

## The case for nutritional supplementation

R H J Verkerk PhD, Alliance for Natural Health ([www.anhcampaign.org](http://www.anhcampaign.org))

In recent years, there has been a rapid expansion of the body of scientific evidence published in peer-reviewed journals which demonstrates that use of food supplements can improve overall nutritional status and key bio-markers for health as well as reduce risk of chronic diseases such as heart disease and cancer. In contrast, there have been a small number of well-publicised studies which have failed to demonstrate beneficial effects, and this has led to some confusion among consumers.

A wealth of evidence from observational and epidemiological studies suggests that diets high in carotenoid, vitamin E and polyphenol-rich fruits and vegetables offer substantially reduced risk of chronic diseases.<sup>1,2,3,4,5,6,7,8,9,10</sup> Basic research also has provided suggestive evidence for plausible mechanisms for these observed effects.<sup>11,12,13</sup> In attempting to understand the nutrients responsible for these

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<sup>1</sup> Buring JE, Hennekens CH. Retinoids and carotenoids. In: DeVita VT Jr, Hellman S, Rosenberg SA, eds. *Cancer: principles and practice of oncology*. 4th ed. Philadelphia: J.B. Lippincott, 1993: 464-74.

<sup>2</sup> Greenwald P. NCI cancer prevention and control research. *Prev Med*, 1993; 22:642-60.

<sup>3</sup> Knekt P, Reunanen A, Jarvinen R, Seppanen R, Heliovaara M, Aromaa A. Antioxidant vitamin intake and coronary mortality in a longitudinal population study. *Am J Epidemiol* 1994; 139: 1180-9.

<sup>4</sup> Klipstein-Grobusch K, Geleijnse JM, den Breeijen JH, et al. Dietary antioxidants and risk of myocardial infarction in the elderly: the Rotterdam Study. *Am J Clin Nutr*, 1999; 69: 261-6.

<sup>5</sup> Kushi LH, Folsom AR, Prineas RJ, Mink PJ, Wu Y, Bostick RM. Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women. *N Engl J Med*, 1996; 334: 1156-62.

<sup>6</sup> Gaziano JM, Manson JE, Buring JE, Hennekens CH. Dietary antioxidants and cardiovascular disease. *Ann N Y Acad Sci*, 1992; 669: 249-59.

<sup>7</sup> Gaziano JM, Manson JE, Branch LG, Colditz GA, Willett WC, Buring JE. A prospective study of consumption of carotenoids in fruits and vegetables and decreased cardiovascular mortality in the elderly. *Ann Epidemiol*, 1995; 5: 255-60.

<sup>8</sup> Lippman SM, Benner SE, Hong WK. Retinoid chemoprevention studies in upper aerodigestive tract and lung carcinogenesis. *Cancer Res*, 1994;54: Suppl:2025s-2028s.

<sup>9</sup> Omenn GS, Goodman G, Thornquist M, et al. The *b*-Carotene and Retinol Efficacy Trial (CARET) for chemoprevention of lung cancer in high risk populations: smokers and asbestos-exposed workers. *Cancer Res*, 1994;54: Suppl:2038s-2043s.

<sup>10</sup> Peto R, Doll R, Buckley JD, Sporn MB. Can dietary beta-carotene materially reduce human cancer rates? *Nature*, 1981; 290: 201-8.

<sup>11</sup> Burton GW, Ingold KU. Beta-carotene: an unusual type of lipid antioxidant. *Science*, 1984; 224: 569-73.

effects, clinical studies have been carried out, these generally involving single, synthetic forms of nutrients, or limited combinations of nutrients. Such clinical studies, however, have tended not to show clear beneficial effects of the nutrients.<sup>14,15,16</sup>

Scientific opinion is increasingly leaning towards the notion that isolated forms of nutrients, particularly synthetic forms of nutrients (especially in the cases of the carotenoids and vitamin E) may not yield the same health protective functions as complexes of nutrients, which can act synergistically, as found in the normal diet. Accordingly, the results of many of the clinical studies conducted on isolated, synthetic nutrients may be less relevant than the observational or epidemiological studies. This also suggests that supplementation with natural complexes of nutrients, similar to those found in dietary sources, is likely to be considerably more beneficial in terms of chronic disease risk reduction than supplementation with isolated nutrients.

A major review of studies on the relationships between vitamin intake and various diseases published between 1966 and 2002 demonstrated that suboptimal levels of vitamin intake are associated with increased risk of contracting a variety of chronic diseases, including cancer, heart disease and osteoporosis.<sup>17</sup> The authors of this study concluded that many physicians may be unaware of common food sources of vitamins or may be unsure which vitamins they should recommend for their patients and given the current status of scientific knowledge it may be prudent for most adults to supplement their diet with a daily multivitamin.<sup>11</sup>

A study that followed 958,000 subjects and their death rates from amyotrophic lateral sclerosis (ALS), a progressive disease of motor nerves in the brain and spinal

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<sup>12</sup> Stich HF, Rosin MP, Vallejera MO. Reduction with vitamin A and betacarotene administration of proportion of micronucleated buccal mucosal cells in Asian betel nut and tobacco chewers. *Lancet*, 1984; 1: 1204-6.

<sup>13</sup> Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol: modifications of low-density lipoprotein that increase its atherogenicity. *N Engl J Med*, 1989; 320: 915-24.

