.03) [14]. The protective associations were strongest for fiber from cereals or fruit. The 2012 European Prospective Investigation into Cancer and Nutrition (EPIC) (521,448 participants; mean age 52 years; 66% women; mean follow-up of 11 years; CRC cases 4,517) found reduced CRC risk by 13% per 10 g total fiber/day [20]. Similar linear inverse associations were observed for colon and rectal cancers and total fiber. For the highest vs lowest quintile of total fiber, there was a significant reduction in CRC risk by 17% and colon cancer risk by 20% (Fig. 17.4a). Also, there was an inverse association (per 10 g/day) for cereal fiber by 11% and fruit and vegetable fiber by 9% for CRC risk. For the highest vs lowest quintile, there was a significantly lower colon cancer risk observed for cereal fiber and fruit and vegetable fibers, but for rectal cancer, the inverse association was only evident for cereal fiber (Fig. 17.4b, c). A 2012 Scandinavian HELGA cohort (108,081 participants; mean age mid-50 years and BMI approx. 26 at baseline; 691 colon cancer and 477 rectal cancer cases; diagnosed during a median 11.3 year-follow-up) observed a significant inverse association between total fiber and reduced risk of colon cancer per 10 g/day by 26% and cereal fiber per 2 g/day by 6% in men [64]. In women, cereal fiber per 2 g/day was insignificantly associated with lower risk of colon cancer by 3%. No associations were shown for rectal cancer. It is important to note that this study population had relatively high fiber intakes, especially of cereal fibers (>17.8 g/day). A 2011 Adventist Health Study (2,818 men and women who had undergone colonoscopy; mean baseline age 72 years; 441 incident cases of colon polyps; 26 years of follow-up) found that higher total fiber intake was associated with significantly reduced colon polyps risk by 29% (p = 0.04) [65]. Fiber from vegetables including legumes significantly reduced the risk of colon polyps by 37% (p = 0.01).

Seven prospective studies [17, 23, 26, 66–69] included in the 2011 WCRF/AICR Continuous Update Project Meta-analysis [12, 15] generally support the protective role of total fiber or specific fiber sources and reduced risk of colonic adenomas or CRC (Table 17.1). These cohort studies found that increased fiber was most effective against distal colon cancer. In populations with low fiber intake, the doubling of total fiber intake was associated with significantly reduced CRC risk, and the most effective sources of fiber in reducing CRC risk were insoluble fiber and cereal, legume, and fruit fiber sources.

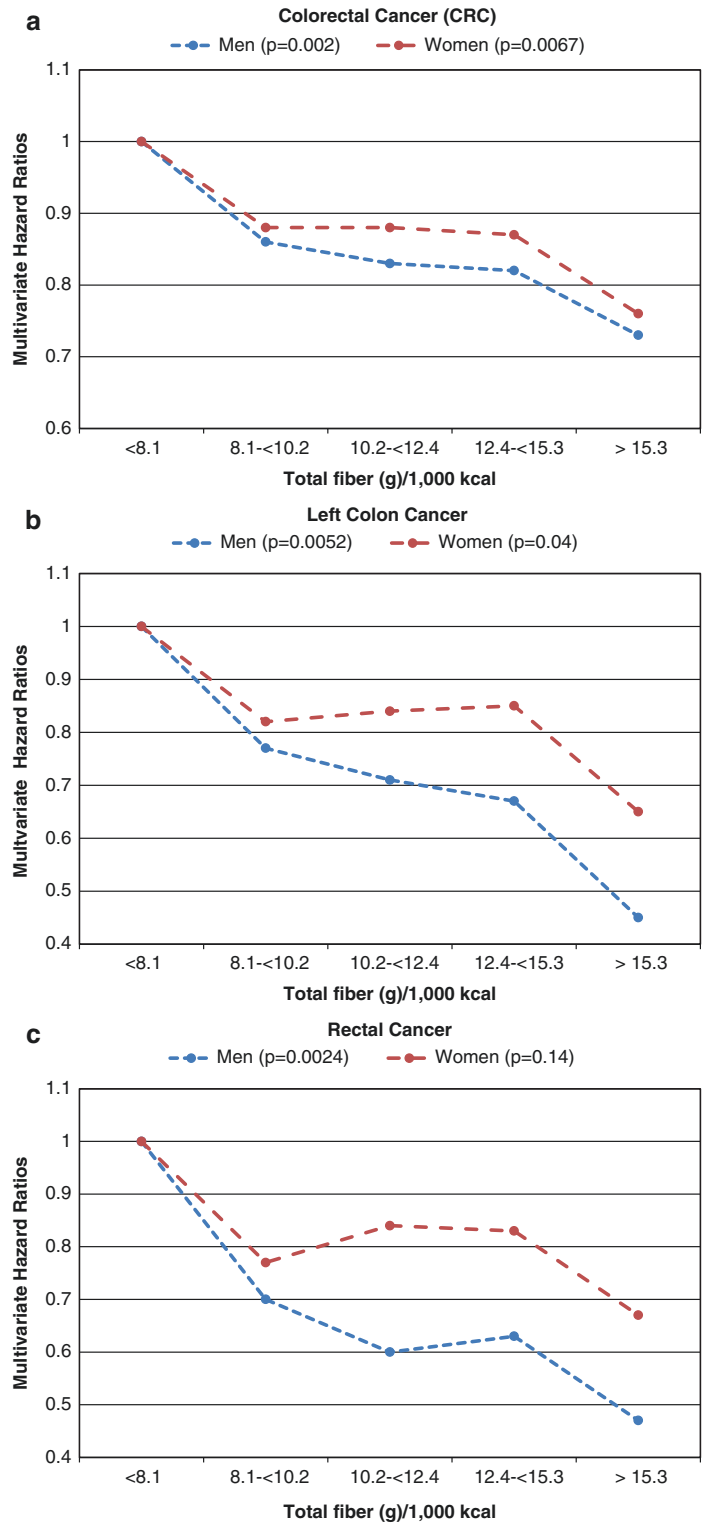

Fig. 17.3 (**a**). Association between total fiber intake and CRC risk in men and women from the Multiethnic Cohort Study over 16 years (1993–2012) [62]. (**b**) Association between total fiber intake and left colon cancer risk in men and women from the Multiethnic Cohort Study over 16 years [62]. (**c**) Association between total fiber intake and rectal cancer risk in men and women from the Multiethnic Cohort Study over 16 years [62]

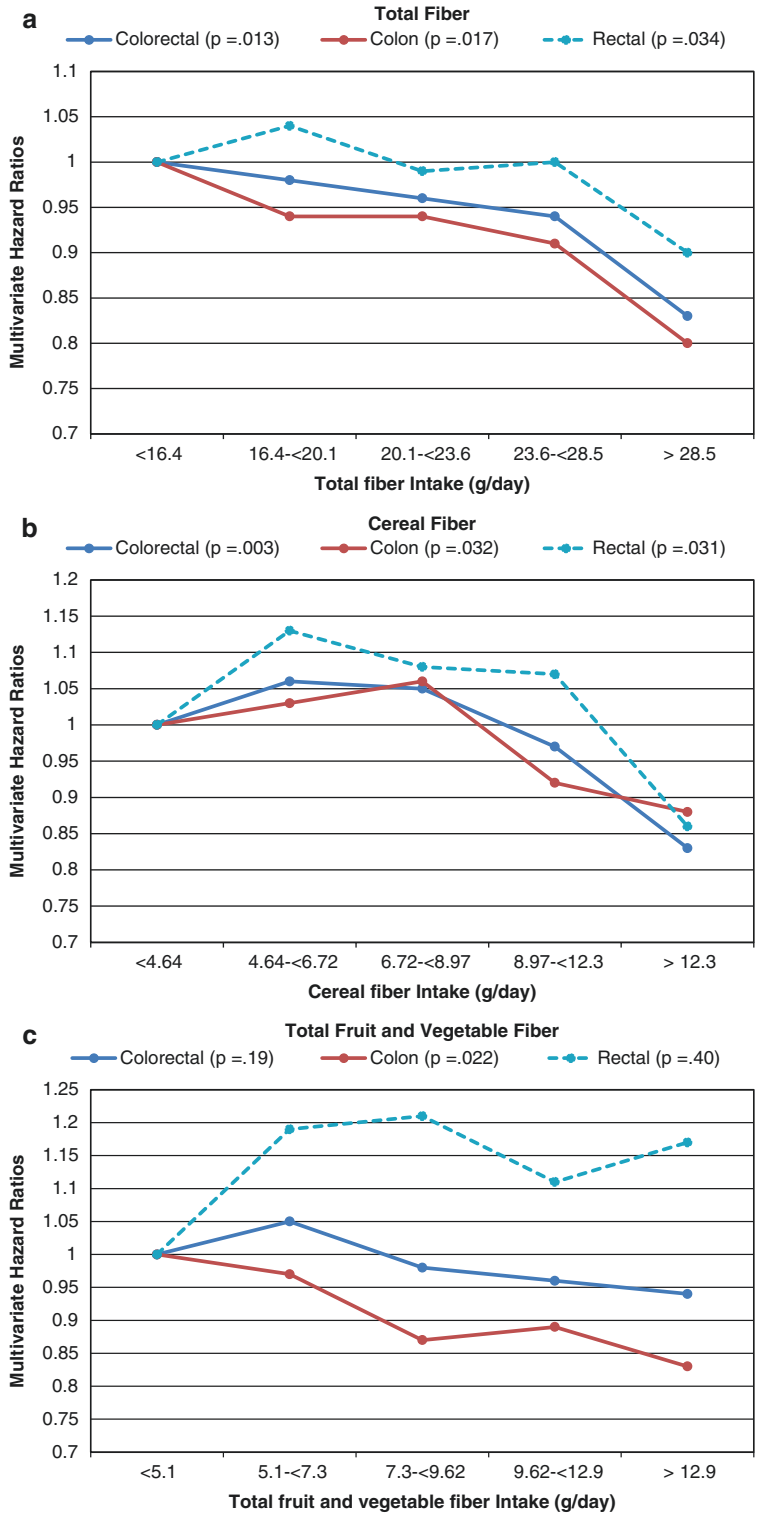

Fig. 17.4 (**a**) Association between total fiber intake and colorectal, colon, and rectal cancer risk from the European Prospective Investigation into Cancer and Nutrition (EPIC) [20]. (**b**) Association between cereal fiber intake and colorectal, colon, and rectal cancer risk from the EPIC study [20]. (**c**) Association between total fruit and vegetable fiber intake and colorectal, colon, and rectal cancer risk from the EPIC study [20]

Case-Control Studies

Table 17.1 summarizes two meta-analyses [59, 60] and eight highlighted case-control studies [52, 70–76] supporting fiber's protective role and mechanisms in reducing the risk of CRC.

Meta-analyses

Two meta-analyses of case-control studies are consistently supportive of the protective effect of fiber in CRC risk management [59, 60]. A 2014 meta-analysis (16 case-control and 4 cohort studies; 150,000 subjects; 10,948 colorectal adenomas) found that for every 10 g fiber consumed daily, the risk of CRC was reduced by 9% for total fiber, 21% for fruit fiber, and 30% for cereal fiber with a significant inverse association with colorectal adenoma development [59]. A 1992 meta-analysis of case-control studies (13 studies; 5,287 CRC cases and 10,470 controls) showed that higher fiber intake reduced CRC risk by 47% (p-trend <0.001) compared to low fiber intake [60].

Specific Case-Control Studies

Eight case-control studies provide specific insights into the relationships between fiber sources, quality of fiber intake measurement methodology, and other dietary and lifestyle factors or mechanisms associated with CRC risk [52, 70–76]. Two US studies provide evidence that lower total fiber intake is associated with increased CRC risk [73, 75]. Two Chinese studies found that fiber from a variety of fiber sources including both soluble and insoluble fiber except for soy fiber is significantly protective against CRC risk [70, 71]. A US study found that higher fiber intake has a protective role against cigarette carcinogens in long-term smoker populations, especially those with high-risk colorectal adenomas, a precursor of colorectal cancer [72]. A Polish study suggests an inverse synergistic association for both the highest level of both calcium and fiber intake and CRC risk especially for colon cancer with a 77% risk reduction [73]. A Danish study found that increased total fiber intake to ≥17 g/day appears to protect against CRC risk in individuals with polymorphisms for low IL-10 levels, in lowering tumor-promoting inflammation compared to those consuming <17 g fiber/day [52]. A nested case-controlled study with seven UK cohort studies suggests that a 4- to 7-day food diary assessment to estimate fiber intake was more likely to support an inverse association between fiber and CRC risk compared to the food frequency questionnaire (FFQ), which may have higher error in fiber intake estimates [75]. This analysis found that the one study estimating fiber intake by using 4- to 7-day food diaries showed that high fiber intake reduced CRC risk by 34% compared to low fiber intake in contrast to six cohort studies using FFQ, which showed a pooled insignificant reduction of CRC risk by 12%.

Cross-sectional Studies

One Chinese cross-sectional study (344 patients with colorectal adenomas vs 344 healthy control subjects; mean age 60 years; 50 female) found that lower-fiber dietary patterns were observed in participants with colorectal adenomas compared to healthy subjects [36]. The healthier individuals had a higher proportion of symbiotic microbiota bacteria including butyrate-producing bacteria and more fecal butyrate, which is consistent with a lower risk of colorectal adenoma and CRC.

Non-supportive Cohort Studies

A pooled analysis and ten cohort studies that do not generally support the protective associations between fiber intake and the risk of CRC are summarized in Table 17.2 [21, 22, 25, 77–84].

Table 17.2 Summaries of observational studies generally not supporting protective associations between fiber and colorectal cancer (CRC) risk (multivariate adjusted)

Objective	Study details	Results
Pooled analyses		
Park et al. Evaluate the association between total fiber and specific fiber intake and CRC risk (Pooling Project of Prospective Studies of Diet and Cancer) [25]	13 prospective cohort studies; 725,628 men and women were followed up for 6–20 years across studies; 8,081 colorectal cancer cases; median energy-adjusted fiber intake ranged from 14 to 28 g/day in men and from 13 to 24 g/day in women	Higher total fiber intake was significantly associated with a 16% reduced CRC risk ($p = 0.002$; age adjusted only) but the association was attenuated to 6%, which was no longer significant after fully adjusting for other risk factors. Participants with fiber intake <10 g/day had an 18% increased risk of CRC compared to those consuming ≥30 g fiber/day. Fiber intake from cereals, fruits, and vegetables was not significantly associated with CRC risk
Prospective cohort studies		
Ward et al. Examine the role of pre-diagnostic total fiber and meat intakes on CRC survival (EPIC; EU) [77]	3789 CRC cases; average 4.1-year follow-up; 1,008 CRC-specific mortality	This study observed that pre-diagnostic intake of total fiber is not associated with CRC survival with an insignificant 16% lower risk ($p = 0.57$). On the other hand, there was a marginal positive trend with higher intake quartiles of processed meat for increased CRC mortality ($p = 0.053$)
Kabat et al. Assess the effect of sugars, total carbohydrate, total fiber, glycemic index (GI) and glycemic load (GL) dietary intake on CRC risk (The Women's Health Initiative; USA) [78]	158,800 postmenopausal women; mean baseline age 63 years; mean BMI 28; dietary intake by FFQ; average follow-up of 7.8 years; 1,476 incident cases of CRC	This study found no significant associations between GI/GL, total carbohydrate, sugars, or total fiber and CRC risk in generally healthy postmenopausal women. Analyses by cancer subsite yielded null results, except for an 84% increased rectal cancer risk with a high GL (p-trend = 0.05)
Otani et al. Investigate the effect of total fiber intake and CRC risk (The Japan Public Health Center-Based Prospective Study) [79]	78,326 subjects; mean age approx. 57 years; mean BMI approx. 23.5; 5.8-year follow-up; 522 CRC cases	This study showed that low total fiber intake significantly increased CRC risk by 1.3-fold in women vs high fiber intake. Higher fiber intake reduced CRC risk in men by 15% (p-trend = 0.48) and in women by 42% (p-trend = 0.21)
Shin et al. Evaluate the associations of dietary intake of calcium, fiber, and vitamins with colorectal cancer risk (Shanghai Women's Health Study; China) [80]	73,314 women; mean baseline age 55 years; median 6 year-follow-up; 283 CRC cases; all subjects were interviewed in-person to obtain information on demographic and lifestyle factors and anthropometric measurement; usual dietary intake was determined using a validated FFQ	This study found no association between total fiber intake, B-vitamins, or antioxidant vitamins (e.g., vitamins A/β-carotene, C and E) and CRC risk. However, high intake of calcium was associated with reduced CRC risk by 40% (p-trend = 0.023)

(continued)

Table 17.2 (continued)

Objective	Study details	Results
Michels et al. Conduct an updated analysis of the association between fiber intake and CRC risk (Nurses' Health Study [NHS] and the Health Professionals Follow-Up Study [HPFS]; USA) [21]	**NHS**: 76,947; baseline age 30–55 years; 16-year follow-up; 744 new cases of colon cancer and 175 new documented cases of rectal cancer; mean intake of AOAC fiber 19.5 g/day; mean follow-up age approx. 58 years. **HPFS**: 47,279; baseline age 40–79 years; 14-year follow-up; 458 new cases of colon cancer and 135 new documented cases of rectal cancer; dietary intake measured by self-administered semi-quantitative FFQ; mean intake of AOAC fiber 21.9 g/day; mean follow-up age 60 years; fiber intake from fruit and vegetables was approx. twofold > than that of cereal fiber	A 5-g/day increase in AOAC fiber intake initially reduced the pooled CRC risk by 9% (limited covariate adjustments) but after fully adjusting for covariates the risk reduction was attenuated to 1%. Fruit fiber had a borderline statistically significant 11% CRC risk reduction per 5 g ($p = 0.20$; fully adjusted), but cereal and vegetable fibers were not associated with reduced CRC risk among women or men
Mai et al. Investigate the association between fiber intake and risk of CRC in a cohort of women (Breast Cancer Detection Demonstration Project; USA) [81]	45,491 women; mean baseline age 62 years; dietary measures from FFQ; mean daily fiber intake ranged from 7.1 g to 16.7 g; 8.5 years of follow-up; 487 CRC cases	This study in postmenopausal women found no significant protective association between higher-fiber intake and lower CRC risk. Higher total fiber reduced CRC risk insignificantly by 6%. Fiber subgroup analyses did not show any fiber source to significantly reduce CRC risk but fiber from beans exhibited the strongest association with a 16% lower CRC risk
Sanjoaquin et al. Examine the relationship of lifestyle and dietary factors with CRC incidence in a cohort that included a large proportion of vegetarians (Oxford Vegetarian Study; UK) [82]	10,998 men and women; vegetarians and non-vegetarians; median baseline age 33 years; median BMI 22; median fiber intake ranged from 17 to 37 g/day; 17-year follow-up; 95 CRC cancer cases	This study does not support the association between fiber intake and reduced CRC risk but missing fiber intake data from 1/3 of the CRC cases appears to be a major confounding factor. On the other hand, frequent intake of white bread (≥15 slices/week resulted in a significantly higher CRC risk by 1.25-fold ($p = 0.006$), which remained highly significant after adjusting for alcohol and smoking. The highest consumption of fresh or dried fruit (10+ vs <5 times/week) reduced CRC risk by 40% ($p = 0.067$)
Terry et al. Investigate the associations between dietary patterns and CRC risk (The Swedish Mammography Screening Cohort) [83]	61,463 women; mean baseline age 52 years; average 9.6 years of follow-up; 460 incident cases of CRC (291 colon cancers, 159 rectal cancers, and 10 cancers at both sites)	This study does not support the protective effect of high total or cereal fiber against CRC risk. Women consuming low amounts of fruit and vegetables (FV) were at the greatest risk for CRC. Specifically, women eating <1.5 FV servings/day had a 65% increased risk of developing CRC (p-trend = 0.001) compared with those consuming >2.5 FV servings/day
Fuchs et al. Examine the influence of fiber on the CRC and adenoma risk in women (Nurses' Health Study; USA) [22]	88,757 women; median baseline age approx. 47 years; no history of cancer, inflammatory bowel disease, or familial polyposis; semi-quantitative FFQ; 16-year follow-up; 787 CRC and 1,012 adenomas of the distal colon and rectum cases	This study does not support an important protective effect of fiber against CRC or adenoma in women after adjustment for age, established risk factors, and total energy intake. Higher total fiber intake reduced CRC risk by 5% ($p = 0.59$). However it was not significantly associated with colorectal adenoma risk

Pooled Analysis

A 2005 pooled analysis of prospective cohort studies (13 studies; 725,628 participants; 6–20 years of follow-up; median fiber intake ranged from 13 to 28 g/day) showed that fiber intake was inversely associated with a 16% lower risk of CRC in age-adjusted analyses, but the association was attenuated to an insignificant 6% after fully accounting for other dietary risk factors [25]. Although high fiber intake was not associated with a reduced CRC risk, several studies show that low fiber intake increased CRC risk.

