cannot be ascribed to prevention of VAD, but indicates other very important roles of VAC.

Everybody agrees that securing an adequate diet and preventing VAD is a goal in itself, but we also predict that if we phase out VAC and replace them by lower doses, we may see a decline in mortality in some subgroups but an increase in mortality in other subgroups. Ideally, we should maintain VAC for those who benefit, even if not suffering from VAD, but stop VAC for those who are harmed, even if they have VAD.

The editorial accompanying the recent meta-analysis stated that' no more placebo-controlled trials of preschool vitamin A supplementation are needed'.[7] Based on the now available evidence, we respectfully disagree. We think the time has come to conduct large-scale multi-centre placebo-controlled VAC trials designed to test the overall effect on mortality of VAC as well as the interactions with sex and other immune-modulating interventions like vaccines. These trials should also include a third arm, with provision of low-dose regular vitamin A supplements. Only this way can we make sure that the children receive the evidence-based interventions that they deserve.

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Response to: Letter to the editor by C Benn, A Fisker and P Aaby

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The context for the views expressed by Benn *et al*. is that response to vitamin A supplements, in doses 100 times recommended daily allowances (RDAs), needs to be separated into: (i) possible effects through vitamin A as a nutrient in normal metabolism (as 100 times RDA doses are seldom found in nature); and (ii) effects through a pharmacological-type response via different mechanisms of the immune system. This seems a useful distinction, especially if, as they suggest, the effect of high-dose supplements may be either beneficial or harmful, and we need to know how to predict these responses.

It seems that the currently available data are not sufficient to address this important question that the authors imply: who benefits from high-dose vitamin A capsules (VACs), whether or not vitamin A-deficient, and who is harmed? Until this question can be answered, it remains questionable whether blanket indiscriminate distribution of high-dose VACs to young children is advisable. Certainly if this distribution had not been already established it would probably not be launched today on the basis of present knowledge.

Our further point is that the resources used for VACs would be better used to combat vitamin A deficiency (for which VACs are largely ineffective); and that the opportunity costs, especially in health personnel diverted to child health days, might be better used for regular health services including urgently needed community-based nutrition programmes. We agree that results of studies to clarify the role

of high-dose VACs might result in broad-based interventions to address vitamin A deficiency (by increasing frequent low-level vitamin A intakes) together with continued targeted use of high-dose VACs for those who would benefit.

However, we would again like to stress that, since VACs are distributed to 1–5-year-old children, they are not relevant to the majority of under 5-year-old deaths (U5MR), which are predominantly in the first few months of life. At most, in some contexts, they might reduce overall U5MR by about 5%. These considerations suggest that there should be higher priorities for use of large-scale programme resources aimed at reducing under-5 child mortality—by all means in contrast to research resources, which are clearly needed.

Mortality rates for same-sex married individuals compared with opposite-sex married individuals: potential analytical problems

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In 2013, Morten Frisch and Jacob Simonsen published the article 'Marriage, cohabitation and mortality in Denmark: national cohort study of 6.5 million persons followed for up to three decades (1982–2011)' in your journal.[1]

Frisch and Simonsen presented an impressive study with data from a national cohort of 6.5 million Danes with 122.5 million person-years of observations during 1982–2011. They set out to explore associations between living arrangements and mortality. By comparing same-sex married persons with opposite-sex married persons, however, an apparent association between sexual orientation and mortality became a significant theme of their article. The authors developed a design where they apparently transcended inherent methodological challenges related to epidemiological studies on marginalized groups by using population-based register data.[2] With reasonably robust indications of sexual orientation (registered partnership/marriage), their work invites generalizations to the target group (the gay and lesbian population).

Analysing overall mortality and cause-specific deaths for the period 2000–11, Frisch and Simonsen concluded that mortality was increased among same-sex married women compared with opposite-sex married women in Denmark [hazard ratio (HR) 1.89], notably from suicide (HR 6.40) and cancer (HR 1.62).[1] Finding these results alarming, we reviewed the approach of the article. In this letter we shall address potential analytical problems that may call for caution in the interpretation of their findings.

The authors wrote about categories for analysis: 'Between 1 January 1982 and 30 September 1989, there were four marital status categories: (i) unmarried (never married), (ii) married, (iii) divorced or (iv) widowed. Since 1 October 1989, three additional categories appeared, namely homosexually married, divorced or widowed, following the implementation of the world's first national law on registered same-sex partnerships; to gain statistical power we combined these categories in (v) current or former same-sex marriage.' A corresponding combination was apparently not established for the comparison groups of opposite-sex married men and women. The HRs, including the period 2000–11, were hence calculated from categories which were not comparable. It is well known that mortality is higher in unmarried, divorced and widowed than in married people. When including data from divorced and widowed individuals in the same-sex married category and not correspondingly in the opposite-sex married category, the main outcome measure (mortality) is biased. One might argue that the impact of this bias is limited, due to the low numbers of divorced and widowed previously same-sex married individuals. However, a comparable pooling for opposite-sex married individuals