

Vitamin K: What You Need to Know





Vitamin K:

What You Need to Know

Table of Contents

Different Forms of Vitamin K	4
Dietary Sources of Vitamin K	5
Consequences of Low Vitamin K	6
What Does Vitamin K Do?	7
How to Replenish Vitamin K	9

What is vitamin K?

It's not a nutrient that gets discussed very often, that's for sure. But that doesn't make it any less important to your health.

Vitamin K is a group of fat-soluble vitamins that's divided into two subsets: vitamin K1 (phylloquinones) and vitamin K2 (menaquinones). Each of them helps support our health in different ways.





Different Forms of Vitamin K

Vitamin K1

Vitamin K1 is produced by plants and is the most common form of this nutrient found in our diets.

Vitamin K2

Vitamin K2 includes many different compounds. The most common forms found in your diet include:

- *MK-4* — Most rapidly absorbed into the body, but is only bioavailable for a few hours.¹
- *MK-7* — Remains bioavailable in the body for up to 48 hours after ingestion, and can even be detected in the blood up to 72 hours after ingestion.²

Studies are also validating the importance of other menaquinones like MK-9, which are associated with cardiovascular protection.³

Vitamin K2 (The Numbering)

Menaquinone molecules vary in length, depending on how many carbon-unit side chains are included.

- Designated as MK-“n,” where “n” is the number of repeated carbon unit side chains
- For example, MK-4 has four repeated carbon unit side chains and MK-7 has seven repeated carbon unit side chains
- The menaquinones can be as large as MK-14 (14 repeated carbon unit side chains!)
- The most well-studied forms of vitamin K2 for health are MK-4 and MK-7, with some studies indicating benefits from other menaquinones like MK-9

Synthetic Vitamin K

There is a third form of vitamin K. Menadione, or vitamin K3, is a synthetic form of the nutrient.

Vitamin K3 is referred to as a provitamin, which means it needs to convert into vitamin K2 (MK-4) to have activity in the body.⁴

Even though the other forms of vitamin K have a longstanding safety profile (even at high doses), the same is not true for the synthetic version. Vitamin K3 can disrupt important antioxidant systems in the body.

Menadione interferes with the function of glutathione, a vital antioxidant for cellular protection. This interference could result in oxidative damage to cell membranes and induce liver toxicity.⁵ So, it's best to avoid this form.



Dietary Sources of Vitamin K

Even though vitamin K is a group of fat-soluble vitamins, the body only stores small amounts.⁵ That's why it's important to get regular dietary intake to maintain vitamin K activity.

Here are some ways to make sure you're getting enough:

Vitamin K1

Where to find it: Dark, leafy green vegetables, Brussels sprouts and broccoli.

Word to the wise: Vegetable content of vitamin K1 varies from crop to crop. Vitamin K1 binds tightly to plant cell structures called chloroplasts, so typically only small fractions of vitamin K1 absorb into the blood stream, making it harder for your body to access Vitamin K1 that comes from plant sources.⁵

Vitamin K2

Where to find it: High-fat dairy products, like cheese, and fermented foods, such natto.^{5,6} Vitamin K2 can also be produced by intestinal bacteria.⁷

Word to the wise: Foods high in saturated fats might not be the best choice if you're concerned about your blood lipid levels. Unfortunately, low-fat versions of these foods tend to have less vitamin K2.⁶ So, it can be very difficult to get optimal amounts from diet alone.



Part 2: Consequences of Low Vitamin K

Fortunately, vitamin K deficiency in healthy adults is uncommon, since it's found in foods like green leafy vegetables and cheese and is created by intestinal bacteria.

But a true deficiency can result in a hemorrhage, which is life-threatening bleeding. You might be at risk for deficiency if you're taking warfarin or another vitamin K antagonist drug, if you're suffering from severe liver disease or have fat malabsorption from digestive issues like inflammatory bowel disease or cystic fibrosis.⁵

If you have any of the following symptoms, please see your doctor to be assessed for vitamin K deficiency or other causes of excessive bleeding: Easy bruising, frequent nose bleeds or bleeding gums, blood in urine or stool, black/tarry stools or excessive heavy menstrual bleeding.

While vitamin K deficiency is rare, *insufficiency* tends to be more common. Several factors can be attributed to this milder condition, including difficulty getting vitamin K1 from plant sources, avoiding foods high in saturated fat and the body simply not storing sufficient levels of vitamin K.

