The effect of vitamin E on mortality is not uniform over the population

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In their systematic review and meta-analysis on vitamins, Fortmann et al. calculated that vitamin E supplementation has no influence on all-cause mortality with 95% CI from -2% to +4% (1). This estimate was based on the pooling of the results of five studies. However, study-level analyses can lead to different conclusions than do corresponding individual-level analysis, a difference which is called the “ecological fallacy” (2).

Recently, we analyzed the heterogeneity in vitamin E effect on the mortality of ATBC Study participants, who were male smokers aged 50-69 years at baseline (3). The combination of age and dietary vitamin C intake modified the effect of vitamin E supplementation, so that the heterogeneity over six subgroups was highly significant (P = 0.0005). In 11,448 ATBC participants aged 50-62 years who had dietary vitamin C intake above the median, vitamin E increased all-cause mortality by 19% (95% CI: 5% to 35%), whereas in 872 participants aged 66-69 years who had vitamin C intake above the median, vitamin E decreased mortality by 41% (95% CI: -56% to -21%). Vitamin E did not influence mortality among men who had vitamin C intake below the median. The modifying effect of vitamin C was not explained by other substances in fruit and vegetables (3). At the biochemical level, the interaction between vitamins C and E is well known (4) and may explain the role of vitamin C as a modifying factor.

Furthermore, the benefit of vitamin E for men aged 66 and over implies that the survival time might be influenced. In a further exploratory analysis, we found that those administered vitamin E lived half a year longer at the upper end of the survival curves (5).

Given the mainly negative findings in the vitamin trials as summarized by Fortmann et al. (1), it seems justified to discourage the general population from taking supplements until we have better knowledge of the restricted groups of people who might benefit. Nevertheless, the pooled vitamin E effect which they calculated does not seem to apply to all people and neither does it indicate in what direction further investigation should proceed. The individual-level analysis of the ATBC Study suggests that trials on vitamins E and C for men older than 70 years are warranted (5).

References
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