Review: high dose vitamin E supplementation is associated with increased all cause mortality


Does vitamin E supplementation increase all cause mortality? Does a dose-response relation exist between vitamin E and all cause mortality?

### Methods

**Data sources:** Medline (1966 to August 2004), Cochrane Central Register of Controlled Trials, bibliographies of relevant studies and reviews, and personal files of the investigators.

**Study selection and assessment:** randomised controlled trials (RCTs) that compared vitamin E supplementation (alone or combined with other vitamins or minerals) with a control or placebo group in men or non-pregnant women; study duration and follow up were >1 year, and >10 deaths occurred.

**Outcomes:** all cause mortality.

### Main Results

19 RCTs (n = 135 967, mean age range 47–84 y) met the selection criteria. 9 RCTs evaluated vitamin E alone, and 10 combined vitamin E with other vitamins or minerals. 16 RCTs were placebo controlled. Vitamin E dose varied between 16.5 and 2000 IU/d. Overall, vitamin E supplementation did not affect all cause mortality (alone or combined with other vitamins or minerals) with a control or placebo group in men or non-pregnant women; study duration and follow up were >1 year, and >10 deaths occurred.

### Conclusions

High dose (≥400 IU/d) vitamin E supplementation is associated with increased risk of all cause mortality. A dose-response relation exists between vitamin E doses ≥150 IU/d and mortality.

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**Table: Vitamin E Dose and All Cause Mortality**

<table>
<thead>
<tr>
<th>Number of trials (n)</th>
<th>Vitamin E dose</th>
<th>RRI (95% CI)</th>
<th>Risk difference per 10 000 persons (CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>19 (135 967)</td>
<td>High and low</td>
<td>1% (–2 to 4)</td>
<td>10 (–18 to 38)</td>
<td>Not significant</td>
</tr>
<tr>
<td>11 (40 950)</td>
<td>High</td>
<td>4% (1 to 7)</td>
<td>39 (3 to 74)†</td>
<td>257 (136 to 3334)</td>
</tr>
<tr>
<td>8 (95 017)</td>
<td>Low</td>
<td>2% (–1 to 4)</td>
<td>16 (–41 to 10)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article. Follow up ranged from 1.4 to 8.2 years. A dose-response regression model was used.

†Favours placebo or no vitamin E.