Vitamin K insufficiency may sound less concerning, but it's likely a contributing factor for chronic cardiovascular and arterial health concerns. Several large population-based studies have assessed dietary vitamin K intake and the

risk of coronary heart disease.^{3,9,10} Combined, they evaluated more than 20,000 subjects with long-term follow-up and found that those with highest intake of vitamin K2 had reduced risks of:

- Coronary heart disease^{3,10}
- Coronary heart disease mortality and all-cause mortality¹⁰
- Severe aortic calcification and coronary calcification⁹

One of the larger population studies followed more than 16,000 women over the course of eight years to determine whether there was an association between dietary vitamin K intake and coronary heart disease. Indeed, there was compelling data suggesting a connection. The mean vitamin K1 intake was 211.7 +/- 100.3 mcg per day and vitamin K2 intake was 29.1 +/- 12.8 mcg per day. After adjusting for traditional risk factors and dietary factors, researchers observed an inverse association between vitamin K2 (mainly MK-7, MK-8, and MK-9) and risk of coronary heart disease.³

That suggests higher intakes of MK-7, MK-8, and MK-9 could protect against coronary heart disease. In fact, the researchers found that vitamin K2 reduced the risk of heart disease by 9% for every 10 mcg consumed per day.³

A study published in 2015 evaluating 451 women for arterial calcification revealed even more dramatic results. Women who were on warfarin

therapy—known to functionally induce vitamin K deficiency—for at least a month or more had a 50% increase in arterial calcification compared to women who did not take this medication. After a follow-up five years later, the women on warfarin had a 75% increase in arterial calcification.¹¹



Vitamin K Deficiency and Newborns

Newborns are at risk of vitamin K deficiency. Before birth, a limited amount of vitamin K is transferred to the baby from the placenta. Even after birth, if a newborn is exclusively breastfed, they may not get enough vitamin K, since amounts are relatively low in human breast milk.⁵

Since normal blood clotting isn't possible without adequate vitamin K, the American Academy of Pediatrics recommends vitamin K1 injections for all newborns.⁸

Part 3: What Does Vitamin K Do?

The Calcium Manager

Vitamin K benefits the body in several different ways. However, its main job is to activate proteins that regulate calcium. These calcium-regulating proteins are referred to as GLA proteins (gamma-carboxyglutamic acid), and they serve your body in different ways:

- *Promoting bone density:* The GLA protein osteocalcin, when activated, binds calcium ions to the matrix of the bone
- *Keeping arteries calcium-free:* Matrix-GLA is another GLA protein, and when it's activated by vitamin K, it moves calcium away from the arteries; calcium build-up in the arteries can be deadly

Keeping Calcium IN Bones and OUT of Arteries

Encouraging calcium to move into the bones is important to keep them healthy. Calcium, after all, provides bone strength and density. But bone health is only part of the story; your heart health depends upon calcium staying *out* of the arteries.

Soft tissue is supposed to be soft, after all. When arteries are soft and elastic, they easily expand and contract with each heartbeat. But when calcium infiltrates the arteries, they lose their flexibility and become stiff—and that's when serious heart health consequences can occur.

Arteries that lose flexibility have trouble expanding and contracting, which leads to higher blood pressure.¹² This, in turn, creates a heavier workload on the heart, as it tries to force blood through rigid arteries. Calcification of the arteries contributes to heart failure.¹³

The role of calcification in coronary arteries (arteries that supply blood to the heart) is very worrisome. Calcification in the arteries can accelerate atherosclerotic plaque narrowing, which leads to coronary artery disease.

Calcification is present in 90% of patients with coronary artery disease.^{14,15} That's why vitamin K's assistance in maintaining the proper movement of calcium is vital not only to the bones, but to heart health as well.

But vitamin K is not a *cure* for these serious health conditions. If you're dealing with low bone density or arterial calcification, in fact, low levels of vitamin K may not be the culprit. Hormone imbalance, deficiencies of other minerals and vitamins, and lack of physical exercise can play a role in both of these health problems. And other cardiovascular risks, such as inflammation and oxidative stress, can lead to arterial calcification. Speak with your doctor rather than making any assumptions.

Calcification Study and Vitamin K

In a cross-sectional study of 564 post-menopausal women that assessed their K1 and K2 intake by asking them to complete food diaries, researchers analyzed whether there was an association of



Warfarin and Vitamin K Safety

For people at risk for developing an unnecessary clot, like those diagnosed with atrial fibrillation, doctors may choose to use a pharmaceutical medication that functions as a vitamin K antagonist, such as warfarin or Coumadin.

