# High Dose Vitamin K2 Builds New Bone

Human trials show that 45 mg a day of vitamin K2 increases bone density and reduces fracture incidence.

Scientifically reviewed by: <u>Dr. Gary Gonzalez</u>, MD, in May 2022. Written by: Michael Downey.

Osteoporosis is astonishingly common in men and women.

Roughly **50%** of American women and **25%** of American men age 50 and older will suffer a **fracture** due to this condition.<sup>1</sup>

These bone breaks are a leading cause of disability. Within a year of suffering a hip fracture, up to 20% of patients over 50 *will die*.<sup>2</sup>

For decades, doctors in Japan have been using **high doses** of **vitamin K2** as a prescription drug to prevent *bone loss* and protect against **fractures**.<sup>3</sup>

It is now available in the U.S. without a prescription.

Clinical trials have demonstrated that 45 mg of vitamin K2 (menaquinone-4) helps to:411

- Slow bone loss,
- Reduce fracture risk, and
- Build *new* bone.

A two-year study of older osteoporosis patients showed that high-dose vitamin K2 cut the number of people suffering a **vertebral** fracture by **half**.<sup>11</sup>

#### The Danger of Osteoporosis

**Osteoporosis** is a condition that causes bones to become weak, brittle, and prone to **fractures**. After suffering one fracture, the risk of future breaks increases by 86%.<sup>2</sup>

Fractures of the **hip** and **vertebra** are particularly associated with loss of mobility and risk of death. People who suffer a **vertebral fracture** have an **eight-fold** increase in mortality compared to other individuals their age.<sup>2</sup>

But almost *any* kind of broken bone increases the risk of death in older people.<sup>12</sup> That's why it is imperative to not just slow, but *reverse* bone loss as soon as it begins to take hold.



Comparing the left (normal) and right (osteoporosis) images, the increase in dark areas involving this crosssection of the femur are simplified visual depictions of the increase in bone marrow fat, and thinning (decrease) in cancellous/ trabecular bone, that occur with osteoporosis.

## How Bone Loss Happens

The body constantly breaks down *old* bone and builds up *new* bone.

In the first decades of life, **bone density** increases. Then it plateaus for about two more decades.

At around age 40, bone density begins to *decrease*. In women, the speed of bone loss accelerates with the onset of menopause.

This *decline in* bone mineral density leads to a *reduction* in bone strength. Bones become brittle and prone to **fractures**, even from minor injuries and **stress fractures** that occur during normal movement.

Osteopenia is the term for the *early* stage of weakening bones.

If no action is taken and bone density continues to drop, **osteoporosis** develops. Osteoporosis means "*bone full of pores or holes*."

Most people who suffer from osteopenia or osteoporosis are unaware of it until it's too late—when they suffer a **fracture**.

#### WHAT YOU NEED TO KNOW

Better Bone Health with High-Dose Vitamin K2

- **Osteoporosis** causes bone loss and increases the risk of serious **fractures**. In people over 50, these fractures are a significant mortality risk.
- High-dose vitamin K2, in the form of MK-4, has been used in Japan for decades as a treatment for osteoporosis.
- Human trials have shown that daily intake of **45 mg** of **vitamin K2** (MK-4) maintains or *increases* bone density and cuts the risk of fractures.
- Other vitamins and minerals, including **calcium** and **vitamin D3**, also support bone health, and help maximize vitamin K2's benefits.

# High-Dose Vitamin K2

The good news: There is something we can do about age-related bone loss and risk of fractures.

In *low* doses of **45-60 mcg**, vitamin K promotes normal blood clotting. This small amount of vitamin K is normally obtained from dietary sources.

Japanese doctors have long been prescribing much **higher doses** of a specific form of **vitamin K2** as a treatment for **osteoporosis**.<sup>3</sup>

They have amassed decades of evidence that **45 mg** (**45,000 mcg**) of vitamin K2 in the form of **menaquinone-4** (**MK-4**), leads to improvements in bone health.<sup>3</sup>

Now scientists have confirmed that oral intake of high-dose **vitamin K2** is critical for bone strength and other aspects of healthy aging.

