



MK4 Osteoporosis Research

Study	Citation	Diagnoses	Design	Volunteers	MK4 Dose	Length	Outcomes	Side Effects
Kodama and Okamoto	Brain & Development. 2017;39(10): 846-850	Osteoporosis in adults with cerebral palsy	Nonrandomized, controlled clinical trial	n = 32; median age 56 years M4 group contained 16 volunteers (7 women and 9 men)	MK4 45 mg/day	12 months	Bone laboratory markers: MK4 improved laboratory markers associated with bone health. Bone density: Bone density improved 5% after six months and 9% after twelve months.	Not reported



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Shikano and Kineko	<i>Internal Medicine.</i> 2016; 55(15): 1997-2003	Prednisone-induced osteoporosis	Prospective, observational study	n = 60 (21 men, 39 women); mean age 55 years.	MK4 45 mg/day orally or no MK4 All volunteers continued to receive prednisone (30-60 mg/day) and all volunteers also took bisphosphonate medications.	18 months	Bone laboratory markers: MK4 improved laboratory markers associated with bone health. Bone density: Bone density was maintained in the MK4 group. Fractures: There were zero fractures in people taking MK4, while 5% of those taking no MK4 fractured.	Not reported



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Huang and Wan	<i>Osteoporosis International</i> . 2015;26(3): 1175-1186	Prednisone-induced osteoporosis	Meta-analysis and review of randomized controlled clinical trials	19 clinical trials with 6,759 women (age ranges 50-75 years old)	MK4 45 mg/day orally vs control groups	12-36 months	Fractures: pooled analysis of studies reporting fractures showed a 53% reduction in fracture risk compared to controls.	Not reported



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Jiang and Zhang	<i>Clinical Intervention in Aging</i> . 2014; 9:121-127	Postmenopausal osteoporosis	Multicenter, randomized, double-blinded, double-dummy, noninferiority, positive drug-controlled clinical trial	n = 213 (all women); mean age 64 years.	MK4 group: 45 mg/day plus calcium 500 mg/day Vitamin D2 (alfacalcidol) group: 0.5 micrograms (mcg)/day plus calcium 500 mg/day	12 months	Bone laboratory markers: MK4 improved laboratory markers associated with bone health. Bone density: MK4 improved bone density 1.2% in the lumbar spine and 2.7% in the hip. Fractures: Fractures were decreased in the MK4 +calcium group compared to those taking just vitamin D2 +calcium.	Minor and not statistically different than taking the vitamin D. The researchers concluded that MK4 "was well tolerated and safe in the study population," and that MK4 "is an effective and safe choice" for people with osteoporosis



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Je and Joo	<i>Journal of Korean Medical Science.</i> 2011; 26(8):1093-1098.	Postmenopausal osteoporosis	Randomized, controlled clinical trial	n = 78 (all women); mean age approx. 68 years	MK4 Group: MK4 45 mg/day, plus calcium 630 mg/day and vitamin D 400 IU/day Control Group: Calcium 630 mg/day and vitamin D 400 IU/day	6 months	Bone density: Bone density improved in the MK4 group, but did not improve in the control group. Bone laboratory markers: Improved lab markers associated with bone health in the MK4 group, but not in the Control Group.	Three people complained of a nausea sensation two times after taking MK4, but no other complaints were reported.



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Shiraki and Itabashi	<i>Journal of Bone and Mineral Metabolism</i> . 2009; 27(3):333-340	Postmenopausal osteoporosis	Randomized, prospective study	n = 109 (all women); mean age approx. 68 years	MK4 Group: 45 mg/day Control Group: Calcium aspartate 1,200 mg/day (providing 133.8 mg elemental calcium)	6 months	Bone laboratory markers: Improved lab markers associated with bone health in the MK4 group, but not in the Control Group.	Minor, and no different than control group.



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Binkley and Harke	<i>Journal of Bone and Mineral Research</i> . 2009; 24(6):983-991	Postmenopausal osteoporosis	Double-blind, placebo-controlled study	n = 381 (all women); mean age 62.5 years	MK4 45 mg/day orally or phylloquinone 1 mg/day orally or placebo	12 months	Bone laboratory markers: Improved lab markers associated with bone health.	None
Inoue and Fujita	<i>Journal of Bone and Mineral Metabolism</i> . 2009; 27(1):66-75	Postmenopausal osteoporosis	Open-labeled	n = 4,378 (all women); mean age 68 years	MK4 45 mg/day orally alone or with calcium (1.2 to 3 grams) orally per day	48 months	Fractures: Fractures were decreased in those taking MK4+calcium.	Minor and statistically lower incidence in MK4 monotherapy group
Knapen and Schurgers	<i>Osteoporosis International</i> . 2007; 18(7): 963–972.	Postmenopausal osteoporosis	Randomized, placebo-controlled	n = 325 (all women); mean age 66 years	45 mg/day orally or placebo	36 months	Bone density: Bone mineral content and bone strength improved in those those taking MK4.	Minor, and no different than placebo group



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Purwosunu and Muharram	<i>Journal of Obstetrics and Gynaecology Research</i> . 2006; 32(2): 230-234.	Postmenopausal osteoporosis	Double-blind, randomized, placebo-controlled	n = 63 (all women); mean age 60 years	MK4 group: MK4 45 mg/day orally plus calcium carbonate 1500 mg/day orally Control group: placebo plus calcium carbonate 1500 mg/day orally	48 weeks	Bone density: MK4 increased bone density 1.74%, while those not taking MK4 lost bone density.	Two minor gastrointestinal symptoms, which subsided after temporary cessation of therapy.