Warfarin works by preventing the recycling of vitamin K, so it can't be reused.⁵ This creates a functional deficiency, resulting in less available vitamin K to activate clotting proteins.

However, this induced deficiency only occurs if we don't introduce more vitamin K into the system, which is why it's vital to talk to your doctor prior to taking any additional vitamin K if you've been prescribed these types of vitamin K antagonists.

vitamin K1 and K2 (MK-4-MK-10) with coronary calcification.

Daily intakes ranged from 18 to 48.5 mcg per day for K2 and from around 210 to 220 mcg/day for K1. They found that those with the highest K2 intake had a 20% lower rate of calcification compared to those with the lowest intake.⁹ Adequate menaquinone intakes could therefore be important for cardiovascular disease prevention.

Can Vitamin K Protect Against Fractures?

One reason why low bone density is a concern is because weaker, lighter bones are more prone to fracture. Might vitamin K help prevent fractures? A large meta-analysis suggests this may be the case.

By pooling data from close to 81,000 individuals, researchers found that higher levels of vitamin K correlated with a lower fracture rate. In fact, for every 50 mcg of vitamin K consumed per day, there was a 3% lower rate of bone fracture. For those at the highest dosage of vitamin K, there was a 22% lower rate of developing a fracture compared with those at the lowest end of the spectrum.²¹

A Word on Calcium

Knowing that calcium build-up in your arteries is dangerous might make you wonder whether you should simply avoid this mineral. But calcium is vital for life, because of its role in so many different life-sustaining activities. For instance, it helps keep your heart beating regularly, since it's involved in the cellular contraction of heart muscles.¹⁶

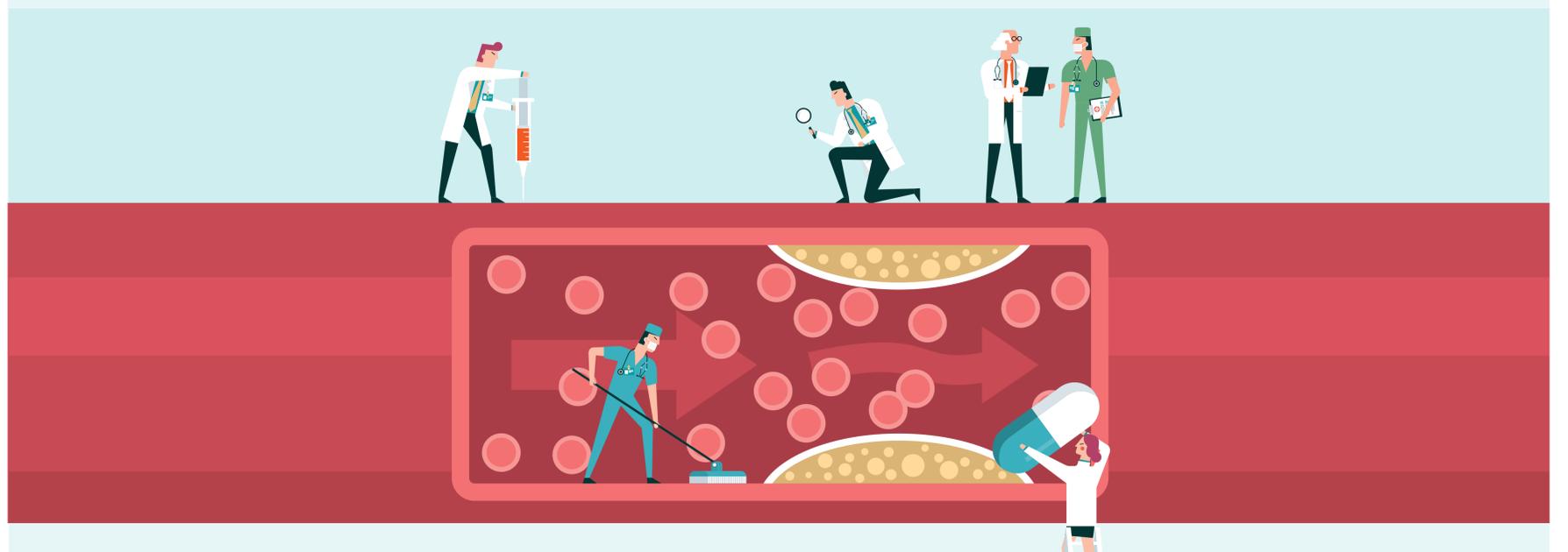
Depriving ourselves of this mineral, therefore, is not the answer. Instead, our goal should be to encourage calcium to be stored where it belongs: in our bones.

