

NUTRIENTS, DIETARY SUPPLEMENTS, AND NUTRICEUTICALS

NUTRITION AND HEALTH

Adrianne Bendich, PhD, FACN, SERIES EDITOR

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NUTRIENTS, DIETARY SUPPLEMENTS, AND NUTRICEUTICALS

Cost Analysis Versus Clinical Benefits

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Series Preface

The Nutrition and Health series of books has, as an overriding mission, to provide health professionals with texts that are considered essential because each includes: (1) a synthesis of the state of the science, (2) timely, in-depth reviews by the leading researchers 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, inter-chapter referrals, (8) suggestions of areas for future research, and (9) balanced, data-driven answers to patient /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(s) has the potential to examine a chosen area with a broad perspective, both in subject matter as well as in the choice of chapter authors. The international perspective, especially with regard to public health initiatives, is emphasized where appropriate. The editors, 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.

“Nutrients, Dietary Supplements and Nutraceuticals: Cost Analysis versus Clinical Benefits,” edited by Ronald R. Watson, Ph.D., Joe K. Gerald, M.D. Ph.D. and Victor Preedy, Ph.D. exemplifies the goals of the Nutrition and Health Series. Unlike many other books in the Series, this text provides a critical assessment of the economic value of dietary interventions studies. Each of the editors has extensive experience in nutrition research and cost analysis and the combined experiences in academia and clinical practice in the US as well as Europe provides a broad perspective on the role of food and food components, diet and diet modifications, nutrients, and many of the nonessential components of the diet on the economic impact of health and disease maintenance.

The editors have chosen 56 internationally recognized experts who are active investigators on the impact of overall diet and individual dietary constituents

on diseases and environmental stressors in different age groups, in different countries throughout the world, and in both sexes and the subsequent effects on health economics. This important, unique text provides practical, data-driven assessments of the cost effectiveness of nutritional interventions and the volume provides the reader with over 2,000 up-to date references and more than 150 well-organized tables and figures that assist the reader in evaluating the health economics associated with the use of vitamins and minerals and other dietary constituents, such as probiotics, long-chain fatty acids, conjugated linoleic acid, certain traditional Chinese medicines, plant polyphenols, tannins, and many other components of foods. Moreover, the critical value of nutrition for at-risk populations including those living with cancer, allergies and/or asthma, autoimmune diseases, the very young, and the very old are extensively reviewed in several unique chapters.

Each chapter begins with comprehensive bulleted Key Points followed by the list of key words, and includes an overview and historic review, examination of the literature with critical focus on comparisons between studies: discussion of the chemical composition of actives where appropriate and conclusions and perspectives on future research areas. The overarching goal of the editors is to provide fully referenced information to health professionals so they may have a balanced perspective on the value of many dietary components that are routinely consumed by patients and clients with the hope that healthy diets and prudent use of supplements and nutraceuticals can reduce overall healthcare costs. This important volume provides health professionals with balanced, data-driven answers to numerous questions about the validity of the science to date and also provides researchers with opportunities to clarify areas where many questions still exist about the effectiveness of specific nutrients/dietary factors on health outcomes and costs of disease prevention as well as treatment.

The editors have organized the volume into six sections that reflect the breadth and depth of current knowledge in the area of dietary factors that affect health and the cost effectiveness of improving nutritional status. In the first introductory section the editors have wisely included four chapters that examine cost effectiveness from a number of perspectives including nutritional options such as fortification, supplementation, and taxation of certain foods while providing subsidies for other, healthier choices. Areas reviewed include the calculation of daily adjusted life years (DALY) and a concept of the least-cost diet containing the minimal daily requirements recommended by national bodies. Unique areas of focus include an analysis of the potential effects of economic incentives on reduction of maternal and childhood under-nutrition. The second section on Influences on Preventive Nutrition Strategies includes three related chapters that describe the complex influences on choosing a healthy diet. Two chapters concentrate on fruit and vegetable choices and agree that price as well as economic status affect the purchase of fruits and vegetables. In depth analyses suggest that food price elasticity is of greater importance in lower and middle income families. Data from China, Brazil, as well as the United States are included. The third chapter examines the influence of ethnicity on the purchase of foods and food patterns. Social psychology models

