

SPECIAL FOCUS ISSUE: CARDIOVASCULAR HEALTH PROMOTION

THE PRESENT AND FUTURE: JACC STATE-OF-THE-ART REVIEW

Supplemental Vitamins and Minerals for CVD Prevention and Treatment



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ABSTRACT

The authors identified individual randomized controlled trials from previous meta-analyses and additional searches, and then performed meta-analyses on cardiovascular disease outcomes and all-cause mortality. The authors assessed publications from 2012, both before and including the U.S. Preventive Service Task Force review. Their systematic reviews and meta-analyses showed generally moderate- or low-quality evidence for preventive benefits (folic acid for total cardiovascular disease, folic acid and B-vitamins for stroke), no effect (multivitamins, vitamins C, D, β -carotene, calcium, and selenium), or increased risk (antioxidant mixtures and niacin [with a statin] for all-cause mortality). Conclusive evidence for the benefit of any supplement across all dietary backgrounds (including deficiency and sufficiency) was not demonstrated; therefore, any benefits seen must be balanced against possible risks. (J Am Coll Cardiol 2018;71:2570–84)
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Treatment and prevention of micronutrient deficiencies with vitamins and minerals in the last two-and-a-half centuries are among the most dramatic achievements in the history of nutritional science. The treatment of scurvy with citrus fruit (vitamin C) by the British Naval Surgeon James Lind in 1747 was, perhaps, the first clinical trial ever conducted (1), in which 12 sailors who had scurvy were (presumably randomly) selected to receive 1 of 6 treatments (2 sailors) per treatment. However, interest in micronutrients has shifted recently from prevention of classic deficiency states to prevention of possible



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subclinical deficiencies and promotion of overall health and longevity using supplemental vitamins and minerals (supplement use). Here, the data are less clear, but supplement use is widespread. Using the National Health and Nutrition Examination Survey data (1999 to 2012) on 37,958 adults, it was estimated that supplement use was high in 2012, with up to 52% of the population taking supplements. Multivitamins were taken by 31% of the population, vitamin D by 19%, calcium by 14%, and vitamin C by 12% (2). In Europe during this period, the European Prospective Investigation into Cancer and Nutrition (EPIC) data on 36,034 men and women indicated a wide range of supplement use, with a strong north-south gradient that was highest in the north (e.g., Denmark: 51% men, 65.8% women) and lowest in the south (e.g., Greece: 2.0% men, 6.7% women), and with higher supplement use by women (3). Despite high supplement use by the general public, there is no general agreement on whether individual vitamins and minerals or their combinations should be taken as supplements for cardiovascular disease (CVD) prevention or treatment. Only the Canadian Cancer Society recommends a supplement (1,000 IU vitamin D to be taken in fall and winter) (4). What is generally recommended internationally is consumption of a good diet as part of a healthy lifestyle. The recent science-based report of the U.S. Dietary Guidelines Advisory Committee, also

concerned with CVD risk reduction, recommended 3 dietary patterns: 1) a healthy American diet low in saturated fat, trans fat, and red meat, but high in fruit and vegetables; 2) a Mediterranean diet; and 3) a vegetarian diet (5). These diets, with their accompanying recommendations, continue the move toward more plant-based diets that are relatively rich in vitamins and minerals, which liberally satisfies requirements (Dietary Reference Intakes) but which are still below the tolerable upper levels of intake of the recommended range in which adverse effects may be seen. Thus, for the general public, the focus has been on meeting requirements through diet, rather than supplements.

Therefore, we reviewed the evidence for supplement use over the last 4 years since the publication of the evidence (6) and guidelines (7) for supplement use of the U.S. Preventive Services Task Force (USPSTF).