Specific Cohort Studies

Ten cohort studies generally support a insignificant association between fiber intake and lower CRC risk [21, 22, 77–84]. The most notable study is the 2005 updated analysis of the Nurses' Health Study and Health Professionals Follow-Up Study (76,947 women; mean age at follow-up 58 years; 16 year-follow-up; 744 colon cancer cases and 175 rectal cancer cases; mean fiber intake 19.5 g/day and 47,279 men; mean age at follow-up 60 years; 14 year-follow-up; 458 colon cancer cases and 135 rectal cancer cases; mean fiber intake 21.9 g/day) that found that a 5 g/day increase in AOAC fiber intake initially reduced the pooled CRC risk by 9% (limited covariate adjustments) but, after fully adjusting for covariates, the risk reduction was attenuated to 1% [21]. Fruit fiber was inversely related to CRC risk with an 11% risk reduction per 5 g increase, but no significant trend across quintiles emerged ($p = 0.20$; fully adjusted). Neither cereal nor vegetable fiber was significantly related to lowering CRC risk among women or men. These findings are generally consistent with five other US, Chinese, and Finnish cohort studies [22, 78, 80, 81, 84]. A UK cohort study observed that vegetarians have a lower CRC risk than non-vegetarians, but did not see a significant fiber-lowering effect because fiber intake was not available for 1/3 of the CRC cases [82]. A Swedish study found no effect of cereal or non-cereal fiber on CRC risk, but it also showed that the consumption of <1.5 servings/day of fruits and vegetables increased CRC risk by 65% (p-trend = 0.001) compared to the consumption of >2.5 servings/day [83]. A Japanese study found a different risk profile between men and women with higher fiber intake reducing CRC risk by 15% for men and 42% for women [79]. Also, women with very low fiber intake had a 130% greater CRC risk than those with a high fiber intake. An EPIC study (3,789 CRC cases; 4.1-year follow-up; 1,008 CRC-specific deaths) showed that pre-diagnostic fiber intake was associated with an insignificant 16% lower CRC risk ($p = 0.57$; multivariate adjusted), but the relative short follow-up time may be a confounding factor [77].

Supportive Randomized Controlled Trials (RCTs)

One pooled analysis [29] and eight RCTs [28, 35, 85–90] support a role for higher fiber intake and lower risk of CRC (Table 17.3).

Table 17.3 Summaries of randomized controlled trials (RCTs) supporting the effects of fiber on reduced colorectal cancer (CRC) risk (multivariate adjusted)

Objective	Study details	Results
Pooled analyses		
Jacobs et al. Determine the pooled effects of increased fiber intake on colorectal adenoma recurrence in men and women from two large clinical intervention trials (The Wheat Bran Fiber Trial (WBF) and the Polyp Prevention Trial (PPT); USA) [29]	3209 participants combined from two trials; mean baseline age approx. 64 years; approx. 64% men; analyzed with logistic regression models to examine the effect of a dietary intervention on colorectal adenoma recurrence. The WBF trial subjects with recent colorectal adenomas removal were randomly assigned to receive either 13.5 or 2.0 g fiber/day as a breakfast cereal (wheat bran) supplement for 3 years. The PPT subjects with recent colonic polyp removal were randomized into an intervention diet of decreased fat and increased fiber, fruit, and vegetables or control diet for 4 years	This pooled analysis shows that increased fiber intake was more effective in lowering colorectal adenoma recurrence in men than in women, which may help to explain some of the discrepant results reported from previous trials. For the total pooled population, the adjusted adenoma recurrence risk was insignificantly reduced by 9%. For men, the intervention was associated with statistically significantly reduced risk of recurrence by 19%; for women, no significant association was observed. There was a statistically significant interaction between fiber intake level and sex ($p = 0.03$)
Fiber-rich diets		
O'Keefe et al. Investigate the acute effects of drastic changes in dietary pattern quality in CRC risk (crossover RCT; USA) [35]	20 healthy African-Americans and 20 rural Africans; age range 40–65 years; BMI 18–35; 2-week controlled intervention, where African-Americans were control fed a high-fiber, low-fat African-style diet, and rural Africans a high-fat, low-fiber Western-style diet; no washout	This trial suggests that drastic dietary changes in the level of total fiber, and level/quality of fat can affect CRC risk properties of the colonic microbiota ecosystem within 2 weeks. African-Americans switching to a rural traditional diet had increased saccharolytic fermentation, butyrogenesis and suppressed secondary bile acid synthesis known to reduce CRC risk. The opposite effect was observed in the rural Africans as they switched to an American style Western diet with an increased colon cancer risk profile
Sansbury et al. Examine the effect of strict adherence to a low-fat, high-fiber, high-fruit and high-vegetable intervention on adenoma recurrence risk (Polyp Prevention Trial; USA) [28]	821 subjects completed 4-year follow-up; super compliers (25.6%), inconsistent compliers (44.6%) and poor compliers (29.8%); mean age 61 years; 63% men; BMI 27.5; super compliers averaged baseline intake of 11.7 g/1000 kcal for fiber, and 2.8 servings/1000 kcal of fruit and vegetables	This secondary trial analysis supports the protective effects of adherence to a moderate low-fat, high-fiber, and high-fruit and high-vegetable diet against recurrence of colorectal adenomas. The super compliers had 32% lower fully adjusted risk of adenoma recurrence and 50% lower risk of multiple and advanced adenoma recurrence compared with low-fiber controls ($p < 0.05$)
Lanza et al. Assess the association between specific fruits, vegetables, and dried pulses on colorectal adenoma recurrence (Polyp Prevention Trial; USA) [85]	1,905 subjects; mean baseline age 61 years; 64% men; mean baseline BMI 27.6; 90% Caucasian; low-fat, high-fiber, high-fruit, and vegetable vs control American diet; 4 years	This trial showed that increased dry bean intake (median intake 42 vs 12 g/day) reduced risk for advanced adenoma recurrence by 65% (p-trend < 0.001) (Fig. 17.5). In addition, vegetables, green beans and peas, and green salad were associated with lower risk for advanced adenoma recurrence

Table 17.3 (continued)

Objective	Study details	Results
Muir et al. Evaluated the effects of combining wheat bran fiber (WBF) with resistant starch (RS) vs WBF control on CRC risk biomarkers ie, fecal bulk, transit time, lower pH, and higher butyrate (Crossover RCT; Australia) [86]	20 subjects with a family history of CRC; WBF (12 g fiber/day) vs WBF/RS (12 g WB fiber/day plus 22 g RS/day); 3-week duration; the major source of protein was lean red meat in all diets	This trial found that compared with the WBF diet control, the WBF/RS diet resulted in greater fecal output by 56% and higher fecal ratio of butyrate to total short-chain fatty acids by 45%, and a shorter transit time by 10 h, lower fecal pH by 0.15 units, and lower concentrations of total phenols by 34% and ammonia by 27%, which are indicators of reduced CRC risk.
Peters et al. Assess the association between fiber intake and colorectal adenoma in an early CRC detection study (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; USA) [87]	33,971 participants who were sigmoidoscopy-negative for polyps; 10-year follow-up; 3,591 cases with at least one histologically verified adenoma in the distal large bowel (i.e., descending colon, sigmoid colon, or rectum)	This trial showed subjects consuming the highest quartile of fiber intake (36.4 vs 12.6 g/day) had a significant 9% reduced risk of distal colon adenoma (p-trend = 0.002). The inverse association was strongest for fiber from cereals (12% reduced risk; p-trend = 0.008; 14.1 vs 3.3 g/day) and fruit (20% reduced risk; p-trend = 0.003; 8.7 vs 1.4 g/day).
Alberts et al. Evaluate dietary intake of wheat bran fiber (WBF) and calcium on fecal bile acids concentration as potential mechanisms for CRC risk reduction (Double-blinded, phase II RCT; USA) [88]	52-patients with history of colon adenoma resection; WBF; 2.0 or 13.5 g/day in the form of cereal and 250 or 1500 mg calcium/day from calcium carbonate; 9 months	This trial supports the hypothesis that high intake of WBF and calcium reduce the risk of colorectal neoplasia and CRC risk by reducing concentrations of fecal bile acids. Compared to baseline, high-dose WBF reduced mean fecal total bile acids concentrations by 52% ($p = 0.001$) and deoxycholic acid by 48% ($p = 0.003$). Also, high-dose calcium supplementation had similar lowering effects on total bile and deoxycholic fecal bile acid concentrations
MacLennan et al. Assess the effects of fat, fiber and beta-carotene on the incidence of colorectal adenomas (Partially double-blinded RCT; Australia) [89]	411 subjects; age 40% < 55 years; diet change 25% energy from fat, 25 g wheat bran/day and other combinations including 20 mg beta-carotene vs a control Western diet; 2 and 4 years; median increase in fiber was 7 g/day in the wheat bran group	This trial suggests that higher wheat bran intake may reduce the rate of transition from smaller to larger adenomas, a step in the progression of adenomas to CRC. The combined dietary intake of lower fat and wheat bran prevented the formation of large adenomas at 2 and 4 years ($p = 0.03$)
Lampe et al. Examine the effects of vegetable and cereal fiber on biomarkers associated with CRC risk (Parallel RCT; USA) [90]	34 subjects; 16 women and 18 men; mean age 27 years; five diets in random order for 23 days each, consisting of a fiber-free liquid diet and quick breads containing 0 g added fiber, 10 g wheat bran fiber (WBF), 30 g fiber as WBF, 10 g fiber as vegetable fiber (VF), and 30 g fiber as VF	This trial showed that the WBF and VF significantly reduced colonic biomarkers associated with CRC risk. Total bile acid concentrations decreased with increased fiber dose ($p < 0.0001$) for both WBF and VF and fecal pH decreased with increased intake of both fibers ($p < 0.005$). WBF wet fecal weights increased by 43% and transit times were faster by 36% compared to VF ($p < 0.0001$). Transit time was 23% faster on 30 g WBF than on 10 g WBF ($p = 0.04$)

(continued)

Pooled RCT Analysis

A 2006 pooled analysis of two large US RCTs (3209 participants from the Wheat Bran Fiber Trial, increased wheat bran intake 13.5 vs 2.0 g/day from cereal, 3 years, and the Polyp Prevention Trial, diet lower in fat, higher in fiber and fruits and vegetables, 4 years; mean baseline age 64 years; 64% men) found that increasing dietary fiber was more effective in preventing adenoma polyp recurrence in men than women which may help to explain some of the inconsistent results reported in other RCTs [29]. For men, the intervention was associated with statistically significantly reduced risk of colorectal polyp recurrence by 19%, but for women, no significant association was observed (multivariate adjusted). Using a likelihood-ratio test, statistically significant interaction between fiber intake and sex ($p = 0.03$) was observed.

Specific RCTs

Eight RCTs provide clinical evidence that the consumption of high-fiber diets may lower the risk of colon adenomas or CRC (Table 17.3) [28, 35, 85–90]. A 2015 crossover RCT (20 healthy African-Americans and 20 rural Africans; middle-aged 40–65 years; 2-week controlled diet; African-Americans were fed a high-fiber, low-fat African-style diet, and rural Africans were fed a high-fat, low-fiber Western-style diet) found that acute dietary change from a Western to traditional diet or vice versa resulted in major change in microbiota profiles and CRC risk within 2 weeks [35]. The African-Americans showed increased butyrogenesis and lower secondary bile acid synthesis and mucosal inflammation associated with lower CRC risk compared to the effects of their usual diets. The rural Africans on the Western-style diet had reduced butyrogenesis and increased secondary bile acid synthesis and mucosal inflammation associated with increased CRC risk. A 2009 reevaluation of the US Polyp Prevention Trial (821 participants who completed the study; 29.8% were classified as poor compliers, 44.6% as inconsistent compliers, and 25.6% as super compliers; 4-year follow-up; mean age 61 years; 63% men; BMI 27.5) found that the super fiber compliers had significantly 32% lower risk of any adenoma recurrence ($p < 0.05$) compared with low-fiber compliant controls [28]. A 2006 reevaluation of the US Polyp Prevention Trial (1,905 subjects; mean baseline age 61 years; 64% men; mean baseline BMI 27.6; low fat, high fiber, high fruit, and high vegetable intake vs control American diet; 4 years; median dry bean intake increased from 11.6 (baseline) to 41.8 g/day) showed that those participants with high dry bean intake (an excellent source of fiber) significantly reduced the risk for advanced adenoma recurrence by 65% (p-trend < 0.001; highest vs lowest intake) (Fig. 17.5) [85]. In addition, vegetables, green beans and peas, and green salad were associated with lower risk for advanced adenoma recurrence. A 2004 Australian crossover RCT (20 subjects with a family history of colorectal cancer; three diets, control, wheat bran fiber (WBF) at 12 g fiber/day, and WBF/resistant starch (RS) at 12 g WB fiber/day plus 22 g RS/day; the major source of protein was lean red meat in all diets; 3weeks) observed that the WBF/RS diet changed fecal composition to lower CRC risk profiles compared to the control WBF diet [86]. Specifically, the WBF/RS group had increased fecal output by 56%, increased fecal ratio of butyrate to total short-chain fatty acids by 45%, shorter transit time by10 h, lower fecal pH by 0.15 units, and lower ammonia by 27%. A 2003 US Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (3971 participants who were sigmoidoscopy-negative for polyps; 10-year follow-up period; 3591 cases with at least one histologically verified adenoma in the distal large bowel) found significantly lower multivariate risk of distal colon adenoma for higher intakes of total fiber by 9% (p-trend = 0.002), cereal fiber by 12% (p-trend = 0.008), and fruit fiber by 20% (p-trend = 0.003) [87]. The risk reductions were similar for advanced and early adenomas, but rectal adenoma was not significantly related to fiber intake. A 1996 US double-blinded, phase II trial (52 patients with history of colon adenoma resection; wheat bran fiber [WBF] 2.0 or 13.5 g/day in

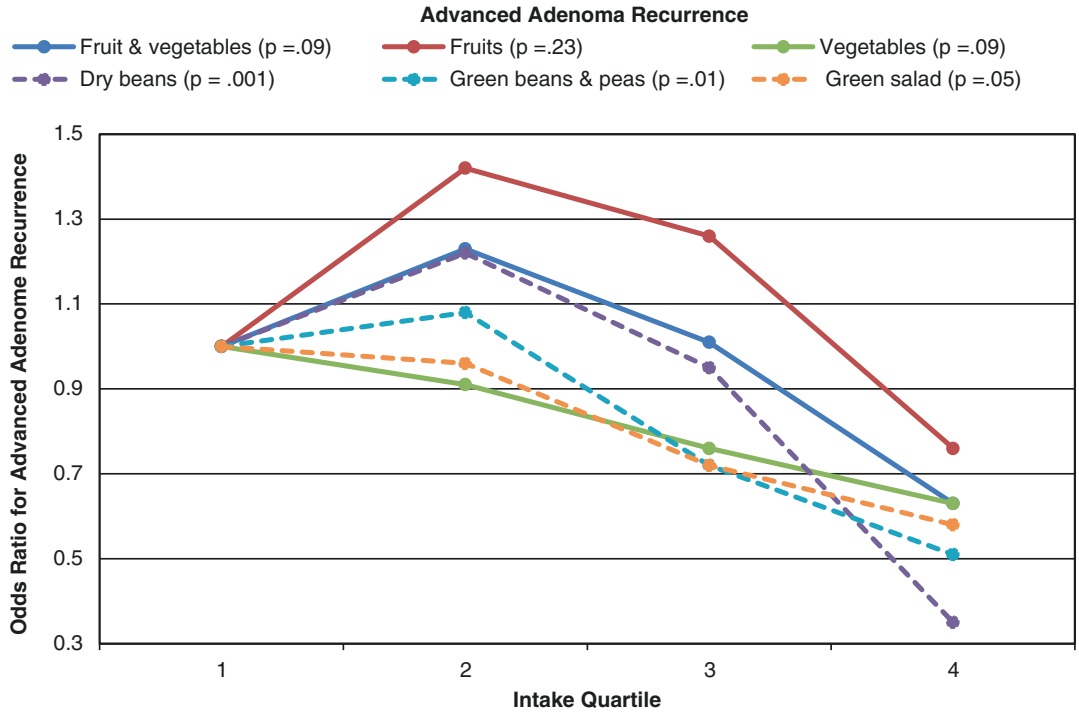

Fig. 17.5 Effect of fruit and vegetables, dry edible beans, green beans and peas, and green salad intake on the risk of advanced adenoma recurrence from the Polyp Prevention Trial [85]

the form of breakfast cereal and 250 or 1500 mg/day elemental calcium; 9 months) showed that fecal concentrations of total primary and secondary bile acids were significantly lower at 9 months on the high-dose WBF and/or calcium vs baseline diets because of additional bulking due to the higher intakes of WBF cereal and calcium [88]. A 1995 Australian double-blinded RCT (411 subjects; age 40% <55 years; diet change 25% energy from fat, 25 g wheat bran/day, and other combinations including 20 mg beta-carotene vs a control Western diet; 2 and 4 years) found that the combined lower fat and wheat bran interventions prevented the development of large adenomas at 2 and 4 years ($p = 0.03$) [89]. This study showed that wheat bran may reduce the transition from smaller to larger adenomas, which are more likely to progress to CRC. A 1992 US wheat bran fiber (WBF) and vegetable fiber (VF) dose-response trial (34 subjects; 16 women and 18 men; mean age 27 years; five diets in random order for 23 days each, consisting of a fiber-free liquid diet and quick breads containing 0 g added dietary fiber; 10 g WBF or 30 g WBF; 10 g VF or 30 g VF) showed that the consumption of both WBF and VF produced a physiological profile associated with a lowered risk for colon cancer [90]. Total bile acid concentrations decreased with increased fiber dose ($p < 0.0001$) with no significant difference between WBF and VF. Fecal pH decreased with increased fiber intake of both WBF and VF ($p < 0.005$). Transit time was 23% faster on 30 g WBF than on 10 g WBF ($p = 0.04$).

