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*Series Editor: Adrienne Bendich*

Donato F. Romagnolo  
Ornella I. Selmin *Editors*

# Mediterranean Diet

Dietary Guidelines and Impact on Health  
and Disease

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# **NUTRITION AND HEALTH**

Adrienne Bendich, Ph.D., FACN, FASN, SERIES EDITOR

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Dietary Guidelines and Impact on Health and Disease

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*This volume is dedicated to the memories of John Milner, Ph.D., and Mary Frances Picciano, Ph.D., international leaders in nutrition research, who were friends, mentors, coeditors, and inspirational figures to the editors of this volume.*



# Foreword

The human diet is complex and ever changing (1). We eat hundreds of individual foods, in thousands of wide-ranging combinations, which we prepare and serve using a diverse array of methods, according to markedly different cultural norms (2). To study the effect of diet on human health, nutrition scientists have attempted to isolate the diet's myriad components, individually and in small groups, to examine what effect, if any, they exert on the body. These studies have led to the suggestion that whole foods may have unique effects on health than individual components (3).

Over the past century, nutrition researchers have made many vital, life-saving advances. The discovery of vitamins in the early twentieth century brought about effective treatments for the deficiency diseases, rickets, beriberi, and scurvy. The 1980s and 1990s saw keen interest in naturally occurring plant substances called phytochemicals that display a wide range of health-promoting, disease-fighting potential (4–20).

But these piecemeal advances have bred a piecemeal understanding in the public's mind. Findings on individual dietary components have indirectly led to the demonization of various nutrients and macronutrients, with damaging effects: health fads that promote the near elimination of carbohydrates or that hold up protein as a panacea (21–35). In response to consumer demand, the food industry floods grocery shelves with low-fat potato chips and cookies. And through it all, the slow, steady ballooning of portion sizes, as well as our waistlines, has proceeded apace (36–38).

As our research methods continue to evolve, and our knowledge expands, it's becoming clear that the big picture is what matters most. Recent studies suggest that our usual patterns of dietary intake and physical activity are more important to wellness than our historically narrow focus on consumption of a few individual foods or nutrients can show (39–48). If we are to move the science forward, it's clear that we must take a step back and examine overall patterns of eating and of living.

## As Data Mounts, Recommendations Evolve

At the American Institute for Cancer Research (AICR), we've had a front-row seat at the steady accretion of new insights and understanding as the evidence linking diet, physical activity, and weight to cancer risk has grown. This mounting evidence has occasioned a shift in focus from individual nutrients and phytochemicals to overall dietary patterns. In 1981, the first scientific reports to evaluate the evidence linking various dietary components to cancer risk were published. Importantly, both *The Causes of Cancer* by Richard Doll and Richard Peto (1981) (49) and the *US National Academy of Sciences Report Diet, Nutrition and Cancer* (1982) (50) concluded by issuing urgent calls for more and better research, and by the mid-1990s thousands of studies had been published on diet and cancer.

To evaluate and synthesize these new studies, in 1997 AICR and the World Cancer Research Fund published an expert report, *Food, Nutrition, and the Prevention of Cancer: A Global Perspective* (51). The report presented our recommendations for cancer prevention, which reflected the then-current state of the science. By 2007 the sheer amount of new evidence demanded that AICR/WCRF produce a second expert report, *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective* (52), and by now physical activity was rightfully acknowledged as an important component of a healthy lifestyle. The report's recommendations were as follows:

1. Be as lean as possible without becoming underweight.
2. Be physically active for at least 30 min every day.
3. Avoid sugary drinks. Limit consumption of energy-dense foods.
4. Eat more of a variety of vegetables, fruits, whole grains, and legumes such as beans.
5. Limit consumption of red meats (such as beef, pork, and lamb) and avoid processed meats.
6. If consumed at all, limit alcoholic drinks to 2 for men and 1 for women a day.
7. Limit consumption of salty foods and foods processed with salt (sodium).
8. Don't use supplements to protect against cancer.
9. It is best for mothers to breastfeed exclusively for up to 6 months and then add other liquids and foods.
10. After treatment, cancer survivors should follow the recommendations for cancer prevention.