<sup>14</sup> Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta-carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med*, 1994; 330: 1029-1035.

<sup>15</sup> Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammer S. Effects of a combination of beta-carotene and vitamin A on lung cancer and cardiovascular disease. *N Engl J Med*, 1996; 334: 1150-1155.

<sup>16</sup> Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med*, 2000; 342(3): 154-60.

<sup>17</sup> Fairfield KM, Fletcher RH. Vitamins for chronic disease prevention in adults: scientific review. *JAMA*, 2002; 287 (23): 3116-26.

cord, from 1989 to 1998 found that those who used vitamin E supplements for 10 years or more had a 62% lower death rate from ALS than those who used no supplements, while those who used vitamin E supplements for less than 10 years had a 41% lower death rate from ALS than non-supplement users.<sup>18</sup>

A study (Established Populations for Epidemiologic Studies of the Elderly) which followed 11,178 people between the ages of 67 and 105 over the period 1984-1993 concluded that the overall risk of death was reduced by 42% for those who took higher dose supplements of vitamins C and E.<sup>19</sup>

A randomised double-blind prevention trial across 7 countries provided conclusive evidence that women who took supplements containing 400 µg folic acid reduced the risk of having babies with neural tube defects such as spina bifida by some 72%.<sup>20</sup>

A large group of 88,756 women from the Nurses' Health Study, who were free of cancer in 1980 and provided updated assessments of diet, including multivitamin supplement use from 1980 to 1994, were followed through for colon cancer. It was found that long term use (over 15 years use), but not short-term use (less than 4 years use) of multivitamins including folic acid markedly reduced (ca. 5-fold) the frequency of colon cancer.<sup>21</sup>

In a further epidemiological study involving 87,245 female nurses, it was found, after adjustment for age and smoking, that long-term vitamin E supplementation alone was associated with a 9% reduction in heart disease.<sup>22</sup> A randomised trial, published in the *Lancet*, showed that subjects consuming vitamin C (1000 mg /day) and E (800 IU /day) supplements had a significantly lower risk of developing arteriosclerosis, compared with the placebo control.<sup>23</sup>

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<sup>18</sup> Ascherio A, Weisskopf MG, O'reilly EJ, Jacobs EJ, McCullough ML, Calle EE, Cudkovicz M, Thun MJ. Vitamin E intake and risk of amyotrophic lateral sclerosis. *Ann Neurol*. 2005, 57(1): 104-10.

<sup>19</sup> Losonczy KG, Harris TB, Havlik RJ. Vitamin E and vitamin C supplement use and risk of all-cause and coronary heart disease mortality in older persons: the Established Populations for Epidemiologic Studies of the Elderly. *Am J Clin Nutr*. 1996; 64(2): 190-6.

<sup>20</sup> MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet*, 1991; 338 (8760): 131-7.

<sup>21</sup> Giovannucci E, Stampfer MJ, Colditz GA, Hunter DJ, Fuchs C, Rosner BA, Speizer FE, Willett WC. Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study. *Ann Intern Med*, 1998; 129 (7): 517-24.

<sup>22</sup> Stampfer MJ, Hennekens CH, Manson JE, Colditz GA, Rosner B, Willett WC. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med*, 1993; 328 (20): 1444-9.

<sup>23</sup> Fang JC, Kinlay S, Beltrame J, Hikiti H, Wainstein M, Behrendt D, Suh J, Frei B, Mudge GH, Selwyn AP, Ganz P. Effect of vitamins E and C on progression of transplant-associated arteriosclerosis: a randomised trial. *Lancet*, 2002; 359 (9312): 1108-13.

In a clinical intervention study (CHAOS) of 2002 coronary patients by Cambridge University scientists, supplementation of up to 800 IU vitamin E (in the alpha-tocopherol form) per day for over two years was associated with reductions in the frequencies of heart attacks by as much as 75%.<sup>24</sup>

A randomised, placebo-controlled trial involving 90 UK schoolchildren showed many children were mineral deficient and that non-verbal intelligence was increased in the group given a multivitamin/mineral supplement, but not in the group receiving a placebo.<sup>25</sup>

A recent placebo-controlled study of 21 Canadian nursing homes showed that subjects (average age 85) without dementia had a significantly lower rate of infections when taking a vitamin and mineral supplement compared with a placebo.<sup>26</sup>

It has been shown that long-term micro-nutritional deficiencies cause damage to DNA much in the same way as radiation and such oxidative stress is likely to contribute to the development of cancer.<sup>27</sup>

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<sup>24</sup> Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ. Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS). *Lancet*, 1996; 347 (9004): 781-6.

<sup>25</sup> Benton D, Roberts G. Effect of vitamin and mineral supplementation on intelligence of a sample of schoolchildren. *Lancet*, 1988; 23: 140-3.

<sup>26</sup> Liu BA, McGeer A, McArthur MA, Simor AE, Aghdassi E, Davis L, Allard JP. Effect of multivitamin and mineral supplementation on episodes of infection in nursing home residents: a randomized, placebo-controlled study. *J Am Geriatr Soc*. 2007; 55(1): 35-42.

<sup>27</sup> Ames BN. Micronutrient deficiencies - A major cause of DNA damage. *Ann New York Acad Sci*, 1999; 889: 87-106.