



## Vitamins C and E from supplements

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Vitamins C and E serve many functions that are essential for general health. Vitamin C, also called ascorbate or ascorbic acid, is needed to produce molecules such as collagen and certain neurotransmitters. In the diet, it is common in citrus fruits, sweet peppers, and Brussels sprouts. Vitamin E refers to a family of eight compounds: four tocopherols and four tocotrienols [1]. Of these, alpha-tocopherol has been considered the most important to human health and is the form that comprises most commercially available vitamin E supplements. Vitamin E is plentiful in green leafy vegetables, sunflower seeds, and almonds.

Both vitamins are “antioxidants” that may reduce oxidative damage, but the benefits of high levels of antioxidant intake have been questioned in recent years with large clinical trials reporting that antioxidant supplements are unlikely to protect from disease in people who are not deficient in the vitamins. Supplementation with some antioxidants including vitamin E may even shorten lifespan and increase the risk of cancer [2; 3; 4].

People with dementia often have low levels of these vitamins, which could be due to poor nutrition, illness, or other changes common in dementia patients. High intake of foods naturally rich in vitamins C and E have, as part of a broad dietary pattern, been tentatively linked to a lower risk of dementia, though supplements do not appear to offer the same protection.

### EVIDENCE AND POTENTIAL BENEFIT FOR BRAIN HEALTH

#### Rated 2/4 based on 3/4 evidence

Multiple meta-analyses and systematic reviews have examined the effects of vitamins C and E on cognitive functions, but the results vary depending on many factors such as the source of the vitamins (i.e., diet versus supplements), the age and health status of the participants, and the methods used to measure vitamin intake and track cognitive function. Little is known about the effects of each vitamin alone.

Randomized controlled trials: Even if vitamins C and E are protective as part of a healthy diet, supplements do not appear as promising. In two randomized controlled trials, vitamin E or vitamin E and C supplements did not help patients with mild cognitive impairment (MCI) [8; 9]. One observational study reported that supplementation with both vitamins C and E failed to slow cognitive decline over a one year period in women over 65 [10], although another prospective observational study reported that vitamin C and E supplementation did slow cognitive decline in both men and women who also took a non-steroidal anti-inflammatory drug [11]. It is possible that supplements will not help people who have sufficient dietary intake (i.e., those targeted in most clinical trials), but they may



still help people who lack sufficient nourishment from their diet. Overall, however, the evidence to-date suggests that vitamin C or E supplementation, alone or in combination, is unlikely to prevent cognitive decline or dementia.

Other human research: In observational research, high dietary intake of vitamins C & E have been linked to a 20–25% lower risk of Alzheimer's disease based on a meta-analysis of 7 observational studies [5] and a more recent 2015 meta-analysis [6]. These results are, however, controversial because the effects of these specific vitamins are difficult to separate from the broader patterns of healthy living and diet that often accompany high vitamins C and E dietary intake. Therefore, the protective association may reflect healthy lifestyle and diet rather than these specific vitamins. There are also concerns on publication bias (e.g., positive results are easier to publish) and measurement errors [3; 7].

Biology: Preclinical animal studies suggest that vitamin E plays neuroprotective roles, including limiting oxidative damage and slowing progression of Alzheimer's disease. For example, vitamin E administration can improve cognitive function in old rats [12] and reduce pathological markers in a mouse model of Alzheimer's disease [13]. However, these results have not been reliably extended to humans.

**APOE4 carriers:** The evidence is mixed and preliminary on whether vitamins C and E selectively affect APOE4 carriers versus non-carriers. In a prospective study, older adults taking a combination of vitamin E and C supplements with a nonsteroidal anti-inflammatory drug (NSAID) experienced less cognitive decline over eight years compared to those taking neither NSAIDs nor vitamins, and this protective effect was evident in APOE4 carriers but not in non-carriers [11]. In contrast, in another prospective cohort study, vitamin E intake from diet was associated with a decreased risk of developing Alzheimer's disease, and this protective effect was observed only in people who were APOE4-negative [14]. An observational study reported that in people without MCI, vitamin E levels were lower in APOE4 carriers compared to non-carriers, but when all subjects were included, neither APOE4 nor MCI was related to vitamin E deficiency [15]. For more information on what the APOE4 gene allele means for your health, read our [APOE4 information page](#).

