

Key Studies

Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease

The population-based Rotterdam Study examined 4,807 subjects to determine whether dietary intake of vitamin K1 and vitamin K2 were related to aortic calcification and coronary heart disease (CHD). Results showed that severe aortic calcification and the relative risk of CHD mortality was reduced with vitamin K2, but not with vitamin K1.

Reference: Geleijnse JM, Vermeer C, Grobbee DE, Schurgers LJ, Knapen MH, van der Meer IM, Hofman A, Witteman JC. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *J Nutr.* 2004 Nov;134(11):3100-5.



A high menaquinone intake reduces the incidence of coronary heart disease

Researchers found that high dietary vitamin K2 intake – but probably not vitamin K1 – was associated with reduced coronary calcification in post-menopausal women. Adequate vitamin K2 intake could therefore be important for prevention of cardiovascular disease.

Reference: Gast GC, de Roos NM, Sluijs I, Bots ML, Beulens JW, Geleijnse JM, Witteman JC, Grobbee DE, Peeters PH, van der Schouw YT. A high menaquinone intake reduces the incidence of coronary heart disease. *Nutr Metab Cardiovasc Dis.* 2009 Sep;19(7):504-10.



The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children

The goal of this study was to demonstrate that MK-7 has a health benefit in healthy prepubertal children. Researchers conducted an 8-week, double-blind, randomized, placebo-controlled trial in which 45 mcg vitamin K2 as MK-7 was given to healthy prepubertal children, and undercarboxylated osteocalcin (ucOC) and carboxylated osteocalcin (cOC) were measured, as well as the the ucOC:cOC ratio (UCR) as an indicator of vitamin K status.

Results showed that with increases in MK-7, the circulating concentration of inactive ucOC reduced and the UCR improved. There were no significant changes in the placebo group. Researchers concluded that supplementation with vitamin K2 as MK-7 increases circulating concentrations of MK-7 and increases osteocalcin carboxylation in healthy, prepubertal children.

Reference: van Summeren MJ et al. The effect of menaquinone-7 (vitamin K2) supplementation on osteocalcin carboxylation in healthy prepubertal children. *Br J Nutr.* 2009 Oct;102(8):1171-8.



Vitamin K status in healthy volunteers

The first aim of this study was to measure circulating ucOC and dp-ucMGP levels across age groups in order to establish the tissue-specific vitamin K status during human life. The second aim was to study the response to vitamin K supplements at different states of vitamin K deficiency.

The study classified healthy children and adults above 40 years as groups with prominent vitamin K deficiency. Researchers established the vitamin K status across age groups based on circulating levels of ucOC and dp-ucMGP, i.e. markers for the vitamin K status of bone and the vasculature, respectively. Accordingly, the study classified healthy children and adults above 40 years as groups with prominent vitamin K deficiency and thus appropriate groups for vitamin K supplementation. The results further showed that more pronounced vitamin K deficiency, reflected by higher baseline values, gave larger responses to MK-7 supplementation.

Reference: Theuwissen E et al. Vitamin K status in healthy volunteers. *Food & Function*. 2014 Feb;5(2):229-34.



Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women

The purpose of the study was to demonstrate that vitamin K2 as menaquinone-7 (MK-7) has a health benefit in apparently healthy postmenopausal women. In a placebo-controlled, randomized clinical trial the effect of an MK-7 supplement was monitored during three years on bone quantity.

Knappen et al. showed for the first time clinically statistically significant protection of the vertebrae and the hip (femoral neck) against osteoporosis. After 3 years of supplementation of 180 mcg vitamin K2 as MK-7 daily, improvements in both bone mineral content and bone mineral density were statistically significant in the vitamin K2 group. Moreover bone strength was statistically improved, demonstrating therapeutic benefits for the MK-7 group as compared to the placebo group. This data indicates that MK-7 supplementation helps postmenopausal women to prevent bone loss.

Reference: Knappen MH, et al. Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporos Int*. 2013 Sep;24(9):2499-507.



Effect of vitamin K2 supplementation on functional vitamin K deficiency in hemodialysis patients: a randomized trial

Aim was to investigate whether daily vitamin K2 (MK-7) supplementation improves the bioactivity of vitamin K-dependent proteins in hemodialysis patients as assessed by circulating dephospho-noncarboxylated MGP (dp-ucMGP), noncarboxylated osteocalcin (ucOC) and noncarboxylated prothrombin (ucFII; PIVKA-II).

This study confirms that most hemodialysis patients have a functional vitamin K deficiency. More importantly, it is the first study showing that inactive MGP levels can be decreased markedly by daily vitamin K2 supplementation.

Reference: Westenfeld R, Effect of vitamin K2 supplementation on functional vitamin K deficiency in hemodialysis patients: a randomized trial. *Am J Kidney Dis.* 2012; 59 (2):186-95.