are used and the theory of planned behavior is discussed as an example of how ethnicity can affect generations of dietary intakes. The third section provides in-depth, separate chapters devoted to the Potential for Cost Effectiveness with Food Interventions that are examined in four chapters. Two chapters discuss the potential for specific foods to be cost effective for children. Development of a lactose-free porridge that can be used as a ready to use therapeutic food in African malnourished children was found to be cost effective in reducing hospital stays. The use of fluoridated milk in needy children who already are provided milk in Chile has also been shown to be cost effective for reducing costs associated with dental care of young children. A broader based program is described for the US underprivileged children entitled the Supplemental Nutrition Assistance program (SNAP) managed by the USDA. By providing children nutrient dense foods and educational materials to parents, this program has shown that it is cost effective to be pro-active about nutrition. In contrast to these three programs, it is difficult to establish the cost effectiveness of nutrition interventions including increases in calcium and vitamin D intakes for improving bone health in children as a means to reduce the costs associated with osteoporosis. Perhaps an alternative strategy would be to look at the association of this intervention and reduction in costs of forearm fractures in prepubertal girls.

The fourth section on Antioxidant Nutrient and Bioactive Food Component Interactions: Potential Economic Benefits includes four chapters that examine the common thread of the importance of optimal antioxidant intakes throughout the lifespan for reducing disease risks and the dermal evidence of aging. One chapter provides a broad overview of the major dietary antioxidants and their concentrations in foods; the chemical structures of these important bioactive molecules are also included. There is a separate, in-depth chapter on zinc and its critical role as an antioxidant as well as a critical component of nonantioxidant enzymes. Options for enhancing zinc levels in the food supply are provided including genetic modification of plants with the goal of enhancing childhood immunity and enhancing the activity of tumor suppressor genes. Another source of antioxidant potential is reviewed in a chapter on a traditional medicine and food source from the hibiscus plant, Roselle. Teas made from parts of the plant have been used as an antioxidant, and also as an antibacterial especially in Mexico and other nations. The final chapter in this section is unique in its comprehensive review of the products used reduce the risk and treat the dermal signs of aging. There is an extensive discussion of the oxidative damage caused by UV light exposure and the importance of lifetime intakes of antioxidant rich diets to reduce environmental dermal damage. Authors of these chapters have been particularly inclusive and objective; extensive references to the published literature are provided.

The fifth section looks mainly at the Economic Effects of Dietary Components in Disease and Prevention Therapy in five chapters. Three of the chapters review the antiviral, antibacterial, antifungal, and anticarcinogenic properties of native plants that have been used as food sources and/or as medicinals. In-depth descriptions of the plants and the components identified as containing the bioactive component and its function are provided for more than 50

distinct plants. One possible way to utilize the antimicrobial properties of plant components is being utilized in food animal production practices. The use of citrus peels that are fed to livestock before slaughter to reduce food-borne pathogens before these enter the food supply is carefully described in another unique chapter. Secondary disease prevention and/or reduction in disease and surgical complications are examined in the last two chapters in this section. Chronic kidney disease is often a consequence of diabetes that is also often linked to obesity. Dietary changes to reduce cholesterol levels and insulin sensitivity can include supplementation with omega-3 fatty acids, antioxidants, B vitamins, and newer plant compounds that have been shown to be beneficial such as those from the olive leaf. These strategies have resulted in cost effective avoidance of dialysis and kidney transplants. Another proven cost effective strategy is the provision of preoperative immunonutrition formulas that contain arginine, omega-3 fatty acids, nucleotides, and other beneficial nutrients. Documentation of cost effectiveness has been shown in gastric cancer surgery patients and is reviewed in the final chapter in this section.

The final section of the volume contains eight chapters that examine the Cost Effectiveness of Dietary Intervention in Cardiovascular Disease and Diabetes. The economic value of the DASH diet is examined for hypertension reduction as well as a means to reduce the costs of care post myocardial infarction. Also, the WHO's evaluation of the global consequences of obesity and noncommunicable diseases are examined from a public health perspective. Changes in food industry choices and incentives for community health initiatives are reviewed. Diabetes prevalence is increasing globally and the potential for low glycemic, high satiety foods to enhance glycemic control are described in detail in two chapters. The third related pragmatic chapter provides practice guidelines and compilations of lifestyle interventions in prediabetics as well as for those with diabetes. The last two chapters explore the new findings from preliminary studies that examine the potential for a plant-based supplement to reduce the microvascular complications associated with diabetes and cardiovascular diseases and compare the cost effectiveness of this intervention with standard pharmacological agents.

