Are We OK on Vitamin K?

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The function of vitamin K was first recognized in 1936 when chickens fed a fat-free diet developed severe bleeding. This essential fat-soluble vitamin is needed for the coagulation, or clotting, of blood. The chickens were not able to absorb the vitamin without adequate fat in their diets and hence their blood did not clot normally. Likewise in humans, when vitamin K is deficient, blood clotting is delayed. Other health problems have also been attributed to reduced levels of this vitamin. There are two forms of vitamin K: K1 (phylloquinone) and K2 (a series of menaquinones).[1] Recently, the K2 form of the vitamin has been suggested to have a role in reducing the risk of bone loss, cardiovascular disease, and potentially, other chronic diseases.[2-5] These roles in disease prevention have inspired supplement manufacturers to bottle and market supplements of vitamin K2. Should we be taking them?

Sources of Vitamin K

Vitamin K1 is found in plants, primarily leafy green vegetables, such as spinach, kale, broccoli, and collard greens; soybeans, vegetable oils, and some fruits are also good sources (see Table). Vitamin K2 is found in small amounts in animal-based foods including fish, meat, eggs, and dairy. Most K2 is synthesized by bacteria, so it is found in fermented foods like cheese and pickled vegetables. One of the best sources is natto, a traditional Japanese dish made from fermented soybeans. Vitamin K2 is also synthesized both in the body from K1 and by the intestinal microbiota.[6] Some of the K2 synthesized in the gut is absorbed and can satisfy part of our requirement for vitamin K.[1]

Vitamin K Content of Food				
Food	Serving size	Vitamin K (mcg)	Primarily K1	Primarily K2
Broccoli, cooked	½ c	110	☐	
Canola oil	1tb	10	☐	
Cheddar cheese	1 oz	3		☐
Chicken breast, broiled	3 oz	13		☐
Collard greens, boiled	½ cup	530	☐	
Egg	1 large	4		☐
Kale, raw	1 cup	113	☐	
Kiwi fruit	1	30	☐	
Natto	3 oz	850		☐
Pumpkin, canned	½ cup	20	☐	
Salmon, broiled	3 oz	0.3		☐
Sauerkraut	½ c	20		☐
Soy beans, boiled	½ c	43	☐	
Spinach, raw	1 cup	145	☐	

Vitamin K in the Body

Both forms of vitamin K act as cofactors for an enzyme that activates vitamin K-dependent proteins, but vitamins K1 and K2 differ in their absorption rates, tissue distribution, and target activity.[2] Vitamin K1 is absorbed more quickly but is also eliminated faster than K2. Once absorbed, K1 is concentrated in the liver, where it activates proteins needed for coagulation. Vitamin K2 is distributed throughout the body where it activates proteins involved in a wide range of

biological functions including those needed to calcify bone and to prevent calcification of blood vessels.[4] These extra-hepatic functions of vitamin K2 are linked to reducing the risk of osteoporosis, cardiovascular disease, and other chronic diseases.[2,7]

The recommended intake for vitamin K is based on the amount of K1 consumed by healthy individuals who do not show signs of delayed blood clotting.[8] Hence, vitamin K status has historically been evaluated by assessing dietary intake or blood clotting time. While deficiency is rare, young infants are at risk because little vitamin K is obtained *in utero* or from breast milk and their gut microbiota has not yet been established.[1,2] Deficiencies may also occur in conditions that disrupt the intestinal microbiota or severely limit intake and/or absorption of fat such as bariatric surgery and malabsorption syndromes, like celiac disease and ulcerative colitis.[1] Medications that increase the risk of deficiency include those that interfere with fat absorption, such as bile sequestrants, and long-term antibiotic use, which kills the gut bacteria that produce vitamin K. The blood thinner warfarin (coumadin) reduces blood clotting by blocking vitamin K activity. Those taking warfarin need to consume adequate and consistent amounts of vitamin K to meet needs without interfering with coagulation; large variations in vitamin K intake can increase or decrease warfarin's anticoagulant effect. Looking beyond the coagulation function of vitamin K, it is now recognized that deficiencies of the K2 form of the vitamin can lead to conditions that reflect the other roles of this form of the vitamin.