### **For Dementia Patients**

The majority of studies report little to no benefit to people with dementia. Deficiencies in both vitamins have been associated with Alzheimer's disease and dementia, but these could be due to decreased nutrient intake and absorption common in this patient population [16].

Several meta-analyses of clinical trials reported that vitamin E supplementation has very little to no protective effects on cognitive function in patients with dementia [8; 17]. A 2012 Cochrane meta-analysis of three high-quality randomized clinical trials concluded that there is no convincing evidence that vitamin E is beneficial in preserving cognitive function in



people with dementia [8]. In one trial, vitamin E supplementation of 800 IU/day resulted in no cognitive improvement in Alzheimer's disease patients [18]. In another trial, moderately severe Alzheimer's disease patients taking 2000 IU/day of vitamin E experienced slower disease progression but no improvement in cognition [19]. The third trial showed that vitamin E supplementation at 2000 IU/day for a 3-year trial did not slow the time to progression from mild cognitive impairment to Alzheimer's disease [20].

Despite these less promising results, the 2014 TEAM-AD (Trial of Vitamin E and Memantine in Alzheimer's Disease) trial reported that patients with mild-to-moderate Alzheimer's disease taking 2000 IU/day of vitamin E experienced slower decline in their ability to carry out daily tasks compared to a group of similar patients given a placebo [21]. These results warrant further investigation.

## SAFETY

### Rated 2/4

While vitamins C and E are essential for good health, excessive supplementation may not be healthy. Vitamin E supplementation of about 225 IU/day has been linked in some studies to a slightly increased risk of death [22; 23], although there is conflicting evidence [24]. Vitamin E supplementation may increase the risk of hemorrhagic stroke but also reduce the risk of ischemic stroke [25]. In patients over 55 years old with diabetes or vascular disease, vitamin E supplementation was shown to increase their risk of heart failure [26]. In men with high selenium levels, vitamin E supplementation at 400 IU/day almost doubled their risk of prostate cancer [27].

Vitamin C supplementation is not associated with many adverse effects but doses beyond 500mg/day may be harmful to people at risk of kidney stones [28]. Detailed information on doses, side effects, and drug interactions with vitamin supplementation can be found at the NIH Office of Dietary Supplements ([vitamin C](#), [vitamin E](#)).

## HOW TO USE

Vitamin supplements are available over-the-counter in different formulations as pills, chewable tablets, or topical creams. Alpha-tocopherol is the most extensively studied type of vitamin E, but recent research is revealing that other vitamin E members, such as gamma-tocopherol and beta-tocotrienol, may also be important for proper health [29]. Because vitamin C absorption is limited to about 400 mg/day [30], higher doses are unlikely to be more beneficial.

Instead of supplements, many experts recommend a healthy diet naturally containing high levels of vitamins C and E in addition to other important nutrients. The [Mediterranean](#), [MIND](#), and [DASH diets](#) have the most evidence to-date for long-term brain health. Citrus



fruits, sweet peppers, and Brussels sprouts are rich in vitamin C. Vitamin E is plentiful in green leafy vegetables, sunflower seeds, and almonds.

### WHAT'S THE FUTURE?

There are currently no ongoing clinical trials that are testing the potential of vitamins C and E in preventing or treating dementia. An ongoing observational study is examining the differences in nutritional status and vitamin levels in healthy people versus those with Alzheimer's disease. Another ongoing clinical trial is testing the effectiveness of vitamin C and vitamin E in treating depression in elderly people and is scheduled to be completed in December 2016. More information about these and other clinical trials can be found at [clinicaltrials.gov](http://clinicaltrials.gov) (U.S.) and at [clinicaltrialsregister.eu](http://clinicaltrialsregister.eu) (Europe).

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