Vitamin K supplementation to improve vascular stiffness in CKD

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Published in:
Journal of the American Society of Nephrology

DOI:
10.1681/ASN.2020020225

Publication date:
2020

Document Version
Peer reviewed version

Supplemental Material

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1. **Supplementary Table: Details of assays used in the trial**

Assay	**Manufacturer**	**Coefficient of variation**	
		Intra-assay	**Inter-assay**
Fetuin A	R+D Systems Quantikine ELISA	3.5-4.2%	8.5-8.8%
Fibroblast Growth Factor 23	Immutopics C-terminal ELISA	3.3-11.5%	3.3-11.5%
Osteocalcin	R+D Systems Quantikine ELISA	5.2-5.4%	7.3-13.8%
Insulin	Alpco ELISA	4.8-6.9%	4.9-13.5%
25-hydroxyvitamin D	Diasorin LIAISON	2.9-8.4%	5.6-10.1%
1,25 dihydroxyvitamin D	Diasorin LIAISON XL	5.3-8.4%	8.2-8.8%
dp-ucMGP	IDS-iSYS InaKtif MGP	≤ 5.0% (between 910 and 7312 pmol/L)	≤ 7.3% between 939 and 7386 pmol/L)
Tartrate-resistant acid phosphatase-5b	Cusabio ELISA	6.9%	6.3-14.3%
N-terminal pro B-type natriuretic peptide	Meso Scale Discovery ELISA	8.0%	13.2-15.5%

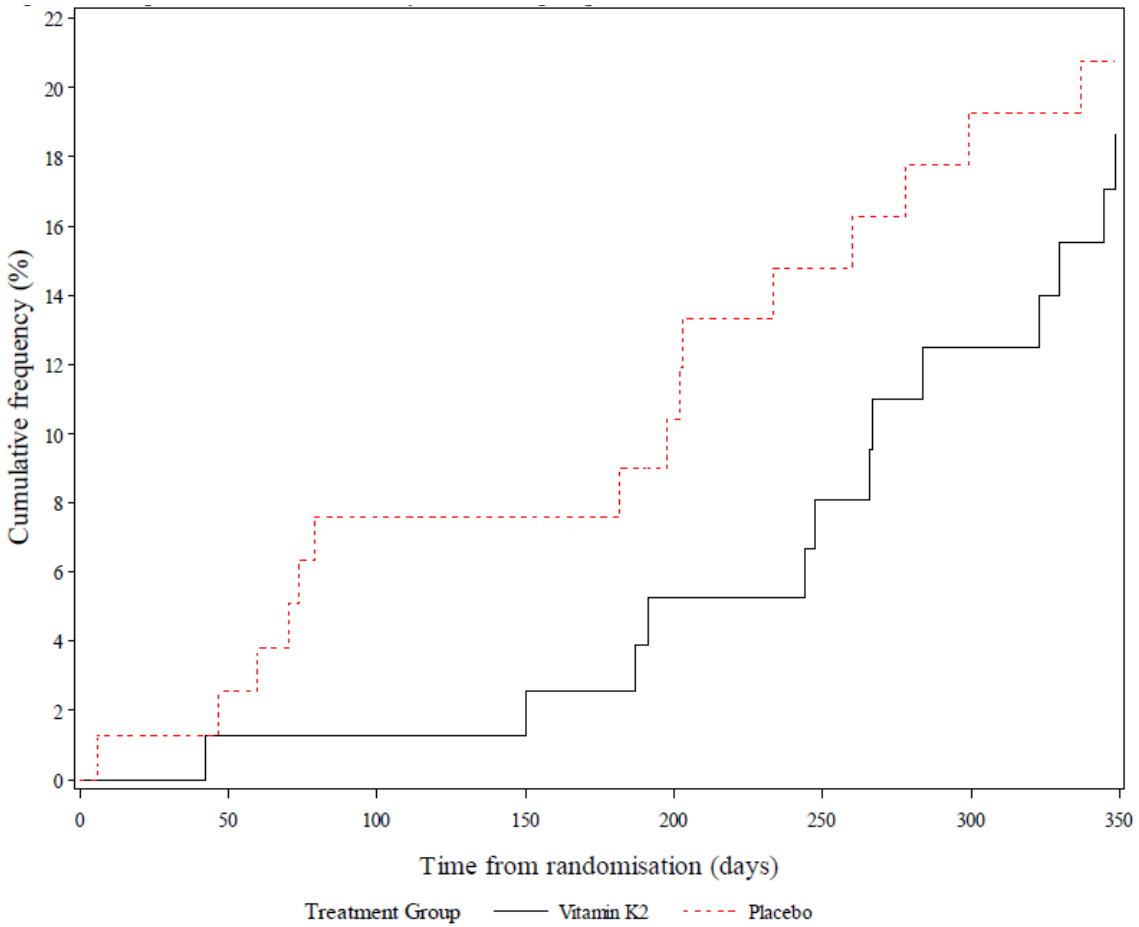
dp-ucMGP: desphospho-uncarboxylated matrix Gla protein

*A threshold of 900 pmol/L was used as the lowest reportable concentration of dp-ucMGP. Assay performance below this concentration was found to be non-linear on dilution testing, thus values below 900 pmol/L cannot be reported with accuracy.