Thus, it is clear that this volume contains a wealth of information concerning the potential for dietary interventions to reduce the costs associated with disease treatments. Additionally, the editors and authors have focussed on assisting those who are unfamiliar with the field of health economics in understanding the critical issues and important new research findings that can impact their fields of interest. Drs. Watson, Gerald, and Preedy have carefully chosen the very best researchers from around the world who can communicate the economic advantage of dietary components for both the maintenance of health and disease management. The authors have worked hard to make their information accessible to health professionals interested in public health, those practicing in medical specialties from pediatrics to geriatrics, those in general medical practice, health economists, public health practitioners, nurses, pharmacists and PharmD.s, educators, graduate students as well as nutrition-related allied health professionals.

In conclusion, "Nutrients, Dietary Supplements, and Nutraceuticals: Cost Analysis versus Clinical Benefits," edited by Ronald Ross Watson, Ph.D.,

Joe K. Gerald, M.D., and Victor R. Preedy, Ph.D. provides health professionals in many areas of research and practice with the most up-to-date, well referenced volume on the economic value of dietary intervention in evaluation of the importance of dietary factors for optimal health. This volume will serve the reader as the most authoritative resource in the field to date and is a very welcome addition to the Nutrition and Health Series.

Adrianne Bendich, Ph.D., FACN
Series Editor

Preface

Food and nutrition are vital keys to controlling morbidity and mortality from many chronic diseases affecting humankind. For millennia the relationship between famine and subsequent death due to disease has been known. Clearly food can be a key preventative agent for such dietary insufficiency-induced diseases. In the past decade, simple and very cheap vitamin A supplements not only prevented ocular damage but extended lifespan in children in developing countries. Documentation of the economic benefits of such dietary remedies is vital to their use in countries where there are insufficient health facilities and where adult diseases may take priority. In industrialized countries the cost to treat one person with a chronic disease like AIDS would pay for nutritional supplements preventing growth and development problems in thousands of children. Both are worthwhile but not always economically possible. Thus this book is crucial as it helps to document for health care agencies and individuals whether various *dietary supplements, nutrients and/or bioactive extracts promote health in a cost-effective manner or not.*

Biomolecules in dietary fruits and vegetables play crucial roles in health maintenance as well as in dietary supplements. They certainly could have different actions beyond their nutrient value in health promotion. For decades, it has been appreciated that oxidative pathways can lead to tissue damage and contribute to pathology. Fortunately, nature has provided us the mechanisms found predominately in plants to defend against such injury. Antioxidant nutritional agents have consequently attracted major attention and rightfully deserve to be studied carefully for possible beneficial roles. One of the main reasons for the interest in antioxidant agents in dietary vegetables, and their products, is their virtually complete lack of harmful side effects. This stands in stark contrast to many drugs that are promoted and studied for possible disease-preventive activity. However, are such bioactive molecules potent enough with an appropriate cost to be economically viable in health promotion? This book documents the potential cost-benefit relationship between major diseases and significant dietary supplements.

The US National Cancer Institute reports that only 18% of adults have the recommended intake of vegetables. Increasingly, Americans, Japanese, and Europeans are turning to the use of dietary vegetables, medicinal herbs, and their extracts or components to prevent or treat cancer. It has been known for decades that those populations with high vegetable consumption have reduced

risks of cancer and other diseases. However, which extracts or components are best to prevent disease or promote health? Some may be useful in experimental studies but the expenses of the supplements may outweigh the benefits. The goal of this book is to examine key ones for which health benefits are known to estimate their economic efficacy or lack thereof.

This book brings together experts working on the different aspects of supplementation, foods, economics and plant extracts and their potential for health promotion and disease prevention. Their expertise and experience provide the most current knowledge to promote future research. The conclusions and recommendations from the various chapters will provide a basis for using dietary supplements for which there is an economic rationale. By using vegetable extracts people can dramatically expand their exposure to protective dietary components and thus readily reduce their risk of multiple diseases. Specific foods, individual fruits or vegetables and their by products are reviewed in order to expand understanding and appropriate use. Yet are the benefits worth the increased costs of vegetables and their extracts? If so for which diseases? Which supplements are economically beneficial in treatment and/or prevention?