Clearly, science doesn't stand still, so we've instituted a process of ongoing review and analysis that ensures our recommendations for cancer prevention reflect the latest science. We have partnered with WCRF International on the Continuous Update Project (53), which reviews and analyzes the relevant research on a rolling basis, cancer site by cancer site.

## **A Focus on Meals, Not Micronutrients**

AICR's education team has turned our recommendations for cancer prevention into understandable and practical messages for the American public and has created a visual plate-based model for healthy eating, the New American Plate. The appeal of this approach is its simplicity and flexibility as well as its emphasis on whole foods and whole meals. At their core, AICR's New American Plate, the USDA's My Plate, and scores of other similar approaches represent an encouraging trend borne out by the research—a desire to address health research and health messaging by shifting away from a piecemeal focus on individual foods and food components to overall dietary patterns.

## **Forest for the (Olive) Trees**

One such pattern, around which a tremendous amount of research has accrued, is the Mediterranean diet. Many of the recommendations included in the 2007 AICR/WCRF Expert Report overlap with those of the Mediterranean pyramid, which:

- Highlights the importance of regular physical activity and avoiding sugary drinks
- Limits the consumption of energy-dense foods
- Recommends intake of more of a variety of vegetables, fruits, whole grains, and legumes such as beans
- Limits the consumption of red and processed meats and alcohol

It is notable that like the AICR/WCRF recommendations, the Mediterranean diet was included in the Scientific Report of the 2015 Dietary Guidelines submitted to the Department of Human Health Services and US Department of Agriculture (54).

As detailed in this volume, the Mediterranean diet includes a variety of healthy foods in moderate amounts. But it is more than just a checklist of specific foods and beverages. The traditional Mediterranean diet represents a truly holistic approach that combines fresh whole foods and plenty of physical activity. As you read about this fascinating research, you may be struck by how simple and appealing this lifestyle seems, in terms of both its day-to-day pleasures and its many long-term health benefits. The editors, Drs. Donato Romagnolo and Ornella Selmin, nutrition and cancer researchers at the University of Arizona, have invited world-renowned experts to highlight the key aspects of the Mediterranean diet and lifestyle.

The volume opens with *Part I, Mediterranean Diet and Lifestyle in a World Contest*. This chapter introduces the foundational elements of the Mediterranean pyramid for improving natural resources sustainability and prevention of chronic diseases including overweight, obesity, cardiovascular, cancer, and diabetes. A key concept emerges: that prevention of chronic diseases requires approaches that go beyond simple food recommendations but also involve increased accessibility to healthier food and better medical and healthcare.

In *Part II, Historical, Behavioral, and Geographical Perspective on the Mediterranean Diet and Lifestyle*, the volume focuses on the historical and geographical differences and overlaps of diets characteristic of the Mediterranean region. Concerns are expressed that even in Mediterranean countries, departure from local agricultural activities has reduced the availability of traditional healthier foods and increased dependency on large-scale, and possibly not as healthy, processed foods. These changes are modifying dietary patterns and possibly contributing to an increased burden of chronic diseases even in less developed and food-insecure communities.

*Part III* discusses the role of *Mediterranean Diet and Lifestyle for Health Promotion*. A key component of the Mediterranean diet is olive oil rich in monounsaturated oleic acid. Fish and nuts provide other sources of fats that positively impact the overall fatty acid profile (i.e., more mono- and polyunsaturated fatty acids compared to a Western diet, which is rich in saturated fatty acids). Authors highlight the beneficial effects of compounds present in olive oil against oxidative processes, cardiovascular disease, cancers, and neurodegenerative disorders. The benefits of the Mediterranean diet extend to improved longevity and reduction of inflammatory processes associated with cardiovascular diseases. Also data are discussed linking adherence to a Mediterranean-like diet and lifestyle and reduced risk of metabolic disorders.

In *Part IV, Aging and Cancer Risk*, authors provide evidence of the benefits of foods—and their wide variety of bioactive compounds—commonly present in the Mediterranean diet (i.e., fruits, vegetables, whole grains, unsaturated fatty acids, lean meat) for reducing or slowing the development of conditions associated with aging (i.e., cognitive decline, dementia, Alzheimer's and Parkinson's). Of particular interest to AICR, which focuses on reducing the cancer burden through nutrition, is the emerging evidence that the Mediterranean diet may have protective effects against the development of breast and colon cancer. Progress in these areas can impact on the development of prevention therapies and reduce cancer mortality associated with breast and colorectal malignancies. A chapter on the developing field of epigenetics clearly points out how dietary exposures to foods and bioactives present in the Mediterranean diet can impact gene expression and, possibly, influence gene expression later in life, or even in subsequent generations.

