



# Lifesaving Vitamin Slashes Heart Disease Risk by 57%

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## STORY AT-A-GLANCE

- › Vitamin K is a fat-soluble vitamin with significant health influence that many don't get enough of. Your body stores very little of it, so it's rapidly depleted without regular dietary intake. Common drugs such as statins and antibiotics can also deplete vitamin K
- › Vitamin K1 is derived from green, leafy vegetables such as spinach, kale, broccoli and cabbage, and is best known for the role it plays in blood clotting
- › Vitamin K2 plays a primary role in bone and heart health. Inside your body, vitamin K2 is synthesized by certain bacteria in your gut. The vitamin K2 MK-4 is found in animal products such as meat, eggs, liver and dairy, while MK-7 is found in fermented foods such as sauerkraut, certain cheeses and natto
- › Recent research shows older individuals with low vitamin K1 status are more likely to have mobility problems and disability than those with higher levels
- › Vitamin K2 inhibits arterial calcification and improves arterial flexibility, thereby reducing your risk of a cardiovascular event (such as a heart attack) or death. It's also important for the prevention of osteoporosis

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Vitamin K is a fat-soluble vitamin with significant health influence that many don't get enough of. Your body stores very little of it, so it's rapidly depleted without regular

dietary intake. Common drugs can also deplete vitamin K, making elevated intake even more important.

There are many vitamin K-dependent proteins in your body, which are involved in things like blood coagulation, bone metabolism and mineralization of your blood vessels. As you'd suspect, that means vitamin K plays a particularly important role in the prevention of bleeding disorders, osteoporosis and heart disease.

There are two main forms of vitamin K, along with several subtypes, all of which can make matters a bit confusing. Here, I'll do my best to break down the basics, starting with the naturally-occurring forms of vitamin K and their basic functions and sources:<sup>1,2</sup>

- 1. Vitamin K1 (phylloquinone)** – Vitamin K1 is derived from green, leafy vegetables such as spinach, kale, broccoli and cabbage, and is best known for the role it plays in blood clotting.

With insufficient K1, your blood cannot clot properly, which can have life-threatening consequences, as you could bleed to death. Excessive intake of dietary or supplemental K1 however, can overcome the anticoagulant effects of blood thinning medications.

As noted by vitamin K expert Leon Schurgers, Ph.D., absorption of vitamin K1 from food is low; only 10% of the vitamin K found in vegetables is absorbed, and there's no way to significantly increase that absorption.

- 2. Vitamin K2 (menaquinones)** – The menaquinones play a primary role in bone and heart health. Inside your body, vitamin K2 is synthesized by certain bacteria in your gut. There are several subtypes of K2, two of the most common of which are:<sup>3</sup>

- a. Menaquinone-4 (MK-4)** – A short-chain form of vitamin K2 found in animal products such as meat, eggs, liver and dairy.<sup>4,5</sup> Source matters, however. For example, pasteurized dairy and products from factory farmed animals are

not high in MK-4 and should be avoided. Only grass fed animals (not grain fed) will develop naturally high levels.

MK-4 has a short biological half-life – about 2.5 hours – making it a poor candidate as a dietary supplement. That said, natural MK-4 from food is important for good health as it plays a role in gene expression. For example, research<sup>6</sup> has found it may lower your risk of liver cancer.

- b. Menaquinone-7 (MK-7)** – Longer-chained vitamin K2 found in fermented foods such as sauerkraut, certain cheeses and natto.<sup>7</sup> There's a variety of these long-chain forms, but the most common one is MK-7. This is the one you'll want to look for in supplements, as this form is extracted from real food, specifically natto,<sup>8</sup> a fermented soy product.

MK-7 is produced by specific bacteria during the fermentation process. However, not all strains of bacteria make it,<sup>9</sup> so not all fermented foods will provide it. Most commercial yogurts, for example, are virtually devoid of vitamin K2, and while certain types of cheeses, such as Gouda, Brie and Edam, are high in K2, others are not.

One of the best ways to ensure a good source of vitamin K2 is to ferment your own vegetables using a special starter culture with bacterial strains that produce vitamin K2. While K1 in vegetables is poorly absorbed, virtually all of the K2 in fermented foods is readily available to your body.

The MK-7 formed in the fermentation process has two major advantages: It stays in your body longer and has a longer half-life than MK-4,<sup>10</sup> which means you can take it just once a day.