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Cockayne and Adamson	Archives of Internal Medicine. 2006;166(12): 1256-1261 of	Postmenopausal osteoporosis	Systematic review and meta-analysis of randomized controlled clinical trials,	13 clinical trials with 1,366 women (mean ages 46-78 years old)	MK4 45 mg/day orally or no MK4	6-36 months	Fractures: After publication, data from three studies were deemed problematic. An analysis without those studies that was published in the original paper still showed a statistically significant 60% reduction of vertebral fractures and 76% reduction in all nonvertebral fractures.	Not reported



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Sasaki and Kusano	<i>Journal of Bone and Mineral Metabolism</i> . 2005; 23(1):41-47	Osteoporosis in people with chronic glomerulonephritis taking prednisone	Randomized, controlled clinical trial	n = 20 (12 men, 8 women), mean age 40 years	MK4 15 mg/day orally plus glucocorticoids (prednisone) or glucocorticoids without MK4	12 months	Bone density: MK4 preserved bone mineral density (BMD) while those not taking MK4 lost BMD.	None
Ochiai and Nakashima	<i>Bone</i> . 2004; 34(3):579-583	Hypoparathyroidism in people with chronic renal failure in patients on dialysis	Randomized, controlled clinical trial	n = 33 (18 men, 15 women) mean age 65 years	MK4 45 mg/day orally or no MK4	12 months	Bone laboratory markers: MK4 improved lab markers associated with bone health.	Not reported



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Yonemura and Fukasawa	<i>American Journal of Kidney Diseases</i> . 2004; 43(1):53-60	Osteoporosis in people with chronic glomerulonephritis taking prednisone	Randomized, controlled	n = 60 (28 men, 32 women), mean age 32 years	Group A: control (glucocorticoids only) Group B:MK4 (45 mg/day) orally plus glucocorticoids Group C: vitamin D alone, plus glucocorticoids Group D: MK4 (45 mg/day) plus vitamin D and glucocorticoids.	24 months	Bone density: Those taking just glucocorticoids lost BMD. Those taking just vitamin D or vitamin D plus MK4 had their bone density maintained. However, those taking just vitamin D also had an increase in serum calcium, while serum calcium did not increase in those taking vitamin D plus MK4.	None

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Nakashima and Yorioka	<i>Bone</i> . 2004; 34(3):579-583.	Hypoparathyroidism in people with chronic kidney failure on dialysis with underlying chronic glomerulonephritis, nephrosclerosis and diabetes mellitus	Randomized, noncontrolled	n = 32 hemodialysis patients (19 men and 13 women) with low parathyroid hormone (PTH); mean age 58 years	MK4 45 mg/day orally	12 months	Bone laboratory markers: MK4 improved bone laboratory markers (eg, undercarboxylated osteocalcin)	None
Iketani and Kiriike	<i>Psychiatry Research</i> . 2003; 117(3):259-69.	Osteoporosis in young women with anorexia nervosa	Controlled	n = 39 (all women); mean age 22 years	MK4 45 mg/day orally or no MK4	10.8 months	Bone density: MK4 preserved bone density compared with those not receiving MK4	None



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Shiomi and Nishiguchi	<i>Psychiatry Research</i> . 2003; 117(3):259-269	Osteoporosis in young women with anorexia nervosa	Controlled clinical trial	n = 39 (all women); mean age 22 years	MK4 45 mg/day orally or no MK4	10.8 months	Bone density: MK4 preserved bone density compared with those not receiving MK4	None
Shiomi and Nishiguchi	<i>American Journal of Gastroenterology</i> , 2002: 97 (4): 978-81.	Osteoporosis in women with cirrhosis of the liver and viral hepatitis	Randomized, controlled	n = 50 (all women); mean age 60 years	MK4 45 mg/day orally or no MK4	24 months	Bone density: MK4 preserved bone density compared with those not taking MK4	None



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Ushiroyama and Ikeda	<i>Maturitas</i> . 2002; 41(3):211-221.	Postmenopausal osteoporosis	Randomized, controlled	n = 172 (all women); mean age 53 years	Group A: MK4 45 mg/day orally Group B: vitamin D3 1 µg/day orally Group C: MK4 plus vitamin D3 Group D: Control group	24 months	Bone density: MK4+Vitamin D increased bone density nearly 5% while those taking MK4 alone had a 0.14% increase in bone density.	None