Non-supportive Randomized Controlled Trials (RCTs)

Two systematic reviews [13, 91] and nine RCTs [18, 19, 92–98] do not provide support to the effect of higher fiber intake and lower risk of CRC (Table 17.4).

Table 17.4 Summaries of randomized controlled trials (RCTs) not supporting the effects of fiber on reduced colorectal cancer (CRC) risk (multivariate adjusted)

Objective	Study details	Results
Systematic reviews		
Clark et al. Evaluate the effects of prebiotic supplementation on CRC risk [91]	Nine RCTs; 1,253 subjects; prebiotics: lactulose ($n = 1$), blend of oligofructose and inulin ($n = 2$), and resistant starch $n = 6$); duration 2 weeks–3 years	Only one RCT found a significant effect of prebiotics on lowering CRC risk, but that study was given a neutral quality rating. Lactulose reduced adenoma recurrence. Resistant starch did not significantly reduce adenoma or CRC risk but appears to have improved gene expression and DNA methylation indicator associated with lower CRC risk
Asano et al. Assess the effect of fiber on the incidence or recurrence of colorectal adenomas and the incidence of CRC (Cochrane Systematic Review) [13]	Five RCTs; 4,349 subjects; wheat bran fiber ($n = 3$), psyllium ($n = 1$), or high-fiber whole food sources ($n = 1$); trial duration ranged from 2 to 4 years	This systematic review of pre-2002 RCTs showed an insignificant difference between the dietary fiber intervention and control groups in subjects with at least one adenoma, more than one adenoma or at least one adenoma 1 cm or greater within a 2- to 4-year period. Other primary and secondary outcomes and sub-analyses by type of fiber intervention were not statistically significant
Fiber-rich diets		
Lanza et al. Follow a sub-cohort of the original cohort for an additional 4 years to further assess the effect of high-fiber, high-fruit and high-vegetable, and low-fat intervention on recurrence of one or more adenomas vs control diet (The Polyp Prevention Trial—Continued Follow-Up Study; USA) [19]	1,192 subjects (63% of the original cohort); 801 confirmed colonoscopy reports; mean age 60 years; 66% men; 8-year follow-up; intake for each of the three dietary goals were still significantly healthier for the intervention vs controls	This subgroup trial continuation from 4 to 8 years showed an insignificant 2% lower adenoma recurrence risk for the higher fiber, fruit and vegetable and lower-fat eating pattern vs the control group. Also, there were no significant intervention-control group differences in the risk for advanced adenoma or multiple adenomas recurrence
Ishikawa et al. Evaluate whether fiber from wheat bran biscuits (WBB), *L. casei*, or a combination can prevent the occurrence of colorectal adenomas (parallel RCT; Japan) [92]	380 subjects; mean baseline age 55 years; approx. 80% men; four groups administered WBB, *L. casei*, both, or neither; WBB composition: energy, 454 kcal/day; 25 g WB/day; protein, 2.9 g/day; lipid, 3.3 g/day; and refined carbohydrate, 17.5 g/day	This trial found no significant difference in the risk of developing new colorectal adenomas with the consumption of either WBB or *L. casei* probiotic. However, the results suggest that *L. casei* probiotic appears to help prevent atypia of colorectal adenomas and WBB appears to increase the number of large adenomas
Alberts et al. Examine the effect of wheat bran fiber (WBF) on fecal bile acid distribution into the solid and liquid phases (subset of Phase III Colorectal Adenomatous Polyp Prevention Trial; USA) [93]	68 subjects; mean age 66 years; 67% men; 28% of these fecal bile acid sub-study participants were in the low WBF (2.0 g/day) intervention group, whereas 72% were in the high WBF (13.5 g/day); median 2.4-year duration	This trial found no significant differences between the low and high WBF groups for aqueous-phase concentrations of secondary bile acids (e.g., lithocholic or deoxycholic bile acids). In contrast, the concentrations of secondary bile acids were significantly lower for the high WBF group in the solid phase stool ($p < 0.05$). Thus, the inability of the high WBF intervention to reduce colorectal adenoma recurrence may be related to its lack of effect on fecal aqueous-phase secondary bile acid concentrations

Table 17.4 (continued)

Objective	Study details	Results
Jacobs et al. Assess the effect of total fiber intake including wheat bran fiber (WBF) and other fiber sources on colorectal adenoma recurrence (Wheat Bran Fiber Trial; USA) [94]	1,208 participants who completed the WBF trial had colonoscopies; mean baseline age 66 years; 68% men; WBF cereal 13.5 or 2.0 g/day; 3-year duration	This trial found that neither high WBF nor total fiber intake significantly lowered CRC risk. For WBF, high intake (>11 g/day) insignificantly lowered adenoma recurrence by 6% vs <1.8 g/day (p-trend = 0.82). For total fiber intake, there was an insignificant 2% risk reduction in adenoma recurrence for those whose total fiber intake was >30.3 g/day compared with those with intake <17.9 g/day (p-trend = 0.82)
Bonithon-Kopp Test the effect of diet supplementation with calcium and fiber on adenoma recurrence (parallel RCT; EU) [95]	665 patients with a history of colorectal adenomas; mean baseline age 59 years; 63% men; three treatment groups: calcium gluconolactate and carbonate (2 g elemental calcium daily), psyllium (3.5 g), or placebo; participants had colonoscopy after 3 year-follow-up	This study suggests that psyllium may adversely affect colorectal adenoma recurrence. Patients developed at least one adenoma in 16% of the calcium group, 29% of the psyllium group, and 20% of the placebo group. Compared to placebo, the psyllium significantly increased adjusted risk for recurrence (p = 0.042), especially when calcium was above the median intake
Schatzkin et al. Investigate the effect of healthy fiber-rich dietary patterns on recurrent colorectal adenomas development (Polyp Prevention Trial; USA) [96]	2,079 subjects; inclusion criteria ≥1 large bowel adenoma removed within 6 months, polyp-free colon post-colonoscopy; mean baseline age 61 years; 64% males; mean baseline BMI 27.6; treatment: dietary targets of 20% of calories from fat, 18 g of dietary fiber/1000 kcal, and 5–8 servings of fruits and vegetables daily vs a control, usual diet and given a standard brochure on healthy eating; 4-year duration	This trial found that adopting a diet low in fat and high in fiber, fruits, and vegetables did not significantly influence the risk of colorectal adenomas recurrence as 40% of subjects in both groups had at least one recurrent adenoma. Among subjects with recurrent adenomas, the mean number of such lesions was approx. 1.9 in both groups, and the rate of recurrence of large adenomas did not differ significantly between the two groups
Alberts et al. Evaluate the effect of WBF from breakfast cereal on the rate of colorectal adenomas recurrence (Phoenix Colon Cancer Prevention Physicians' Network; USA) [18]	1,429 subjects as outpatients in Phoenix, Arizona; mean baseline age 66 years; 66% men; removal of ≥1 colonic adenoma(s) ≥3 mm at colonoscopy within 3 months of study entry; treatment: WBF 13.5 g/day vs control WBF 2.0 g/day; baseline total fiber intake approx. 19 g/day; median duration 3 years	This trial showed that high intake of WBF from breakfast cereal did not protect against recurrent colorectal adenomas. At the end of the trial, >one adenoma had been identified in 47% of the high-WBF group and in 51.2% of the low-WBF group. There was a 12% lower risk for recurrent adenoma in the high-WBF vs low-WBF (p = 0.28)
Alberts et al. Evaluate the potential mechanisms for WBF and calcium to reduce the development or recurrence of rectal adenomas in patients at increased risk (double-blinded phase II RCT; USA) [97]	100 subjects; mean age approx. 66 years; approx. 70% men; dietary WBF (2.0 or 13.5 g/day) from breakfast cereal and calcium carbonate (250 or 1500 mg/day elemental calcium); thymidine labeling index percentages in rectal mucosal crypts and 24-h in vitro outgrowth cultures; measurements were made at baseline vs. 9 months	This trial found that high-dose WBF from breakfast cereal and calcium carbonate supplementation in study participants with a history of recently resected colorectal adenomas did not have a significant effect on cellular proliferation rates in rectal mucosal biopsies, comparing 9-month results to baseline

(continued)

Table 17.4 (continued)

Objective	Study details	Results
McKeown-Eyssen et al. Assess the effect of a low-fat and high-fiber diet on colorectal polyp's recurrence (parallel RCT; Canada) [98]	201 subjects; mean baseline age 58 years; approx. 55% men; subjects received counseling on a diet low in fat (the lesser of 50 g/day or 20% of energy) and high in fiber (50 g/day) (LFHF) or to follow a control Western diet, high in fat and low in fiber; actual diet estimates: fat consumption was about 25% of energy in the LFHF group and 33% in the control group; fiber intake was 35 g and 16 g, respectively; 2-year follow-up; primary outcome: number of subjects with at least one recurrent adenoma	This trial found gender-specific associations between diet and fecal bile acid concentrations on risk of colorectal neoplasia recurrence. An intention-to-treat analysis showed no significant difference in incidence rates for recurrence of neoplastic polyps, between dietary groups. However, an exploratory analysis conducted among 142 persons with substantial diet counseling indicated a reduced risk of neoplastic polyp recurrence in women by 50% associated with reduced concentrations of fecal bile acids while on the LFHF diet, but men did not have a reduction in risk of recurrence or fecal bile acids

Systematic Reviews

Two systematic reviews of RCTs do not support the protective effects of fiber intake on CRC risk. A 2012 systematic review that evaluated the effects of prebiotics on CRC risk (nine trials; 1,253 subjects; colonoscopy adenomas, CRC, and Lynch syndrome; lactulose ($n = 1$), blend of oligofructose and inulin ($n = 2$), and resistant starch ($n = 6$); duration 2 weeks–3 years) showed that prebiotics had limited effects on CRC risk [91]. Only one study found a significant change in a direct CRC endpoint, but that study received a neutral quality rating. Lactulose reduced adenoma recurrence. Although resistant starch had no significant effect on adenoma development or CRC risk, there was some evidence that gene expression and DNA methylation were somewhat improved with resistant starch consumption. A 2002 Cochrane systematic review (5 RCTs; 4,349 subjects; wheat bran fiber ($n = 3$), psyllium ($n = 1$), or high-fiber whole food diets ($n = 1$); 2–4 years; US, EU, Australian, and Canadian) found that high fiber intake did not significantly reduce CRC risk in subjects with at least one adenoma or adenomas ≥1 cm within a 2- to 4-year period [13, 88, 95–98].

Specific RCTs

Nine RCTs evaluating high-fiber fruits and vegetables and low-fat diets or wheat bran fiber supplementation among patients with a history of colorectal polyps found that increased fiber intake had no significant effect on colorectal polyps or secondary bile acids [18, 19, 92–98]. However, all these trials had several limitations, including relatively poor dietary compliance and the relatively short duration (2–4 years). The 2007 US Polyp Prevention Trial—Continued Follow-Up Study which extended the trial from 4 years to 8 years (801 confirmed colonoscopies; 405 intervention and 396 control; mean age 60 years; 66% men; target diet, high fiber (18 g/1000 kcal), high fruit and vegetable (3.5 servings/1000 kcal), and low fat 20% of total energy vs habitual Western diet control; 8 years) found that the higher-fiber intervention group had an insignificant 2% lower risk of recurrent adenomas than the control group [19]. A 2005 Japanese parallel RCT (380 subjects; mean baseline age 55 years; approx. 80% men; wheat bran biscuits composition included 454 total kcal, 25 g WB, 2.9 g protein, 3.3 g lipid, 17.5 g refined carbohydrate, *L. casei*, *L. casei* and WBB combination vs control; 4 years) showed no significant difference in the number of new colorectal tumors with the consumption of either wheat

bran biscuits or *L. casei* probiotic. However, the results suggest that *L. casei* prevented atypical colorectal tumors, and wheat bran biscuits may increase the number of large adenomas [92]. A 2003 evaluation of a sub-study of the US Phase III Colorectal Adenomatous Polyp Prevention Trial (68 subjects; mean age 66 years; mean 67% men; 15.5 vs 2.0 g/day of wheat bran fiber [WBF]; median 2.4 years) reported no significant differences between the low- and high-WBF groups on mean and median aqueous-phase concentrations of secondary bile acids, which may be a factor associated with the risk of colorectal adenoma recurrence [93]. A 2002 US Wheat Bran Fiber Trial sub-study (1,208 participants with colonoscopy; mean age 66 years; 68% men; 13.5 g or 2.0 g WBF; 3 years) found that consuming >11.0 g WBF/day resulted in an insignificant 6% lower risk for adenoma recurrence compared to <1.8 g WBF/day [94]. For total fiber intake, there was an insignificant 2% risk reduction for those consuming >30.3 g/day compared with those with intake <17.9 g/day. A 2002 EU trial (665 patients with a history of colorectal adenomas; mean baseline age 59 years; 63% men; three treatment groups, 2 g elemental calcium daily, 3.5 g psyllium daily, or placebo; 3 years) showed that the psyllium increased adjusted risk of adenoma recurrence ($p = 0.042$) with 29% of the psyllium group having ≥one adenoma recurrence compared to 20% of the placebo group [95]. A 2000 US Polyp Prevention Trial (2,079 subjects; inclusion criteria ≥1 large bowel adenoma removed within 6 months, polyp-free colon post-colonoscopy; mean baseline age 61 years; 64% males; mean baseline BMI 27.6; treatment, dietary targets of 20% of calories from fat, 18 g of dietary fiber/1000 kcal, and 5–8 servings of fruits and vegetables daily vs a control, given a standard brochure on healthy eating and assigned to follow their usual diet; 4 years) found that approx. 40% of subjects in both groups had at least one recurrent adenoma with no difference in risk observed between groups [97]. The mean number of such lesions was approx. 1.9 in both groups, and the rate of recurrence of large adenomas did not differ significantly between the two groups. A 2000 US Phoenix Colon Cancer Prevention Physicians' Network (1,429 subjects as outpatients in Phoenix, Arizona; mean baseline age 66 years; 66% men; removal of ≥1 colonic adenoma(s) ≥3 mm at colonoscopy; treatment: WBF 13.5 g/day vs control WBF 2.0 g/day; median duration 3 years; baseline fiber intake 19 g/day) repoted >one adenoma in 47% of the high-WBF group and in 51.2% of the low-WBF group, and an significant reduced risk for recurrent adenoma by 12% in the high-WBF vs low-WBF ($p = 0.28$). A 1997 US double-blinded, phase II RCT (100 subjects; dietary WBF 2.0 or 13.5 g/day from cereal and 250 or 1500 mg/day calcium from calcium carbonate; 9-month duration) found that high-dose WBF from cereal and calcium supplementation in participants with a history of recently resected colorectal adenomas did not have a significant effect on cellular proliferation rates in rectal mucosal biopsies, when comparing 9-month results to baseline [97]. A Canadian parallel RCT (201 subjects; mean baseline age 58 years; approx. 55% men; received counseling on a diet low in fat and high in fiber or to follow a control Western diet; fiber intake was 35 g and 16 g, respectively; 2 years) showed no significant difference in incidence rates for recurrence of neoplastic polyps between the dietary groups [98]. However, an exploratory analysis conducted among 142 persons with substantial low fat and high fiber dietary counseling showed a 50% lower risk of neoplastic polyp recurrence and reduced concentrations of fecal bile acids in women but not for men compared to control diets.

Conclusion

In 2015, there were 1.7 million cases of CRC globally, which caused 832,000 deaths. CRC rates have doubled since the 1970s and incidence is strongly associated with the Western lifestyle and aging populations. Dietary factors have an important influence on CRC and colorectal adenoma risk. Examples of known or suspected dietary-related CRC or CRA risk factors are higher intake of alcohol and red meat; lower intakes of dietary fiber, calcium, and folate; and elevated BMI. The 1970s fiber

hypothesis stimulated a surge of observational and intervention studies, but the early findings were inconsistent, due to differences in the type and amount of fiber consumed, study populations (e.g., US vs European), length of follow-up time, poor dietary compliance, and tumor site heterogeneity. Despite these early inconsistencies, there is now convincing evidence that higher intake of fiber-rich foods reduces CRC risk and that low fiber intake is associated with an increased risk of CRC. Dose-response meta-analyses found that each daily 10 g increase in total or cereal fiber reduced CRC risk by 10% (in prospective studies) and reduced CRA risk by 9% and 30% for total fiber and cereal fiber, respectively (primarily in case-control studies). Two large US-based randomized controlled trials (RCTs), the Wheat Bran Fiber Trial and the Polyp Prevention Trial, indicated that increased intake fiber-rich foods did not significantly lower the risk of CRA recurrence, but there were several trial limitations including relatively poor dietary compliance and short duration (2–4 years). However, a pooled analysis of these two trials found that increased intake of dietary fiber significantly reduced the risk of CRA recurrence in men by 19%, and a reanalysis of the US Polyp Prevention Trial found that subjects with the highest fiber intake had a significantly 32% lower risk of CRAs compared with low fiber controls. CRC-protective mechanisms depend on the fiber's properties: (1) soluble fermentable fiber lowers colonic pH, inhibiting pathogenic bacteria and increasing butyrogenic bacteria to promote healthy colonic mucosal cells, reduces colon inflammation, and inhibits cancer cell proliferation and facilitates apoptosis; and (2) insoluble fiber dilutes or inactivates potential carcinogens by bulking stools and binding carcinogens to reduce their exposure to the colon and rectum. Also, fiber-rich foods tend to be lower in energy density compared to more processed foods for better weight control, and they are major contributors of potential cancer-protective nutrients such as folate, antioxidant nutrients such as vitamins C and E, and phytochemicals such as phenolics and carotenoids.

Appendix 1. Fifty High Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (Garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multi-grain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

Dietary Guidelines Advisory Committee. Scientific Report of the 2015Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Chapter 1: Food and nutrient intakes and health: Current status and trends. 2015; 97–8; Table D1.8

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Chapter 18
Fiber and Other Dietary Factors in Breast Cancer

Keywords Dietary fiber • Premenopause • Postmenopause • Adolescence • Tumor receptor subtype • Body fat • Abdominal fat • Weight gain • Estrogen • C-reactive protein • Insulin resistance • Hot flashes

Key Points

- As with many cancers, consuming a healthy fiber-rich dietary pattern and maintaining a healthy body weight are important for lowering breast cancer (BC) risk and/or improving post-diagnosis survival. For example, postmenopausal women with higher healthy lifestyle scores had a 26% lower risk of BC compared to those with lower healthy lifestyle scores.
- Potential mechanisms by which increased dietary fiber (fiber) intake supports the reduction of BC risk and/or improves survival include lowering women's risk of excess weight or abdominal fat gain, reducing elevated C-reactive protein, attenuating insulin resistance, and decreasing circulating estrogen levels.
- The relationship between weight and fiber intake on BC risk is complex, as it varies at different times of life. Higher BMI at age 18 years was inversely associated with BC risk, but weight gain after age 18 years was positively associated with BC risk after menopause, in those who never used hormone therapy. Also, weight gain by ≥15 lb compared to no weight change over a 4-year period was associated with increased BC risk, especially in premenopausal women. Higher fiber intake during adolescence and early adulthood reduced the risk of adult BC risk, especially in premenopausal women.
- Prospective cohort meta-analyses show that each 10 g of fiber intake was inversely associated with a 4–7% lower BC risk in all women. In postmenopausal women, an increased fiber intake by 15 g/day above typical intake was associated with reduced BC risk by 7–12%.
- A meta-analysis of two large RCTs and a cohort study of breast cancer survivors showed that post-diagnostic diets lower in fat and higher in fruits, vegetables, and fiber significantly reduced BC recurrence risk by 23% and BC mortality risk by 17%. In RCTs with BC survivors, dietary patterns high in vegetables, fruits, and fiber and low in fat were more effective in lowering risk of recurrent BC events in women without hot flashes at baseline, suggesting that higher fiber intake lowered circulating estrogen concentrations.
- For both pre- and postmenopausal women, increased intake of non-starchy vegetables (estrogen receptor negative BC women only), plant foods rich in carotenoids and diets high in calcium were associated with lower BC risk.