### Increased Bone Density

**Human trials** have demonstrated that vitamin K2 maintains or even *increases* bone mineral density. It also helps prevent **fractures**, even in older patients who have already developed **osteoporosis**.<sup>4-11</sup>

In one of these studies, Japanese researchers randomized older osteoporosis patients into two groups. One received **150 mg**/day of **calcium** alone. The other received this same modest **calcium** dose plus **45 mg** of **vitamin K2** (as **MK-4**) daily.<sup>11</sup>

Over a two-year period:11

- Patients who received *only* calcium continued to lose **bone density**, dropping by about **3%**.
- Patients receiving **vitamin K2** in addition to **calcium** largely maintained their bone mineral density.

A **10%** drop in bone density more than *doubles* the risk for **fractures** of the vertebra and hip.<sup>13</sup> This suggests that patients in this study who were treated *only* with calcium may have an increased **risk of fracture**.

But adding vitamin K2 to calcium largely arrested bone loss, possibly preventing an increase in fracture risk."

Patients receiving K2 also had a significant *increase* in levels of active **osteocalcin**.<sup>11</sup> This protein binds calcium to bone, helping the body turn calcium into healthy *new bone*.<sup>14</sup>

#### MEDICATIONS THAT PROMOTE OSTEOPOROSIS

Many common drugs can contribute to bone loss and osteoporosis risk, including:

- **Cancer-fighting drugs** that inhibit sex hormones. These include **anti-androgen** therapies (which reduce levels of testosterone) and **aromatase inhibitors** (which reduce estrogen activity).<sup>36,37</sup>
- Corticosteroids like prednisone, hydrocortisone, dexamethasone, and many others.<sup>38,39</sup>
- Warfarin (Coumadin<sup>®</sup>), which is used to treat blood clots.<sup>40,42</sup>
- Proton-pump inhibitors used to reduce stomach acid, including Nexium<sup>®</sup>, Prilosec<sup>®</sup>, and Prevacid<sup>®</sup>.<sup>43</sup>

No one should stop taking these medications unless directed by their doctor. But people using any of these drugs may want to carefully monitor their bone mineral status.

### **Preventing Fractures**

In the same study, scientists assessed the effect of vitamin K2 on the incidence of bone fractures.

During the two-year study, the group receiving **calcium alone** sustained **35 fractures**, compared to only **14 fractures** in the **vitamin K2** group.<sup>11</sup>

In another Japanese clinical trial, scientists evaluated the effect of vitamin K2 on women with osteoporosis.<sup>6</sup>

Taking 45 mg of oral vitamin K2 daily:6

• Maintained **mineral density** to a significantly greater degree than in the untreated group, and

• *Reduced* the incidence of vertebral **fractures** to a degree similar to the drug **etidronate**.

Etidronate (most commonly sold as Didronel<sup>®</sup>) is from the class of drugs known as **bisphosphonates**. It is used to treat **Paget's disease**, a condition characterized by bones that are soft, weak, or easily broken.

It is sometimes used to treat osteoporosis, but its side effects can include nausea, diarrhea, heartburn, chest pain, and skin blisters.<sup>15</sup> Vitamin K2, on the other hand, is not associated with significant side effects.

#### VITAMIN K2'S HEART BENEFITS

Vitamin K2 promotes new bone growth in part by increasing calcification, the buildup of calcium deposits, in the bone.

In *soft tissues*, calcification can be dangerous. In blood vessels, for example, it leads to the buildup of atherosclerotic plaque associated with <u>cardiovascular disease</u>.

Research has shown that while vitamin K2 *causes* beneficial calcification in bones, it *prevents* harmful calcification in soft tissues, including blood vessels.<sup>44,45</sup> This occurs because it activates **matrix Gla protein**, which *inhibits* calcification of blood vessels.

For this reason, vitamin K2 may be protective against cardiovascular disease.<sup>46</sup>

Anyone taking **warfarin**, a powerful anti-coagulant, should consult a physician before deciding to take any form of vitamin K.

Warfarin functions by blocking vitamin K activity in the body. Those taking warfarin are told to restrict vitamin K intake even from healthy vegetables. Newer drugs like Eliquis<sup>®</sup>, Pradaxa,<sup>®</sup>, and Xarelto<sup>®</sup> provide anticoagulant effects without the need to restrict vitamin K intake.

### How Vitamin K2 Keeps Bones Strong

Vitamin K2 works by restoring a healthy balance between the two types of bone cells that influence <u>bone</u> <u>density</u>: osteoclasts and osteoblasts.

Osteoclasts break down old bone. Osteoblasts build new bone.

Healthy bone relies on a *balance* of activity between these two types of cells.