Research<sup>11</sup> has shown MK-7 helps prevent inflammation by inhibiting proinflammatory markers that can cause autoimmune diseases like rheumatoid arthritis. And, while vitamin K1 has been found to moderately reduce the risk of bone fractures,<sup>12</sup> MK-7 is more effective than vitamin K1 at

reaching (and protecting) your bone.<sup>13,14</sup>

## Vitamin K2 Plays Key Role in Heart Health

The difference between vitamins K1 and K2 was clearly established in The Rotterdam Study,<sup>15</sup> published in 2004, which focused on their effects on the heart. As it turns out, K1 has no effect on the heart at all, whereas K2 does.

That doesn't mean K1 is useless – far from it. According to a 2019 study<sup>16</sup> in the Journal of Gerontology, older individuals with low vitamin K1 status are more likely to have mobility problems and disability than those with higher levels. In reality, you need the whole suite of vitamin K, but vitamin K2 does have important benefits that K1 does not.

One of the reasons why vitamin K2 is so important for both bone and heart health in particular has to do with a complex biochemistry involving the enzymes matrix gla-protein (MGP, found in your vascular system<sup>17</sup>), and osteocalcin, found in your bone.

"Gla" stands for glutamic acid, which binds to calcium in the cells of your arterial wall and removes it from the lining of your blood vessels. Once removed from your blood vessel lining, vitamin K2 then facilitates the integration of that calcium into your bone matrix by handing it over to osteocalcin, which in turn helps "cement" the calcium in place inside your bone.

Vitamin K2 activates these two proteins, so without it, this transfer process of calcium from your arteries to your bone cannot occur, which raises your risk of arterial calcification.<sup>18</sup>

Calcium deposits in the arteries are responsible for atherosclerosis, hardening and narrowing of the arteries, slowly blocking blood flow. It's a common cause of heart attacks, strokes and peripheral vascular disease.

Indeed, studies<sup>19,20</sup> have demonstrated vitamin K2 inhibits arterial calcification and

improves arterial flexibility, thereby reducing your risk of a cardiovascular event (such as a heart attack) or death.<sup>21</sup>

One 2019 study<sup>22</sup> proposed therapeutic supplementation with vitamin K2 could prevent or halt progression of vascular calcification that may occur with excessive calcium intake, and previous research has demonstrated those eating the highest amount of vitamin K2 have the lowest risk of developing cardiovascular disease.

In the Rotterdam study,<sup>23</sup> those who had the highest amount of vitamin K2 were 52% less likely to experience severe calcification in their arteries and 57% less likely to die from heart disease over a seven- to 10-year period.

People who consumed 45 micrograms (mcg) of K2 daily lived on average seven years longer than people getting just 12 mcg per day. This was a profound discovery, because such a correlation did not exist for K1 intake.

In a subsequent trial called the Prospect Study,<sup>24</sup> 16,057 women were followed for an average of 8.1 years. Here, they found that each additional 10 mcg of K2 in the diet resulted in 9% fewer cardiac events. Again, vitamin K1 had no apparent impact on heart disease risk.

## **Vitamin K2 Is an Important Ally Against Osteoporosis**

To explain the importance of vitamin K2 for bone health and prevention of osteoporosis a bit further, this goes back to its influence over osteocalcin.<sup>25</sup>

Osteocalcin is a protein produced by your osteoblasts (cells responsible for bone formation), and is utilized within the bone as an integral part of the bone-forming process.

However, osteocalcin must be "carboxylated" before it can be effective. Vitamin K functions as a cofactor for the enzyme that catalyzes the carboxylation of osteocalcin.

A systematic review and meta-analysis<sup>26</sup> published in 2006 found vitamin K2, in this case MK-4, reduced bone loss and had "a strong effect on incident fractures." MK-4 supplementation was linked to a 60% reduction in vertebral fractures, a 77% reduction in hip fractures and an 81% lower risk for all nonvertebral fractures.

Another three-year-long placebo-controlled study<sup>27</sup> done in the Netherlands found that postmenopausal women taking 180 mcg of MK-7 per day increased their bone strength, decreased the rate of age-related bone mineral decline and reduced bone density loss, compared to placebo.

## **Vitamin K2 'Kills Two Birds With One Stone'**

Oftentimes, osteoporosis (precipitated by insufficient calcium in your bones) goes hand in hand with heart disease, and vitamin K2's interrelationship with MGP and osteocalcin is one of the reasons for that.

In short, both osteoporosis and heart disease are related to vitamin K2 deficiency, and can be prevented by ensuring sufficient amounts.

