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Nutrient Reference Values for Australia and New Zealand
Including Recommended Dietary Intakes

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VITAMIN E

BACKGROUND

Vitamin E is the name given to a group of water-insoluble, plant-derived substances. There are eight naturally-occurring isomers and a number of semisynthetic or synthetic homologues. The naturally-occurring *d*- (or RRR) alpha-tocopherol is the most biologically active form and vitamin E activity is traditionally expressed in terms of equivalents of this isomer (mg alpha-tocopherol equivalents or α-TE). Other tocopherols such as gamma-tocopherol also have vitamin E activity. There are four tocopherol homologues (*d*-α-, *d*-β-, *d*-γ- and *d*-δ-) and four tocotrienols. Other forms of vitamin E occur in lower amounts in foods and are less active in animal bioassay. The usual form in supplements is synthetic *dl*- (or all-rac) α-tocopherol that consists of a mixture of active and inactive stereoisomers, because natural vitamin E from wheat germ oil is expensive. The equivalence of the various forms is shown below:

Form	Alternative name	mg α-tocopherol equivalence
d-α-tocopherol	RRR-α-tocopherol	1
d-α-tocopherol acetate	RRR-α-tocopherol acetate	0.91
d-α-tocopherol acid succinate	RRR-α-tocopherol acid succinate	0.81
dl-α-tocopherol	all-rac-α-tocopherol	0.74
dl-α-tocopherol acetate	all-rac-α-tocopherol	0.67
d-β-tocopherol	RRR-β-tocopherol	0.25–0.40
d-γ-tocopherol	RRR-γ-tocopherol	0.10
α-tocotrienol		0.25–0.30

The major role of vitamin E is to protect polyunsaturated fatty acids (PUFA) from oxidation. It acts as an anti-oxidant in the lipid phase of cell membranes. Vitamin E requirements have been reported to increase when intakes of PUFA are increased (Dam 1962, Horwitt 1962) and a ratio of at least 0.4 mg α-tocopherol per gram of PUFA has been recommended (Bieri & Evarts 1973, Horwitt 1974, Witting & Lee 1975). Most dietary sources of polyunsaturated fat are also relatively rich in vitamin E. However supplements of fish oils or other pure n-3 fatty acids may not provide the amount of vitamin E needed.

The activity vitamin E complements that of selenium-dependent glutathione peroxidase in protecting the membrane PUFAs from free radical damage. Although vitamin E is mainly located in cells and organelle membranes, its concentration may be very low, suggesting that after its reaction with free radicals it is rapidly regenerated, possibly by other antioxidants such as selenium, ubiquinols and vitamin C (Doba et al 1985, Niki et al 1982, Stoyanovsky et al 1995).

The main source of vitamin E is fats and oils. It is also found in some vegetables, in the fats of meat, poultry and fish and, to lesser degrees, in cereals and dairy foods. About half the tocopherol in wheat germ, sunflower, safflower, canola, olive and cottonseed oils is α-tocopherol but soybean and corn oils contain about 10 times as much γ-tocopherol as α-tocopherol. Most vitamin E is found in foods containing fat. Absorption requires micelle formation and chylomicron secretion in the gut (Muller et al 1974) together with biliary and pancreatic secretions. Efficiency of absorption is low, but the precise rate is unknown.

Vitamin E is transported in the blood by the plasma lipoproteins and erythrocytes. Tocopherols are carried from the gut to the liver in chylomicrons where they are incorporated as chylomicron remnants. Catabolism of chylomicrons takes place in the systemic circulation through the action of cellular lipoprotein lipase. Vitamin E can be transferred to high density lipoprotein (HDL) and then

to low density liopoprotein (LDL) and very low density lipoprotein (VLDL). Most α-tocopherol enters peripheral tissues within the intact lipoprotein through the LDL receptor pathway.

Although all tocopherol homologues are absorbed similarly, α-tocopherol predominates in blood and tissue as the binding proteins take it up preferentially. Plasma vitamin E and tissue concentrations vary little over a wide range of dietary intake and the brain is particularly resistant to depletion (Bourne & Clement 1991).

The main oxidation product of α-tocopherol is tocopheryl quinone which is conjugated to glucuronate and is excreted in bile or further degraded in the kidneys to α-tocopheronic acid before excretion in bile (Drevon 1991). Some may be excreted through the skin (Shiratori 1974).