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Introduction

Overview

In 2015, there were 17.5 million cancer cases and 8.7 million cancer deaths worldwide with a 33% increase between 2005 and 2015 [1]. In women, breast cancer (BC) was the most common cancer overall, with an estimated 2.4 million cases in 2015. BC was also the leading cause of cancer deaths (523,000 deaths) and disability-adjusted life years (15.1 million years) for women. The odds of developing BC between birth and 79 years are 1 in 14 for women globally, but these odds increase to 1 in 9 for women in the highest-income countries such as in North America, Western Europe, and Australia. The worldwide rise in BC incidence, despite continuous improvements in BC prognosis, is primarily due to longer life expectancy, increased aging populations, and the adoption of Western diets and lifestyles [2, 3]. Hormones, such as estrogen, progesterone, insulin, and growth factors, which peak with puberty, pregnancy, and lactation, may influence the lifetime risk of BC because they modulate the structure, growth, and epigenetics of tumor cells. Risk doubles each decade until menopause, when the increase slows down or remains stable, but breast cancer is more common after menopause. In many countries, the 5-year survival rate for women diagnosed with Stage I/II BC (only spread to tissues or nodes under the arm) is 80–90%, but if the cancer stage is more advanced (spread to distant lymph nodes or organs), the survival rate falls to about 25%. With routine screening, BC can often be detected at a relatively early, localized stage [2, 3]. In US women, the 5-year relative survival rate for BC has improved from 63% in the early 1960s to 91% currently, but BC survivors have a higher risk of recurrence compared to the general population [4]. Breast cancer is a heterogeneous disease with various subtypes [5]. Common molecular subtype biological markers include the presence or absence of estrogen receptors (ER+/ER−), progesterone receptors (PR+/PR−), and human epidermal growth factor receptor 2 (HER2+/ HER2−). Only <5–10% of BC can be primarily attributed to an inherited genetic mutation, such as early-onset (BRCA1 or 2) genes and p53 which result in very high BC risk but account for only 2–5 percent of total cases. More typically, BC risk and survival are associated with lifestyle, reproductive, and other environmental factors, including aging, early age at menarche, lactation, late menopause, first full-term pregnancy, the use of exogenous hormones (oral contraceptives and combined postmenopausal hormone replacement therapy), alcohol consumption, excess weight, insulin resistance, diet, and physical activity [2–6]. Among the dietary factors, the role of fiber in BC risk has been debated for decades. The objective of this chapter is to review the effects of fiber in BC risk, recurrence and survival.

Diet and Lifestyle

It has been estimated that up to 90% of overall cancer risk may be attributable to environmental and lifestyle factors [6, 7]. World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) [8, 9] and American Cancer Society (ACS) [10] guidelines for healthy weight, a diet rich in fiber-containing plant foods, and physical activity are important for lowering overall cancer risk, including BC prevention and improved post-diagnosis survival (Table 18.1) [10]. For the WCRF/AICR cancer prevention guidelines, the EpiGEICAM case-control study (973 incident cases of BC and 973 controls from 17 Spanish regions; age range 22–71 years) found a linear association between the degree of diet and lifestyle noncompliance and BC risk [11]. This study compared women who met six or more recommendations as reference women meeting less than three recommendations showed a ≥ three-fold increased BC risk, which as, especially true for postmenopausal women [11]. A high intake of energy dense foods and drinks that promote weight gain increased BC risk by 86%,

Table 18.1 Adult guidelines for nutrition and physical activity for cancer prevention

World Cancer Research Fund (WCRF)/ American Institute for Cancer Research (AICR) [8, 9]	American Cancer Society (ACS) guidelines [10]
Maintain a healthy lean body weight without being underweight	Achieve and maintain a healthy lean body weight throughout life
Be physically active for at least 30 minutes every day	Be as lean as possible throughout life without being underweight
Limit consumption of energy-dense foods (particularly processed foods high in added sugar, or low in fiber, or high in fat)	Avoid excess weight gain at all ages. For those who are currently overweight or obese, losing even a small amount of weight has health benefits and is a good place to start
Eat mostly plant foods including a variety of vegetables, fruits, whole grains, and legumes.	Engage in regular physical activity and limit consumption of high-calorie foods and beverages as key strategies for maintaining a healthy weight
Limit animal foods such as red and processed meats	Adopt a physically active lifestyle. Adults should engage in at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity activity weekly spread over the week
Limit alcoholic beverages (two for men and one for women a day)	Limit sedentary behavior such as sitting, lying down, watching television, or other forms of screen-based entertainment. Doing some physical activity above usual activities, no matter what one's level of activity, can have many health benefits
Limit consumption of salty foods and foods processed with salt	Choose foods and beverages in amounts that help achieve and maintain a healthy weight
Meet nutritional needs through diet	Limit consumption of processed meat and red meat
Breast feeding exclusively for up to 6 months	Eat at least 2.5 cups of vegetables and fruits each day
Cancer survivors should follow the recommendations for cancer prevention	Choose whole grains instead of refined-grain products
	If you drink alcoholic beverages, limit consumption. Drink no more than one drink per day for women or two per day for men

especially in premenopausal women. The low intake of healthy plant foods increased BC risk by 65%, especially in postmenopausal women. The Women's Health Initiative (65,838 postmenopausal women; mean age 63 years at baseline; mean 12.6 years follow-up; 8,632 cancer cases; 2,356 cancer deaths) found that women with the highest ACS guideline scores had significantly lower multivariate adjusted risk for any cancer by 17%, for BC by 22%, and for colorectal cancer by 52% and similar risk reduction for cancer mortality (Fig. 18.1a, b) [12].

The WCRF/AICR Continuous Update Project (CUP) supports ongoing expert panels to review the effects of diet and lifestyle on BC risk and survival. The 2017 report on the effect of food, nutrition, and physical activity on BC risk are summarized in Table 18.2 [2]. For premenopausal women, there is probable evidence that lactation, body fatness, and vigorous physical activity decreases and alcoholic beverages and greater birthweight increase BC risk, and suggestive evidence that physical activity, non-starch vegetables (ER-BC only), dairy products, foods containing carotenoids and diets rich in calcium decrease BC risk. For postmenopausal women, there was convincing evidence that alcoholic beverages, body fatness, and adult weight gain increase BC risk, probable evidence that physical activity, body fatness in young adulthood and lactation decrease BC risk, and suggestive evidence that non-starch vegetables (ER-BC only), foods containing carotenoids and diets rich in calcium decrease BC risk. The 2014 report on the effect of food, nutrition, and physical activity on BC survival and outcomes are summarized in Table 18.3 [3]. Before BC diagnosis, there is suggestive evidence that higher intake of dietary fiber-rich diets and physical activity decrease BC risk; and higher body fatness, total and saturated fat intake increase BC risk. Twelve months or more after BC diagnosis, there is suggestive evidence for improved survival odds with increased intake of fiber and soy rich diets and physical activity, whereas higher body fatness reduces survival odds.

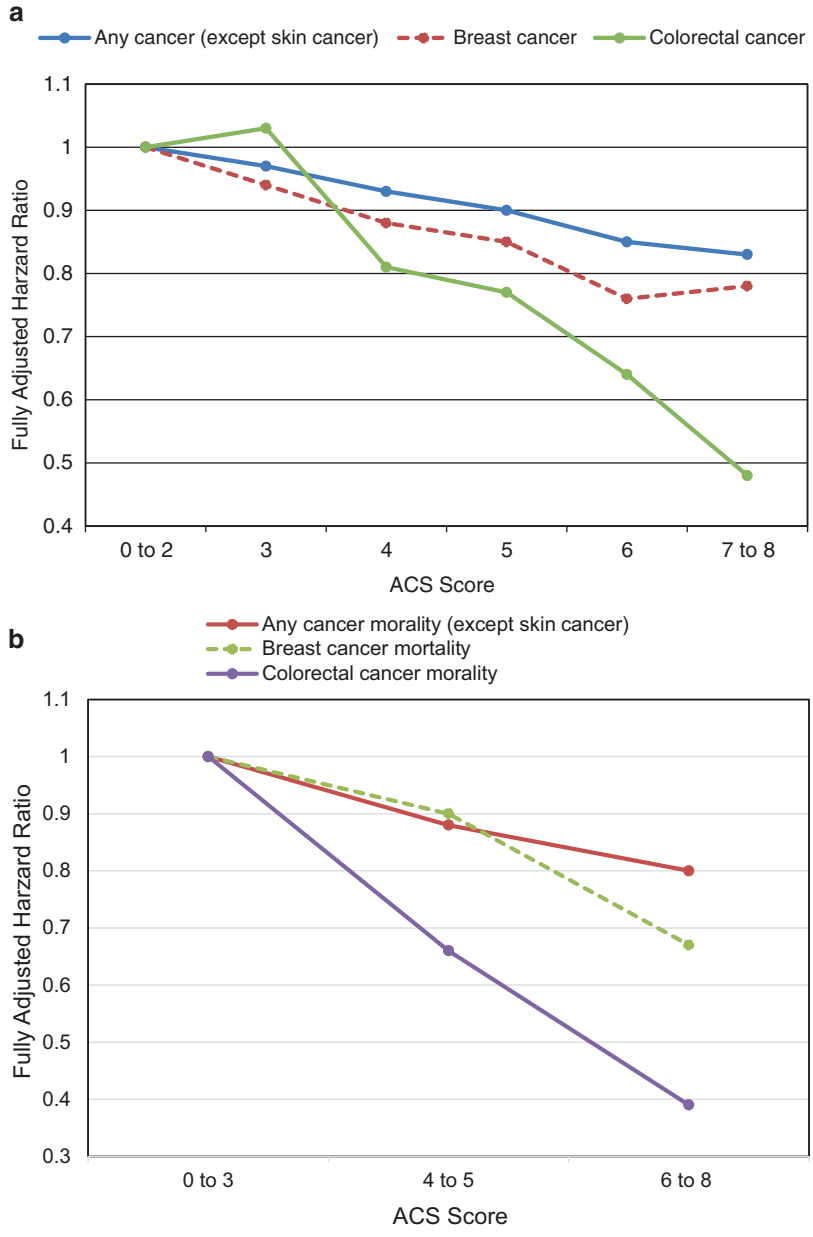

Fig. 18.1 (**a**) For postmenopausal cancer risk, the effect of American Cancer Society (ACS) cancer prevention score based on adherence to nutrition and physical activity guidelines from the US Women's Health Initiative (all cancers $p < 0.001$) [12]. (**b**) For postmenopausal cancer mortality, the effect of American Cancer Society (ACS) cancer prevention score based on adherence to nutrition and physical activity guidelines from the US Women's Health Initiative (all cancers $p < 0.001$) [12]

Table 18.2 Food, nutrition, and physical activity and breast cancer (BC) risk: 2017 consensus guidelines [2]

	Decrease risk	Increase risk
Premenopause Women		
Convincing		Adult attained height[a]
Probable	Vigorous physical activity Body fatness Lactation	Alcoholic beverages Greater birth weight
Limited—suggestive	Physical activity[b] Non-starchy vegetables (ER – BC only) Foods containing carotenoids Diets high in calcium Dairy products	
Postmenopause Women		
Convincing		Alcoholic beverages Body fatness Adult weight gain Adult attained height
Probable	Physical activity Lactation Body fatness in young adulthood	
Limited—suggestive	Non-starchy vegetables (ER – BC only) Foods containing carotenoids Diets high in calcium	

[a]Unlikely to directly modify BC risk as it is a marker of genetic, environmental, hormonal, and nutritional factors affecting growth during the period from preconception to completion of linear growth
[b]All type household, occupational, and recreational

Table 18.3 Food, nutrition, and physical activity and breast cancer (BC) survival: 2014 consensus guidelines [3]

By timeframe							
		Before diagnosis		Less than 12 months after diagnosis		12 months or more after diagnosis	
		Decreases risk	Increases risk	Decreases risk	Increases risk	Decreases risk	Increases risk
Limited evidence	Suggestive	Physical activity	Body fatness		Body fatness	Physical activity	Body fatness
		Fiber-rich foods	Total fat			Fiber-rich foods	
			Saturated fat			Soy foods	
By outcome							
		All-cause mortality		**Breast cancer mortality**		**Second primary breast cancer**	
		Decreases risk	**Increases risk**	**Decreases risk**	**Increases risk**	**Decreases risk**	**Increases risk**
Limited evidence	Suggestive	Physical activity	Body fatness	Physical activity	Body fatness		Body fatness
		Fiber-rich foods	Total fat				
		Soy foods	Saturated fat				

European Prospective Investigation into Cancer and Nutrition (EPIC) Cohorts

The multinational EPIC prospective study assessing the healthy lifestyle index score [HLIS], which is an index of combined healthy behaviors including diet, physical activity, smoking, alcohol consumption, and anthropometry with the highest health at 20 points (242,918 postmenopausal women; median age 53 years at follow-up; median 10.9-year follow-up; 7,756 BC cases) suggests that an improvement of each HLIS point equates to a 3% lower BC risk. Postmenopausal women with a high score (≥16 points) had reduced adjusted BC risk by 26% vs women with a low health score (≤5 points) (Fig. 18.2a)

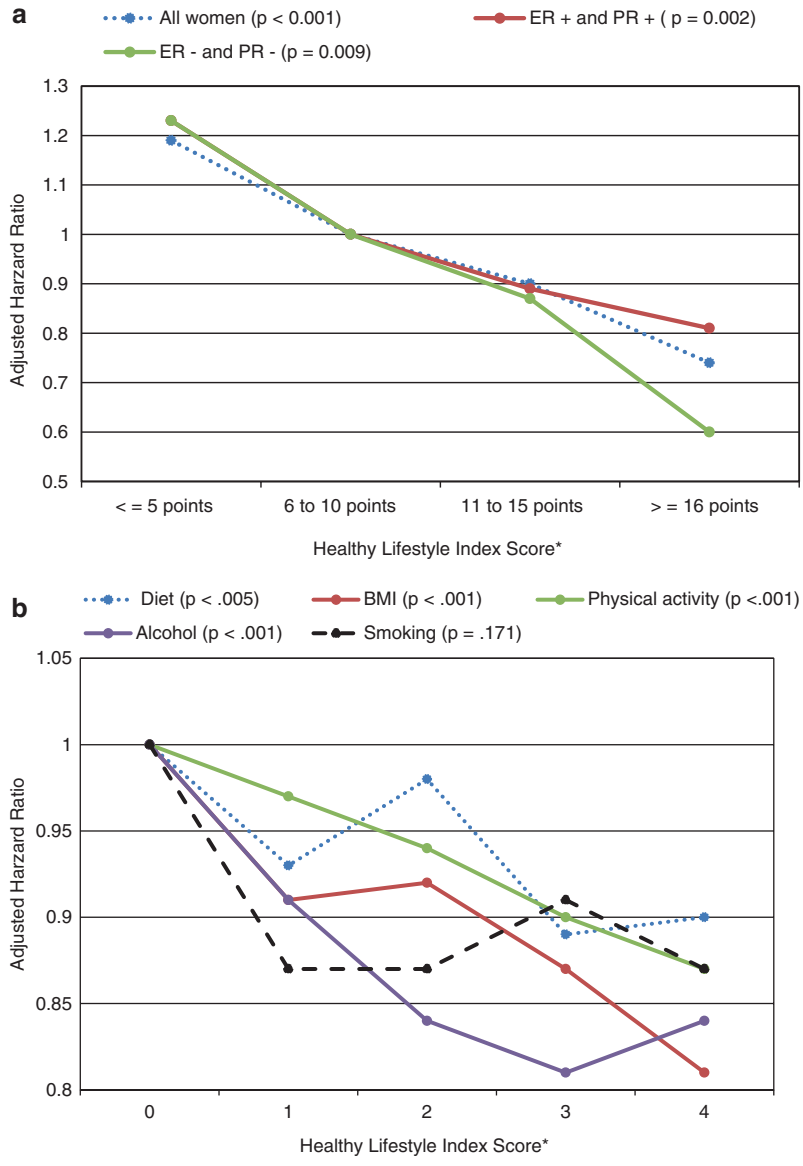

Fig. 18.2 (**a**) Association between healthy lifestyle index score (HLIS) and postmenopausal breast cancer risk from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study (n = 242,918; median 10.9-year follow-up; 7,756 breast cancer cases) [13]. (**b**) Association between healthy lifestyle index score (HLIS) and postmenopausal breast cancer risk from the EPIC cohort study over a median of 10.9 years [13]. *HLIS was constructed from five factors (diet, physical activity, smoking, alcohol consumption, and anthropometry) by assigning scores of 0–4 to categories of each component, for which higher values indicate healthier behaviors

[13]. For specific subtypes of BC, a healthier score was associated with a lower risk for hormone receptor double-positive BC by 19% and hormone receptor double-negative breast cancer by 40%. The effect for specific health behaviors on lowering BC risk is summarized in Fig. 18.2b.

Nurses' Health Study (NHS) Cohorts

A review of NHS I and NHS II cohort articles on BC incidence and survival published from 1976 to 2016 provides an excellent overview of lifestyle factors including diet, body weight, physical activity, and alcohol in BC risk [14].

Weight and Weight Change

The relationship between weight and BC risk is complex, as it varies across the lifespan [14]. Levels of body fatness in childhood and BMI at age 18 years are inversely associated with adult plasma insulin-like growth factor 1 (IGF-1) levels, a hormone similar in molecular structure to insulin which plays an important role in childhood growth and continues to have anabolic effects in adults. Also, early-life body size was inversely associated with percentage of mammographic density, which is a strong BC risk factor. Although higher BMI at age 18 years was inversely associated with both pre- and postmenopausal risk, weight gain after age 18 years was positively associated with risk after menopause, in those who never used hormone therapy (HT). In a subsequent analysis with 26 years of follow-up, it was observed that among women who never used HT, those who had lost more than 10 kg since menopause and maintained their weight loss had a lower risk of BC than women with stable weight since menopause. Finally, short-term gain over 4 years by $\geq$15 lb was associated with increased BC risk that was stronger for premenopausal than postmenopausal women compared to no weight change [15].

Alcohol

The most consistent dietary risk factor for BC risk is alcohol [14]. NHS II observed that alcohol consumption, even at low levels of consumption (10 g/day), both in early and later adult life was independently, significantly associated with increased BC risk.

Dietary Fat

Dietary fat intake was long hypothesized to be associated with higher rates of BC in affluent countries, based primarily on strong international correlations with BC incidence and fat intake, especially in animal studies [14]. However, NHS did not observed a significant association between dietary fat intake and BC risk.

