

# **Supplemental Material**

**Table S1. International Classification of Disease codes used to determine validated cases of atherosclerotic cardiovascular disease**

<b>Validated Diagnosis</b>	<b>ICD codes (ICD-8; ICD-10)</b>	<b>Follow-up</b>
Myocardial infarction	I21	10-02-1994 to 04-07-2013
Peripheral artery disease	I702, I702A, I739A, I739B, I739C	14-11-1994 to 07-12-2009
Ischemic stroke	I63	04-03-1994 to 30-11-2009

The methods for validating these cases have been published previously<sup>35-39</sup>.

**Table S2. Anatomical Therapeutic Chemical codes for antihypertensive medications**

Use of antihypertensive medication was defined by the usage of any combination of at least two of the seven different drugs classes at the same time.	<p><u>Non-Loop</u>: Thiazides C02L, C02DA, C07B, C07D, C09XA52, C03A, C03EA;</p> <p><u>Low-ceiling diuretics (excl. thiazides)</u>: C03B, C03X, C07C, C08G, C09BA, C09DA; potassium-sparing agents (spiron): C03D, C03E, C03EB</p> <p><u>Loop</u>: high-ceiling diuretics (Loop) C03C, C03EB</p> <p><u>Antiadrenergic agents</u>: C02A, C02B, C02C</p> <p><u>Beta-blockers</u>: C07A, C07B, C07C, C07D, C07F</p> <p><u>Vasodilators</u>: C02DB, C02DD, C02DG</p> <p><u>Calcium channel blockers</u>: C08, C09BB, C09DB</p> <p><u>Renin angiotensin system inhibitors and angiotensin II receptor blockers</u>: C09AA, C09BA, C09BB, C09CA, C09DA, C09DB, C09XA02, C09XA52</p>
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**Table S3. Intakes and main dietary sources of vitamin K<sub>1</sub> and vitamin K<sub>2</sub> in the Danish Diet Cancer and Health cohort**

Vitamin K	Median [IQR] intake (µg/day)	Main dietary sources
Vitamin K <sub>1</sub>	113.8 [80.7 – 151.2]	Margarine (12.5%), lettuce (12.0%), broccoli (6.8%), wholemeal bread (6.9%), spinach (5.5%)
Vitamin K <sub>2</sub>	43.7 [31.1 – 61.5]	
MK-4	19.0 [13.4 – 25.4]	Eggs (15%), butter (9.4%), cheese (6.8%)
MK-5	0.4 [0.3 – 0.5]	Hard cheese (69.8%)
MK-6	0.6 [0.4 – 0.8]	Hard cheese (33.7%)
MK-7	0.6 [ 0.4 – 0.9]	Hard cheese (44.6%)
MK-8	5.3 [3.8 – 9.7]	Hard cheese (59.1%), brie cheese (6.6%)
MK-9	13.2 [9.0 – 26.9]	Hard cheese (71.2%), brie cheese (9.4%), blue cheese (6.2%)
MK-10	0.7 [ 0.4 – 1.7]	Hard cheese (85.4%)

**Table S4. Association between incident atherosclerotic cardiovascular disease and vitamin K<sub>1</sub> intake, stratified by tertiles of total vegetable intake**

Baseline vegetable intake tertile		Vitamin K <sub>1</sub> intake quintiles				
		Q1	Q2	Q3	Q4	Q5
<b>1</b>	No. events	1 916	1 063	412	106	24
	HR (95% CI)	ref.	0.97 (0.90, 1.06)	0.93 (0.85, 1.02)	0.85 (0.74, 0.98)	0.74 (0.55, 0.99)
<b>2</b>	No. events	201	693	922	687	216
	HR (95% CI)	ref.	0.84 (0.73, 0.96)	0.79 (0.67, 0.92)	0.76 (0.65, 0.88)	0.61 (0.50, 0.75)
<b>3</b>	No. events	25	107	355	733	1 266
	HR (95% CI)	ref.	0.88 (0.79, 0.97)	0.78 (0.64, 0.95)	0.72 (0.55, 0.93)	0.73 (0.58, 0.93)