Plant extracts as dietary supplements are now a multi-billion-dollar business, built upon moderate research data. The bioactive extracts constitute many non-traditional medicines. In many cases these materials have been largely unregulated with limited requirements to show efficacy let alone economic efficiency compared to pharmaceutical drugs. Recently the US Food and Drug Administration has pushed this industry, with the support of Congress, to base its claims and products on scientific research. Therefore, the key area of dietary herbal medicine in this book will focus on efficacy or lack thereof in health promotion with emphasis on their economic benefits. Since common dietary vegetables and over-the-counter extracts are readily available, this book will be useful to health providers who treat clients and modify their lifestyles, as well as to the growing nutrition, food science, and natural product community. Increasingly, the lay public is requesting advice and is using more bioactive natural products in treatment and prevention of certain diseases including cancer, encouraging the medical community to become more knowledgeable. This book focuses on the growing body of knowledge on the role of diet, supplements and various dietary plants in reducing disease and whether the cost of such dietary changes equals or exceeds their economic benefits. As such the book will be essential reading for nutritionists, pharmacologist, health care professionals, research scientists, cancer workers, pathologists, molecular or cellular biochemists, physicians, general practitioners as well as those interested in diet and nutrition.

Our overall goal is to provide the most current, concise, scientific appraisal of the cost-benefits of nutritional supplements and bioactive components (nutriceuticals) of foods in improving the quality of life. The *basic outline* of the book involves concise chapters in sections: (A) *Introduction and Overview* which focuses on economics design in nutrition policy and value of dietary supplements; (B) *Influences on Preventive Nutrition Strategies* which focuses on benefits of fruits and vegetables versus costs; (C) *Cost-benefits of Food Interventions* which range from dental caries to malnourished children;

(D) *Nutrients and Bioactive Food Components and Interactions: Economic Benefits* which focuses on items such as natural antioxidants and zinc relative to their costs; (E) *Economic Effects of Dietary Components in Disease and Prevention Therapy* which focuses on cost benefits of citrus and vegetables on cancer and viruses; and (F) *Cost Effectiveness of Dietary Intervention in Cardiovascular Disease and Diabetes* which is the major section and shows the importance of dietary supplements relative to their costs. The excellent volunteer work of a wide variety of experts is greatly appreciated as it made this book possible.

Acknowledgments

The work of editorial assistant, Bethany L. Stevens, in communicating with authors, working with the manuscripts and the publisher was critical to the successful completion of the book and is much appreciated. Her daily responses to queries and collection of manuscripts and documents were extremely helpful. Support for her work was graciously provided by the National Health Research Institute as part of its mission to communicate to scientists about bioactive foods and dietary supplements was vital (<http://www.naturalhealthresearch.org>). This was part of their efforts to educate scientists and the lay public on the health and economic benefits of nutrients in the diet as well as supplements. Finally Nguyen T. Nga and Mari Stoddard of the Arizona Health Sciences library were instrumental in finding the authors and their addresses in the early stages of the book's preparation. The support of Humana Press staff as well as the input by the series editor, Adrienne Bendich is greatly appreciated for the improved organization of this book.

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Biography

Ronald R. Watson, Ph.D., attended the University of Idaho but graduated from Brigham Young University in Provo, Utah, with a degree in chemistry in 1966. He earned his Ph.D. in biochemistry from Michigan State University in 1971. His postdoctoral schooling in nutrition and microbiology was completed at the Harvard School of Public Health, where he gained 2 years of postdoctoral research experience in immunology and nutrition.

From 1973 to 1974 Dr. Watson was assistant professor of immunology and performed research at the University of Mississippi Medical Center in Jackson. He was assistant professor of microbiology and immunology at the Indiana University Medical School from 1974 to 1978 and associate professor at Purdue University in the Department of Food and Nutrition from 1978 to 1982. In 1982 Dr. Watson joined the faculty at the University of Arizona Health Sciences Center in the Department of Family and Community Medicine of the School of Medicine. He is currently professor of health promotion sciences in the Mel and Enid Zuckerman Arizona College of Public Health.

Dr. Watson is a member of several national and international nutrition, immunology, cancer, and alcoholism research societies. He is presently funded by the National Heart Blood and Lung Institute to study heart disease. In addition he has an NIH grant from NCCAM to study dietary supplements in modulating immune function and thus heart structure and function. For 30 years he was funded by Wallace Research Foundation to study dietary supplements in health promotion. Dr. Watson has edited more than 35 books on nutrition and another 53 scientific books. He has published more than 500 research and review articles.