As noted in a 2015 paper,<sup>28</sup> "By striking the right balance in intake of calcium and K2, it may be possible to fight osteoporosis and simultaneously prevent the calcification and stiffening of the arteries."

The following graphic from the 2014 paper,<sup>29</sup> "Vitamin K: An Old Vitamin in a New Perspective," illustrates the effect of vitamin K on bone and vascular health.

vitamin k effect bone vascular health

Keep in mind that vitamin K2 also works in tandem with vitamin D and magnesium. So, it's important to remember that vitamin K2 needs to be considered in combination with calcium, vitamin D and magnesium, as these four all have a synergistic relationship that impacts your bone and heart health.<sup>30</sup>

## Other Health Benefits of Vitamin K2

Vitamin K2 is also important for a variety of other health reasons and conditions, including the following:

**Dental health** — Preserving enamel helps reduce cavity formation. Your enamel is made of hollow tubes that extend into the dentin. The enamel is made of nonliving cells, while the dentin has live cells called odontoblasts.

These cells release proteins using vitamin K2 to help prevent tooth decay through an immune response.<sup>31</sup> Research<sup>32</sup> has demonstrated osteocalcin may be found in inflamed tissue, and researchers consider the protein to have a reparative role in dental pulp.

You teeth, like your bones, are storehouses of calcium, which supports the structure and hardness of the teeth.<sup>33</sup> The way calcium is deposited in your teeth will either increase the hardness of your tooth or make it more brittle.

Vitamin K2 once again acts like the traffic cop, telling calcium where and how to be used in your teeth. Working together with vitamin D, it also promotes a reduction in tooth decay or cavities.<sup>34</sup>

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**Cancer** — Cancer prevention is another health benefit of vitamin K2. As noted in the 2010 European Prospective Investigation into Cancer and Nutrition (EPIC) study,<sup>35</sup> high intake of vitamin K2 — not K1 — reduces cancer risk and lowers cancer mortality by 28%. Findings published in 2008 showed men who consumed the greatest amounts of K2 had a 63% reduced incidence of advanced prostate cancer.<sup>36</sup>

The evidence also suggests vitamin K2 may reduce your risk for Non-Hodgkin lymphoma. Mayo Clinic researchers discovered that people with the highest intake of vitamin K2 (108 mcg/day or higher) had a 45% lower risk for this type of cancer, compared to those with the lowest vitamin K2 intake (39 mcg/day or

less).<sup>37</sup>

They attribute this effect to vitamin K2's ability to inhibit inflammatory cytokines, which are related to this type of lymphoma, and its role the life cycle of your cells.

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**Inflammatory conditions** – The inflammatory response is a crucial component in many chronic diseases and diseases of aging. Scientific evidence suggests both vitamin K1 and K2 have anti-inflammatory activity, in part by inhibiting nuclear factor kappa-B.<sup>38</sup>

In one meta-analysis,<sup>39</sup> researchers found evidence the family of vitamin K plays a protective role in chronic aging conditions, inflammation and cardiovascular disease. Another study<sup>40</sup> confirmed the role the MK-7 form specifically has in the modulation of inflammatory biomarkers.

The researchers evaluated natural vitamin K2 for its potential to inhibit gene expression and production of pro-inflammatory markers in vitro, finding MK-7 inhibited gene expression in a dose-dependent manner.

Other research<sup>41</sup> has demonstrated a reduction in C-reactive protein, a common biomarker used to evaluate inflammation in patients with rheumatoid arthritis. C-reactive protein is a risk marker for a wide range of diseases and the researchers concluded higher intake of vitamin K2 may lower overall risk.

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**Kidney health** – There is also accumulating evidence suggesting vitamin K2 may play a role in chronic kidney disease.

A pre- and post-intervention clinical trial,<sup>42</sup> which included patients with a diagnosis of chronic kidney disease who took 360 mcg of MK-7 for four weeks, found it significantly reduced calcification in the patients' blood vessels.

Patients with chronic kidney disease with a subclinical vitamin K deficiency may also benefit from a greater intake of the vitamin.<sup>43</sup> As noted in a 2016 study<sup>44</sup> in EBioMedicine, "MGP not only inhibits calcification in larger arteries but also may



be renoprotective."

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**Testosterone** — Yet another role vitamin K2 plays in your body is the optimal production of sex hormones. At least two studies<sup>45,46</sup> have shown MK-4, found in animal foods such as meat and dairy products, can help balance testosterone production.