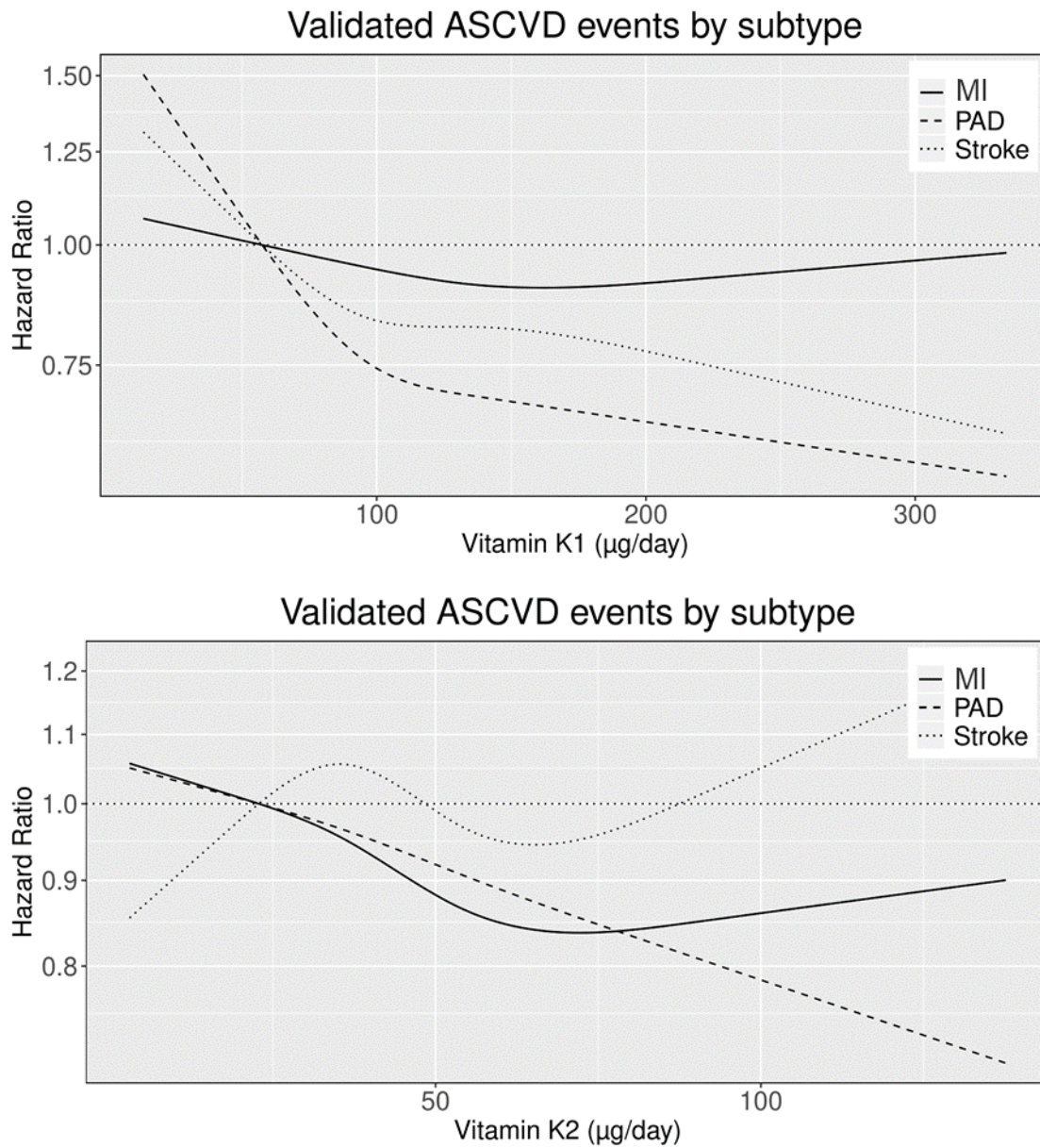
Hazard ratios (95% CI) for atherosclerotic cardiovascular disease hospitalisations during 23 years of follow-up, obtained from Cox proportional hazards models using Model 1b for adjustment: age, sex, BMI, smoking status, physical activity, alcohol intake, social economic status (income), and education.