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Bunyaratavej and Penkitti	<i>Journal of the Medical Association of Thailand.</i> 2001; 84 Suppl 2: S553-559	Osteoporosis	Randomized, controlled clinical trial	n = 83 (all women)	MK4 group: MK4 45 mg/day orally plus calcium 800 mg/day orally Control group: calcium 800 mg/day orally	12 months	Bone density: MK4 improved bone density compared to those taking calcium alone. Bone laboratory markers: MK4 Improved lab markers associated with bone health compared to those taking calcium alone.	Two cases of mild skin rash that subsided upon discontinuation of MK4



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Inoue and Sugiyama	<i>Endocrine Journal</i> . 2001; 48(1):11-8.	Osteoporosis in children taking prednisone who have Juvenile rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, muscular gravis, autoimmune hepatitis, lymphoid interstitial pneumonia, IgA nephropathy, nephrotic syndrome, membranoproliferative glomerulonephritis dystrophy, or myasthenia gravis	Randomized, controlled clinical trial	n = 18 (5 boys, 13 girls), ages 4 to 14 years	Group A: MK4 (2 mg/kg/day) plus glucocorticoid Group B: MK4 (2 mg/kg/day) plus Vitamin D (0.03 µg/kg/day) plus glucocorticoid	12 weeks	Bone density: MK4 maintained bone density while those not taking MK4 lost bone density.	None

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Nishiguchi and Shimoi	<i>Journal of Hepatology</i> . 2001; 35(4):543-545.	Osteoporosis in people with primary biliary cirrhosis (PBC) stages I-IV	Randomized, controlled clinical trial	n = 30 (all women); mean age 55 years	MK4 45 mg/day orally or no MK4	24 months	Bone density: MK4 increased bone density by 0.3%, while those not taking MK4 lost 3.5%.	None
Iwamoto and Takeda	<i>Journal of Orthopaedic Science</i> . 2000; 5(6):546-551.	Postmenopausal osteoporosis	Randomized clinical trial	n = 92 (all women); mean age 64 years	Group A: vitamin D3 0.75 µg/day orally Group B: MK4 45 mg/day orally Group C: MK4 plus vitamin D3 Group D: calcium lactate 2000 mg /day orally	24 months	Bone density: MK4 plus Vitamin D increased bone density compared to all other groups.	None



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Shiraki and Shiraki	<i>Journal of Bone and Mineral Research.</i> 2000; 15(3):515-521.	Postmenopausal osteoporosis	Randomized, open-label, controlled trial	n = 241 (all women); mean age 67 years	Group A: MK4 45 mg/day orally plus calcium 150 mg/day orally Group B: calcium 150 mg/day orally	24 months	Fractures: MK4 group experienced 60% fewer fractures compared with the calcium-only group, including a 54% decrease in vertebral fractures. Bone density: MK4 maintained bone density compared to those not taking MK4.	Not reported

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Iwamoto and Kosha	<i>Maturitas</i> . 1999; 31(2):161-164.	Postmenopausal osteoporosis	Randomized, controlled clinical trial	n = 72 (all women)	<p>Group A: no intervention control</p> <p>Group B: conjugated equine estrogen 0.625 mg/day orally and medroxyprogesterone 2.5 mg/day orally</p> <p>Group C: vitamin D3 1000 mg/day</p> <p>Group D: MK4 45 mg/day</p>	12 months	Bone density: MK4 increased bone density while bone density decreased in the control group.	Not reported



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Sato and Honda	<i>Bone</i> . 1998; 23(3):291-296	Osteoporosis in people with hemiplegia following stroke	Randomized, controlled clinical trial	n = 108 (65 men, 78 women); mean age 66 years	MK4 45 mg/day orally or no MK4	12 months	Bone density: MK4 increased bone density by 4.7% compared to a loss of 4.7% in the group not taking MK4 Fractures: There were no fractures in the MK4 group and one fracture in the group not taking MK4.	None



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Somekawa and Chigughi	<i>The Journal of Clinical Endocrinology and Metabolism</i> . 1999; 84(8): 2700-2704	Osteoporosis in women with estrogen-dependent diseases (eg, endometriosis and leiomyomas) being treated with leuprolide	Randomized, controlled clinical trial	n = 110 (all women); mean age 46.2 years	Group A: leuprolide (Lupron, Eligard) Group B: leuprolide plus MK4 45 mg/day orally Group C: leuprolide plus vitamin D3 0.5 µg/day orally Group D: leuprolide plus MK4 and vitamin D3	6 months	Bone density: MK4 slowed the bone loss from estrogen deprivation.	Not reported

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Sugiyama and Tanaka	<i>Journal of Bone and Mineral Research.</i> 1999; 14(8):1466-1467.	Osteoporosis in a girl with Arnold-Chiari deformity	Case report	n = 1 (girl); age 8 years	MK4 2 mg/kg/day and vitamin D3 0.5 mg/kg/day	15 months	Bone density: MK4 plus vitamin D increased bone density.	None
Nagasawa and Fujii	<i>Lancet.</i> 1998; 351(9104):724	High cholesterol in people with chronic renal failure on peritoneal dialysis		n = 17 (8 men, 9 women); ages 36-70 years	MK4 45 mg/day orally	1 year	Total Cholesterol: MK4 significantly reduced total cholesterol.	Not reported