



Title	Vitamin K to Prevent Fractures in Older Women: A Systematic Review and Economic Evaluation
Agency	NETSCC, HTA, NIHR Evaluation and Trials Coordinating Centre Alpha House, University of Southampton Science Park, Southampton, SO16 7NS, United Kingdom; Tel: +44 2380 595 586, Fax: +44 2380 595 639; hta@soton.ac.uk, www.hta.ac.uk
Reference	Volume 13.45, ISSN 1366-5278. www.hta.ac.uk/project/1712.asp

Aim

To determine the clinical and cost effectiveness of vitamin K in preventing osteoporotic fractures in postmenopausal women.

Conclusions and results

It is uncertain whether vitamin K₁ is more cost effective than alendronate (the current first-line treatment). Literature searches identified 1078 potentially relevant articles. Of these, 14 articles met the review inclusion criteria. The articles relate to 5 trials that compared vitamin K with a relevant comparator in postmenopausal women with osteoporosis or osteopenia. The double-blind ECKO trial compared 5 mg of phylloquinone (vitamin K₁) with placebo in Canadian women with osteopenia but without osteoporosis. Four open-label trials used 45 mg of menatetrenone (vitamin K₂) in Japanese women with osteoporosis; the comparators were no treatment, etidronate, or calcium. The methodological quality of the ECKO trial was good, but all 4 menatetrenone trials were poorly reported, and 3 were very small ($n < 100$ in each group). Phylloquinone was associated with a statistically significant reduction in the risk of clinical fractures relative to placebo (relative risk 0.46, 95% confidence interval [CI] 0.22 to 0.99). These data were not reported by fracture site. The smaller menatetrenone trials found an association with a reduced risk of morphometric vertebral fractures relative to no treatment or calcium. The larger Osteoporosis Fracture (OF) study found no evidence of a reduction in vertebral fracture risk. The 3 smaller trials found no significant difference between treatment groups in nonvertebral fracture incidence. These data were not reported in the OF study. In the ECKO trial, phylloquinone was not associated with an increase in adverse events. In the menatetrenone trials, adverse event reporting was generally poor. In the OF study, menatetrenone was associated with a significantly higher incidence of skin and skin appendage lesions. Since we found no published economic evaluations of vitamin K, a mathematical model was constructed to estimate the cost effectiveness of vi-

tamin K₁. Comparators were alendronate, risedronate, and strontium ranelate. Vitamin K₁ and alendronate were more cost effective than either risedronate or strontium ranelate. Base-case results favored vitamin K₁, but relied on many assumptions, particularly on the efficacy of preventing hip and vertebral fractures. Calculation of the expected value of sampled information assumed an RCT of 5 years' duration comparing alendronate with vitamin K₁.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1712.asp.

Methods

The scope of this assessment was to determine the clinical and cost effectiveness of vitamin K in preventing osteoporotic fractures in postmenopausal women compared to no intervention or specific drugs licensed in the UK for prevention or treatment of postmenopausal osteoporosis. Relevant outcome measures included incident vertebral and nonvertebral fractures, health-related quality of life, all-cause mortality, and adverse effects of treatment.

Further research/reviews required

Further research is required to resolve uncertainty over whether vitamin K₁ is more cost effective than alendronate. Calculation of the expected value of sampled information shows that an RCT of 2000 women per arm would be a cost effective use of resources.