METHODS

We conducted a systematic review and meta-analysis of existing systematic reviews and meta-analyses and single randomized controlled trials (RCTs) published in English from January 2012 (1 year before the census, when this field was reviewed comprehensively by the

ABBREVIATIONS AND ACRONYMS

CI	= confidence interval
CVD	= cardiovascular disease
GRADE	= Grading of Recommendations Assessment, Development, and Evaluation
MI	= myocardial infarction
NNT	= number needed to treat
RCT	= randomized controlled trial
RR	= risk ratio
USPSTF	= U.S. Preventive Services Task Force

Canada, Pulse Canada, Kellogg's Company, Quaker Oats, Procter & Gamble Technical Centre Ltd., Bayer Consumer Care, Pepsi/Quaker, International Nut & Dried Fruit (INC), Soy Foods Association of North America, the Coca-Cola Company (investigator-initiated, unrestricted grant), Solae, Haine Celestial, the Sanitarium Company, Orafit, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, the Canola and Flax Councils of Canada, the Calorie Control Council, the CIHR, the Canada Foundation for Innovation, and the Ontario Research Fund; has received in-kind supplies for trials as a research support from the Almond Board of California, Walnut Council of California, American Peanut Council, Barilla, Unilever, Unico, Primo, Loblaw Companies, Quaker (Pepsico), Pristine Gourmet, Bunge Limited, Kellogg Canada, and WhiteWave Foods; has been on the speakers panel, served on the scientific advisory board, and/or received travel support and/or honoraria from the Almond Board of California, Canadian Agriculture Policy Institute, Loblaw Companies Ltd., the Griffin Hospital (for the development of the NuVal scoring system), the Coca-Cola Company, EPICURE, Danone, Diet Quality Photo Navigation, Better Therapeutics (FareWell), Verwywell, True Health Initiative, Institute of Food Technologists, Saskatchewan Pulse Growers, Sanitarium Company, Orafit, the American Peanut Council, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, Herbalife International, Pacific Health Laboratories, Nutritional Fundamental for Health, Barilla, Metagenics, Bayer Consumer Care, Unilever Canada and Netherlands, Solae, Kellogg, Quaker Oats, Procter & Gamble, the Coca-Cola Company, the Griffin Hospital, Abbott Laboratories, the Canola Council of Canada, Dean Foods, the California Strawberry Commission, Haine Celestial, PepsiCo, the Alpro Foundation, Pioneer Hi-Bred International, DuPont Nutrition and Health, Spherix Consulting and WhiteWave Foods, the Advanced Foods and Material Network, the Canola and Flax Councils of Canada, the Nutritional Fundamentals for Health, Agriculture and Agri-Food Canada, the Canadian Agri-Food Policy Institute, Pulse Canada, the Saskatchewan Pulse Growers, the Soy Foods Association of North America, the Nutrition Foundation of Italy, Nutra-Source Diagnostics, the McDougall Program, the Toronto Knowledge Translation Group (St. Michael's Hospital), the Canadian College of Naturopathic Medicine, The Hospital for Sick Children, the Canadian Nutrition Society (CNS), the American Society of Nutrition (ASN), Arizona State University, Paolo Sorbini Foundation, and the Institute of Nutrition, Metabolism and Diabetes; has received an honorarium from the United States Department of Agriculture to present the 2013 W.O. Atwater Memorial Lecture; has received funding and travel support from the Canadian Society of Endocrinology and Metabolism to produce mini-cases for the Canadian Diabetes Association; is a member of the International Carbohydrate Quality Consortium (ICQC); his wife is a director and partner of Glycemic Index Laboratories, Inc.; and his sister received funding through a grant from the St. Michael's Hospital Foundation to develop a cookbook for one of his studies. Dr. Spence is an officer of Vascularis, Inc.; and has received lecture fee from Bristol-Myers Squibb. Dr. Kendall has received grants or research support from the Advanced Food Materials Network, Agriculture and Agri-Foods Canada, Almond Board of California, American Pistachio Growers, Barilla, Calorie Control Council, CIHR, Canola Council of Canada, International Nut and Dried Fruit

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