Peer-reviewed | Manuscript received: February 17, 2017 | Revision accepted: August 08, 2017

Vitamin K – an update

Part 2: Medical aspects

Alexandra Schek

Reference	Subjects	Vitamin K_1 intake	Significant results
Risk of fracture			
Feskanich et al., 1999 [103]	n = 72,326 100 % ♀ 38–63 years	median (range): 163 (45–563) µg/day	10-year follow-up: 30 % lower risk of hip fracture in the case of K_1 intake > 109 µg/day compared to < 109 µg/day, but p not significant for trend
Chan et al., 2011 [104]	n = 2,944 55 % ♂ > 65 years	median: ♀: 239 µg/day ♂: 242 µg/day	7-year follow-up: no association between vitamin K_1 intake and risk of fracture (hips, pelvis, arm, hand, leg, foot, ribs, shoulder, face, etc.)
Apalset et al., 2011 [105]	n = 2,807 56 % ♀ 71–75 years	61.6 % of the study > 1 µg/kg/day	10-year follow-up: every 10 µg/day increase in vitamin K_1 intake was associated with a 3 % lower risk of hip fracture. There was a 57 % higher risk of hip fracture in the lowest quartile (♀ < 42, ♂ < 53 µg/day) compared to the highest quartile (♀ > 109, ♂> 114 µg/day). No association between K_2 intake and risk of fracture.
Risk of fracture and BMD			
Booth et al., 2000 [106]	n = 888 62 % ♀ 75 ± 5 years	mean value ± SD: ♀: 163 ± 115 µg/day ♂: 143 ± 97 µg/day	7-year follow-up: 65 % lower risk of hip fractures in the highest quartile (254 µg/day) compared to the lowest quartile (56 µg/day) of K_1 intake, but no association with BMD
BMD			
Booth et al., 2003 [107]	n = 2,591 57 % ♀ 59 ± 9 years	mean value ± SD: ♀: 171 ± 103 µg/day ♂: 153 ± 115 µg/day	cross-over study: in the case of women, there was lower BMD in the lowest dietary intake quartile (70 µg/day) compared to the highest quartile (309 µg/day). No association in the case of men.
Rejnmark et al., 2006 [108]	n = 1,869 100 % ♀ 43–68 years	median (range): 67 (45–105) µg/day	5-year follow-up (n = 1,139): no association between vitamin K_1 intake and BMD (femoral neck, lumbar spine)
Macdonald et al., 2008 [109]	n = 3,199 100 % ♀ 49–54 years	at the beginning (n = 898): 100 ± 39 µg/day in the end (n = 2,301): 109 ± 55 µg/day	7-year follow-up: higher BMD was observed in the femoral neck of those in the third dietary intake quartile (116 µg/day) compared to the first (59 µg/day) and second quartiles (91 µg/day), but not in the fourth quartile (162 µg/day).
Bulló et al., 2011 [110]	n = 362 55 % ♀ 55–80 years	mean value ± SD: ♀: 230 ± 12 µg/day ♂: 334 ± 17 µg/day	cross-over study; 2-year follow-up of n = 200: every additional 100 µg/day of vitamin K_1 intake was associated with a 0.006 g/cm² increase in BMD in the calcaneus in the adjusted model[a].

Tab. 5: **Prospective cohort and cross-over studies on the effect of vitamin K_1 on risk of fracture and BMD**

[a] 162 subjects reduced their vitamin K_1 intake by an average of 156 µg/day, and 74 increased it by an average of 104 µg/day, but no explanation is given of how this occurred. BMD in the calcaneus reduced significantly more in the study participants who reduced their vitamin K_1 intake (-0.023 g/cm²) than in those who increased their vitamin K_1 intake (-0.009 g/cm²). Furthermore, an increase in vitamin K_1 intake was associated with less progression of age-related porosity and elasticity of the bones. The test subjects had a sub-clinical vitamin D deficiency.

SD = standard deviation

Reference	Subjects	Vitamin K intake	Significant results
Osteoarthritis			
Oka et al., 2009 [123]	n = 719 62 % ♀ > 60 years	MK-7 from nattō (amount not specified) questionnaire completed autonomously and on one occasion	cross-over study: inverse association between the vitamin K intake level (75th percentile: 286 µg/day, 50th percentile: 206 µg/day, 25th percentile: 141 µg/day) and the severity of arthritic changes in the knee
Type 2 diabetes mellitus			
Beulens et al., 2010 [9]	n = 38,094 74 % ♀ 20–70 years	mean value ± SD: K_2: 31 ± 7 µg/day K_1: 200 ± 98 µg/day FFQ on one occasion	10-year follow-up: inverse relationship between K_2 intake (highest dietary intake quartile: 49 µg/day, lowest dietary intake quartile: 15 µg/day) and risk of diabetes; inverse relationship trend in the case of vitamin K_1 (highest dietary intake quartile: 333 µg/day, lowest dietary intake quartile: 96 µg/day; p = 0.08)
Cancer			
Nimptsch et al., 2008 [8]	n = 11,319 100 % ♂ 40–64 years	median (range): K_2: 35 (26–46) µg/day K_1: 94 (71–123) µg/day FFQ on one occasion	9-year follow-up: inverse relationship between K_2 intake (> 46 µg/day in highest vs. < 26 µg/day in lowest dietary intake quartile) and incidence of advanced prostate cancer (RR 0.37; 95 % CI: 0.16–0.88; p for trend = 0.03); non-significant inverse relationship in the case of overall incidence of prostate cancer (RR 0.65; 95 % CI: 0.39–1.06); no association with vitamin K_1
Nimptsch et al., 2010 [137]	n = 24,340 53 % ♀ 35–64 years	median (range): K_2: 32 (23–42) µg/day (♀), 35 (26–46) µg/day (♂) K_1: not specified FFQ on one occasion	10-year follow-up: inverse relationship between K_2 intake and cancer-related mortality (HR 0.72; 95 % CI: 0.53–0.98; p for trend = 0.03); non-significant inverse relationship in the case of overall incidence of cancer (HR 0.86; 95 % CI: 0.73–1.01); the reduction in the risk of cancer was greater in men (especially with regard to prostate and lung cancer) than in women; no association with vitamin K_1
Juanola-Falgarona et al., 2014 [136]	n = 7,216[a] 57 % ♀ 55–80 years	mean value dietary intake quartiles: K_2: Q1: 18 µg/day Q4: 57 µg/day K_1: Q1: 170 µg/day Q4: 626 µg/day FFQ on one occasion	baseline vitamin K_1 intake inversely associated with cancer risk and all-cause mortality risk; 5-year follow-up: association between increase in K_2 intake (n = 2,752) and both reduction in cancer-related mortality risk and all-cause mortality risk, but not cardiovascular mortality risk (CVD); for K_1 (n = 3,141), there was also a reduction in CVD risk

Tab. 6: **Prospective cohort and cross-over studies on the effect of vitamin K on osteoarthritis, diabetes, and cancer**

[a] The study participants had type 2 diabetes mellitus and/or ≥ 3 cardiovascular risk factors.

95 % CI = 95 % confidence interval; HR = hazard ratio; RR = relative risk; SD = standard deviation