In a healthy body, 99% of calcium is stored in the bones.¹⁷ The other 1% circulates in the blood, but is tightly controlled by hormones, like parathyroid hormone and calcitonin, as well as by vitamin D3.

Most adults require 1000 to 1200 mg of calcium per day.¹⁸

A smart approach to daily calcium intake is consuming 700 mg of calcium and relying on food sources for the additional 300-500 mg.

That way, when calcium is regulated properly by healthy levels of hormones and balanced nutrition with vitamin D and K, it's very unlikely that the recommended daily intake would accelerate soft tissue calcification.^{19,20}



Part Four: How to Replenish Vitamin K?

What amount of vitamin K do you need to ensure you are getting the health benefits? Here are some studies based on various doses:

Vitamin K1 & Aortic Valve Calcification

Patients taking vitamin K showed less of a progression in aortic valve calcification (AVC) compared to those who did not take this nutrient, according to a 12-month prospective, single-center, open label, randomized interventional trial of 72 men and women with mild to no symptoms of this disease. Subjects who received 2000 mcg of vitamin K1 saw an AVC volume score progression of 10% compared to a 22% progression in the placebo group.²²

Bone Density Studies in Postmenopausal Women

Two placebo-controlled clinical trials used a daily dose of 1500 mcg of MK-4 in healthy, postmenopausal women. The studies demonstrated better maintenance of bone density and higher levels of activated osteocalcin (indicating more new bone formation) for those receiving the MK-4.^{23,24}

In one of the studies, the researchers measured forearm bone mineral density. The placebo group continued to show progressive bone loss in the forearm over the year of the study, while the MK-4 group remained stable.²⁴

The Link Between Vitamin K, Bone Density and Arterial Health

A group of researchers followed 244 healthy postmenopausal women for three years to assess the effect of 180 mcg of MK-7 on both bone and arterial health.^{25,26}

The researchers found that the ratio of inactive to active osteocalcin improved by 58% in the MK-7 group, in addition to significant improvements in bone mineral content, bone mineral density and bone strength.²⁵

When their arterial health was assessed, the MK-7 group displayed improved arterial flexibility when compared to the placebo group that had worsening arterial stiffness. The researchers further observed that those in the MK-7 group who had more advanced arterial stiffness improved the most.²⁶

Coronary Heart Disease & Vitamin K

Only recently have other menaquinones become available in ingredient form. Therefore, specific clinical trials have yet to be performed on them. But observational studies suggest there are many benefits of including more menaquinones in your diet.

For example, in the large population study mentioned earlier, the researchers concluded that higher intakes of vitamin K2 (including MK-7 and MK-9) reduced the risk of coronary heart disease by 9% for every 10 mcg consumed per day.³



We can infer that it may be necessary to achieve higher-than-average dietary intakes of MK-9 (and other menaquinones) than were reported in this study.

Diet

As discussed earlier, there are limitations to obtaining sufficient vitamin K from food.

Even if you eat large amounts of leafy greens, you may not be absorbing adequate amounts of vitamin K1 due to its poor bioavailability.²⁷

Consuming green leafy vegetables with some dietary fat may help facilitate the absorption of K1,

but since vitamin K1 is bound to chloroplasts within cell walls, the bioavailability can still be an issue. And for anyone avoiding foods high in saturated fat, it can be very difficult to obtain clinically relevant doses of vitamin K2 from diet alone.

Food Equivalencies

To achieve 2000 mcg of vitamin K1 from diet alone, you would have to eat almost 14 cups of spinach per day.²⁸ To get 1500 mcg of MK-4 from food, you would have to consume over 32 pounds of hard cheese like cheddar.²⁹ And to get 180 mcg of MK-7, you would need to consume more than 17 pounds of hard cheese like cheddar.²⁹



Vitamin K and Clotting: Myth vs. Reality

Vitamin K not only regulates proteins involved in calcium balance for bone and arterial health, but it is also required for activating protein clotting factors. Without vitamin K, we cannot form a clot to stop bleeding.

