

population and dose of antioxidants might be important determinants of the effect of antioxidants on cancer and mortality. The effect of antioxidant supplements could also depend on baseline antioxidant status. Antioxidant supplements could influence the balance between oxidative stress and apoptosis in human cells, resulting in undesirable health consequences. We discussed this issue at length in our review.

The SU.VI.MAX results<sup>4</sup> are interesting and may not in fact contradict our findings (different population, different doses of antioxidants, and differential use of selenium). However, the positive SU.VI.MAX results originate from subgroup analyses, which must be interpreted with caution.<sup>5</sup>

Finally, results of recent and ongoing randomised clinical trials, when incorporated into our meta-analysis, will provide more precise, evidence-based facts about the potential influence of antioxidant supplements on our health.

We declare that we have no conflict of interest.

\**Goran Bjelakovic, Dimitrinka Nikolova, Rosa G Simonetti, Christian Gluud*  
goranb@junis.ni.ac.yu

Cochrane Hepato-Biliary Group, Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

- 1 Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for preventing gastrointestinal cancers (Cochrane Review). *Cochrane Database Syst Rev* 2004; **4**: CD004183.
- 2 Kjærgard LL, Villumsen J, Gluud C. Reported methodological quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 2001; **135**: 982–89.
- 3 Miller ER III, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; **142**: 37–46.
- 4 Hercberg S, Galan P, Preziosi P, et al. The SU.VI.MAX study: a randomised, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. *Arch Intern Med* 2004; **164**: 2335–42.
- 5 Oxman AD, Guyatt GH. A consumer's guide to subgroup analyses. *Ann Intern Med* 1992; **116**: 78–84.

The prospect raised by Goran Bjelakovic and colleagues<sup>1</sup> that vitamins might not only do no good but also kill their consumers is a scary one. We agree with their careful interpretation of the study's results. However, reporting by the media of a lack of effect of most vitamins is unfortunate, since insufficient dietary intake of micronutrients, including vitamins, is still a common health problem worldwide.

Data consistently show that vitamin D deficiency is frequent in Europe among healthy adults. The optimum values for serum vitamin D concentrations are about 80 nmol/L.<sup>2</sup> However, epidemiological studies in Europe indicate that 75% of healthy adults in France have vitamin D serum concentrations less than 78 nmol/L and 14% have values below 30 nmol/L.<sup>2</sup> In Finland, 86% of women age 31–43 years had serum values of vitamin D less than 80 nmol/L.<sup>3</sup> Little is being done to tackle this problem, and the public and even health professionals seem unaware of the situation.

Widespread vitamin D deficiency could have a serious effect on public health. There is a well-established link between vitamin D and bone health and cardiovascular disease.<sup>4</sup> The public should be informed about the importance of vitamin D and those deficient for the nutrient identified and provided with supplements or advised about appropriate food groups.

The design and the nutritional status of the study populations of trials that have not detected a positive effect of antioxidants on cancer or cardiovascular disease prevention<sup>1,5</sup> should be examined carefully, since in most of these studies supplements were given to individuals without evidence of deficiency for vitamins or antioxidants. The probability of observing a clinical benefit is, therefore, low and the likelihood of an adverse effect high. Supplementation with vitamin A, for example, is

unlikely to result in a clinical benefit in countries where low vitamin A intake is uncommon, but in low-income countries where inadequate vitamin A intake is frequent, this clinical benefit is obvious.

We declare that we have no conflict of interest.

\**Rodrigo Moreno-Reyes, Marleen Boelaert, Sylvain Meuris*  
rmorenor@ulb.ac.be

\*Department of Nuclear Medicine, Erasme Hospital (RM-R) and Laboratory of Experimental Hormonology (SM), Université Libre de Bruxelles, Route de Lennik 808, B-1070 Brussel Belgium; and Institute of Tropical Medicine, Antwerp, Belgium (MB)

- 1 Bjelakovic G, Nikolova D, Simonetti RG, Gluud C. Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis. *Lancet* 2004; **364**: 1219–28.
- 2 Chapuy MC, Preziosi P, Maamer M, et al. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 1997; **7**: 439–43.
- 3 Lamberg-Allardt CJ, Outila TA, Karkkainen MU, Rita HJ, Valsta LM. Vitamin D deficiency and bone health in healthy adults in Finland: could this be a concern in other parts of Europe? *J Bone Miner Res* 2001; **16**: 2066–73.
- 4 Scragg R, Jackson R, Holdaway IM, Lim T, Beaglehole R. Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D3 levels: a community-based study. *Int J Epidemiol* 1990; **19**: 559–63.
- 5 Vivekananthan DP, Pen MS, Sapp SK, Hsu A, Topol EJ. Use of antioxidant vitamins for the prevention of cardiovascular diseases: meta-analysis of randomised trials. *Lancet* 2003; **361**: 2017–23.

## Malaria vaccine: 3 or 6 months' protection?

The results of the trial of the RTS,S/AS02A malaria vaccine reported by Alonso and colleagues (Oct 16, p 1411)<sup>1</sup> are exciting and show clearly a protective effect against severe malaria and delays in the time to a first attack of clinical malaria and to the appearance of parasites in the blood after vaccination. However, the authors' conclusions that protection against clinical disease showed no evidence of waning during the 6 month follow-up and that there was only limited waning of the efficacy against malaria infection

Rights were not granted to include this image in electronic media. Please refer to the printed journal.