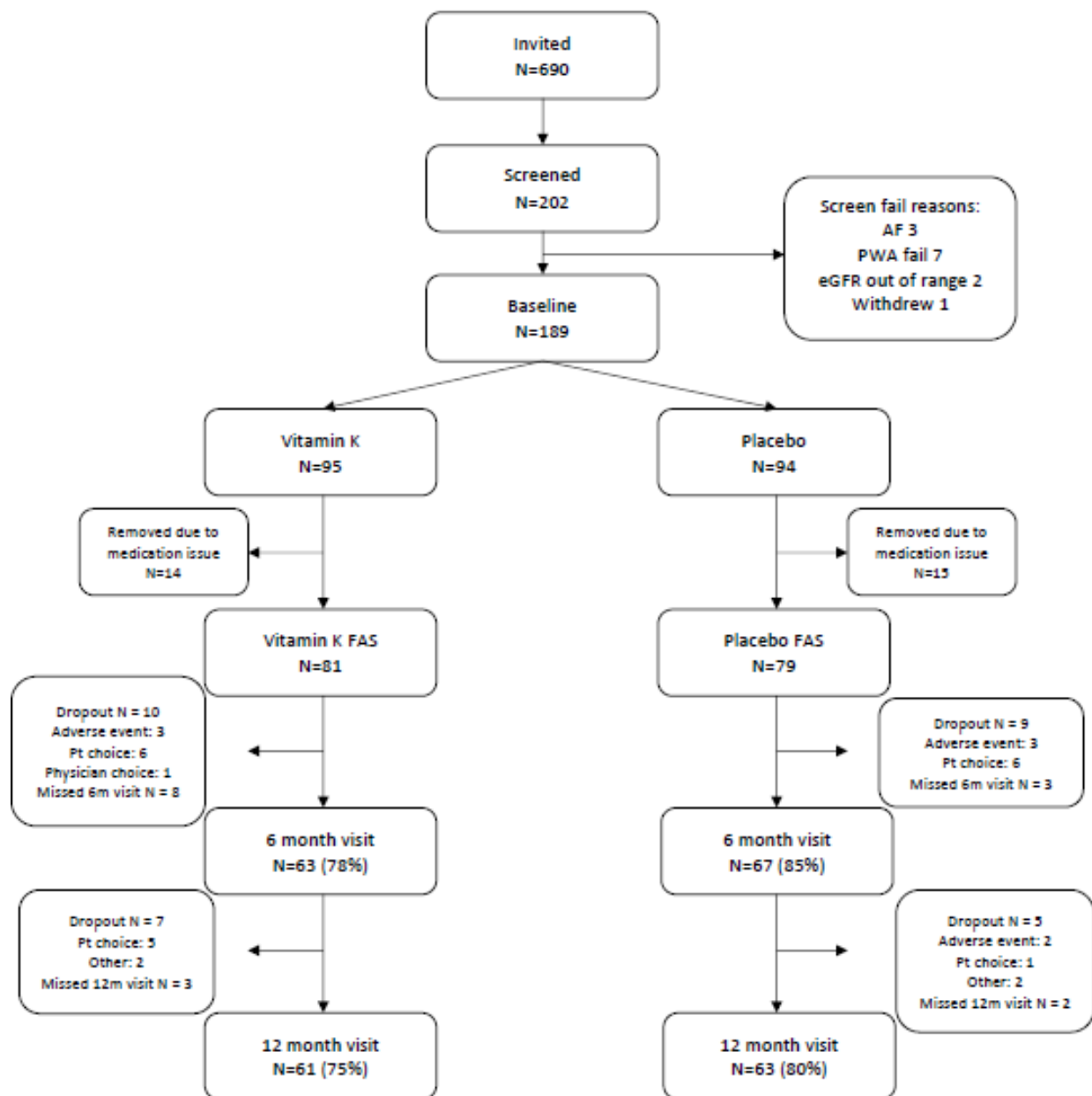


Participant flow



Baseline characteristics

		Vitamin K (n=81)	Placebo (n=79)
Mean age (years) (SD)		67.3 (10.9)	65.7 (13.5)
Female sex (%)		33 (41)	30 (38)
White ethnicity (%)		77 (95)	77 (98)
Cause of renal dysfunction (%)	Hypertension	19 (24)	13 (17)
	Diabetes mellitus	18 (22)	16 (20)
	Glomerulonephritis	10 (12)	8 (10)
	Polycystic kidney disease	7 (9)	5 (6)
	Vascular disease	5 (6)	7 (9)
	Other	29 (36)	32 (41)
	Not known	5 (6)	5 (6)
Cardiovascular comorbidity (%)	Ischaemic heart disease*	10 (12)	15 (19)
	Stroke	7 (9)	7 (9)
	Heart failure	2 (3)	4 (5)
	Peripheral vascular disease	6 (7)	4 (5)
	Hypertension	70 (86)	63 (80)
	Diabetes mellitus	26 (32)	27 (34)
Previous fragility fracture (%)		5 (6)	3 (4)
Walking aids (%)		19 (23)	12 (15)
Current smoker (%)		6 (7)	12 (15)
Median number of medications (IQR)		7 (4,10)	7 (4,10)
Medication use:	ACEi/ARB	50 (62)	50 (63)
	Phosphate binder	1 (1)	0 (0)
	EPO	4 (5)	5 (6)
	Iron	12 (15)	7 (9)
Mean eGFR (ml/min/1.73m ²) (SD)		29 (8)	30 (8)
CKD stage 3b vs 4 (%)		38 vs 43 (47% vs 53%)	35 vs 44 (44% vs 56%)
Mean pulse wave velocity (m/s) (SD)		11.9 (3.5)	11.4 (3.2)
Mean augmentation index (%) (SD)		26 (11)	25 (10)
Mean office BP (mmHg) (SD)		147/78 (26/11)	137/74 (19/10)
Mean postural BP drop (mmHg) (SD)		15/5 (18/8)	9/3 (18/9)
Mean 24 hour BP (mmHg) (SD)		129/69 (16/11)	130/70 (17/10)
Mean SPPB (SD)		9.2 (2.6)	9.4 (2.6)
Mean handgrip strength (kg) (SD)	Males	31.7 (12.1)	30.2 (9.8)
	Females	14.7 (6.1)	16.6 (6.1)
Median B-type natriuretic peptide (IQR) (pg/ml)		1494 (415,4133)	2274 (585, 5801)
Dp-uc-Matrix Gla protein			
Median Fetuin (IQR) (ng/ml)		1237 (1005,1535)	1359 (1090, 1847)
Median FGF-23 (IQR) (RU/ml)		170 (126,255)	156 (113,218)
Median Parathyroid hormone (IQR) (pmol/L)		14 (9,22)	13 (8,19)
Median TRACP-5b (IQR) (mIU/ml)		0.41 (0.28, 0.88)	0.55 (0.30, 1.27)
Median Osteocalcin (ng/ml)		37 (24, 62)	36 (24, 52)
25-hydroxyvitamin D (nmol/L)		48 (29)	44 (23)
1,25-hydroxyvitamin D (pmol/L)		74 (33)	69 (29)
Adjusted calcium (mmol/L)		2.33 (0.11)	2.33 (0.14)