This might lead people to think that taking vitamin K leads to an increased risk of developing unnecessary clots. That's not the case. Only small amounts of vitamin K are required to fully saturate the proteins required for blood clotting. So, adding more vitamin K does not increase thrombotic risk.³⁰

For example, the following doses were used in studies without adverse events or excessive clotting risk:

- 2000 mcg of vitamin K1 for a year²²
- 10000 mcg of vitamin K1 for two years^{31,32}
- 45000 mcg of MK-4³¹⁻³³
- 360 mcg of MK-7³⁴

In Japan, MK-4 at doses of 45000 mcg are used daily as an approved drug to treat osteoporosis.³⁵⁻³⁸ The reality is, there is no known toxic dose of vitamin K1 or vitamin K2.5 This alarming misconception about how vitamin K works in coagulation may be an attributing factor to the epidemic of cardiovascular disease.



References:

1. Shearer M, Fu X, Booth SL. Vitamin K Nutrition, Metabolism, and Requirements: Current Concepts and Future Research. *Advances in Nutrition*. 2012 Mar 1; 3(2):182-195
2. Sato T, Schurgers LJ, Uenishi K. Comparison of menaquinone-4 and menaquinone-7 Bioavailability in Healthy Women. *Nutr J*. 2012 Nov 12; 11:93
3. Gast GC, et al. A high menaquinone intake reduces the incidence of coronary heart disease. *Nutr Metab Cardiovasc Dis*. 2009 Sep;19(7):504-10
4. Nakagawa K, et al. Identification of UBIAD1 as a Novel Human menaquinone-4 Biosynthetic Enzyme. *Nature*. 2010 Nov 4; 468(7320):117-21
5. Booth SL, Mayer J. Micronutrient Information Center, Vitamin K. Linus Pauling Institute. 2014; <https://lpi.oregonstate.edu/mic/vitamins/vitamin-K>. Accessed July 2, 2020.
6. Fu X, Harshman SG, Shen X, et al. Multiple Vitamin K Forms Exist in Dairy Foods. *Curr Dev Nutr*. 2017 Jun;1(6):e000638
7. Palermo A, et al. Vitamin K and Osteoporosis: Myth or Reality? *Metabolism*. 2017. May; 70:57-71
8. Controversies Concerning Vitamin K and the Newborn. American Academy of Pediatrics Committee on Fetus and Newborn. *Pediatrics*. 2003 Jul; 112(1 Pt 1):191-2
9. Beulens JW, Bots ML, Atsma F, et al. High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis*. 2009 Apr;203(2):489-93
10. Geleijnse JM, Vermeer C, Grobbee DE, et al. 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
11. Tantisattamo E, Han KH, O'Neill WC. Increased vascular calcification in patients receiving warfarin. *Arterioscler Thromb Vasc Biol*. 2015 Jan;35(1):237-42
12. Kalra SS, Shanahan CM. Vascular calcification and hypertension: cause and effect. *Ann Med*. 2012 Jun;44 Suppl 1:S85-92
13. Leening MJ, Elias-Smale SE, Kavousi M, et al. Coronary calcification and the risk of heart failure in the elderly: the Rotterdam Study. *JACC Cardiovasc Imaging*. 2012 Sep;5(9):874-80
14. Liu YC, Sun Z, Tsay PK, Chan T, Hsieh IC, Chen CC, Wen MS, Wan YL. Significance of coronary calcification for prediction of coronary artery disease and cardiac events based on 64-slice coronary computed tomography angiography. *Biomed Res Int*. 2013;2013:472347.
15. Eisen A, Tenenbaum A, Koren-Morag N, et al. Coronary and aortic calcifications inter-relationship in stable angina pectoris: A Coronary Disease Trial Investigating Outcome with Nifedipine GITS (ACTION)--Israeli spiral computed tomography substudy. *Isr Med Assoc J*. 2007 Apr;9(4):277-80
16. Marks AR. Calcium and the heart: a question of life and death. *J Clin Invest*. 2003 Mar;111(5):597-600
17. Bonjour JP. Calcium and phosphate: a duet of ions playing for bone health. *J Am Coll Nutr*. 2011 Oct;30(5 Suppl 1):438S-48S. Review
18. National Institutes of Health, Office of Dietary Supplements. Calcium Fact Sheet for Health Professionals. 2020 Mar 26. <https://ods.od.nih.gov/factsheets/Calcium-Health-Professional/>. Accessed July 2020.