Finally, *Part V, Building a Mediterranean-Like Pyramid* translates the research concepts presented in the opening and health promotion papers into practical suggestions. First, authors highlight the health benefits of physical activity, which is a key component of the Mediterranean pyramid and other lifestyle behaviors. This is a behavioral component that can cut across cultural and geographical differences and contribute to correcting/preventing excessive energy balance and diseases associated

with overconsumption. The closing chapters of the volume illustrate selected Mediterranean recipes that include information about ingredients, cooking methods, and nutritional value. In the last chapter, the editors and coauthors have translated the information from each recipe into a week-long dietary plan inspired by the Mediterranean pyramid. The recipe information used to build this dietary plan is an instructional material developed by the editors for the Mediterranean Diet and Health Study Abroad Program. This program is held in Italy every year for students, nutrition professionals, and adults who wish to learn about the health benefits of the Mediterranean diet and lifestyle (55).

In closing, our understanding of diet and health has progressed rapidly. Yet today, we are beset by illnesses related directly to poor diets, inactivity, and soaring obesity rates. We applaud the editors and contributors of this volume, a work that supplies a wider, much-needed perspective on an overall pattern of living.

Washington, DC

Susan Higginbotham, Ph.D., RD.  
Glen Weldon

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# Preface

Death incidence attributable to chronic diseases is projected to increase due to the growing and aging population. The rampant increase in the prevalence of overweight and obesity in the USA and other world populations has been attributed to a combination of dietary, socioeconomic, and behavioral causes. These include an imbalance between dietary recommendations and behavior combined with an increasingly sedentary lifestyle. To reduce the burden of chronic diseases, various dietary guidelines are being released by health organizations in the USA and around the world to promote a rebalancing of calories and more physical activity. International efforts are underway to formulate dietary recommendations that prevent chronic diseases and improve quality of life. Unfortunately, socioeconomic constraints contribute to the paradoxical coexistence of noncommunicable diseases with food insecurity.

Various dietary guidelines and patterns emphasize the importance of variety, proportionality, and moderation in food selections. These include the *Mediterranean diet* which, in 2013, was inscribed by UNESCO in the Representative List of the Intangible Cultural Heritage of Humanity. In 2015, the Scientific Report of the Dietary Guidelines for Americans to the US Department of Human Health Services Department of Agriculture recommended the Mediterranean-style pattern among those dietary patterns associated with health promotion. The impetus for developing this volume stems from the wealth of research evidence suggesting that dietary habits and lifestyle characteristic of the Mediterranean region may offer protection against chronic diseases and improve longevity. Contributors have summarized the most up-to-date research evidence related to foods and dietary behaviors that contribute to a healthy Mediterranean diet and lifestyle, the biochemical mechanisms through which bioactive compounds usually found in Mediterranean foods impact on biological processes associated with disease, and opportunities and challenges for implementing a Mediterranean-like dietary pattern in developed and emerging economies. Twenty chapters were assembled by world-renowned experts who conducted a systematic review of the relevant literature and provided an assessment of chronic disease prevention opportunities using diet and food components characteristic of the Mediterranean region. The tone of this text is to establish a “proof of principle” about the importance of the Mediterranean diet and lifestyle approach for disease prevention. The editors regret that because of space limitations not all areas of research related to the Mediterranean diet and lifestyle could be adequately addressed, and acknowledge that geographical differences around the world impose limitations in the choice of foods and dietary customs.

This volume has been organized into five parts to aid in the assimilation of the materials provided. *Part I, Mediterranean Diet and Lifestyle in a World Context*, introduces the challenges and opportunities for maintaining or adopting a Mediterranean-like diet and lifestyle. Emphasis is placed on the realization that sustainability of natural resources is intimately related to agricultural production, food supply, and availability, which in turn impact on dietary behavior and disease risk. Adoption of Mediterranean dietary patterns and lifestyles that have been traditionally associated with reduced incidence of chronic diseases is recommended. Implementation of a Mediterranean-like diet and lifestyle may benefit populations residing in the USA and abroad. Major challenges include globalization

of food supplies, food insecurity, and socioeconomic constraints that limit access to healthier foods, affordable education, and medical care.