**Table S5. Hazard ratios of colorectal cancer hospitalisations by quintiles of vitamin K intake**

	Vitamin K intake quintiles				
	Q1	Q2	Q3	Q4	Q5
<b>Vitamin K<sub>1</sub></b>					
Model 1b	ref.	1.02 (0.92, 1.13)	1.02 (0.91, 1.14)	0.99 (0.88, 1.13)	0.93 (0.82, 1.07)
<b>Vitamin K<sub>2</sub></b>					
Model 1b	ref.	1.02 (0.93, 1.12)	0.98 (0.88, 1.10)	0.91 (0.80, 1.02)	0.89 (0.78, 1.01)

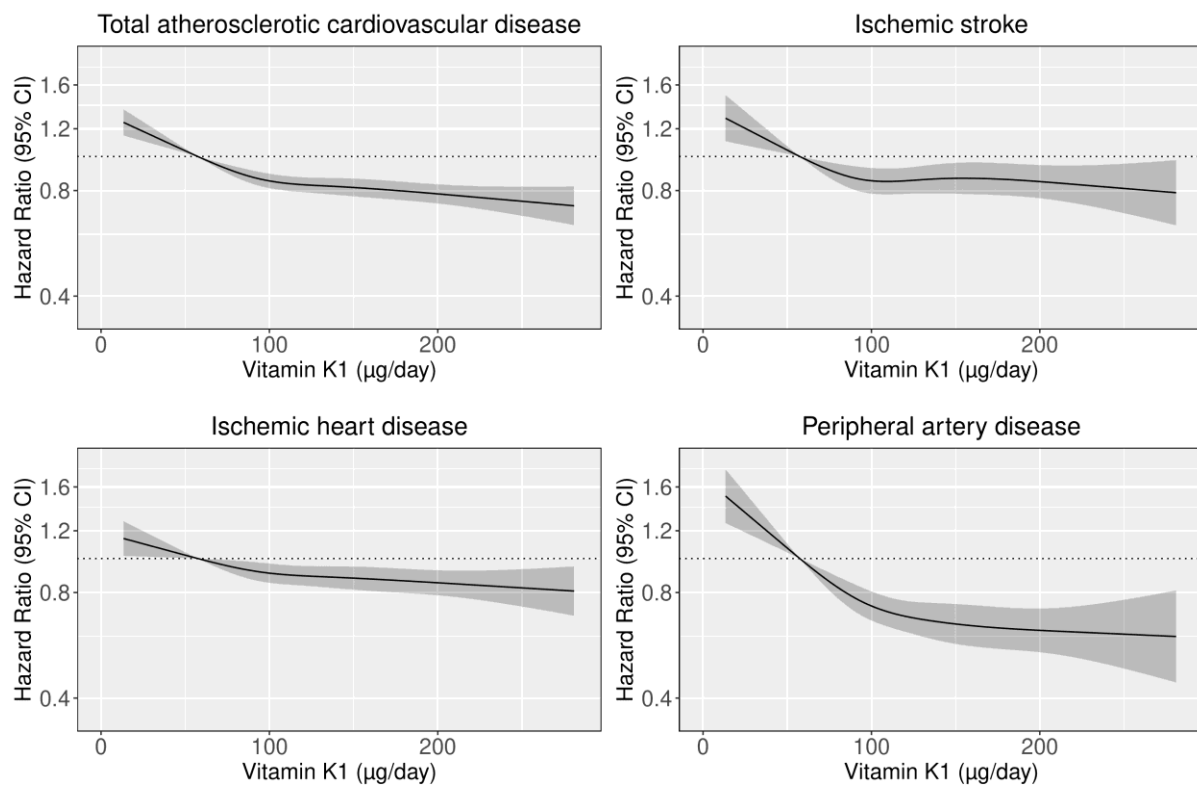
Hazard ratios (95% Confidence Intervals) for colorectal cancer hospitalisations (n = 1 716) during 23 years of follow-up, obtained from restricted cubic splines based on Cox proportional hazards models. Model 1b adjusted for age, sex, BMI, smoking status, physical activity, alcohol intake, social economic status (income), and education.