19. Bhakta M, Bruce C, Messika-Zeitoun D, et al. Oral calcium supplements do not affect the progression of aortic valve calcification or coronary artery calcification. *J Am Board Fam Med*. 2009 Nov-Dec;22(6):610-6.
20. Manson JE, Allison MA, Carr JJ, et al. Calcium/vitamin D supplementation and coronary artery calcification in the Women's Health Initiative. *Menopause*. 2010 Jul;17(4):683-91
21. Hao G, Zhang B, Gu M, et al. Vitamin K intake and the risk of fractures: A meta-analysis. *Medicine (Baltimore)*. 2017 Apr;96(17):e6725
22. Brandenburg VM, et al. Slower Progress of Aortic Valve Calcification With Vitamin K Supplementation. *Circulation*. 2017 May 23;135(21):2081-2083
23. Koitaya N, Ezaki J, Nishimuta M, et al. Effect of low dose vitamin K2 (MK-4) supplementation on bio-indices in postmenopausal Japanese women. *J Nutr Sci Vitaminol (Tokyo)*. 2009 Feb;55(1):15-21
24. Koitaya N, Sekiguchi M, Tousen Y, et al. Low-dose vitamin K2 (MK-4) supplementation for 12 months improves bone metabolism and prevents forearm bone loss in postmenopausal Japanese women. *J Bone Miner Metab*. 2014 Mar;32(2):142-50
25. Knapen MH, Drummen NE, Smit E, 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
26. Knapen MH, Braam LA, Drummen NE, et al. Menaquinone-7 supplementation improves arterial stiffness in healthy postmenopausal women. A double-blind randomised clinical trial. *Thromb Haemost*. 2015 May;113(5):1135-44
27. Gijssbers BL, Jie KS, Vermeer C. Effect of food composition on vitamin K absorption in human volunteers. *Br J Nutr*. 1996 Aug;76(2):223-9
28. Available at: <https://nutritiondata.self.com/facts/vegetables-and-vegetable-products/2626/2>. Accessed March 8, 2019
29. Marles RJ, Roe AL, Oketch-Rabah HA. US Pharmacopeial Convention Safety Evaluation of menaquinone-7, and form of vitamin k. *Nutr Rev*. 2017. July 1. 75(7):553-578
30. Beulens JW, Booth SL, van den Heuvel EG, Stoecklin E, Baka A, Vermeer C. The role of menaquinones (vitamin K) in human health. *Br J Nutr*. 2013 Oct;110(8):1357-68
31. Schwalfenberg GK. Vitamins K1 and K2: The Emerging Group of Vitamins Required for Human Health. *J Nutr Metab*. 2017; 2017:6254836
32. Therapeutic Research Center. Natural Medicines – Professional Monograph, Vitamin K. 2017. <https://naturalmedicines.therapeuticresearch.com/>
33. Cockayne S, et al. Vitamin K and the Prevention of Fractures: Systemic Review and Meta-Analysis of Randomized Controlled Trials. *Arch Intern Med*. 2006 June 26; 166(12):1256-61.
34. Theuwissen E, et al. Low-dose menaquinone-7 Supplementation Improved Extra-Hepatic Vitamin K Status, but Had No Effect on Thrombin Generation in Healthy Subjects. *Br J Nutr*. 2012 Nov 14; 108(9):1652:7
35. Iwamoto J, Takeda T, Ichimura S. Combined treatment with vitamin K2 and bisphosphonate in postmenopausal women with osteoporosis. *Yonsei Med J*. 2003 Oct 30;44(5):751-6.
36. Kaneki M, Hodges SJ, Hosoi T, et al. Japanese fermented soybean food as the major determinant of the large geographic difference in circulating levels of vitamin K2: possible implications for hip-fracture risk. *Nutrition*. 2001 Apr;17(4):315-21.
37. Tanaka S, Miyazaki T, Uemura Y, et al. Design of a randomized clinical trial of concurrent treatment with vitamin K2 and risedronate compared to risedronate alone in osteoporotic patients: Japanese Osteoporosis Intervention Trial-03 (JOINT-03). *J Bone Miner Metab*. 2014 May;32(3):298-304.
38. Iwamoto J. Vitamin K therapy for postmenopausal osteoporosis. *Nutrients*. 2014 May 16;6(5):1971-80

Have a health question?

We have the answers... You can speak with a Life Extension Wellness Specialist toll-free at 1-800-226-2370. This informational service is staffed by doctors, nurses, and other health practitioners and is free.



LifeExtension.com