Prudent (Healthy) Dietary Patterns Rich in Fiber

NHS analyses have identified several specific connections between prudent dietary patterns characterized by higher intakes of fiber-rich fruits, vegetables and whole grains, low-fat dairy, fish, and poultry and lower BC risk [14]. ER-negative tumors were shown to be inversely associated with non-starchy vegetable intake, which is consistent with carotenoids potential inhibition of BC tumor progression and proliferation. Early-life dietary factors can affect premenopausal BC risk with higher intake of red meat during high school years increasing risk by 43% higher and higher fiber intake during adolescence lowering risk by 16% risk [14]. Fifty high fiber plant foods in rank order are provide in Appendix 1.

Physical Activity

Physical activity is postulated to decrease BC risk by lowering ovarian hormone levels. NHS analyses suggest women who reported participating in ≥7 h of moderate or vigorous physical activity weekly had an 18% lower BC risk. In follow-up analyses, the cumulative and recent physical activities of postmenopausal women were inversely associated with BC risk, and among younger women lifetime physical activity was inversely associated with risk of premenopausal BC with a 33% risk reduction, comparing the most with the least active women. Also, NHS studies indicate that physical activity is important for survival after breast cancer diagnosis. For improved BC survival, benefits are observed for physical activity equivalent to walking 3–5 h weekly at an average pace or for those who follow the US recommendations of at least 30 min daily of moderate physical activity for at least 5 days weekly, independent of activity level before diagnosis.

Fiber Mechanisms

There are several potential biological mechanisms supporting a role for fiber in the prevention and survival of BC by attenuating: the risk of weight gain, body fatness and insulin resistance, and elevated circulating C-reactive protein (CRP) and estrogen (Fig. 18.3) [16]. Fiber intake is a major shortfall "nutrient," especially in highly developed countries such as the USA with high energy-dense diets where <5% of the populations consume adequate fiber with the mean intake being only about half of the recommended intake [17–21]. Analyses of US NHANES data found increasing fiber intake was significantly negatively associated with obesity (BMI > 30 kg/m^2), metabolic syndrome rate, and elevated CRP (≥3.0 mg/L), after multivariate adjustments [22].

Weight Gain and Body Fatness

The effect of weight gain and body fatness on BC risk depends on menopausal status. In postmenopausal women, a high BMI and abdominal fat increase circulating estrogen levels which are associated with increased BC risk, whereas in premenopausal women, the effects of body fatness and

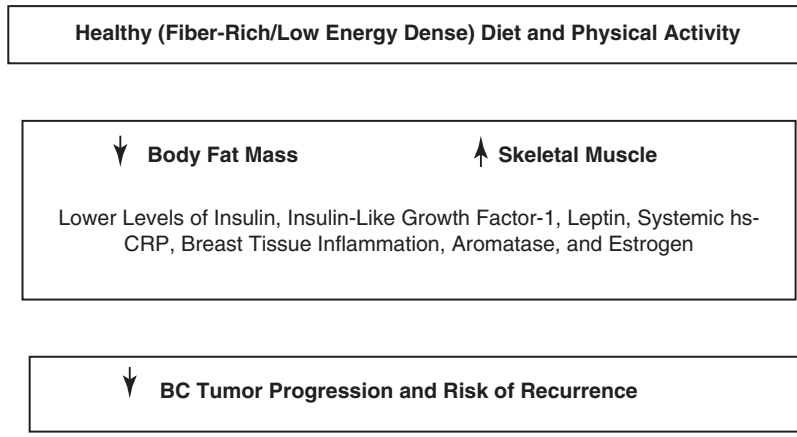

Fig. 18.3 Potential mechanisms mediating the impact of a healthy fiber and phytochemical-rich diet and exercise on breast cancer BC recurrence [16]

estrogen are not related to BC risk [2, 3, 14–16]. Significant excessive weight and abdominal fat gain after menopause is associated with an increased risk of estrogen-dependent BC [23], and short-term weight gain (4-year weight gain of ≥15 lb versus no change (≤5 lb)) in premenopausal women is associated with increased estrogen-independent BC risk [15]. In postmenopausal women, excessive visceral, subcutaneous, and breast fat results in chronic low-grade inflammation which is associated with the activation of NFkB signaling and elevated levels of aromatase, the rate-limiting enzyme in estrogen biosynthesis. The main source of estrogen in premenopausal women is the ovaries, but in postmenopausal women, it is adipose tissue. Interventions aimed at modifying weight, including diet and exercise, are associated with changes in adipose tissue inflammation and estrogen production that are likely to impact BC risk, especially ER+ tumors which depend on estrogen for growth.

Populations consuming higher-fiber and lower-energy-density dietary patterns tend to be leaner than those with low-fiber and higher-energy-density diets [24–29]. The US Scientific Report of the 2015 Dietary Guidelines Advisory Committee found that a prudent dietary pattern (adequate fiber and lower energy-dense plant-based whole foods) is associated with lower body weight outcomes, whereas a Western dietary pattern (inadequate fiber and high energy density higher in meats and refined plant foods) tends to increase weight [19]. A systematic review of 43 prospective cohort, case-control, and randomized trials found moderately strong evidence that fiber-rich foods have a protective role against weight gain and increased waist size [30]. In a study of 52 overweight/obese and 52 normal-weight adults matched for sex, age, and height, intake of fiber and daily servings of fruit were inversely related to percent body fat ($p = 0.01$) after controlling for potential confounding factors [27]. A prospective cohort study with 252 women over 20 months showed that increasing dietary fiber and the associated reduced energy intake over time significantly reduce the risk of gaining weight and body fat in women, independent of several potential confounders, including physical activity, dietary fat intake, and others [26]. The Finnish Diabetes Prevention Trial found that high-fiber and low-fat diets were the most effective dietary patterns to reduce body weight over time (Fig. 18.4) [24]. In middle-aged women, weight

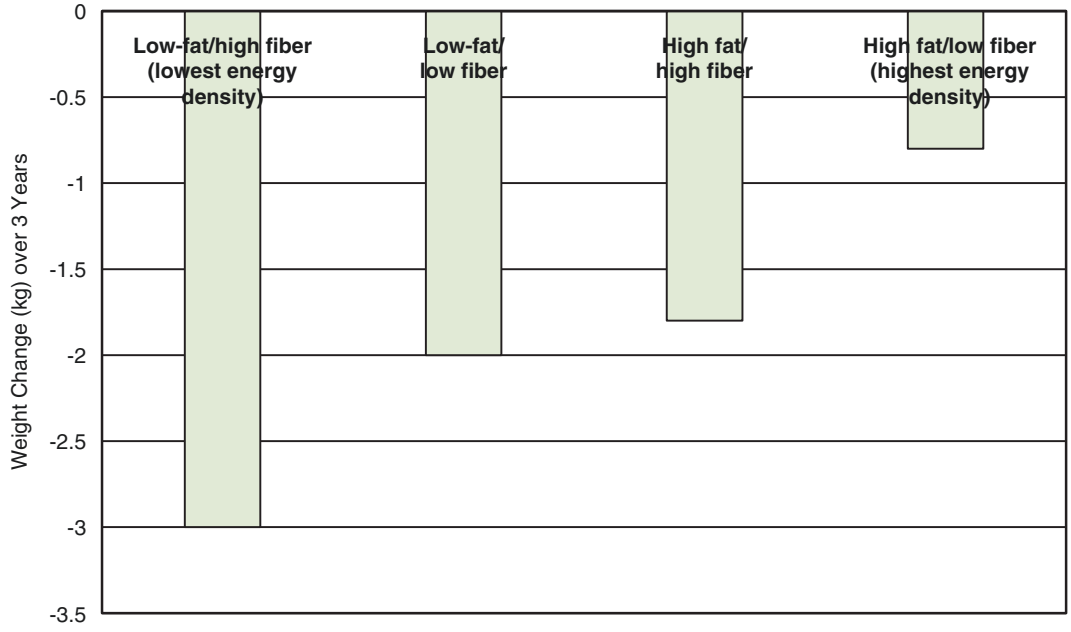

Fig. 18.4 Mean weight loss from baseline to year 3 in overweight middle-aged men ($n = 172$) and women ($n = 350$) with impaired glucose tolerance from the Finnish Diabetes Prevention Trial (adjusted for age, sex, baseline weight, baseline fiber and fat intake, and baseline and follow-up physical activity) [24]

gain was inversely associated with the intake of high-fiber and whole-grain foods but positively related to the intake of refined-grain foods, which indicated the importance of distinguishing whole-grain products from refined-grain products to aid in weight control [28]. The US Cancer Prevention Study II Nutrition Cohort (56,795 women; mean baseline age 69 years; 11.7 years of follow-up; 2,509 BC cases) found that in postmenopausal women after adjusting for age, race, education, reproductive characteristics, and family history, high vs low dietary energy density (1.7 vs 1.2 kcal/g) was associated with a statistically significantly higher risk of BC by 20% (p-trend = 0.03) [31].

The mechanisms associated with fiber's effect on body weight regulation include providing lower energy density, better satiation/satiety, and nutrient bioavailability to thereby improve energy intake control, hunger control, macronutrient metabolism, and reduced metabolizable energy via fecal excretion of macronutrients [32]. Fiber has an energy density in the range of 2 kcal/g compared to 4 kcal/g for digestible carbohydrates such as sugar and starch, and fiber-rich foods are often lower in fat content, which combined are important contributing factors for a lower dietary pattern energy density [33–35]. Fiber-rich foods are generally more physically dense and are slower to eat and digest than lower-fiber foods and can promote satiation/satiety by increasing gastric distention and suppressing food intake by altering intestinal satiety hormones such as peptide YY, cholecystokinin (CCK), and glucagon-like peptide-1 (GLP-1) [32, 36–39]. Fiber-rich foods tend to decrease the efficiency of macronutrient bioavailability, especially that of dietary fat, leading to higher fecal macronutrient excretion compared to low-fiber foods [40]. The consumption of >25 g fiber/day can lead to the excretion of 3–4% macronutrient energy in the feces, which is equivalent to 80 kcal in a 2000 kcal diet.

Insulin Resistance

Insulin resistance associated with prediabetes and type 2 diabetes (diabetes) increases the risk of BC in both pre- and postmenopausal women [41–44]. A systematic review and meta-analysis (22 observational studies; 33,405 women) found that insulin resistance (HOMA-IR) levels were significantly higher in BC patients ($p < 0.00001$) than in normal glycemic women [41]. Women with insulin resistance had higher BC risk for premenopausal women by 98% and postmenopausal women by 29% [42]. In women with diabetes, a meta-analysis (17 cohort studies; 48,315 women) found that insulin resistance is independently associated with poor overall BC survival by 51% [43]. Another meta-analysis (16 cohort studies; 891,426 women) showed that women with prediabetes were associated with an increased BC risk by 15% [44]. The potential biological mechanisms underlying insulin resistance and BC prognosis are complex [45–48]. Prediabetes and diabetes may directly influence BC prognosis through hyperinsulinemia and insulin-like growth factors, endogenous sex hormones, and inflammatory markers. Hyperinsulinemia and insulin-like growth factors may play roles in promoting BC development. Chronic pro-inflammatory conditions and oxidative stress induced by impaired glucose metabolism may promote tumor initiation and progression.

There is a strong association between high adherence to healthy dietary patterns and diets adequate in fiber intake (>25 g/day) and lower diabetes risk. A meta-analysis (15 cohort studies) found a 21% lower diabetes risk for the highest adherence compared to the lowest adherence to healthy dietary patterns compared to a 44% increase in risk for the highest adherence compared to the lowest adherence to unhealthy dietary patterns ($p < 0.005$) [49]. Several meta-analyses of prospective studies show an inverse association between fiber intake and diabetes risk, especially for total fiber, cereal fiber, and whole-grain intake [50, 51]. Three large US cohort studies (74,248 women from the NHS 1, 90,411 women from the NHS 2, and 40,498 men from the Health Professionals Follow-Up Study; followed for 18–24 years) showed that diets high in glycemic index or load and low in cereal fiber are associated with a significantly 50% higher diabetes risk [52]. Increasing fiber intake, particularly by consuming

healthy dietary patterns rich in fiber and low in energy density and glycemic foods, is highly likely to reduce insulin resistance and diabetes risk and increase overall health and wellness. Three long-term RCTs over 3–6 years including PREvención con Dieta MEDiterránea [PREDIMED] Diabetes Prevention, Da Qing Diabetes, and Finnish Diabetes Prevention trials support the importance of consuming healthy fiber-rich diets (>25 g fiber/day) for reduced risk of developing diabetes by 18–58% [53–55]. An Italian RCT with 180 middle-aged adults with metabolic syndrome consuming a Mediterranean-style diet (32 g fiber/day including 487 g/day of whole grains, vegetables, fruit, legumes, and nuts) found significantly lower insulin resistance (HOMA-IR scores), serum insulin, and plasma glucose compared to those on a control lower-fiber prudent diet (15 g fiber/day including 201 g/day of whole grains, vegetables, fruit, legumes, and nuts) over 2 years [56].

CRP Levels

Aging is generally associated with increased chronic low-grade systemic inflammation, known as "inflammaging" [57]. Consequently, postmenopausal women are more likely than premenopausal women to have chronic elevated circulating CRP levels, a sensitive widely used marker of systemic inflammation, and other pro-inflammatory mediators, which may play a role in a higher risk of carcinogenesis, including cancer initiation, promotion, progression, metastasis, and other clinical features that may be related to breast cancer development and survival [58, 59]. A meta-analysis (15 cohort and case-control studies; 107,199 women primarily postmenopausal; 5,286 BC cases) found that each natural log unit increase in CRP levels was associated with a 16% increased BC risk [60]. The association was stronger in Asian populations with a BC increased risk by 57% compared with an increase of 12% for Europeans and 8% for Americans. Two other meta-analyses show modest but significant elevated BC risk with increasing CRP levels in a dose-response manner [61, 62]. A case-cohort analysis nested within the Women's Health Initiative Observational Study (875 BC cases and 839 controls) showed that postmenopausal women not using hormone theraphy with elevated CRP levels had increased BC risk by 67% compared to women with CRP levels (*P*-trend = 0,029) [63]. Also, meta-analysis found elevated CRP to be predictive of poorer BC survival [59].

Numerous observational studies and RCTs are generally supportive of the protective role of increased fiber intake in decreasing CRP levels. The Health, Eating, Activity, and Lifestyle (HEAL) study, a cross-sectional multicenter, multiethnic cohort (698 early-stage breast cancer survivors; 24-month post-study assessment), showed that diets with 20 g fiber or more/day were associated with lower risk of elevated CRP (defined as >3.0 mg/L) by 49% (p-trend = 0.053) vs diets with <5.4 g fiber/day [64]. A meta-analysis (14 RCTs) showed that increasing fiber intake by ≥8 g/day above control diet significantly lowered CRP levels by 0.5 mg/L in overweight or obese adults and when baseline CRP was ≥3 mg/dL, there was a lowering of CRP levels by 0.72 mg/L for higher fiber intake ($p = 0.06$) [65]. A systematic review found that in six of seven RCTs with high-fiber diets, ≥14 g fiber/1000 kcal, in the presence of weight loss and healthier dietary fat intakes, significantly lowered CRP concentrations by 25–54% vs control diets [66]. The Finnish Diabetes Prevention Study reported that fiber intake was inversely associated with CRP after adjustments for BMIs [67]. A Mediterranean diet RCT (180 metabolic syndrome subjects, 99 men and 81 women; 2 years) found that subjects on 32 g fiber/day diets had significantly lower hs-CRP by 39% ($p = 0.01$) than those on 15 g fiber/day diets [56]. For the DASH dietary pattern, people consuming 30 g fiber/day from diet alone or from 18 g psyllium fiber supplementation/day added to the usual diet had significantly reduced CRP levels by 14 and 18%, respectively, after 3 weeks compared to those on 12 g fiber/day diets ($p < 0.05$) [68]. Fiber related CRP lowering mechanisms include: reducing the risk of weight gain, promoting microbiota health, and improving cardiometabolic health [66, 69–70].

Estrogen Levels

The relationship between circulating estrogen levels and BC risk is complex involving BMI, menopausal status, diet during adolescence, and estrogen-only hormone replacement therapy (HRT) [71–74]. An estrogen modeling study predicts a decrease in the relative risk of BC by 3% per unit increase in BMI for premenopausal women and an increase in risk by 4% per unit increase in BMI for postmenopausal women who are not HRT users [72]. In postmenopausal women, higher serum levels of estrogens (e.g., estradiol) and androgens and lower levels of sex hormone-binding globulin (SHBG), which determines the pool of estrogens that can enter cells, have been associated with increased BC risk after adjusting for mammographic density [74–76]. For early-stage BC survival after diagnosis, a nested case-control cohort of women from Women's Healthy Eating and Living [WHEL] RCT (153 cases vs 153 control) found a significant independent association between serum concentrations of total, bioavailable, and free estradiol and risk for BC with a doubling of recurrence risk for women with an average total estradiol concentration of 22.7 versus 10.8 pg/mL ($p = 0.05$) [77].

Diets high in fiber have been hypothesized to reduce BC incidence by decreasing estrogen circulating levels [78, 79]. Mechanisms for the effect of fiber on estrogen include sequestration of estrogen in the digestive system and reduction of β-D-glucuronidase activity in the digestive system, resulting in increased estrogen excretion in the feces [80–83]. Since conjugated estrogens in the liver are excreted into the bile and reabsorbed in the intestine, unfermented fiber has the capacity to bind estrogens or reduce the rate of hydrolysis of conjugated estrogens in the colon during the enterohepatic circulation to increase the fecal excretion of estrogens resulting in less reabsorption of estrogens and lower serum levels. Three meta-analyses of prospective studies all found moderate but significant inverse associations for 10 g fiber/day increments resulting in 4–7% lower BC risk [84–86]. Generally, the evidence on fiber intake and BC risk is based on studies in which women were enrolled during midlife or later with minimal studies on the effects of fiber on estrogen changes during adolescence or early adulthood and BC incidence until recently with the new findings from the Nurses' Health Study II (NHSII) cohort [87–89]. A 2003 NHSII analysis found that higher vs lower fiber intake during adolescence was inversely related to the incidence of proliferative benign breast disease (BBD), an early step in breast carcinogenesis, and a 25% lower adult BC risk (p-trend = 0.05; multivariate adjusted) [87]. A follow-up 2010 NHS II analysis confirmed that increased fiber intake during adolescence was inversely associated with proliferative BBD and showed that among the fiber-rich food sources, total nuts and peanuts were the most effective in significantly lowering BBD risk (Fig. 18.5) [88]. A 2016 NHS II analysis showed that higher fiber intakes during adolescence and early adulthood reduced BC risk. For the average of fiber intake during adolescence and early adulthood, 25–28 g total fiber/day vs 15–18 g total fiber/day reduced BC risk by 25% (p-trend = 0.004) [89].