Vitamin K2 and Bone Health Vitamin K is important for bone health because it is needed to activate osteocalcin, a protein that facilitates the deposition of calcium into bone, as well as several other proteins important for healthy bones. Observational and interventional studies have investigated the effect of vitamin K on bone mineral density and fracture risk in healthy and osteoporotic individuals. Many studies link higher vitamin K intakes with higher bone mineral density and/or lower hip fracture incidence.[1,6,9] Some studies support the use of vitamin K2 supplements for the prevention of osteoporosis. For example, a meta-analysis of randomized controlled trials of K2 supplementation in

postmenopausal women found a positive association between supplements and bone mineral density and reduced fracture incidence.[10] However, small study sample sizes and differences in the population studied and the type of supplement used have made it difficult to draw definitive conclusions about whether to recommend vitamin K2 supplements to prevent and treat osteoporosis.[5,6]

Vitamin K2 and Heart Health. Vitamin K2 appears to play a pivotal role in two important chronic health problems that involve calcium – bone loss and calcification of soft tissue.[11] Several vitamin K-dependent proteins are involved in preventing calcification of the arteries, which can lead to atherosclerosis and high blood pressure. Some studies have found an association between high vitamin K2 intake and reduced vascular calcification and cardiovascular disease risk, but supplements have not consistently been found to prevent the progression of these conditions.[12,13] Available studies are small and heterogeneous in terms of the type and dose of vitamin K administered, the population studied, and the outcomes measured.[14] More well controlled long-term studies are needed to confirm a role for K2 supplements in preventing vascular calcification and consequently atherosclerosis and hypertension.

Vitamin K2 and Other Chronic Diseases The relationship between vitamin K and other chronic diseases is less clear than its roles in osteoporosis or cardiovascular disease. While no large long-term clinical trial results are available, there are many small studies showing interrelationships between vitamin K2 status, intake, and/or supplementation and various chronic diseases. The potential roles of vitamin K2 in kidney disease, diabetes, arthritis, and cancer are hypothesized to be related to the activation of extrahepatic vitamin K-dependent proteins as well as its function in cell proliferation, inflammation, and as an antioxidant.[2,5,7] The role of vitamin K in chronic kidney disease (CKD) is multifactorial. Vitamin K status is often poor in patients with CKD due to dietary restrictions as well as to medications, such as phosphate binders, that reduce bioavailability of the vitamin. Poor vitamin K status has been associated with increased proteinuria and renal function decline. In addition, vitamin K plays a role in both vascular calcification and decreased

bone density, complications that increase as CKD progresses. Supplemental K2 has been shown to slow the progression of the disease and reduce these complications.[15] In diabetes, vitamin K2 supplementation has been shown to promote the proliferation of insulin-producing beta cells and to increase insulin sensitivity.[4,7] The antioxidant and anti-inflammatory properties of K2 have been suggested to play a role in reducing the symptoms of rheumatoid arthritis.[3] Supplemental vitamin K2 has also been studied in the treatment of several cancers with promising results.[2] While some studies have found vitamin K2 supplements to improve disease outcomes, more research is needed to elucidate mechanisms and confirm the effectiveness of vitamin K2 for these conditions.

Do We Get Enough K2?

Although reduced blood clotting due to vitamin K deficiency is rare, low vitamin K2 status has been documented in older adults and in people with age-related diseases, including osteoporosis, cardiovascular disease, and CKD.[2,12] As discussed above, there are many small studies that show supplemental K2 may help prevent or slow the progression of these ailments.[9,12,15] Despite these data, it is not possible to definitively conclude that we get don't get enough vitamin K2. This is due in part to the fact that studies of vitamin K intake consider primarily K1 because food composition data for K2 are limited. [1,16] In addition, we don't know how much K2 we get from synthesis by the microbiota or from conversion of K1 to K2 in the body. The recognition that current recommendations may be insufficient to provide for all of the functions of the vitamin has led to the suggestion there be a separate recommendation for vitamin K2.[16]

Should You Take a K2 Supplement? There is increasing evidence that our intake of vitamin K2 is too low to support optimal health. And no adverse effects of vitamin K2 from food or supplements have been reported in healthy adults.[8,16] Therefore, it seems logical that we should increase our vitamin K2 intake. While ideally, we should obtain our nutrients from food, it is difficult to significantly increase dietary K2 without supplements. Other than natto, there are few foods that are naturally high in vitamin K2, and not many that are fortified with this vitamin. Although there is not sufficient information to make a specific

recommendation, the risk of taking a vitamin K2 supplement is minimal for healthy individuals. If you decide to supplement vitamin K2, make sure the product you choose contains vitamin K2. Multivitamin supplements typically provide vitamin K1, shown on the label ingredient list as phylloquinone (natural vitamin K1) or phytonadione (synthetic vitamin K1). Vitamin K2, listed on the label as menaquinone-4 and/or menaquinone-7, is more often found in individual supplements or those advertised for bone health.