**Figure S1. Hazard ratios from Cox proportional hazards models using restricted cubic spline curves describing the association between vitamin K<sub>1</sub> and vitamin K<sub>2</sub> intake (µg/day) and validated cases of myocardial infarction (MI), peripheral artery disease (PAD), and ischemic stroke.**



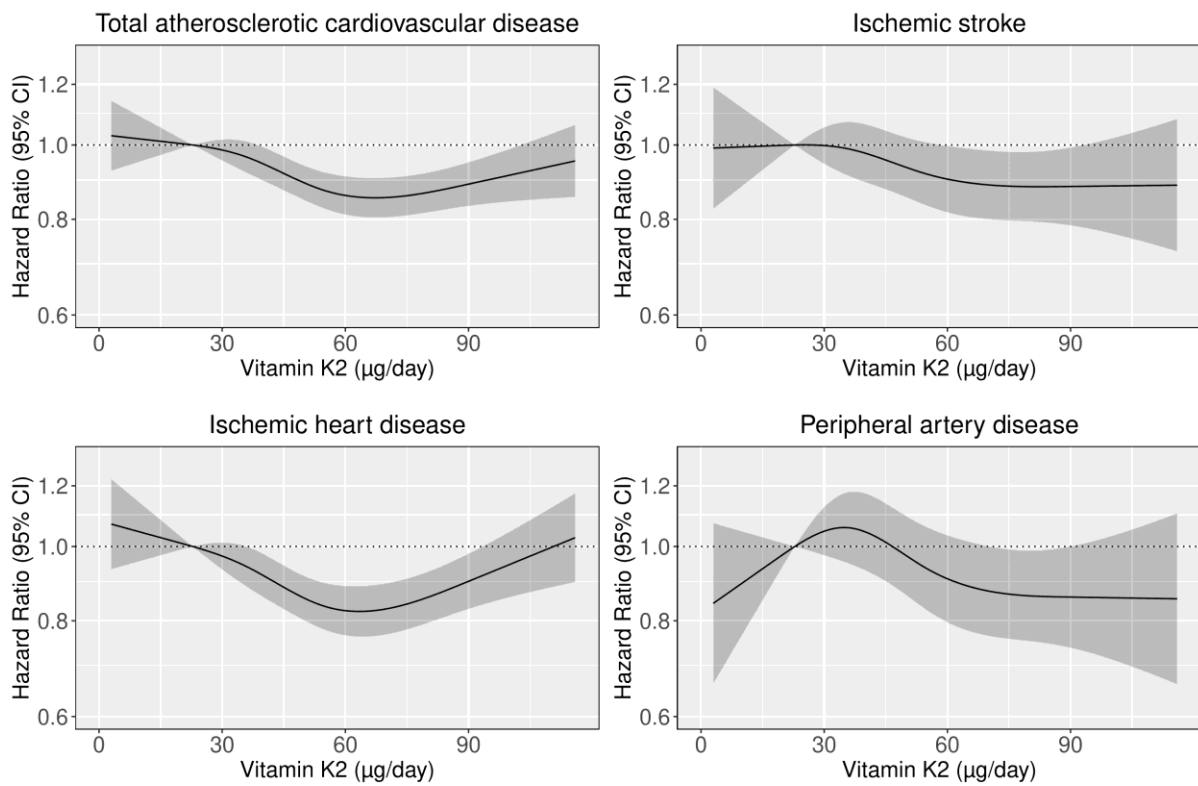
Hazard ratios are based on Cox proportional hazards models adjusted for age, sex, BMI, smoking status, social economic status (income), physical activity, alcohol intake, and education (Model 1b), and are comparing the specific level of vitamin K intake (horizontal axis) to the median intake for participants in the lowest intake quintile (vitamin K<sub>1</sub>: 57 µg/day and vitamin K<sub>2</sub>: 23 µg/day).

**Figure S2. The association between vitamin K<sub>1</sub> intake ( $\mu\text{g}/\text{day}$ ) and both total atherosclerotic cardiovascular disease (ASCVD) hospitalisations and subtypes of ASCVD hospitalisations (ischemic heart disease; peripheral artery disease; and ischemic stroke), after censoring participants upon prescription of a vitamin K antagonist.**