Overt deficiency symptoms in normal individuals consuming diets low in vitamin E have never been described. It occurs only as a result of genetic abnormalities, fat malabsorption syndrome (Rader & Brewer 1993, Sokol 1993) or protein-energy malnutrition (Kalra et al 1998, Laditan & Ette 1982). The main symptom is a peripheral neuropathy. Other symptoms include spinocerebellar ataxia, skeletal myopathy and pigmented retinopathy (Sokol 1988).

In epidemiological studies, higher intakes of vitamin E have been related to reduction in cardiovascular disease risk (Gey et al 1991, Rimm & Stampfer 1993, Stampfer et al 1993), diabetic complications (Baynes 1991, Mullarkey et al 1990, Semenkovich & Heinecke 1997), certain cancers (Comstock et al 1997, Eichhlozer et al 1996, Yong et al 1997) and cataracts (Jacques & Chylack 1991, Knekt et al 1992, Leske et al 1991). Not all studies, however, have confirmed a relationship and clinical trials with supplements in high risk groups, have shown little benefit. Further discussion of these trials is given in the 'Chronic disease' section.

Indicators that have been used to estimate vitamin E requirements include lipid peroxidation markers, oxidation products of DNA or proteins, vitamin E metabolite excretion, vitamin E biokinetics, vitamin E deficiency symptoms, plasma α-tocopherol concentration, hydrogen peroxide-induced haemolysis or the relationship of vitamin E to chronic disease status. However, erythrocyte fragility studies have been the most widely used.

The US DRI review in 2000 used the data of Horwitt (1960, 1963). These same data had been used in setting the earlier US RDIs but were interpreted differently in 2000, leading to considerably increased recommendations. In the US DRI review of 2000, the amount of dietary vitamin E required to bring plasma α-tocopherol to a level where per cent haemolysis was low was used to estimate an EAR (Horwitt 1960, 1963). However, the interpretation of these data is problematic in relation to level of plasma α-tocopherol at which adverse effects are seen, as there were no data available for plasma α-tocopherol concentrations between 5 and 12 μmol/L. All four subjects below 6 μmol/L plasma α-tocopherol (range 2–5 μmol/L) had haemolysis of about 80% or above and all 6 subjects with concentrations between 12 and 22 μmol/L, had haemodialysis of 12% or less. There has been disagreement as to whether the 'adequacy' cut off should be midway between these two clusters or at the lowest point showing low haemolysis. The data are dichotomous, not continuous, thus preventing an accurate dose-response analysis. Changing the cut-off point makes a large difference to the estimated requirement. In addition, the authors of the key paper themselves expressed concern about the validity of the technique for assessing vitamin E requirements (Horwitt 1960, 1963, 2001).

Given these uncertainties, an AI rather than an EAR was set for vitamin E based on median population intakes in Australia and New Zealand – both healthy populations with no apparent vitamin E deficiency. Recommendations for infants were based on the median concentration in breast milk of healthy mothers.

RECOMMENDATIONS BY LIFE STAGE AND GENDER

Infants	**AI**	**Vitamin E (as α-tocopherol equivalents)**
0–6 months	**4 mg /day**	
7–12 months	**5 mg /day**	

***Rationale*:** The AI for 0–6 months was calculated by multiplying the average intake of breast milk (0.78 L/day) by the average concentration of vitamin E in breast milk of 4.9 mg/L (Boersma et al 1991, Chappell et al 1985, Jansson et al 1981, Lammi-Keefe et al 1985, 1990) and rounding. Two of these studies reported only α-tocopherol data but Boersma et al (1991) showed that the tocopherol content of breast milk is almost entirely comprised of α-tocopherol. For 7–12 months, the AI was extrapolated from younger infants on a body weight basis and rounded.

Children & adolescents	**AI**	**Vitamin E (as α-tocopherol equivalents)**
All		
1–3 yr	**5 mg/day**	
4–8 yr	**6 mg/day**	
Boys		
9–13 yr	**9 mg/day**	
14–18 yr	**10 mg/day**	
Girls		
9–13 yr	**8 mg/day**	
14–18 yr	**8 mg/day**	

***Rationale*:** As there are no specific data on which to base an EAR for children and adolescents, an AI was set based on the median intakes in Australia and New Zealand from the National Nutrition Surveys with rounding up to the nearest milligram (ABS 1998, MOH 1999, 2003).