Aging disrupts this delicate balance. Osteo*clast* activity overtakes osteo*blast* activity. Bone is broken down faster than new bone is built up. Bone **density** drops and **osteopenia** and **osteoporosis** result.

Vitamin K2 has been shown, in preclinical studies, to promote:14,16

- An increase in bone-building osteoblast activity, and
- A *reduction* in bone-destroying **osteoclast** activity.

With this balance restored, *more* bone is built, *less* is destroyed, and **bone mineral density** is maintained or increased.

Additionally, in order to lay down new bone, osteoblasts need the protein **osteocalcin**. Vitamin K2 helps convert osteocalcin into its *active* form.<sup>14,17</sup>

# Nutrients That Support Vitamin K2

The bone-rebuilding effects of vitamin K2 are even greater when supported by several other **nutrients**. The following vitamins and minerals support strong, healthy bones:

- **Calcium** is the major mineral that forms the hard matrix of bone. Most studies show that oral calcium decreases the rate at which bone breakdown and mineral loss occur.<sup>18-20</sup>
- Vitamin D helps absorb calcium from the gut after a meal and stimulates the production of **osteocalcin**.<sup>17</sup> It also facilitates the transfer of calcium from the blood and other extracellular fluids to the surface of bones, where it makes them stronger and less likely to break.<sup>21</sup> Vitamin D helps the body absorb the bone-strengthening trace elements zinc and manganese as well.<sup>22,23</sup>
- **Magnesium**, like calcium, makes up the mineral matrix of bone and is needed to maintain healthy bone density.<sup>24</sup>
- Zinc, Manganese, Silicon, and Boron. These minerals have been shown to be important for optimal bone formation and health. *Low* intake of each of these minerals is associated with bone *loss*, and increased intake improves bone health in animals and in humans.<sup>25-35</sup>

Supported by these nutrients, vitamin K2 can provide powerful protection against fractures and bone loss.

# Combining Vitamin K2 with Osteoporosis Drugs

**Bisphosphonates** are a group of drugs prescribed to slow the bone loss of osteoporosis. They include **etidronate** (Didronel®), **alendronate** (Fosamax®), **risedronate** (Actonel®), and others.

Research shows that vitamin K2 does *not* interfere with bisphosphonates and can safely be used at the same time.

Some data suggest that they may have an *additive* effect. This means they may protect bone density better together than either one does alone.<sup>47</sup>

### Summary

Age-related **bone loss** and **osteoporosis** lead to frequent fractures in people over 50.

**High-dose vitamin K2** can help. It improves bone health by restoring balance to the process of bone breakdown and formation.

Doctors in Japan have prescribed it to treat osteoporosis for decades.

Human trials demonstrate that a daily intake of **45 mg** of vitamin K2 maintains or increases **bone mineral density** and reduces the risk of **fractures**.

If you have any questions on the scientific content of this article, please call a **Life Extension**® Wellness Specialist at 1-866-864-3027.

## References

- 1. Available at: <u>https://www.nof.org/patients/what-is-osteoporosis/</u>. Accessed October 5, 2020.
- 2. Available at: https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosisand-fragility-fractures. Accessed July 7, 2020,

