Association of dietary vitamin K and risk of coronary heart disease in middle-age adults. The Hordaland Health Study Cohort.

Teresa R Haugsgjerd, MSc[1], Grace M Egeland, PhD[1,2], Ottar K Nygård, MD PhD[3,4], Kathrine J Vinknes, PhD[5], Gerhard Sulo, MD Phd[6,7], Vegard Lysne, PhD[4], Jannicke Igland, PhD[1], Grethe S Tell, PhD[1,8]

[1]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

[2]Health Registries, Research and Development, Norwegian Institute of Public Health, Bergen, Norway

[3]Department of Heart Disease, Haukeland University Hospital, Bergen, Norway

[4]Centre for nutrition, Department of Clinical Science, University of Bergen, Bergen, Norway

[5]Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Oslo, Norway

[6]Centre for Disease Burden, The Norwegian Institute of Public Health, Bergen, Norway

[7]Oral Health Centre of Expertise in Western Norway, Bergen, Norway

[8]Division of Mental and Physical Health, Norwegian Institute of Public Health, Bergen, Norway

Correspondence

Teresa Risan Haugsgjerd

Teresa.Haugsgjerd@uib.no

Phone: +47 40634711

Supplementary table 1 Associations between intake of energy-adjusted vitamin K1 and K2 and incident coronary heart disease (CHD)[a]. Sex-specific quartiles with 1279 men and 1708 women. Missing data are imputed with multiple imputation.[b]
The Hordaland Health Study (HUSK).

Exposure	Intake, µg/day mean (SD)	N	CHD, N(%)	Model 1 HR (95% CI)[c] N = 2987	Model 2 HR (95% CI)[d] N = 2987	Model 3 HR (95% CI)[e] N = 2987
Vitamin K1						
		2987	112			
Q1	63 (25)	746	33 (4.4)	1 (ref)	1 (ref)	1 (ref)
Q2	83 (27)	747	18 (2.4)	0.47 (0.27 to 0.85)	0.49 (0.27 to 0.87)	0.47 (0.26 to 0.84)
Q3	122 (32)	748	31 (4.1)	0.84 (0.51 to 1.39)	0.83 (0.50 to 1.36)	0.77 (0.47 to 1.27)
Q4	269 (191)	746	30 (4.0)	0.91 (0.55 to 1.49)	0.93 (0.56 to 1.53)	0.71 (0.40 to 1.25)
P for trend[f]				0.64	0.60	0.60
Continuous, Per 10 µg				1.00 (0.99 to 1.02), p = 0.57	1.00 (0.99 to 1.02), p = 0.61	0.99 (0.97 to 1.01), p = 0.26
Vitamin K2						
		2987	112			
Q1	10 (4)	746	35 (4.7)	1 (ref)	1 (ref)	1 (ref)
Q2	13 (4)	747	30 (4.0)	0.79 (0.48 to 1.29)	0.80 (0.49 to 1.31)	0.86 (0.52 to 1.42)
Q3	17 (4)	747	29 (3.9)	0.77 (0.47 to 1.26)	0.79 (0.48 to 1.30)	0.90 (0.52 to 1.53)
Q4	26 (8)	747	18 (2.4)	0.50 (0.28 to 0.88)	0.50 (0.28 to 0.88)	0.60 (0.30 to 1.19)
P for trend[f]				0.02	0.02	0.17
Continuous, Per 10 µg				0.71 (0.50 to 0.99), p = 0.04	0.70 (0.50 to 0.98), p = 0.04	0.80 (0.52 to 1.25), p = 0.33

[a]HR are presented as Q2 vs. Q1, Q3 vs. Q1, Q4 vs. Q1.
[b]Missing values for physical activity, smoking and education were imputed using ordinal logistic regression as the imputation model in MICE (multiple imputation using chained equation) with 20 imputations.
[c] Cox proportional hazards regression analysis adjusted for age, sex and total energy intake.

[d]Adjusted in addition for physical activity, smoking and education.
[e] Vitamin K1 is adjusted in addition for energy-adjusted fiber and folate, while vitamin K2 is adjusted in addition for energy-adjusted calcium and saturated fatty acids.
[f] P – trend, to test for linear trends across quartiles, we modelled the median intake of each quartile as a continuous variable.
SD, standard deviation; N, number of participants; CHD, incident coronary heart disease; HR, hazard ratio; CI, confidence interval; Q, quartile

Supplementary table 2 Associations between intake of absolute (not energy adjusted) vitamin K1 and K2 and incident coronary heart disease (CHD)[a]. Sex-specific quartiles with 1279 men and 1708 women. The Hordaland Health Study (HUSK).

Dietary intake	Intake, µg/day mean (SD)	N	CHD, N(%)	Model 1 HR (95% CI)[b] N = 2987	Model 2 HR (95% CI)[c] N = 2792[e]	Model 3 HR (95% CI)[d] N = 2792[e]
Vitamin K1						
		2987	112			
Q1	51 (13)	747	34 (4.6)	1 (ref)	1 (ref)	1 (ref)
Q2	86 (10)	747	26 (3.5)	0.89 (0.52 to1.50)	0.97 (0.55 to 1.71)	0.92 (0.52 to 1.62)
Q3	127 (16)	747	26 (3.5)	0.94 (0.54 to 1.62)	0.97 (0.54 to 1.74)	0.86 (0.47 to 1.55)
Q4	274 (188)	746	26 (3.5)	1.03 (0.58 to 1.84)	1.04 (0.55 to 1.96)	0.72 (0.35 to 1.48)
P for trend[f]				0.79	0.87	0.37
Continuous, Per 10 µg				1.00 (0.99 to 1.02), p = 0.57	1.00 (0.99 to 1.02), p = 0.62	0.99 (0.97 to 1.01), p = 0.27
Vitamin K2						
		2987	112			
Q1	9 (2)	749	33 (4.4)	1 (ref)	1 (ref)	1 (ref)
Q2	13 (2)	745	35 (4.7)	1.15 (0.70 to 1.87)	1.27 (0.75 to 2.17)	1.38 (0.80 to 2.40)
Q3	18 (2)	748	27 (3.6)	0.94 (0.54 to 1.62)	1.00 (0.56 to 1.78)	1.21 (0.64 to 2.29)
Q4	27 (7)	745	17 (2.3)	0.62 (0.32 to 1.22)	0.72 (0.36 to 1.45)	0.97 (0.41 to 2.28)
P for trend[f]				0.12	0.25	0.83
Continuous, Per 10 µg				0.71 (0.50 to 0.99), p = 0.04	0.74 (0.52 to 1.05), p = 0.09	0.82 (0.51 to 1.30), p = 0.39

[a]HRs are presented as Q2 vs. Q1, Q3 vs. Q1, Q4 vs. Q1.

[b]Cox proportional hazards regression analysis adjusted for age, sex and total energy intake.

[c]Adjusted in addition for physical activity, education and smoking habits.

[d] Vitamin K1 is adjusted in addition for energy-adjusted fiber and folate, while vitamin K2 is adjusted in addition for energy-adjusted calcium and saturated fatty acids.
[e] Analyses were based on a reduced number of participants (n=2792) and CHD events (n=100) due to listwise deletion when covariates were missing.
[f] P – trend, to test for linear trends across quartiles, we modelled the median intake of each quartile as a continuous variable.
SD, standard deviation; N, number of participants; CHD, incident coronary heart disease; HR, hazard ratio; CI, confidence interval; Q, quartile