Professor Victor R. Preedy is currently Professor of Nutritional Biochemistry in the Department of Nutrition and Dietetics, King's College London and Professor of Clinical Biochemistry in the Department of Clinical Biochemistry, King's College London. He is also Director of the Genomics Centre, Kings College London. Professor Preedy graduated in 1974 with a Degree in Biology and Physiology with Pharmacology. He gained his Ph.D. in 1981 in the field of Nutrition and Metabolism, specializing in protein turnover. In 1992 he received his Membership of the Royal College of Pathologists, based on his published works and in 1993 he gained a D.Sc. degree for his outstanding contribution to protein metabolism. At the time, he was one of the university's youngest

recipients of this distinguished award. Professor Preedy was elected as a Fellow to the Royal College of Pathologists in 2000. Since then he has been elected as a Fellow to the Royal Society for the Promotion of Health (2004) and The Royal Institute of Public Health (2004). In 2009 he was elected as a Fellow of the Royal Society for Public Health. Professor Preedy has written or edited over 550 articles, which includes over 160 peer-reviewed manuscripts based on original research and 85 reviews and 30 books. He has a wide interest in health related matters, particularly nutrition and diet.

Joe K. Gerald, MD, Ph.D., joined the Division of Community, Environment and Policy in the Mel and Enid Zuckerman College of Public Health in March of 2009. Dr. Gerald is the director of the undergraduate program in public health. His prior contributions to undergraduate education were recognized in 2001 as the recipient of the Ellen-Gregg-Ingalls/University of Alabama at Birmingham National Alumni Society Award for Excellence in Classroom Teaching. He currently teaches Health Care in the US and Health Economics and Policy.

Dr. Gerald completed a Ph.D. in Health Services Administration and post-doctoral fellowship in outcomes research at the University of Alabama at Birmingham. His research focuses on health outcomes, comparative effectiveness and economic research with an emphasis on the cost-effectiveness of interventions targeting children with asthma. His most recent work on the cost-effectiveness of school-based asthma screening was published in the *Journal of Asthma and Clinical Immunology*. This research used a novel short-cycle Markov Model approach to evaluate a 5 asthma health state model. He is currently investigating the cost-effectiveness of hand hygiene practices and their impact on asthma exacerbations.

Dr. Adrienne Bendich is Clinical Director, Medical Affairs at GlaxoSmithKline (GSK) Consumer Healthcare where she is responsible for leading the innovation and medical programs in support of many well-known brands including TUMS and Os-Cal. Dr. Bendich had primary responsibility for GSK's support for the Women's Health Initiative (WHI) intervention study. Prior to joining GSK, Dr. Bendich was at Roche Vitamins Inc. and was involved with the groundbreaking clinical studies showing that folic acid-containing multivitamins significantly reduced major classes of birth defects. Dr. Bendich has coauthored over 100 major clinical research studies in the area of preventive nutrition. Dr. Bendich is recognized as a leading authority on antioxidants, nutrition and immunity, and pregnancy outcomes, vitamin safety and the cost-effectiveness of vitamin/mineral supplementation.

Dr. Bendich is the editor of nine books including "Preventive Nutrition: The Comprehensive Guide For Health Professionals" coedited with Dr. Richard Deckelbaum, and is Series Editor of "Nutrition and Health" for Humana Press with 29 published volumes including "Probiotics in Pediatric Medicine" edited by Dr. Sonia Michail and Dr. Philip Sherman; "Handbook of Nutrition and Pregnancy" edited by Dr. Carol Lammi-Keefe, Dr. Sarah Couch, and Dr. Elliot Philipson; "Nutrition and Rheumatic Disease" edited by Dr. Laura Coleman; "Nutrition and Kidney Disease" edited by Dr. Laura Byham-Grey, Dr. Jerrilynn

Burrowes, and Dr. Glenn Chertow; “Nutrition and Health in Developing Countries” edited by Dr. Richard Semba and Dr. Martin Bloem; “Calcium in Human Health” edited by Dr. Robert Heaney and Dr. Connie Weaver and “Nutrition and Bone Health” edited by Dr. Michael Holick and Dr. Bess Dawson-Hughes.

Dr. Bendich served as Associate Editor for “Nutrition” the International Journal; served on the Editorial Board of the Journal of Women’s Health and Gender-based Medicine, and was a member of the Board of Directors of the American College of Nutrition.

Dr. Bendich was the recipient of the Roche Research Award, is a *Tribute to Women and Industry* Awardee and was a recipient of the Burroughs Wellcome Visiting Professorship in Basic Medical Sciences, 2000–2001. In 2008, Dr. Bendich was given the Council for Responsible Nutrition (CRN) Apple Award in recognition of her many contributions to the scientific understanding of dietary supplements. Dr Bendich holds academic appointments as Adjunct Professor in the Department of Preventive Medicine and Community Health at UMDNJ and has an adjunct appointment at the Institute of Nutrition, Columbia University P&S, and is an Adjunct Research Professor, Rutgers University, Newark Campus. She is listed in Who’s Who in American Women.

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