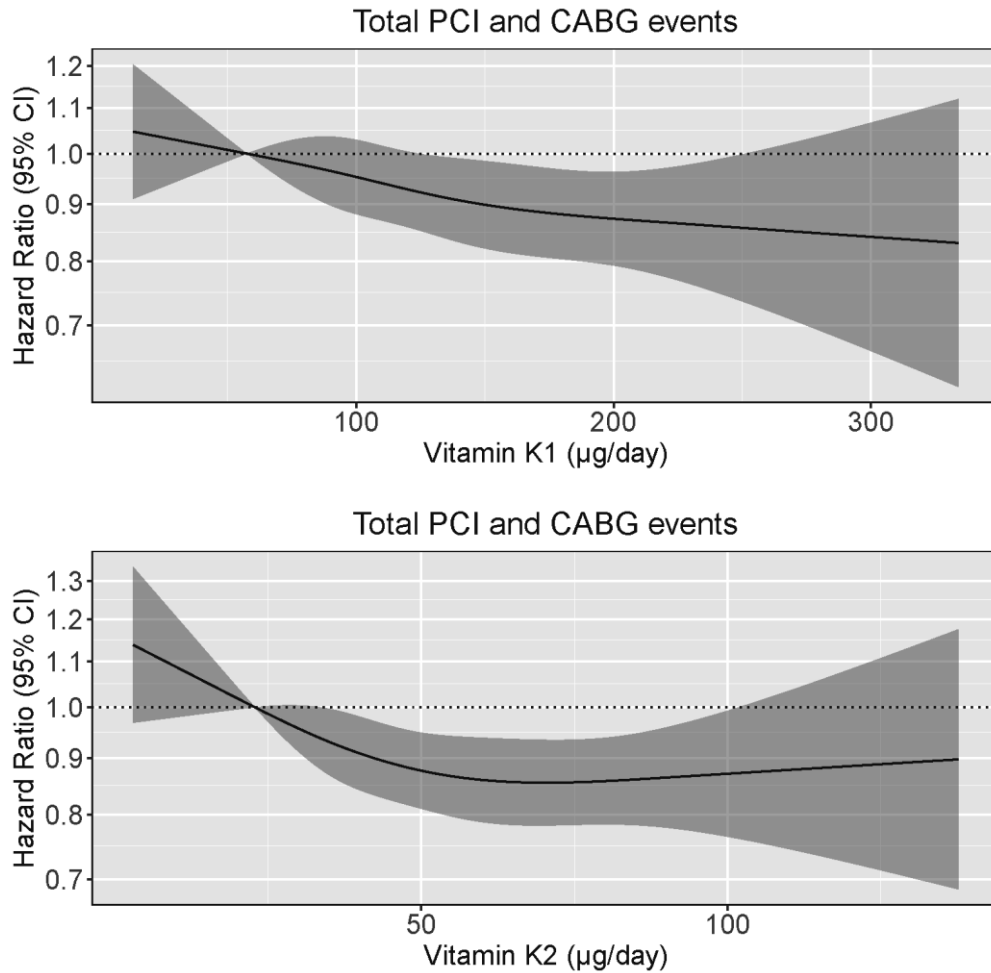
Hazard ratios are derived from Cox proportional hazards model with restricted cubic spline curves adjusting for age, sex, BMI, smoking status, social economic status (income), physical activity, alcohol intake, and education (Model 1b), and are comparing the specific level of vitamin K<sub>1</sub> intake (horizontal axis) to the median intake for participants in the lowest intake quintile (57  $\mu\text{g}/\text{day}$ ).

**Figure S3. The association between vitamin K<sub>2</sub> intake (µg/day) and both total atherosclerotic cardiovascular disease (ASCVD) hospitalisations and subtypes of ASCVD hospitalisations (ischemic heart disease; peripheral artery disease; and ischemic stroke), after censoring participants upon prescription of a vitamin K antagonist.**



Hazard ratios are derived from Cox proportional hazards model with restricted cubic spline curves adjusting for age, sex, BMI, smoking status, social economic status (income), physical activity, alcohol intake, and education (Model 1b), and are comparing the specific level of vitamin K<sub>2</sub> intake (horizontal axis) to the median intake for participants in the lowest intake quintile (23 µg/day).

**Figure S4. Hazard ratios from Cox proportional hazards models using restricted cubic spline curves describing the association between vitamin K intake ( $\mu\text{g}/\text{day}$ ) and both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) procedures.**



Hazard ratios are based on Cox proportional hazards models adjusted for age, sex, BMI, smoking status, social economic status (income), physical activity, alcohol intake, and education (Model 1b), and are comparing the specific level of vitamin K intake (horizontal axis) to the median intake for participants in the lowest intake quintile (vitamin K<sub>1</sub>: 57  $\mu\text{g}/\text{day}$  and vitamin K<sub>2</sub>: 23  $\mu\text{g}/\text{day}$ ).