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**Polycystic ovarian syndrome (PCOS)** — Vitamin K2 has an effect in women as well, as the vitamin may be helpful in the management of PCOS. This is now the most common hormonal disorders in young women, causing enlarged ovaries and a heightened risk for fertility problems.<sup>47</sup>

In one randomized study,<sup>48</sup> 60 vitamin D deficient women with PCOS took either a placebo or a combination of calcium, vitamin D and vitamin K for eight weeks. Those in the treatment group enjoyed greater decrease in testosterone and symptoms than the placebo group.

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**Insulin sensitivity** — An unexpected discovery was made when researchers found bone was an endocrine organ, contributing to the regulation of a number of physiological processes, including glucose homeostasis.<sup>49</sup>

There's evidence to suggest vitamin K2 supplementation may improve insulin sensitivity via osteocalcin metabolism,<sup>50</sup> and may help prevent the development of Type 2 diabetes.<sup>51</sup>

The evidence is not conclusive, however, as a systematic review<sup>52</sup> of controlled trials found K2 supplementation had no effect on insulin sensitivity. Part of the problem may have something to do with the form of vitamin given. Numerous studies have demonstrated synthetic vitamin K2 supplements are not as effective as natto-derived K2 supplements.

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**Mitochondrial health** — Research<sup>53</sup> published in the journal Science in 2012 found vitamin K2 serves as a mitochondrial electron carrier, thereby helping maintain

normal ATP production in mitochondrial dysfunction, such as that found in Parkinson's disease.

**Macular degeneration** — According to a 2014 paper<sup>54</sup> on vitamin K, MK-7 in particular may offer benefits for age-related macular degeneration.

## Signs and Symptoms of Vitamin K2 Deficiency

The major problem we face when it comes to optimizing vitamin K2 is that there's no easy way to screen or test for vitamin K2 sufficiency. Vitamin K2 cannot at present be measured directly, so it's measured through an indirect assessment of undercarboxylated osteocalcin. This test is still not commercially available, however.

Without testing, we're left with looking at various lifestyle factors that predispose you to deficiency. As a general rule, if you have osteoporosis, heart disease or diabetes, you're likely deficient in vitamin K2.

That said, it's believed that the vast majority of people are in fact deficient these days and would benefit from more K2. One reason for this is because very few (Americans in particular) eat enough vitamin K2-rich foods.

So, if you do not have any of the health conditions listed, but do not regularly eat high amounts of the following foods, then your likelihood of being vitamin K2 deficient is still very high:

- Certain fermented foods such as natto, or vegetables fermented using a starter culture of vitamin K2-producing bacteria
- Certain cheeses such as Brie and Gouda (these two are particularly high in K2)
- Grass fed organic animal products such as egg yolks, liver, butter and dairy

Use of certain drugs may also affect your vitamin K2 status and make you more prone to deficiency. For example, research<sup>55</sup> shows statins deplete vitamin K2, and there's

scientific evidence<sup>56</sup> suggesting statin drugs may indeed increase calcification in the arteries.

Vitamin K2 depletion may be an explanation for that. So, if you're on a statin, you'll want to make sure you're taking extra vitamin K2, as well as ubiquinol or coenzyme Q10, which is also being depleted by the drug.

As discussed in "Vitamin K2 Deficiency Is a Significant Cause of Cardiovascular Disease," warfarin, antibiotics, anti-tuberculosis drugs, anticonvulsants can also raise your risk of vitamin K deficiency.

## Dosage Recommendations

As for a clinically useful dosage of vitamin K2, some studies – including the Rotterdam study<sup>57</sup> – have shown as little as 45 mcg per day may be sufficient. As a general guideline, I recommend getting around 150 mcg of vitamin K2 per day.

Others recommend slightly higher amounts; upward of 180 to 200 mcg. Fortunately, you don't need to worry about overdosing on K2, as it appears to be completely nontoxic.

If you opt for a vitamin K2 supplement, make sure it's MK-7. (The exception is if you're on vitamin K antagonists, i.e., drugs that reduce blood clotting by reducing the action of vitamin K. If so, you should avoid MK-7 supplements.<sup>58</sup>) Also remember to take it with fat since it's fat-soluble and won't be properly absorbed otherwise, and to balance it with calcium, vitamin D and magnesium.

As a last tip, keep in mind that vitamin K2 may not necessarily make you "feel better" per se. Its internal workings are such that you're not likely to feel the difference physically.

Compliance can therefore be a problem, as people are more likely to take something that has a noticeable effect. This may not happen with vitamin K2, but that certainly

does not mean it's not doing anything.

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