#### **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%			

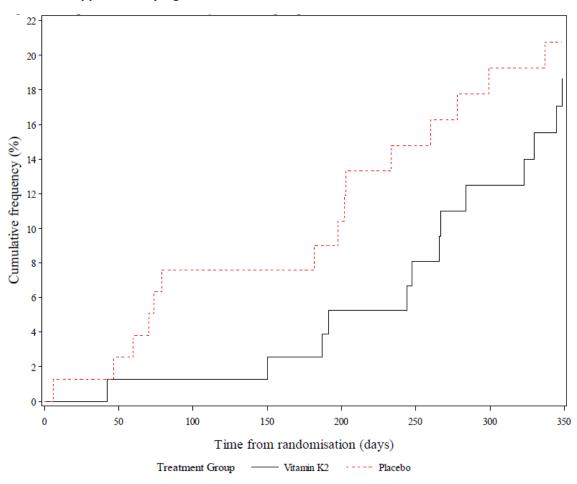
dp-ucMGP: desphospho-uncarboxylated matrix Gla protein

<sup>\*</sup>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 <sup>33</sup>	2004	Netherlands	121	Healthy	K1 +Multivitamin (incl vitamin D)	1000	Multivitamin (incl vitamin D)	36	Compliance coefficient (mm²/kPa)	
Shea <sup>34</sup>	2009	USA	295	Older adults	K1 +Multivitamin (incl vitamin D)	500	Multivitamin (incl vitamin D)	36	Coronary artery calcification score	
Knapen <sup>35</sup>	2015	Netherlands	244	Postmenopausal women	K2-MK7	180	Placebo	36	Pulse wave velocity (SphygmoCor)	
Kurnatowska <sup>16</sup>	2015	Poland	40	CKD	K2-MK7 + Vitamin D	90	Vitamin D	9	Coronary artery calcification score	
Fulton <sup>18</sup>	2016	Scotland	80	Older adults, vascular disease	K2-MK7	100	Placebo	6	Pulse wave velocity (SphygmoCor)	
Brandenburg <sup>36</sup>	2017	Germany	72	Aortic stenosis or sclerosis	K1	2000	Placebo	12	Aortic valve calcification score	
Oikonomaki <sup>37</sup>	2019	Greece	102	Patients undergoing haemodialysis	K2-MK7	200	Usual care	12	Abdominal aortic calcification score	
Zwakenberg <sup>39</sup>	2019	Netherlands	68	Patients with type 2 diabetes mellitus	K2-MK7	360	Placebo	6	Femoral artery calcification score	
De Vriese <sup>38</sup>	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	Placebo	Treatment effect* (95% CI)	р
	Mean (SD)	Mean (SD)		
Mean Aortic calcification score (SD)	4.8 (5.1)	4.2 (5.3)	-0.3 (-0.8 to 0.2)	0.31
at 12 months				
	[3 (0,8)]	[3 (0,5)]		
[Median (Q1,Q3)]				
Mean Aortic calcification score (SD)	7.0 (4.8)	6.5 (5.3)	-0.3 (-1.1. to 0.42)	0.37
at 12 months (excluding zero scores)				
Change in aortic calcification score	0.0 (1.4)	0.3 (1.4)	-0.3 (-0.8 to 0.2)	0.31
between baseline and 12 months				
(SD)				
No detectable calcification at	18 (30.0)	22 (36.7)		
baseline (%)			Odds ratio	0.30
No detectable calcification at 12	19 (31.7)	21 (35.6)	0.2 (0.0 to 4.3)	
months (%)				

#### 5. Forest plots – vascular calcification

## a) Excluding current trial

		Vita	min K		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Kurnatowska 2015	28	21.7	32.7	12	18.7	26.9	<u> </u>	3.05	[-16.39; 22.48]	8.1%	13.5%
Shea 2009	149	89.5	259.3	146	108.8	151.1	* j		[-67.67; 28.97]		3.1%
Brandenburg 2017	38	9.8	18.9	34	21.7	23.0		-11.81	[-21.62; -2.01]	31.8%	26.2%
De Vriese 2020	42	9.2	14.6	46	15.1	29.5	<del> </del>	-5.90	[-15.50; 3.70]	33.1%	26.6%
Oikonomaki 2019	22	33.0	51.7	30	33.7	51.1	<del></del>	-0.71	[-29.02; 27.60]	3.8%	7.8%
Zwakenberg 2019	33	4.1	24.0	27	-7.1	22.6		11.23	[ -0.58; 23.05]	21.9%	22.9%
Fixed effect model Random effects mode	312			295					[ -8.81; 2.24] [-11.18; 6.51]	100.0%	 100.0%
Heterogeneity: $I^2 = 49\%$ ,	-	r', p = 0.	80					-2.33	[-11.10, 0.51]		100.0 /0
							-60 -40 -20 0 20 40 60				
				% C	HANG	E IN CA	LCIFICATION				

## b) Including current trial

		Vita	min K		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean Difference	MD	95%-CI	(fixed)	(random)
Kurnatowska 2015	28	21.7	32.7	12	18.7	26.9	<del>-   -</del>	3.05	[-16.39; 22.48]	6.4%	9.8%
Shea 2009	149	89.5	259.3	146	108.8	151.1	·	-19.35	[-67.67; 28.97]	1.0%	2.0%
Brandenburg 2017	38	9.8	18.9	34	21.7	23.0	- <del>   </del>	-11.81	[-21.62; -2.01]	25.3%	22.1%
Witham 2020	60	0.2	28.7	59	6.9	32.2	<del>-   -  </del>	-6.68	[-17.64; 4.28]	20.3%	19.9%
De Vriese 2020	42	9.2	14.6	46	15.1	29.5	-	-5.90	[-15.50; 3.70]	26.4%	22.5%
Oikonomaki 2019	22	33.0	51.7	30	33.7	51.1	<del></del>	-0.71	[-29.02; 27.60]	3.0%	5.3%
Zwakenberg 2019	33	4.1	24.0	27	-7.1	22.6	-	11.23	[ -0.58; 23.05]	17.4%	18.5%
Fixed effect model	372			354					[-8.91; 0.96]	100.0%	
Random effects mode	-	_						-3.31	[-10.35; 3.72]		100.0%
Heterogeneity: $I^2 = 41\%$ , 1	$t^{-} = 33.3$	p = 0.	12								
							-60 -40 -20 0 20 40 60				
				% C	HANG	E IN CA	ALCIFICATION				