*Part II, Historical, Behavioral, and Geographical Perspective on the Mediterranean Diet and Lifestyle*, addresses the historical and behavioral origins of the Mediterranean diet, regional differences in dietary profiles, and the evolution of traditional Mediterranean diet into modern dietary guidelines. The traditional Mediterranean diet reflects the interactions of diverse populations and civilizations that have occupied the Mediterranean basin over thousands of years. In modern times, specific indexes to measure adherence to Mediterranean dietary patterns and their impact on health status have been developed. A key concept that emerges from this section is that food consumption in Mediterranean countries is a cultural element that goes beyond the need to satisfy nutrition needs. Nevertheless, concerns have mounted that modern diet and lifestyle continue to depart from the traditional Mediterranean “Genius loci” as a result of globalization and technological modifications leading to drastic changes in food behavior and increased susceptibility to chronic diseases.

*Part III* presents evidence of the benefits of the *Mediterranean Diet and Lifestyle for Health Promotion*. In addition to olive oil, which is the main source of fats in the Mediterranean region, this section presents other sources of fats that contribute to the overall profile of fatty acids found in the Mediterranean diet. Authors highlight that micronutrients and microconstituents with antioxidant and other properties are common in vegetable oils used in Mediterranean households. These bioactive compounds protect fatty acids from oxidation and are potentially important for reducing chronic disease risk. Olive oil is convincingly recognized as a food that reduces the risk of cardiovascular diseases, and possibly, certain cancers and neurodegenerative disorders. Research evidence is also presented suggesting that the Mediterranean diet decreases inflammatory parameters and risk of mortality. In Chap. 8, the authors conclude that the coordinated actions of phenolic compounds found in red wine and alcohol exert various health effects including a reduced risk of atherosclerosis. Regular and moderate consumption of red wine, 1–2 drinks a day with meals, is recommended. However, sound clinical judgment is needed to determine if alcohol consumption is appropriate based on age, medical history, gender, and predisposition to dependency. No more than one glass of wine/day is recommended for women and two glasses of wine/day for men. Metabolic syndrome has been recognized as a health concern and clinical challenge. There is general agreement that clinical parameters associated with metabolic syndrome can be greatly improved through adoption of lifestyle and dietary changes characteristic of the Mediterranean diet pattern. For example, research evidence from Mediterranean studies suggested a positive correlation between adherence to diets low in saturated fat, trans-fat, cholesterol, added sugar, and sodium; and high in unsaturated fats, complex unrefined carbohydrates, fruits, vegetables, and fish, with improvement of metabolic abnormalities. Unequivocally, these are dietary features typical of the traditional Mediterranean diet. The adoption of metabolomic approaches may offer new opportunities to monitor the health impact of individual food components and Mediterranean-like diets on metabolic syndrome and chronic disease risk.

*Part IV, Aging and Cancer Risk*, gives attention to the fact that the Mediterranean diet relies heavily on components such as fruits, vegetables, whole grains, unsaturated fatty acids, and lean meats and offers a regimen of nutrient-dense foods that provide viable, healthy and gradual weight loss while reducing a number of chronic health conditions that are so prevalent in the aging population. Of these, cognitive decline, dementia, and Alzheimer’s and Parkinson’s disease are age-related conditions that affect mature adults worldwide. Risk factors for cognitive diseases include hypercholesterolemia, obesity, diabetes, and cardiovascular factors, such as hypertension and inflammation. Studies suggest that the Mediterranean diet pattern may be beneficial for preventing and/or attenuating biological processes associated with cognitive impairment. Research data on extra virgin olive oil, the main source of saturated fat in the Mediterranean diet, suggest protective effects of olive oil components on markers of neurodegenerative diseases. Mediterranean-like diet and lifestyle are discussed as options to improve brain mitochondrial functions and for treatment of cognitive impairment and neurodegeneration. Turning to causes impacting cancer death, breast cancer remains the most commonly