- Iwamoto J. Vitamin K(2) therapy for postmenopausal osteoporosis. *Nutrients*. 2014 May 16;6(5):1971-80.
- 4. Binkley N, Harke J, Krueger D, et al. Vitamin K treatment reduces undercarboxylated osteocalcin but does not alter bone turnover, density, or geometry in healthy postmenopausal North American women. *J Bone Miner Res.* 2009 Jun;24(6):983-91.
- 5. Iwamoto J, Takeda T, Ichimura S. Effect of combined administration of vitamin D3 and vitamin K2 on bone mineral density of the lumbar spine in postmenopausal women with osteoporosis. *J Orthop Sci.* 2000;5(6):546-51.
- 6. Iwamoto J, Takeda T, Ichimura S. Effect of menatetrenone on bone mineral density and incidence of vertebral fractures in postmenopausal women with osteoporosis: a comparison with the effect of etidronate. *J Orthop Sci.* 2001;6(6):487-92.
- 7. Jiang Y, Zhang ZL, Zhang ZL, et al. Menatetrenone versus alfacalcidol in the treatment of Chinese postmenopausal women with osteoporosis: a multicenter, randomized, double-blinded, double-dummy, positive drug-controlled clinical trial. *Clin Interv Aging*. 2014;9:121-7.
- 8. Purwosunu Y, Muharram, Rachman IA, et al. Vitamin K2 treatment for postmenopausal osteoporosis in Indonesia. *J Obstet Gynaecol Res.* 2006 Apr;32(2):230-4.
- 9. Takahashi M, Naitou K, Ohishi T, et al. Effect of vitamin K and/or D on undercarboxylated and intact osteocalcin in osteoporotic patients with vertebral or hip fractures. *Clin Endocrinol* (*Oxf*). 2001 Feb;54(2):219-24.
- Ushiroyama T, Ikeda A, Ueki M. Effect of continuous combined therapy with vitamin K(2) and vitamin D(3) on bone mineral density and coagulofibrinolysis function in postmenopausal women. *Maturitas*. 2002 Mar 25;41(3):211-21.
- 11. Shiraki M, Shiraki Y, Aoki C, et al. Vitamin K2 (menatetrenone) effectively prevents fractures and sustains lumbar bone mineral density in osteoporosis. *J Bone Miner Res.* 2000 Mar;15(3):515-21.
- 12. Tran T, Bliuc D, Hansen L, et al. Persistence of Excess Mortality Following Individual Nonhip Fractures: A Relative Survival Analysis. *J Clin Endocrinol Metab.* 2018 Sep 1;103(9):3205-14.
- 13. Available at: https://www.ncbi.nlm.nih.gov/books/NBK45525/. Accessed September 28, 2020.
- 14. Palermo A, Tuccinardi D, D'Onofrio L, et al. Vitamin K and osteoporosis: Myth or reality? *Metabolism.* 2017 May;70:57-71.
- Available at: <u>https://medlineplus.gov/druginfo/meds/a682581.html#side-effects</u>. Accessed November 5, 2020.
- 16. Akbari S, Rasouli-Ghahroudi AA. Vitamin K and Bone Metabolism: A Review of the Latest Evidence in Preclinical Studies. *Biomed Res Int.* 2018;2018:4629383.
- 17. van Ballegooijen AJ, Pilz S, Tomaschitz A, et al. The Synergistic Interplay between Vitamins D and K for Bone and Cardiovascular Health: A Narrative Review. *Int J Endocrinol.* 2017;2017:7454376.
- 18. Straub DA. Calcium supplementation in clinical practice: a review of forms, doses, and indications. *Nutr Clin Pract.* 2007 Jun;22(3): 286-96.
- 19. Bischoff-Ferrari HA, Rees JR, Grau MV, et al. Effect of calcium supplementation on fracture risk: a double-blind randomized controlled trial. *Am J Clin Nutr*. 2008 Jun;87(6):1945-51.
- 20. Kalluru R, Ames R, Mason B, et al. Bone density in healthy men after cessation of calcium supplements: 20-month follow-up of a randomized controlled trial. *Osteoporos Int.* 2015 Jan;26(1):173-8.
- 21. Schild A, Herter-Aeberli I, Fattinger K, et al. Oral Vitamin D Supplements Increase Serum 25-Hydroxyvitamin D in Postmenopausal Women and Reduce Bone Calcium Flux Measured by 41Ca Skeletal Labeling. J Nutr. 2015 Oct;145(10):2333-40.
- 22. Claro da Silva T, Hiller C, Gai Z, et al. Vitamin D3 transactivates the zinc and manganese transporter SLC30A10 via the Vitamin D receptor. *J Steroid Biochem Mol Biol.* 2016 Oct;163:77-87.
- 23. Newmark HL, Heaney RP, Lachance PA. Should calcium and vitamin D be added to the current enrichment program for cereal-grain products? *Am J Clin Nutr*. 2004 Aug;80(2):264-70.
- 24. Matsuzaki H. [Prevention of osteoporosis by foods and dietary supplements. Magnesium and bone metabolism]. *Clin Calcium.* 2006 Oct;16(10):1655-60.