Dietary Fiber and Breast Cancer Prevention

Supportive Observational Studies

Meta-analyses

Meta-analyses of observational studies consistently show that increased fiber intake is associated with moderate but significantly lower BC risk (Table 18.4) [84–86, 90]. Three meta-analyses of cohort studies (up to 20 cohorts and 3,662,421 women; up to 51,939 BC cases; 1 to 20-year follow-up) found that fiber is inversely associated with BC risk with a 4–7% lower risk per 10 g fiber/day [84–86]. An increase in fiber intake by 15 g/day reduced BC risk by 7–12% especially in postmenopausal women. A meta-analysis of case-control studies (12 studies; 4,427 cases and 6,095 controls) showed that a

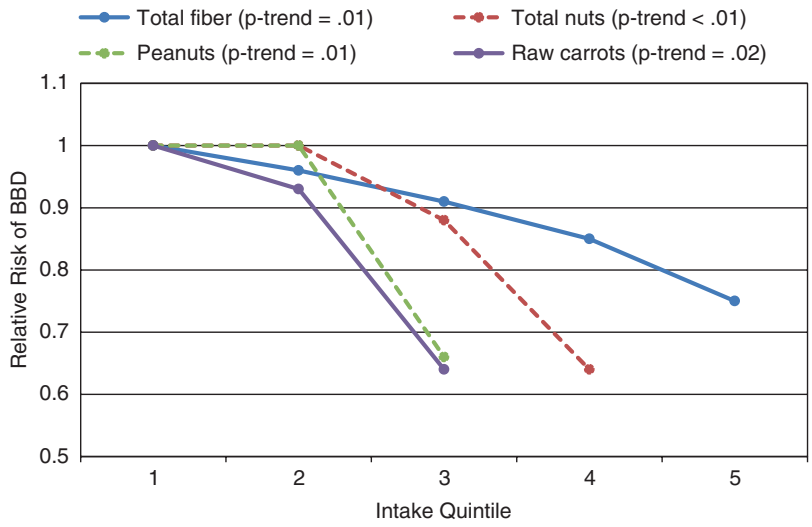

Fig. 18.5 Effect of level of total fiber, total nuts, peanuts, and carrots consumed during adolescence on adult risk of proliferative benign breast disease (BBD): total fiber (mean intake 15.1–27.5 g/day), total nut intake (1 oz.; <1/month to ≥2/week), peanuts (1 oz.; <1/month to >1/week), and carrots (2–3 servings/month to >1 serving/week) [87]

20 g increased total fiber intake significantly reduced BC risk in all women by 15%, postmenopausal women by 17%, and premenopausal women by 11% [89].

Prospective Cohort Studies

Table 18.4 summarizes ten cohort studies supporting increased fiber intake effects in reducing BC risk [78, 87–89, 91–96]. Three cohort studies from the NHS II showed significant effects of higher total fiber and fiber-rich diets during adolescence and early adulthood resulting in lower proliferative benign breast disease (BBD) and BC risk in adult women [87–89]. For women with proliferative BBD; in youth two NHS II analyses found that increasing fiber intake during adolescence was inversely associated with BC risk in adult women by 25% (median 27.5 vs 15.1 g total fiber/day; *p*-trend = 0.01; multivariate adjusted) [87, 88]. There was a significant inverse association between increasing intake of total fiber, tree nuts, peanuts, and raw carrots on proliferative BBD risk (Fig. 18.5) [87]. Similar results were observed in another study with nuts and apples [88]. For BC risk, a NHS II analysis (90,534 premenopausal women who completed a dietary questionnaire in 1991; 20 years of follow-up; 2,833 BC cases) found that the highest vs lowest quintiles of fiber intake during adolescence and early adult life reduced adult BC risk by 25% (*p*-trend = 0.004; multivariate adjusted) [89]. Figure 18.6 summarizes the significant effects of early fiber intake on reducing adult premenopausal BC risk. The effect of increased total fiber intake during adolescence and early adulthood lowered postmenopausal BC risk insignificantly by 13–15%. A 2013 EPIC analysis (334,849 women; mean baseline age 50 years; 11.5-year follow-up; 11,576 BC cases) showed modest significantly reduced BC risk with increased intake (highest vs lowest quintiles) of total fiber by 5% and vegetable fiber (excluding potatoes, legumes, soy, and tomato products) by 10% [78]. All observed associations were consistent with a protective fiber effects from vegetables by menopausal and ER status, with the largest protective association observed in ER (−) and PR (−) (Fig. 18.7). In premenopausal women, high fiber(>26 g/day) and low fat (≤63 g/day) diets reduced BC risk by 34% compared to high fat and low fiber diets (≤63 g/day). The 2009 US NIH-AARP Diet and Health study (185,598 postmenopausal women; mean baseline age 62 years; mean 7-years of follow-up; 5,461 BC cases) found that mean total fiber/day intake (26 g vs 11 g) was inversely associated with multivariate BC risk by 13%

Table 18.4 Summaries of observational studies supporting an association between fiber and reduced breast cancer (BC) risk (multivariate adjusted)

Objective	Study details	Results
Systematic reviews and meta-analyses		
Chen et al. Update previous meta-analysis on the effectiveness of total fiber intake on BC risk [84]	20 cohort and 4 case-control studies; 3,662,421 participants; 51,939 cases; USA ($n = 8$), Canada ($n = 2$), Europe ($n = 12$), China ($n = 1$), and Malaysia ($n = 1$); 1 to 20-year follow-up	This analysis showed that the highest total fiber intake significantly reduced BC risk by 12%, particularly in postmenopausal women ($p = 0.027$) vs lowest intake. Dose-response analysis found that every 10 g total fiber intake was inversely associated with a 4% reduction in BC risk ($p < 0.002$)
Aune et al. Assess the effectiveness of total fiber and specific fiber source intake on BC risk by systematic review and meta-analysis [85]	16 cohort studies, 500,000–1,000,000 participants; 15,000–26,000 cases	This analysis found an overall 7% lower BC risk for higher total fiber intake, but significant risk reduction was only observed among studies with fiber intake increased by ≥13 g/day vs <13 g or total fiber intake ≥25 g fiber/day vs <25 g/day. Dose-response analyses showed lower BC risk per 10 g total fiber by 5%, soluble fiber by 9%, insoluble fiber by 5%, fruit fiber by 5%, and cereal fiber by 4% but only 1% for vegetable fiber
Dong et al. Examine the association between total fiber intake and risk of BC by conducting a meta-analysis of prospective cohort studies [86]	10 cohort studies; 712,195 participants; 16,848 cases; North America ($n = 5$), Europe ($n = 4$), and China ($n = 1$); studies with premenopausal women ($n = 2$), postmenopausal women ($n = 5$), both ($n = 3$); follow-up period ranged from 4.3 to 18 years, with a median of 8 years	This analysis found a significant 11% lower BC risk based on all women with a total fiber intake increased by 15 g/day. Of these studies, two studies reported a statistically significant inverse effect, and six studies showed an inverse trend between fiber intake and risk of BC. Dose-response analysis found a significant 7% reduction in BC risk for every 10 g/day increment fiber intake (p-trend = 0.004) based on six of the studies with no evidence of heterogeneity
Howe et al. Evaluate the effect of dietary factors on BC risk from case-control studies [90]	12 case-control studies; 4,427 cases and 6,095 controls	This analysis showed that high fiber intake was associated with a significant 15% reduction in BC risk. An increased intake of 20 g total fiber/day significantly reduced BC risk by 15% for all women ($p = 0.001$), 17% for postmenopausal women ($p = 0.002$), and 11% for premenopausal women ($p = 0.15$). However, the difference in BC risk between post- and premenopausal women was not significant
Prospective cohort studies		
Farvid et al. Evaluate fiber intake during adolescence and early adulthood in relation to BC risk (Nurses' Health Study II, USA) [89]	90,534 women; mean baseline age 36.4 years; 20-year follow-up; 2,833 women were diagnosed with BC; 44,263 of these women had data on adolescent fiber intake; 1,118 women were diagnosed with BC	This study suggests that higher fiber intake during adolescence and early adulthood may be especially important in reducing BC risk. Higher total fiber intake in adolescence and early adult life reduced BC risk by 25% (p-trend = 0.004). Higher total fiber intake during adolescence was associated with a 16% lower BC risk (p-trend = 0.04). Among all women, higher total fiber intake in early adulthood significantly lowered BC risk by 19% (p-trend = 0.002); higher intakes of soluble fiber lowered risk by14% (p-trend = 0.02); and insoluble fiber reduced risk by 20% (p-trend < 0.001). Fig. 18.6 summarizes the effects of early age fiber intake on reducing adult premenopausal BC risk

Table 18.4 (continued)

Objective	Study details	Results
Chhim et al. Assess the relation between alcohol intake and the risk of hormone-dependent breast cancer and investigate whether fiber intake modulated these associations (Supplémentation en Vitamines et Minéraux AntioXydants study, France) [91]	3,771 women; completed at least six valid 24-h dietary records during the first 2 years of follow-up. After a median 12-year follow-up, 158 BC cases were found	This study suggests that high alcohol consumption and low fiber intake may cumulate and act synergistically to increase hormone-dependent BC risk. Overall, high alcohol intake was directly associated with the increased risk of hormone-dependent BC by 70% (p-trend = 0.04). In stratified analyses, the combination of low fiber intake and high alcohol intake was directly associated with hormone-dependent BC risk increase by 1.5-fold (p-trend = 0.02) but not among women with higher fiber intake (p-trend = 0.8)
Ferrari et al. Investigate associations between total fiber and its main food sources (vegetables, fruit, cereals, and legumes) and BC risk (the European Prospective Investigation into Cancer and Nutrition [EPIC]) [78]	334,849 women; mean baseline age 50 years (35–70 years); tumor subtypes, estrogen receptor (ER) + and ER− tumors, progesterone receptor (PR) + and PR-tumors, and human epidermal growth factor receptor (HER) 2+ and HER2− tumors; median follow-up of 11.5 years; 11,576 invasive BC cases	This study found that diets rich in total fiber and, particularly, vegetable fiber modestly and significantly reduced BC risk, independently of menopausal status. Total fiber was inversely associated with BC risk by 7% for each 10 g total fiber intake. Total fiber (<17.6 to >26.3 g/day) lowered BC risk by 5%; (p-trend = 0.03). In premenopausal women, there was a significant 34% lower risk (p-trend = 0.02) for those consuming both high-fiber (>26 g/day) and low-fat (≤63 g/day) diets compared with high-fat (>89 g/day) and low-fiber (≤18 g/day) diets but this interaction between fiber and fat intake was not significant in post-menopausal women. For vegetable fiber, BC was reduced by 15% for each 5 g/day intake (p-trend = 0.01; excluding potatoes, legumes, and soya and tomato products), independent of menopausal status. For tumor subtype, vegetable fiber was significantly protective for all BC risk regardless of menopausal or hormone receptor status (Fig. 18.7)
Su et al. Examine associations between adolescent fiber intake and proliferative benign breast disease (BBD), a marker of increased breast cancer risk (Nurses' Health Study II, USA) [88]	Among 29,480 women who completed a high school diet questionnaire in 1998; 682 proliferative BBD cases were identified and confirmed by centralized pathology review	This study supports the adequate intake of total fiber during adolescence and subsequent lower risk of BBD and protection against BC. Women in the highest quintile (median intake 27.5 g/day) of adolescent fiber intake had a 25% lower risk of proliferative BBD (p-trend = 0.01) than women in the lowest quintile (median 15.1 g/day). High school intake of nuts and apples was also related to significantly reduced BBD risk
Park et al. Evaluate the relation of fiber intake to BC by hormone receptor status and histologic type among postmenopausal women (National Institutes of Health-AARP Diet and Health Study, USA) [92]	185,598 postmenopausal women; mean age, 62 years; average 7-years of follow-up; 5,461 BC cases were identified, of which 3,341 cases had known ER and PR status	This study suggests that fiber can play a role in preventing BC through non-estrogen pathways among postmenopausal women. Higher total fiber intake was inversely associated with a 13% lower BC risk (p-trend = 0.02). The association was stronger for ER^-/PR^- tumors with lower risk by 44% (p-trend = 0.008) than for ER+/PR+ tumors with a lower risk by 5% (p-trend = 0.47). BC risk for lobular tumors was reduced by 34% (p-trend = 0.04), and ductal tumors was reduced by 10% (p-trend = 0.10). Fruit was the most effective dietary fiber source in reducing BC risk. Soluble fiber intake was inversely associated with BC by 17% (p-trend = 0.02). Total fiber effects on lowering the risk of BC were independent of the level of dietary fat intake (p = 0.08)

(continued)

Table 18.4 (continued)

Objective	Study details	Results
Sonestedt et al. Examine the association between fiber, plant foods, and breast cancer, especially related to estrogen receptor (ER) BC (Malmo Diet and Cancer cohort, Sweden) [93]	15,773 women, baseline age 46–75 years; 544 invasive BC cases; mean age at diagnosis 63 years; mean follow-up of 10.3 years; dietary information collected by a modified diet history method	High intake of fiber-rich bread was associated with reduced BC by 25% (median 65 vs 0 g/day; $p = 0.04$). The highest quintile of total fiber was associated with a nonsignificant decreased risk of BC by 18% (median 26 vs 12 g/day; $p = 0.40$). Other plant foods were not significantly associated with BC incidence. There was a tendency for an inverse association for high-fiber bread with ERα (+) breast cancer (p-trend = 0.06) and ERβ (+) breast cancer (p-trend = 0.06). Fried potatoes were statistically significantly associated with increased risk of ERβ (−) breast cancer ($p = 0.01$)
Suzuki et al. Evaluate the association between total fiber and fiber subtypes on ER/PR-defined BC risk stratified by postmenopausal hormone (PMH) use, alcohol intake, and family history of breast cancer (Swedish Mammography Screening Cohort) [94]	51,823 postmenopausal women; mean baseline age approx. 59 years; average 8.3-year follow-up; 1,188 BC cases with known ER/PR status were diagnosed	This study showed nonsignificant inverse associations between higher total fiber intake and the risk of all BC tumor subtypes by 15% (p-trend = 0.09; 29 vs 17 g/day). For PMH users, total fiber reduced all BC tumors risk by 50% (p-trend < 0.0001; 29 vs 17 g/day) Fruit fiber significantly reduced overall BC risk by 34% (p-trend = 0.007) and for ER/PR (+) tumors by 38% (p-trend = 0.022). Cereal fiber, among PMH users, was significant inverse association with lower risk of all BC by 56% and ER/PR (+) tumors by 59% (p-trend < 0.001). For never PMH users, vegetable fiber was inversely associated with BC risk by 35% (p-trend = 0.003)
Cade et al. Examine associations between total fiber and fiber source on BC risk in a cohort including large numbers of vegetarians (the UK Women's Cohort Study) [95]	35,792 women (17,781 postmenopausal women and 15,951 premenopausal women at baseline); mean baseline age 52 years (mean 45 years premenopausal and 59 years menopausal); 18% vegetarian; 10-year follow-up; cases of invasive BC (350 postmenopausal and 257 premenopausal); total fiber intake ranged from <20 g/day up to >30 g/day	This study supports the protective role of total fiber against premenopausal BC. Higher total fiber intake was significantly inversely related to BC risk by 52% (p-trend = 0.01; 30+ vs <20 g/day). Also, higher cereal fiber was inversely associated with BC risk by 41% (p-trend = 0.05; 13+ vs <4 g/day), and fruit fiber had a borderline inverse BC risk-lowering effect by 19% (p-trend = 0.09; 6+ vs <2 g/day). No significant BC-lowering effects were seen for postmenopausal women
Mattisson et al. Investigate the associations between intakes of plant foods, fiber, and dietary fat on BC risk (the Malmo¨ Diet and Cancer cohort, Sweden) [96]	11,726 postmenopausal women; 342 BC cases; 11-year follow-up	This study supports the hypothesis that dietary patterns high in fiber and low/moderate in fat are associated with lower risk of postmenopausal BC. High fiber intakes were associated with a lower risk of postmenopausal BC by 42% (25.9 vs 12.5 g/day; p-trend = 0.056). A significant interaction ($p = 0.049$) was found between fiber and fat tertiles with higher-fiber and lower-fat dietary patterns having the optimal impact for reducing postmenopausal BC risk
Baer et al. Examine associations between components of adolescent diet and risk of proliferative benign breast disease (BBD), a marker for breast cancer (Nurses' Health Study II, USA) [87]	29,494 women; age 33–53 years; completed a questionnaire on adolescent diet in 1998; 7-year follow-up; 470 new cases of proliferative BBD	This study found that increasing intake of vegetable fat, vitamin E, and fiber during adolescence is inversely associated with adult proliferative BBD risk. There was a significant inverse association between the increasing intake of total fiber, nuts, and raw carrots on proliferative BBD risk (Fig. 18.5). There was a reduction by 25% for women in the highest vs lowest quartile of fiber intake during adolescence (p-trend = 0.05)

Table 18.4 (continued)

Objective	Study details	Results
Case-control studies		
Tajaddini et al. Investigate the association between resistant starch (RS) fiber-containing foods and BC risk (Iran) [97]	306 women newly diagnosed with BC and 309 healthy women; mean age approx. 44 years; mean BMI 28; validated, semiquantitative FFQ	This study suggests that certain RS fiber-containing foods can reduce BC risk. Higher intake of RS rich foods such as whole-grain breads, boiled/baked potatoes, and legumes significantly reduced BC risk by 47%, 62% and 99%, respectively. In contrast, the high intake of lower RS fiber foods such as white bread and biscuits was positively related to increased BC risk by 44% and 50%, respectively ($p < 0.001$)
Liu et al. Evaluate the associations between total fiber intake during adolescence and adult BC risk (Canada) [98]	2,865 BC cases and 3,299 controls; mean age 56 years; diets when the subjects were aged 10–15 years were assessed by FFQ	This study observed an inverse association between total fiber, vegetable protein, vegetable fat, and nut intake during adolescence and BC risk after adjusting for adult intake. Significant lower BC risks were shown for the highest intake of total fiber by 34% (p-trend = 0.001), for vegetable protein by 20% (p-trend = 0.01), vegetable fat by 26% (p-trend = 0.002), and for nuts by 24% (tree nuts, peanuts and peanut butter; ≥1 serving/day vs <1 serving/day; p-trend = 0.04) vs the lowest intake
Sulaiman et al. Examine the association of premenopausal and postmenopausal BC risk with dietary carbohydrate, fiber, and sugar intake (Malaysia) [99]	382 BC patients and 382 controls; mean age 50 years; food intake pattern was assessed via an interviewer-administered FFQ	This study found that sugar and total fiber intake were independently related to pre- and postmenopausal BC risk. For a higher total fiber intake, there was a significantly lower BC risk among premenopausal women by 69% (p-trend = 0.009) and postmenopausal women by 77% (p-trend = 0.031). For higher sugar intake, there was a significant twofold increased BC risk among premenopausal (p-trend = 0.001) and postmenopausal (p-trend = 0.045) women
Li et al. Evaluate the effect on BC risk by the type of fiber consumed, the patient's menopausal status, and the tumor's hormone receptor status (Yale–New Haven Study; USA) [100]	557 BC cases and 536 age controls; dietary intakes from in-person interviews with a semiquantitative FFQ; soluble fiber >6.2 vs <3.6 g/day	This study showed that among premenopausal women, higher intake of soluble fiber was associated with a reduced risk of BC by 62% (p-trend = 0.08). When further restricted to premenopausal women with ER (−) tumors, BC risk was significantly lowered by 85% (p-trend = 0.02) for soluble fiber intake. Among postmenopausal women, no reduced risk of BC was observed for either soluble or insoluble fiber intakes or among ER (+) or ER (−) tumor groups
Zhang et al. Investigate the link between total fiber and fiber fraction intake and BC risk by ER and PR status in a hospital-based case-control study among Chinese women [101]	438 cases with primary BC and 438 controls matched by age and residence (rural/urban); dietary intake through a face-to-face interview with a validated FFQ	This study suggests that the higher intake of total fiber and vegetable and fruit fiber was inversely associated with BC risk. There was a significantly lower BC risk for the highest quartile intake of total fiber by 69% (p-trend < 0.001), soy fiber by 27% (p-trend = 0.013), vegetable fiber by 52% (p-trend < 0.001), and fruit fiber by 46% (p-trend = 0.001) vs the lowest fiber intake. The inverse association was stronger in all ER/PR tumors subtypes