Adults	**AI**	**Vitamin E (as α-tocopherol equivalents)**
Men		
19–30 yr	**10 mg/day**	
31–50 yr	**10 mg/day**	
51–70 yr	**10 mg/day**	
>70 yr	**10 mg/day**	
Women		
19–30 yr	**7 mg/day**	
31–50 yr	**7 mg/day**	
51–70 yr	**7 mg/day**	
>70 yr	**7 mg/day**	

***Rationale*:** As there are not sufficient data on which to base an EAR for adults, an AI was set based on the median intakes in Australia and New Zealand from the National Nutrition Surveys with rounding up to the nearest milligram (ABS 1998, MOH 1999). The values set for men and women were the highest median intake for any respective adult age band.

Pregnancy	**AI**	**Vitamin E (as α-tocopherol equivalents)**
14–18 yr	**8 mg/day**	
19–30 yr	**7 mg/day**	
31–50 yr	**7 mg/day**	

***Rationale*:** There is no evidence of increased needs for vitamin E in pregnancy, so the AI is set at that for the non-pregnant woman.

Lactation	**AI**	**Vitamin E (as α-tocopherol equivalents)**
14–18 yr	**12 mg/day**	
19–30 yr	**11 mg/day**	
31–50 yr	**11 mg/day**	

***Rationale*:** The AI for lactation is set at that for the non-lactating woman plus an allowance for the vitamin E secreted in milk.

UPPER LEVEL OF INTAKE - VITAMIN E - (as α-tocopherol equivalents)

Infants	
0–12 months	**Not possible to establish. Source of intake should be breast milk, formula and food only**
Children	
1–3 yr	**70 mg/day**
4–8 yr	**100 mg/day**
Boys	
9–13 yr	**180 mg/day**
14–18 yr	**250 mg/day**
Girls	
9–13 yr	**180 mg/day**
14–18 yr	**250 mg/day**
Adults 19+ yr	
Men	**300mg/day**
Women	**300mg/day**
Pregnancy	
All ages	**300 mg/day**
Lactation	
All ages	**300 mg/day**

***Rationale*:** In recent years, several clinical intervention trials have assessed the effects of high doses of vitamin E on chronic disease outcomes, including the CHAOS Heart trial which used 268–567 mg *d*-α-tocopherol/day (Stephens et al 1996), the GISSI study with 300 mg vitamin E as synthetic α-tocopherol (GISSI-Prevenzione Investigators 1999), the ATBC study using 55 mg *dl* α-tocopherol (ATBC 1994, Heinonen et al 1998), the HOPE study using 268 mg vitamin E (Yusuf et al 2000), the Primary Prevention Study using 300 mg/day synthetic α-tocopherol (Collaborative group of the Primary Prevention Study 2001) and the Heart Protection Study with 600 mg of vitamin E (Heart Protection Study Collaborative Group, 2002). In addition, there have been a number of experimental trials using supplements ranging from 540 to 970 mg *d*-α-TEs. With the exception of an increase in subarachnoid haemorrhaging in smoking hypertensives in the ATBC study (Leppanen et al 2000a,b), a non-significant increase in stroke (relative risk 1.17) in the HOPE study and a tendency to haemorrhage in aspirin users in the Primary Prevention Project, no adverse events have been recorded. However, most studies were not specifically designed to assess adverse events to Vitamin E alone.

Meydani et al (1998) undertook an experimental, dose-dependent study in 88 healthy volunteers aged >65 years, with one control group and three varying dose groups (equivalent to 34, 134 or 537 mg *d*-α-TEs), over 4 months. This study had the most comprehensive assessment of potential adverse events. There were no subjective side effects and no effects on glutathione peroxidase, superoxide dismutase, immunoglobulin, anti-DNA or anti-thyroglobulin antibodies, body weight, total plasma proteins, albumin, glucose, lipids or lipoprotein profile, total bilirubin, serum liver enzymes, blood count, platelet number, bleeding time, haemoglobin, haematocrit or urinary or serum creatinine. The NOAEL established from this study was 540 mg/day. A UF of 2 was applied to cover inter-individual differences in sensitivity. A larger UF was not considered necessary because data from a number of other less well controlled studies showed no adverse effects at considerably higher intakes. The UL for vitamin E was therefore established as 270 mg/day for adults and rounded to 300 mg/day. The ULs for other age groups were derived on a relative body weight basis.

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