References

[1] U.S. Department of Health and Human Services. National institutes of Health. Office of Dietary Supplements. Vitamin K. https://ods.od.nih.gov/factsheets/vitaminK-HealthProfessional/#h3. Accessed September 13, 2023.

[2]Simes DC, Viegas CSB, Araújo N, Marreiros C. Vitamin K as a Diet Supplement with Impact in Human Health: Current Evidence in Age-Related Diseases. *Nutrients*. 2020; 12(1):138. https://doi.org/10.3390/nu12010138

[3]Schwalfenberg GK. Vitamins K1 and K2: The Emerging Group of Vitamins Required for Human Health. J Nutr Metab. 2017;2017:6254836. doi: 10.1155/2017/6254836. Epub 2017 Jun 18.

[4]Halder M, Petsophonsakul P, Akbulut AC, et al. Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *Int J Mol Sci*. 2019;20(4):896. Published 2019 Feb 19. doi:10.3390/ijms20040896

5]Harshman SG, Shea MK. The Role of Vitamin K in Chronic Aging Diseases: Inflammation, Cardiovascular Disease, and Osteoarthritis. Curr Nutr Rep. 2016 Jun;5(2):90-98. doi: 10.1007/s13668-016-0162-x. Epub 2016 Mar 31.

[6]Palermo A, Tuccinardi D, D'Onofrio L, et al. Vitamin K and osteoporosis: Myth or reality? *Metabolism*. 2017;70:57-71. doi:10.1016/j.metabol.2017.01.032

[7] Popa DS, Bigman G, Rusu ME. The Role of Vitamin K in Humans: Implication in Aging and Age-Associated Diseases. Antioxidants (Basel). 2021 Apr 6;10(4):566. doi: 10.3390/antiox10040566.

[8]Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Institute of Medicine (US) Panel on Micronutrients. Washington (DC): National Academies Press (US); 2001.

https://www.ncbi.nlm.nih.gov/books/NBK222299/

[9]Rodríguez-Olleros Rodríguez C, Díaz Curiel M. Vitamin K and Bone Health: A Review on the Effects of Vitamin K Deficiency and Supplementation and the Effect of Non-Vitamin K Antagonist Oral Anticoagulants on Different Bone Parameters. J Osteoporos. 2019 Dec 31;2019:2069176. doi: 10.1155/2019/2069176.

[10]Ma ML, Ma ZJ, He YL, et al. Efficacy of vitamin K2 in the prevention and treatment of postmenopausal osteoporosis: A systematic review and meta-analysis of randomized controlled trials. *Front Public Health*. 2022;10:979649. Published 2022 Aug 11. doi:10.3389/fpubh.2022.979649

[11]Mandatori D, Pelusi L, Schiavone V, Pipino C, Di Pietro N, Pandolfi A. The Dual Role of Vitamin K2 in "Bone-Vascular Crosstalk": Opposite Effects on Bone Loss and Vascular Calcification. *Nutrients*. 2021;13(4):1222. Published 2021 Apr 7. doi:10.3390/nu13041222

[12] Hariri E, Kassis N, Iskandar J-P, et al. Vitamin K2 —a neglected player in cardiovascular health: a narrative review. Open Heart 2021;8:e001715. doi:10.1136/ openhrt-2021-001715

[13]Shioi A, Morioka T, Shoji T, Emoto M. The Inhibitory Roles of Vitamin K in Progression of Vascular Calcification. *Nutrients*. 2020;12(2):583. Published 2020 Feb 23. doi:10.3390/nu12020583

[14]Vlasschaert C, Goss CJ, Pilkey NG, McKeown S, Holden RM. Vitamin K Supplementation for the Prevention of Cardiovascular Disease: Where Is the Evidence? A Systematic Review of Controlled Trials. *Nutrients*. 2020;12(10):2909. Published 2020 Sep 23. doi:10.3390/nu12102909

[15]]Bellone F, Cinquegrani M, Nicotera R, Carullo N, Casarella A, et al. Role of Vitamin K in Chronic Kidney Disease: A Focus on Bone and Cardiovascular Health. Int J Mol Sci. 2022 May 9;23(9):5282. doi: 10.3390/ijms23095282.

[16]Akbulut AC, Pavlic A, Petsophonsakul P, Halder M, Maresz K, et al. Vitamin K2 Needs an RDI Separate from Vitamin K1. *Nutrients*. 2020; 12(6):1852. doi.org/10.3390/nu12061852