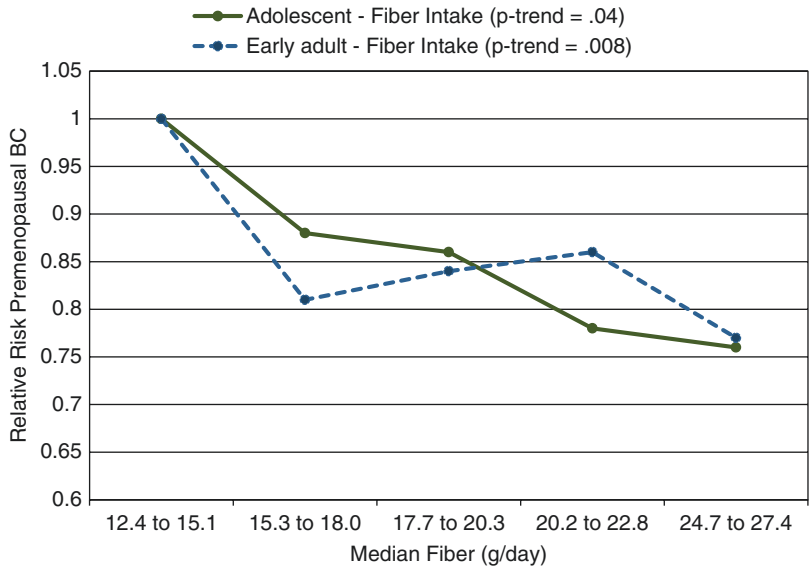

Fig. 18.6 Effect of adolescent and early adulthood fiber intake on adult premenopausal breast cancer risk [89]

(p-trend = 0.02) with an insignificant interaction with total fat intake (p = 0.08) [92]. The inverse association was stronger for ER (−)/PR (−) tumors by 44% (p-trend = 0.008) and lobular tumors by 44% (p-trend = 0.04). Of the fiber sources and types, fruit fiber and soluble fiber had the strongest effects on reducing BC risk. For postmenopausal women, three Swedish cohort studies generally support the BC risk-lowering effects of increased intake of total fiber or fiber-rich foods such as fiber-rich bread [93, 94, 96]. For premenopausal women, the UK Women's Cohort Study (35,792 women; mean baseline age 52 years; 10-year follow-up) found that the consumption M ≥30 g fiber/day vs. vs <20 g/day reduced BC risk by 52% (p-trend = 0.01) [95]. The French Supplémentation en Vitamines et Minéraux AntioXydants study (3,771 women; baseline age 46–75 years; 12-year follow-up; 158 BC cases) showed that the combination of high alcohol and low total fiber increased hormone-dependent BC risk by 153% (p-trend = 0.02), but there was no significant increase among women with higher fiber intake [91].

Case-Control Studies

Table 18.4 summarizes five case-control studies supporting the effects or increased fiber intake on reducing BC risk [97–101]. Two studies show that high-fiber foods or foods rich in resistant starch including whole-grain breads, baked potatoes, and legumes significantly lower BC risk by 47–99% and highly refined carbohydrates such as white bread, biscuits, and sugar may significantly increase BC risk by 44–200% in pre- and postmenopausal women [97, 99]. A US study (557 BC cases and 536 controls) found that in all premenopausal women higher soluble fiber intake (>6.2 vs <3.6 g/day) reduced multivariate BC risk by 62% (p-trend = 0.08) and ER (−) premenopausal women by 85% (p-trend = 0.02) [100]. A study among Chinese women (438 cases and 438 controls) reported significantly reduced BC risk for higher total fiber by 69% and fruit and vegetable fiber by 27–52% with higher reduction in all ER/PR tumor subtypes [101]. A large Canadian study (2,865 BC cases and 3,200 controls; dietary intake at age 10–15 years) showed higher total fiber intake in adolescent diets significantly lowered adult BC risk by 34% (p-trend = 0.01) and similar significant BC-lowering effects were observed for high vegetable protein and fat, tree nut, peanut, and peanut butter intake [98].

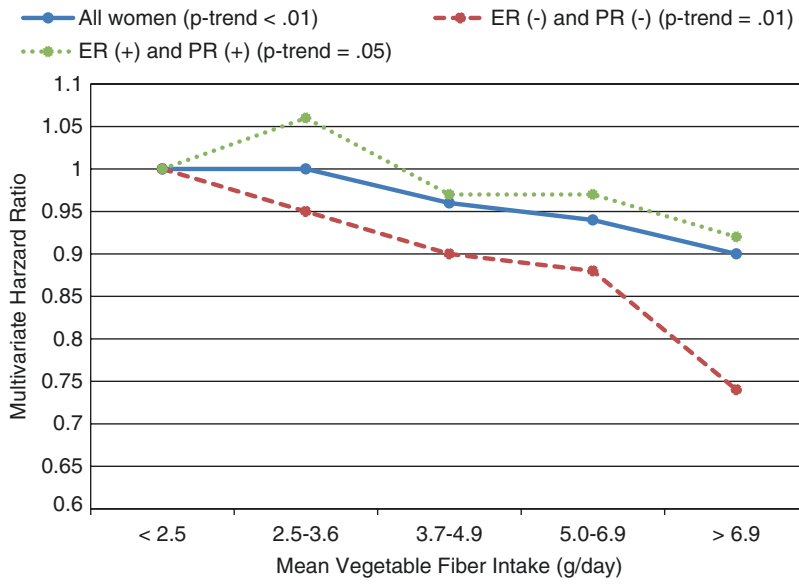

Fig. 18.7 Effect of vegetable fiber intake (excluding potatoes, legumes, soy, and tomato products) on breast cancer risk for all women and by hormone receptor status [78]

Non-supportive Studies

Table 18.5 summarizes one RCT [102] and eight cohort studies [79, 103–109] generally do not support an association or show inconsistent associations between increased fiber intake, specific fiber sources or subtypes, and lower BC risk.

Randomized Controlled Trial

The 2006 US Women's Health Initiative trial (40 US clinical centers; 48,835 postmenopausal women; age range 50–79 years; without prior BC; promoted dietary change with the goals of reducing intake of total fat to 20% of energy, and increasing consumption of vegetables and fruit to at least five servings daily, and grains to at least six servings daily; the control group was asked to maintain habitual diet; average 8.1-year follow-up) found a 9% lower BC risk trend for women in the dietary intervention group compared with women in the control group ($p = 0.07$) [102]. The lack of significant results may be related to relatively low total fiber intake (18 vs 15 g fiber/day) compared to adequate fiber intake (≥25–28 g/day) and the small 3 g fiber/day difference between the groups. Thus, this study does not exclude the potential BC protective role for adequate fiber intake. Also, a secondary analysis showed a significantly lower BC risk among the most dietary adherent women, among women having a healthier diet at baseline, and dietary effect on BC risk varied by hormone receptor characteristics of the tumor.

Prospective Cohort Studies

Although five cohort studies found no overall significant lowering association between the midlife intake of fiber and fiber types on BC risk, these findings do not exclude the possibility that adequate fiber intake (>25–28 g/day) diets may modestly reduce BC risk [79, 103–109]. Two cohort studies, despite reporting no association between total fiber and most fiber subtypes, with BC risk found large

significant lower multivariate BC risk for vegetable fiber by 50% (p-trend = 0.03) [103] and for legume fiber by 21% (p-trend = 0.04) [106]. A 2002 Canadian National Breast Screening Study (89,835 women aged 40–59 years; 16.2-years of follow-up; 2,536 BC cases were diagnosed; total fiber intake varied from 15 to 26 g/day) showed that total fiber intake insignificantly lowered BC risk by 8% ($p = 0.16$; highest to lowest quintile of intake; multivariate adjusted) [107]. The effects of total

Table 18.5 Summaries of a randomized controlled trial (RCT) and prospective cohort studies generally not supporting an association between fiber and reduced breast cancer (BC) risk (multivariate adjusted)

Objective	Study details	Results
RCT		
Prentice et al. Determine the effect of adopting a healthier dietary pattern in the middle to later decades of life reduces the risk for BC (Women's Health Initiative (WHI) trial, USA) [102]	40 US clinical centers; 48,835 postmenopausal women; age range 50–79 years; without prior BC; 19% minority race/ethnicity; dietary intervention goals of reducing intake of total fat to 20% of energy and increasing intake of vegetables and fruits to at least five servings daily and grains to at least six servings daily; the control group asked to maintain habitual diet; average 8.1-year follow-up	This trial showed a strong trend for a healthier diet to reduce BC risk in postmenopausal women. The dietary intervention implemented in the WHI resulted in a significant and sustained reduction in fat intake and an increase in vegetable and fruit intake, but the difference in total fiber between the groups was only approx. 3 g/day (18 vs 15 g fiber/day) with both groups consuming inadequate fiber (as adequate fiber intake ≥25 g/day). After 8.1 years of follow-up, BC incidence was 9% lower for women in the dietary intervention group compared with women in the control group ($p = 0.07$). Secondary analyses suggest a lower BC risk among adherent women, provide greater evidence of risk reduction among women having a healthier diet at baseline, and suggest a dietary effect that varies by hormone receptor characteristics of the tumor
Prospective studies		
Deschasaux et al. Investigate the association with total fiber and fiber subtypes on BC risk, (Supplémentation en Vitamines et Minéraux AntioXydants, France) [103]	4,684 women; mean baseline age 47 years; median 12.6-year follow-up; 167 invasive BC cases were diagnosed; at least three 24-h dietary records within the first 2 years of follow-up	Total fiber intake was not associated with BC risk (p-trend = 0.5) nor was fiber intake from cereals (p-trend = 0.1), fruits (p-trend = 0.9), or legumes (p-trend = 0.3). However, vegetable fiber intake significantly decreased BC risk by 50% (p-trend = 0.03)
Wen et al. Evaluate the association of dietary carbohydrates, glycemic index, glycemic load, and total fiber with BC risk, and determine whether these dietary intakes are modified by age and selected insulin- or estrogen-related risk factors (Shanghai Women's Health Study, China) [104]	74,942 women; mean baseline age 52.5 years; average of 7.4-years follow-up, 616 incident BC cases; dietary intake assessed by in-person interviews	This study showed that the median intake of total fiber from 16 vs 8 g/day was insignificantly associated with premenopausal or postmenopausal BC risk. Also, high dietary available carbohydrate intake or glycemic load may be associated with twofold higher BC risk (p-trend = 0.001) in premenopausal women when consuming 344 vs 258 g available carbohydrate intake
Giles et al. Investigate associations between dietary carbohydrate, fiber, glycemic index (GI), and glycemic load (GL) on postmenopausal BC risk (Melbourne Collaborative Cohort Study, Australia) [105]	12,273 postmenopausal women; average 9.1-year follow-up; 324 BCs diagnosed	Higher fiber intake had heterogeneous effects on BC risk. There was a modest insignificant association between total fiber and the incidence of localized, low-grade, and ER (+)/PR (+) tumors and a significant lower risk for ER (−)/PR (−) tumors by 35% ($p = 0.005$)

Table 18.5 (continued)

Objective	Study details	Results
Holmes et al. Evaluate the association of total fiber, fiber fractions, carbohydrate, glycemic index (GI) and glycemic load (GL) with the risk of BC (Nurses' Health Study, USA) [79]	88,678 participants; mean age 56.5 years at assessment; 68% postmenopausal and 38% on hormone replacement; 18-year follow-up; 4,092 BC cases; mean total fiber intake 18.1 g/day; 25 vs 12 g total fiber/day	This study found no overall significant association between the midlife intake of fiber, fiber types, and carbohydrate quality on BC risk. However, these findings do not exclude the possibility that diets including a very high intake of fiber (>30 g/day) may reduce BC risk. Among premenopausal women there was no association of dietary GI, GL, total fiber, and cereal, fruit, or vegetable fiber with BC risk. In postmenopausal women, there was a positive association between GI and BC risk by 15% (p-trend = 0.02). The association was stronger among women whose BMI was <25 with doubling of risk to 28% (p-trend = 0.003). There were no significant associations for total fiber or specific fiber types except for a fruit fiber trend to reduce BC risk by 8% (p = 0.08)
Cho et al. Examine effect of dietary fiber, carbohydrate, GI, and GL on BC risk (Nurses' Health Study II, USA) [106]	90,655 premenopausal women; mean baseline age 36 years; diet was assessed by FFQ; median intake total fiber 24.8 g vs 12.5 g/day; 8-year follow-up; 714 cases of BC	Total fiber intake was minimally related to BC risk. Higher intake of total fiber insignificantly reduced BC risk by 12% (p-trend = 0.60). Food fiber sources from cereals, fruits, vegetables, or soluble and insoluble fiber did not have a statistically significant relation to a reduced risk of BC. However, there was a significant inverse association between intake of legume fiber and lower BC risk by 21% (p-trend = 0.04)
Terry et al. Evaluate the relationships between total dietary fiber, dietary fiber fractions, and BC risk (Canadian National Breast Screening Study) [107]	89,835 women aged 40–59 years; 16.2-year follow-up; 2,536 BC cases were diagnosed; self-completed questionnaire regarding diet and physical activity; total fiber intake varied from 15 to 26 g/day	Total fiber and specific fiber fractions or types were weakly associated with reduced BC risk (Fig. 18.8). Increasing total fiber intake insignificantly lowered BC risk by 8% (p = 0.16; highest to lowest quintile of intake). There were similar insignificant risk reductions for intakes of other specific fiber fractions, including soluble and insoluble fiber, fiber from cereals, fruit, and vegetables. For lignin, there was an 11% BC risk reduction trend which approached statistical significance (p = 0.06)
Verhoeven et al. Examine the role of antioxidant vitamins and total fiber on BC risk (the Netherlands Cohort Study) [108]	62,573 women aged 55–69 years; 4.3-year follow-up; 650 BC cases	This study does not support a strong role for intake of vitamins C and E, β-carotene, retinol, total fiber, vegetables, fruit, and potatoes on BC risk over a 4-year follow-up. Higher total fiber insignificantly lowered BC risk by 17% (p = 0.16; 34.5 vs 16.9 g fiber/day)
Willett et al. Evaluate the hypothesis that dietary fat increases and fiber decreases BC risk (Nurses' Health Study, USA) [109]	89,494 women; 34–59 years of age; 8-year follow-up; 1,439 incident cases of BC, including 774 among postmenopausal women; ≥22 to ≤11 g total fiber/day and mean total fiber intake 17 g/day	This study does not support a protective role for total fiber intake on BC risk in pre- or postmenopausal women over 8 years (p = 0.62). Since total fiber consists of a variety of subcomponents and types, the possibility cannot be excluded that some specific fraction may lower BC risk. Also, this study did not find an adverse effect of high levels of dietary fat on BC risk

fiber and specific fiber fractions insignificantly reduced BC risk, except for lignin which lowered risk by 11%, which approached statistical significance (p = 0.06; Fig. 18.8). A 2006 Melbourne Collaborative Cohort Study (12,273 postmenopausal women; 9-year follow-up; 324 BC cases) found that total fiber intake had heterogeneous effects on BC risk depending on hormone receptor status with increased fiber significantly lowering BC risk for ER (−)/PR (−) tumors by 35% (p = 0.005) or for ER (−) by 11% (p = 0.07) [105].

Dietary Fiber and Breast Cancer Recurrence and Survival

Randomized Controlled Trials

Table 18.6 summarizes a RCT meta-analysis [110] and five specific RCTs [111–115] on the effects of healthier diets including low fat, increased fruit and vegetables, and increased total fiber on risk of BC recurrence and survival. A meta-analysis of two RCTs and one large cohort study (Women's Intervention Nutrition Study [WINS] followed 2437 women for 60 months; Women's Healthy Eating and Living [WHEL] followed 3,088 women for 7.3 years; the Collaborative Women's Longevity Study (CWLS) followed 4,441 women for 5.5 years) found that post-diagnostic diets lower in fat and higher in fruits, vegetables, and fiber reduced the risk of BC recurrence by 23% (p = 0.009) and reduced BC-related mortality by 17% (=0.05) [110]. A 2004 sub-study analysis of

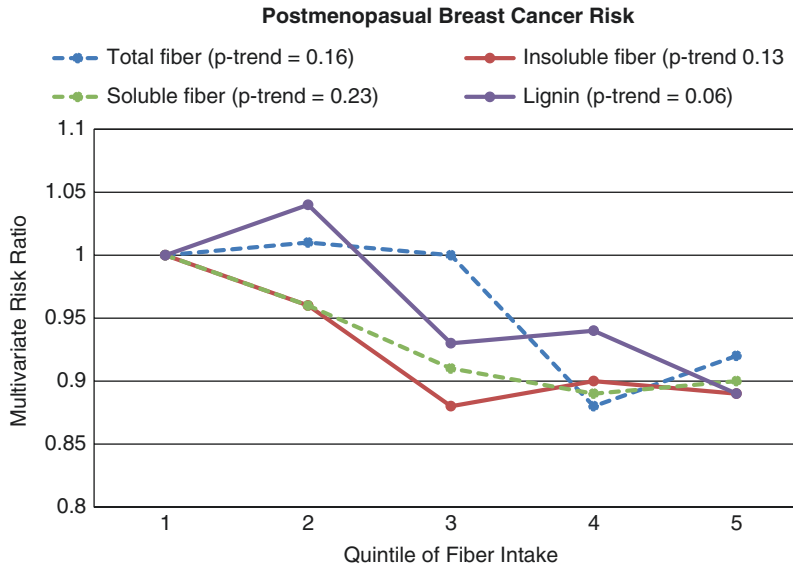

Fig. 18.8 Effects of total fiber and fiber fractions on postmenopausal BC risk from 89,835 women in the Canadian Breast Cancer Screening Study [107]

the US WHEL trial (291 women with a history of BC; mean age 55 years; mean BMI 27; 1 year) showed that higher total fiber intake (29 g/day vs 22 g/day) significantly reduced bioavailable estradiol concentration by 16 pmol/L ($p = 0.05$) from baseline to 1 year in the intervention, which may play a role in reducing recurrent BC risk [115]. A 2006 US WINS trial (2,437 postmenopausal women with resected, early-stage BC receiving conventional cancer management; lower dietary fat and energy and higher fiber diets vs the usual diet; median 60-months) found that the healthier intervention diet significantly prolonged relapse-free survival compared with the control group by 24% ($p = 0.034$) [114]. This dietary intervention had a greater effect on relapse-free survival in women with ER (−) cancer compared to women with ER (+) cancer. The 2007 US WHEL trial (3088 women survivors of early-stage BC; mean baseline age 53 years; mean 7.3-years follow-up; daily diet targets of five vegetable servings plus 16 oz. of vegetable juice; three fruit servings; 30 g of fiber; and 15–20% of energy intake from fat vs a control 5-a-day fruit and vegetable diet) found no difference in BC events or mortality between the intervention and control groups despite increased servings of vegetables by 65%, fruit by 25%, total fiber by 30%, and decreased energy intake from fat by 13% over the first 4 years of the 7.3-year trial [113]. Specifically, after 7.3 years, BC event risk was insignificantly lower by 4% ($p = 0.63$; 256 vs 262 women), and mortality risk was insignificantly lower by 9% ($p = 0.43$; 155 vs 160 women). The absence of an observed effect on BC events or all-cause mortality over a 7.3-year follow-up does not rule out the possibility of improved longer-term survivorship within this cohort. Two WHEL trial secondary analyses of peri- and postmenopausal BC survivors with hot flashes (HF) or without HF found a reduced risk of recurrent BC events among women without HFs at baseline [111, 112]. In a 2008 analysis, women without baseline HFs in the higher fruit and vegetable fiber intervention group had a 47% lower risk of recurrent BC compared to a 31% reduced risk for those women in the 5-a-day control group, which may be related to the effects of fiber on lowering circulating estrogen levels [112]. In a 2009 follow-up analysis, women without baseline HF at 1 year, who were also the highest baseline fiber consumers (mean 31.5 g/day), had significantly lower risk of BC recurrence compared to the lowest baseline fiber consumers (mean 12.4 g/day) ($p = 0.02$). Those with the lowest fiber intake had 54% increased BC events compared to an 18% increase in events for those in the highest fiber intake [111]. Overall, these secondary WHEL trials showed that a dietary pattern high in vegetables, fruit, and fiber and low in fat did not lower risk of recurrent BC events for all BC survivors but did appear to lower the risk in women without HF, a status suggesting higher circulating estrogen concentrations. These analyses suggest that the greatest effect occurred among women who were already eating significant amounts of vegetables, fruits, and fiber at baseline compared to the study intervention because of short study duration and potentially low or inconsistent dietary compliance.