2. Supplementary Table: Details of studies included in the meta-analysis

Author	Year	Country	Baseline N	Population	Intervention	Dose (mcg/day)	Comparator	Duration (months)	Outcome measure
Braam[33]	2004	Netherlands	121	Healthy	K1 +Multivitamin (incl vitamin D)	1000	Multivitamin (incl vitamin D)	36	Compliance coefficient (mm^2/kPa)
Shea[34]	2009	USA	295	Older adults	K1 +Multivitamin (incl vitamin D)	500	Multivitamin (incl vitamin D)	36	Coronary artery calcification score
Knapen[35]	2015	Netherlands	244	Postmenopausal women	K2-MK7	180	Placebo	36	Pulse wave velocity (SphygmoCor)
Kurnatowska[16]	2015	Poland	40	CKD	K2-MK7 + Vitamin D	90	Vitamin D	9	Coronary artery calcification score
Fulton[18]	2016	Scotland	80	Older adults, vascular disease	K2-MK7	100	Placebo	6	Pulse wave velocity (SphygmoCor)
Brandenburg[36]	2017	Germany	72	Aortic stenosis or sclerosis	K1	2000	Placebo	12	Aortic valve calcification score
Oikonomaki[37]	2019	Greece	102	Patients undergoing haemodialysis	K2-MK7	200	Usual care	12	Abdominal aortic calcification score
Zwakenberg[39]	2019	Netherlands	68	Patients with type 2 diabetes mellitus	K2-MK7	360	Placebo	6	Femoral artery calcification score
De Vriese[38]	2020	Belgium	88	Patients undergoing haemodialysis with atrial fibrillation	K2-MK7 + Rivaroxaban	857	Rivaroxaban	18	Coronary artery calcification score

3. Supplementary Figure. Time to first fall



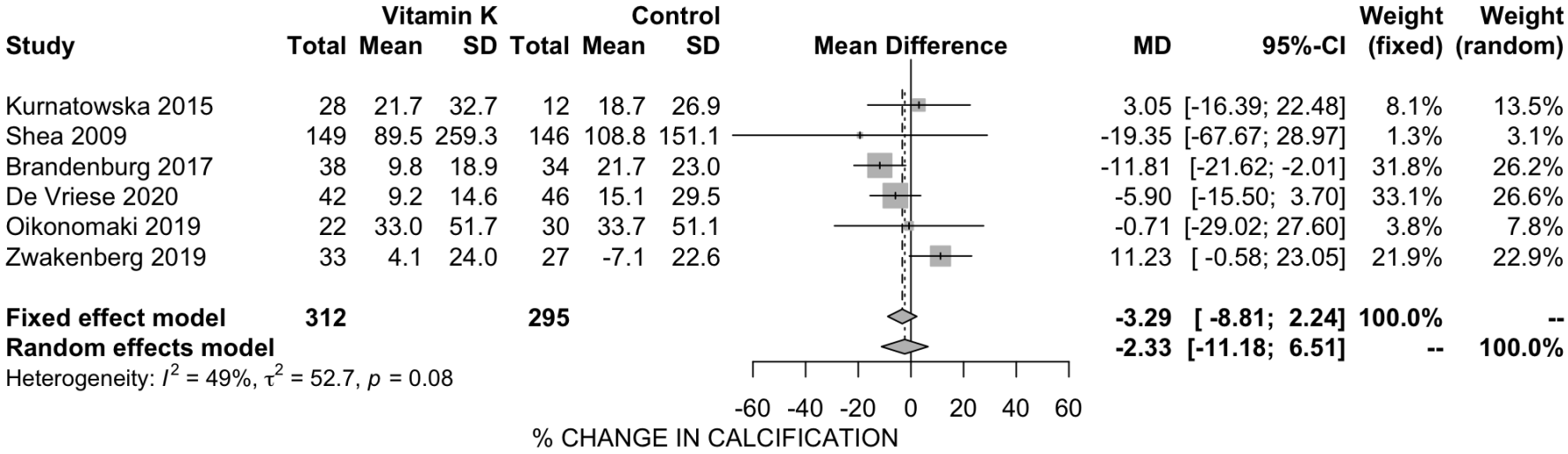
Time to first fall: HR 0.79 (95% CI 0.37 to 1.69, p=0.54)

4. Vascular calcification results

	Vitamin K Mean (SD)	Placebo Mean (SD)	Treatment effect* (95% CI)	p
Mean Aortic calcification score (SD) at 12 months [Median (Q1,Q3)]	4.8 (5.1) [3 (0,8)]	4.2 (5.3) [3 (0,5)]	-0.3 (-0.8 to 0.2)	0.31
Mean Aortic calcification score (SD) at 12 months (excluding zero scores)	7.0 (4.8)	6.5 (5.3)	-0.3 (-1.1. to 0.42)	0.37
Change in aortic calcification score between baseline and 12 months (SD)	0.0 (1.4)	0.3 (1.4)	-0.3 (-0.8 to 0.2)	0.31
No detectable calcification at baseline (%)	18 (30.0)	22 (36.7)	Odds ratio 0.2 (0.0 to 4.3)	0.30
No detectable calcification at 12 months (%)	19 (31.7)	21 (35.6)		

5. Forest plots – vascular calcification

a) Excluding current trial



b) Including current trial