- 25. Aydin H, Deyneli O, Yavuz D, et al. Short-term oral magnesium supplementation suppresses bone turnover in postmenopausal osteoporotic women. *Biol Trace Elem Res.* 2010 Feb;133(2):136-43.
- 26. Bae YJ, Kim JY, Choi MK, et al. Short-term administration of water-soluble silicon improves mineral density of the femur and tibia in ovariectomized rats. *Biol Trace Elem Res.* 2008 Aug;124(2):157-63.
- 27. Dimai HP, Porta S, Wirnsberger G, et al. Daily oral magnesium supplementation suppresses bone turnover in young adult males. *J Clin Endocrinol Metab.* 1998 Aug;83(8):2742-8.
- 28. Hyun TH, Barrett-Connor E, Milne DB. Zinc intakes and plasma concentrations in men with osteoporosis: the Rancho Bernardo Study. *Am J Clin Nutr*. 2004 Sep;80(3):715-21.
- 29. Kim MH, Bae YJ, Choi MK, et al. Silicon supplementation improves the bone mineral density of calcium-deficient ovariectomized rats by reducing bone resorption. *Biol Trace Elem Res.* 2009 Jun;128(3):239-47.
- 30. Nielsen FH. Studies on the relationship between boron and magnesium which possibly affects the formation and maintenance of bones. *Magnes Trace Elem.* 1990;9(2):61-9.
- 31. Nielsen FH, Lukaski HC, Johnson LK, et al. Reported zinc, but not copper, intakes influence wholebody bone density, mineral content and T score responses to zinc and copper supplementation in healthy postmenopausal women. *Br J Nutr*. 2011 Dec;106(12):1872-9.
- 32. Rico H, Gallego-Lago JL, Hernandez ER, et al. Effect of silicon supplement on osteopenia induced by ovariectomy in rats. *Calcif Tissue Int.* 2000 Jan;66(1):53-5.
- 33. Strause L, Saltman P, Smith KT, et al. Spinal bone loss in postmenopausal women supplemented with calcium and trace minerals. *J Nutr.* 1994 Jul;124(7):1060-4.
- 34. Yamaguchi M. Role of nutritional zinc in the prevention of osteoporosis. *Mol Cell Biochem.* 2010 May;338(1-2):241-54.
- 35. Yamaguchi M, Weitzmann MN. Zinc stimulates osteoblastogenesis and suppresses osteoclastogenesis by antagonizing NF-kappaB activation. *Mol Cell Biochem*. 2011 Sep;355(1-2):179-86.
- 36. Lumachi F, Luisetto G, Basso SM, et al. Endocrine therapy of breast cancer. *Curr Med Chem.* 2011;18(4):513-22.
- 37. Mazziotti G, Canalis E, Giustina A. Drug-induced osteoporosis: mechanisms and clinical implications. *Am J Med.* 2010 Oct;123(10):877-84.
- 38. Briot K, Roux C. Drug-induced osteoporosis: beyond glucocorticoids. *Curr Rheumatol Rep.* 2008 Apr;10(2):102-9.
- 39. Mirza F, Canalis E. Management of endocrine disease: Secondary osteoporosis: pathophysiology and management. *Eur J Endocrinol.* 2015 Sep;173(3):R131-51.
- 40. Cranenburg EC, Schurgers LJ, Vermeer C. Vitamin K: the coagulation vitamin that became omnipotent. *Thromb Haemost.* 2007 Jul;98(1):120-5.
- 41. Namba S, Yamaoka-Tojo M, Hashikata T, et al. Long-term warfarin therapy and biomarkers for osteoporosis and atherosclerosis. *BBA Clin.* 2015 Dec;4:76-80.
- 42. Namba S, Yamaoka-Tojo M, Kakizaki R, et al. Effects on bone metabolism markers and arterial stiffness by switching to rivaroxaban from warfarin in patients with atrial fibrillation. *Heart Vessels*. 2017 Aug;32(8):977-82.
- 43. Kopic S, Geibel JP. Gastric acid, calcium absorption, and their impact on bone health. *Physiol Rev.* 2013 Jan;93(1):189-268.
- 44. El Asmar MS, Naoum JJ, Arbid EJ. Vitamin k dependent proteins and the role of vitamin k2 in the modulation of vascular calcification: a review. *Oman Med J*. 2014 May;29(3):172-7.
- 45. van den Heuvel EG, van Schoor NM, Lips P, et al. Circulating uncarboxylated matrix Gla protein, a marker of vitamin K status, as a risk factor of cardiovascular disease. *Maturitas*. 2014 Feb;77(2):137-41.
- 46. 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):90-8.
- 47. Plaza SM, Lamson DW. Vitamin K2 in bone metabolism and osteoporosis. *Altern Med Rev.* 2005 Mar;10(1):24-35.