Prospective Cohort Studies

Table 18.6 summarizes seven cohort studies evaluating the effect of fiber and other dietary factors on BC recurrence and survival [64, 116–121]. Five of these studies found that increased fiber from plant-based diets improves overall survival after BC diagnosis, especially in postmenopausal women by 31–52%.

Table 18.6 Summaries of randomized controlled trials (RCTs) and cohort studies on diets lower in fat and higher in fruits, vegetables, and fiber on breast cancer (BC) recurrence and survival (multivariate adjusted)

Objective	Study details	Results
RCT		
Meta-analyses		
Xing et al. Evaluate the effect of diets lower in fat and higher in fruits, vegetables, and fiber on breast cancer (BC) recurrence and survival by meta-analysis [110]	Two RCTs (5,525 BC women): (1) Women's Intervention Nutrition Study (WINS), 2,437 women, median 60 months of duration, and (2) Women's Healthy Eating and Living (WHEL) study, 3,088 women, mean 7.3 years; plus Collaborative Women's Longevity Study (CWLS), a large multicenter prospective cohort study with 4,441 BC patients for 5.5-year follow-up	This meta-analysis of the pooled data from two large RCTs and one large prospective study found that post-diagnostic diets lower in fat and higher in fruits, vegetables, and fiber reduced the risk of BC recurrence by 23% ($p = 0.009$) and BC related mortality by 17% (=0.05)
Specific RCTs		
Pierce et al. Secondary analysis of the baseline quartiles of fiber, fiber-to-fat ratio, and vegetable-fruit intake effects in hot flash negative (HF−) BC survivor subgroup (WHEL trial, USA) [111]	896 early-stage BC survivors not experiencing HF- at baseline (one-third of total trial population); fiber intake by 24-h recall as the primary dietary assessment measure for the study; intervention increased daily servings of vegetables and fruits a higher fiber and lower energy from fat; 7.3 years	The greatest effect on lowering additional BC events occurred among HF-women who were already eating significant amounts of vegetables, fruits, and fiber at baseline rather than the degree of intervention dietary change that was achieved. At 1 year, the highest baseline fiber consumers (mean 31.5 g/day) had significantly lower risk of BC recurrence compared to the lowest baseline fiber consumers (mean 12.4 g/day) ($p = 0.02$); those with the lowest fiber intake had 54% increase in BC events compared to an 18% increase in events for highest fiber intake. After 4 years, there were fewer BC events observed for higher vegetable-fruit and fiber consumption compared to the control group ($p = 0.01$)
Gold et al. Secondary evaluation of the effect of a low-fat diet high in vegetables, fruits, and fiber on the prognosis in BC survivors with hot flashes (HF) or without HF at baseline (WHEL trial, USA) [112]	2,967 BC survivors; age 18 to 70 years; 2,067 HF-positive women (70%), 900 women (30%) in the HF-negative group; intervention increased intake of vegetable/fruit servings per day (54% higher; 10 vs 6.5 servings/day), fiber (31% higher; 25.5 vs 19.4 g/day), and reduced percent energy from fat (14% lower; 26.9% vs 31.3%) vs 5-a-day diet; 7.3 years	This trial found that peri- and postmenopausal women without HF at baseline assigned to the intervention had 31% fewer BC events than those assigned to the control group ($p = 0.02$). The intervention did not affect prognosis in the women with baseline HFs. Also, compared with women without HF assigned to the lower-fiber control group, HF-positive women had significantly fewer events independent of diet group. Thus, a diet with higher vegetable, fruit, and fiber and lower fat intakes than the 5-a-day diet may reduce risk of additional events in BC survivors without HF symptoms, and these effects may be related to fiber's effects on circulating estrogen concentrations

Table 18.6 (continued)

Objective	Study details	Results
Pierce et al. Assess effects of increased vegetables, fruits, and fiber intake above the 5-a-day recommendations along with reduced fat intake on BC recurrence and all-cause mortality among women with previously treated early-stage BC (WHEL, USA) [113]	3,088 women; mean baseline age 53 years; intervention (n = 1,537) and control (n = 1,552) groups; daily diet targets of five vegetable servings plus 16 oz. of vegetable juice; three fruit servings; 30 g of fiber; and 15% to 20% of energy intake from fat; 7.3 years	In this study among survivors of early-stage BC, adoption of a diet that was very high in vegetables, fruits, and fiber and low in fat did not reduce additional BC events or mortality after 7.3 years compared to a 5-a-day fruit and vegetable group. Specifically, 256 women in the intervention group (16.7%) vs 262 in the comparison group (16.9%) had an insignificant 4% lower BC event risk (p = 0.63; adjusted), and 155 intervention group women (10.1%) vs 160 comparison group women (10.3%) died. The intervention group achieved and maintained the following dietary changes vs the 5-a-day fruit and vegetable group through 4 years: higher servings of vegetables by 65%, fruit by 25%, and fiber by 30% and lower energy intake from fat by 13%
Chlebowski et al. Evaluate the effect of a healthier dietary intervention significantly lower in dietary fat and energy and higher in total fiber on prolonged relapse-free survival in women with resected BC (the Women's Intervention Nutrition Study [WINS], USA) [114]	2,437 postmenopausal women with resected, early-stage BC receiving conventional cancer management; 975 women in dietary intervention group and 1,462 women in the control group; median 60-month follow-up; at 12-month dietary fat (33.3 vs 51.3 g/day), daily energy (1460 vs 1531 kcal/day), and total fiber (19.5 vs 17.3 g/day); weight loss 2.3 kg	The dietary intervention significantly prolonged relapse-free survival compared with the control group by 24% (p = 0.034). Exploratory analyses suggest a differential effect of the dietary intervention based on hormonal receptor status. The dietary intervention had a greater effect on relapse-free survival in women with ER (−) cancer by reducing mortality risk by 42% compared to women with ER (+) with 15% lower risk (interaction test, p = 0.15)
Rock et al. Testing whether post-diagnosis dietary modification can influence estrogen levels and BC recurrence and survival (WHEL study, USA) [115]	291 women with a history of breast cancer; mean age 55 years; mean BMI 27; dietary goals for the intervention group were increased total fiber, vegetables, and fruits intakes and reduced fat intake; 1 year	This trial found that the intervention group reported a significantly lower intake of energy from fat (21% vs 28%), higher total fiber intake (29 g/day vs 22 g/day) (p < 0.001), and mean weight loss of 1 kg. There was a significant reduction in bioavailable estradiol concentration from baseline to 1 year in the intervention by 16 pmol/L vs the control group (p = 0.05). Change in total fiber (but not fat) intake was significantly and independently related to change in serum bioavailable estradiol (p = 0.01) and total estradiol (p = 0.05) concentrations, which may play a role in lowering BC recurrent risk
Prospective cohort studies		
Villasenor et al. Examine associations between total fiber and serum concentrations of C-reactive protein (CRP) and serum amyloid-A (SAA) in BC survivors (Health, Eating, Activity, and Lifestyle (HEAL) study, USA) [64]	698 BC survivors; age range 18–64 years; 24 months	Among BC survivors who consumed >15.5 g/day of insoluble fiber, there was a 49% lower risk of elevated CRP concentrations compared to those who consumed <5.4 g/day (p = 0.053). These findings suggest that diets high in fiber may benefit BC survivors via reductions in systemic inflammation, as elevated inflammation may be prognostic for reduced survival

(continued)

Table 18.6 (continued)

Objective	Study details	Results
Belle et al. Investigate associations of fiber with BC prognosis in survivors (HEAL study, USA) [116]	688 stage 0 to IIIA BC survivors; mean baseline age 55 years; median of 6.7-year follow-up; after diagnosis	Compared with lower total fiber intakes, moderate to high intake of fiber may lead to a better clinical outcome after a BC diagnosis. Women with a fiber intake of >18.3 g/day had a 47% lower risk of death from any cause than women with <8.8 g fiber/day. These findings were similar in direction and magnitude for BC mortality and nonfatal BC recurrence, although the results for those outcomes were not statistically significant. Still, the findings suggest increased dietary fiber may be a useful addition to a BC treatment plan
Beasley et al. Examine the relation between post-diagnosis dietary factors and breast cancer and all-cause survival in women with a history of BC (Collaborative Women's Longevity Study [CWLS], USA) [117]	4,441 women without a history of breast cancer recurrence prior to completing the questionnaire; age range 20–79 years; mean 5.5-year follow-up; 525 deaths, of which 26% (137) were attributed to BC	This study provides little evidence for an association between dietary intake and BC survival but provides additional support for an adverse relationship between saturated and trans-fat intake and overall survival following a BC diagnosis. There was a nonsignificant inverse trend (highest vs lowest quintile) between calcium intake by 41% (p-trend = 0.09) and total fiber by 25% (p-trend = 0.24) on BC morality
Buck et al. Estimate the effect of total fiber on survival after postmenopausal BC (Germany) [118]	2,653 postmenopausal BC patients; median 6.4 years of follow-up; total of 321 deaths occurred, of which 235 were due to breast cancer	Higher fiber intake was associated with a significantly lowered all-cause mortality risk by 48% and BC mortality risk by 36% (p = 0.01; 29 vs 13 g/day)
Holmes et al. Examine whether, after a BC diagnosis, high intake of animal fat was associated with increased BC mortality and high intake of fiber was associated with decreased BC mortality (NHS, USA) [119]	3,846 women; mean age at diagnosis 58 years; 446 BC deaths and 91 additional BC recurrences in women who did not die during follow-up. Median follow-up 83 months and maximum follow-up 321 months	Animal fat intake significantly increased BC death risk by 42–67%, and cereal fiber intake was reduced BC death risk by about 50%. However, physical activity attenuates these dietary factors to insignificant levels
McEligot et al. Investigate the influence of diet, including dietary fat (percentage energy), fiber, vegetable, and fruit intakes, and micronutrients (folate, carotenoids, and vitamin C) on overall survival in women diagnosed with BC (USA) [120]	516 postmenopausal women diagnosed with BC; mean age at diagnosis 65 years; mean survival time of 80 months; 96 deaths, of which 41 (43%) were due to BC; FFQ prior to diagnosis	This study found significantly lower mortality risk for the highest level of fiber intake by 52%, vegetables by 43%, and fruit by 37%. Other healthy nutrients including folate, vitamin C, and carotenoid intakes were also significantly associated with reduced mortality risk (p-trend $\leq$ 0.05). The highest vs lowest tertile of total fat increased mortality risk. A plant-based, high-fiber diet appears to improve overall survival in postmenopausal women after BC diagnosis
Holmes et al. Examine the relation of intake of dietary components to breast carcinoma survival (NHS, USA) [121]	121,700 female registered nurses; mean age 54 years at BC diagnosis; mean follow-up 157 months; 378 patients died, 326 (86%) died from BC	After BC diagnosis, healthy dietary components were effective in reducing all-cause mortality risk: total fiber by 31% (p-trend = 0.02), protein by 35% (p-trend < 0.001), calcium by 34% (p-trend = 0.007), and lutein by 13% (p-trend = 0.04). However, no survival advantage was found for a low-fat diet after a diagnosis of BC

Conclusions

BC is the most common cancer in women, with an estimated 2.4 million cases in 2015. BC was also the leading cause of cancer deaths (523,000 deaths) and disability-adjusted life-years (15.1 million years) for women. As for most cancers, consuming a healthy fiber-rich dietary pattern and maintaining a healthy body weight are important for lowering breast cancer (BC) risk and/or improving post-diagnosis survival. For example, postmenopausal women with higher healthy lifestyle scores had a 26% lower risk of BC compared to those with lower healthy lifestyle scores. Potential mechanisms by which increased dietary fiber intake supports the reduction of BC risk and/or improves survival include lowering women's risk of excess weight or abdominal fat gain, reducing elevated C-reactive protein, attenuating insulin resistance, and decreasing circulating estrogen levels. The relationship between weight and fiber intake on BC risk is complex, as it varies at different time of life. Higher BMI at age 18 years was inversely associated with BC risk, but weight gain after age 18 years was positively associated with BC risk after menopause, in those who never used hormone therapy. Also, weight gain by ≥15 lb compared to no weight change over a 4-year period was associated with increased BC risk, especially in premenopausal women. Higher fiber intake during adolescence and early adulthood reduced the risk of adult BC risk, especially in premenopausal women. Prospective cohort meta-analyses found that each 10 g of total fiber intake was inversely associated with 4–7% lower BC risk in all women. In postmenopausal women, an increased total fiber intake by 15 g/day above typical intake was associated with reduced BC risk by 7–12%. A meta-analysis of two large RCTs and a cohort study in breast cancer survivors showed that post-diagnostic diets lower in fat and higher in fruits, vegetables, and fiber significantly reduced BC recurrence risk by 23% and BC mortality risk by 17%. In RCTs with BC survivors, dietary patterns high in vegetables, fruits, and fiber and low in fat were more effective in lowering risk of recurrent BC events in women without hot flashes at baseline, suggesting that higher fiber intake lowered circulating estrogen concentrations. For both pre- and postmenopausal women, increased intake of non-starchy vegetables (estrogen receptor negative BC women only), plant foods rich in carotenoids and diets high in calcium were associated with lower BC risk.

Appendix 1. Fifty High Fiber Foods Ranked by Amount of Fiber Per Standard Food Portion[a]

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
High fiber bran ready-to-eat cereal	1/3–3/4 cup (30 g)	9.1–14.3	60–80	2.0–2.6
Navy beans, cooked	1/2 cup cooked (90 g)	9.6	127	1.4
Small white beans, cooked	1/2 cup (90 g)	9.3	127	1.4
Shredded wheat ready-to-eat cereal	1–1 1/4 cup (50–60 g)	5.0–9.0	155–220	3.2–3.7
Black bean soup, canned	1/2 cup (130 g)	8.8	117	0.9
French beans, cooked	1/2 cup (90 g)	8.3	114	1.3
Split peas, cooked	1/2 cup (100 g)	8.2	114	1.2
Chickpeas (Garbanzo) beans, canned	1/2 cup (120 g)	8.1	176	1.4
Lentils, cooked	1/2 cup (100 g)	7.8	115	1.2
Pinto beans, cooked	1/2 cup (90 g)	7.7	122	1.4
Black beans, cooked	1/2 cup (90 g)	7.5	114	1.3
Artichoke, global or French, cooked	1/2 cup (84 g)	7.2	45	0.5
Lima beans, cooked	1/2 cup (90 g)	6.6	108	1.2
White beans, canned	1/2 cup (130 g)	6.3	149	1.1

(continued)

Appendix 1 (continued)

Food	Standard portion size	Dietary fiber (g)	Calories (kcal)	Energy density (calories/g)
Wheat bran flakes ready-to-eat cereal	3/4 cup (30 g)	4.9–5.5	90–98	3.1–3.3
Pear with skin	1 medium (180 g)	5.5	100	0.6
Pumpkin seeds. Whole, roasted	1 ounce (about 28 g)	5.3	126	4.5
Baked beans, canned, plain	1/2 cup (125 g)	5.2	120	0.9
Soybeans, cooked	1/2 cup (90 g)	5.2	150	1.7
Plain rye wafer crackers	2 wafers (22 g)	5.0	73	3.3
Avocado, Hass	1/2 fruit (68 g)	4.6	114	1.7
Apple, with skin	1 medium (180 g)	4.4	95	0.5
Green peas, cooked (fresh, frozen, canned)	1/2 cup (80 g)	3.5–4.4	59–67	0.7–0.8
Refried beans, canned	1/2 cup (120 g)	4.4	107	0.9
Mixed vegetables, cooked from frozen	1/2 cup (45 g)	4.0	59	1.3
Raspberries	1/2 cup (65 g)	3.8	32	0.5
Blackberries	1/2 cup (65 g)	3.8	31	0.4
Collards, cooked	1/2 cup (95 g)	3.8	32	0.3
Soybeans, green, cooked	1/2 cup (75 g)	3.8	127	1.4
Prunes, pitted, stewed	1/2 cup (125 g)	3.8	133	1.1
Sweet potato, baked	1 medium (114 g)	3.8	103	0.9
Multi-grain bread	2 slices regular (52 g)	3.8	140	2.7
Figs, dried	1/4 cup (about 38 g)	3.7	93	2.5
Potato baked, with skin	1 medium (173 g)	3.6	163	0.9
Popcorn, air-popped	3 cups (24 g)	3.5	93	3.9
Almonds	1 ounce (about 28 g)	3.5	164	5.8
Whole wheat spaghetti, cooked	1/2 cup (70 g)	3.2	87	1.2
Sunflower seed kernels, dry roasted	1 ounce (about 28 g)	3.1	165	5.8
Orange	1 medium (130 g)	3.1	69	0.5
Banana	1 medium (118 g)	3.1	105	0.9
Oat bran muffin	1 small (66 g)	3.0	178	2.7
Vegetable soup	1 cup (245 g)	2.9	91	0.4
Dates	1/4 cup (about 38 g)	2.9	104	2.8
Pistachios, dry roasted	1 ounce (about 28 g)	2.8	161	5.7
Hazelnuts or filberts	1 ounce (about 28 g)	2.7	178	6.3
Peanuts, oil roasted	1 ounce (about 28 g)	2.7	170	6.0
Quinoa, cooked	1/2 cup (90 g)	2.7	92	1.0
Broccoli, cooked	1/2 cup (78 g)	2.6	27	0.3
Potato baked, without skin	1 medium (145 g)	2.3	145	1.0
Baby spinach leaves	3 ounces (90 g)	2.1	20	0.2
Blueberries	1/2 cup (74 g)	1.8	42	0.6
Carrot, raw or cooked	1 medium (60 g)	1.7	25	0.4

[a]Dietary Guidelines Advisory Committee. Scientific Report of the 2010 Advisory Guidelines Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Part B. Section 2: Total Diet. 2010; Table B2.4

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