Phosphate (mmol/L)	1.17 (0.19)	1.18 (0.20)
Median HOMA IR (IQR)	2.36 (1.46, 3.66)	2.02 (1.44, 3.78)
Median Urinary protein/creatinine ratio (IQR)	37 (6,147)	40 (5,104)
Median aortic calcification score (IQR)	3.5 (0,9)	2 (0,6.5)

TRACP-5b: Tartrate-resistant acid phosphatase 5b. FGF: Fibroblast growth factor. ACEi: Angiotensin converting enzyme. ARB: Angiotensin receptor blocker. EPO: Erythropoietin (or analogs)

*previous myocardial infarction, percutaneous coronary angioplasty, coronary artery bypass grafting or diagnosis of angina

Outcome measures

Primary outcome: Carotid-femoral Pulse Wave Velocity (m/s)

	Vitamin K	Placebo	Treatment effect* (95% CI)	p
6 months	11.7 (3.2)	11.1 (3.1)	0.17 (-0.61 to 0.95)	0.67
12 months	11.7 (3.2)	11.7 (3.6)	-0.12 (-0.93 to 0.69)	0.77
Repeated measures			0.05 (-0.63 to 0.72)	0.89
Multiple imputation: 12 month			-0.04 (-0.82 to 0.74)	0.91

*Adjusted for age, sex, eGFR, site and baseline values

Secondary outcomes – vascular and physical function

		Vitamin K	Placebo	Treatment effect* (95% CI)	p
Office systolic blood pressure (mmHg)	6 months	139 (22)	134 (18)	0 (-5 to 5)	0.99
	12 months	139 (23)	137 (21)	-2 (-8 to 4)	0.58
	Repeated measures			-1 (-5 to 4)	0.80
Office diastolic blood pressure (mmHg)	6 months	76 (11)	74 (10)	1 (-2 to 3)	0.69
	12 months	75 (10)	74 (10)	-1 (-4 to 1)	0.32
	Repeated measures			-1 (-3 to 2)	0.66
Augmentation index (%)	6 months	24 (10)	23 (11)	0 (-3 to 2)	0.66
	12 months	25 (10)	25 (9)	0 (-2 to 2)	0.97
	Repeated measures			0 (-2 to 2)	0.91
Log [BNP (pg/ml)]	12 months	7.46 (1.29)	7.47 (1.53)	0.10 (-0.20 to 0.39)	0.51
Mean Aortic calcification score (SD) [Median (IQR)]	12 months	4.8 (5.1) [3 (0,8)]	4.2 (5.3) [3 (0,5)]	-0.3 (-0.8,0.2)	0.31
SPPB	6 months	9.3 (2.8)	9.6 (2.2)	0.1 (-0.5 to 0.7)	0.70
	12 months	9.1 (3.0)	9.8 (2.2)	-0.4 (-1.0 to 0.3)	0.29
	Repeated measures			-0.1 (-0.6 to 0.4)	0.76
Grip strength (kg)	6 months	23.9 (11.5)	25.5 (10.7)	-0.3 (-1.7 to 1.2)	0.71
	12 months	24.1 (11.9)	23.8 (10.6)	-0.2 (-2.1 to 1.8)	0.88
	Repeated measures			-0.4 (-1.9 to 1.0)	0.56
Number with at least one fall		13	15		
Falls / months of fall diary data (falls rate per month)		18/765 (0.024)	128/795 (0.161)	0.146** (0.089 to 0.239)	<0.001

*Adjusted for age, sex, eGFR, site and baseline values

**incident rate ratio

Secondary outcomes – bloods at 12 months

	Vitamin K	Placebo	Treatment effect* (95% CI)	p
eGFR (ml/min/1.73m ²)	29 (9)	29 (10)	0 (-2 to 2)	0.96
Log [HOMA-IR]	0.68 (0.79)	0.90 (1.01)	-0.32 (-0.57 to -0.08)	0.01
Log [Osteocalcin (ng/ml)]	2.70 (0.77)	3.62 (0.69)	-0.93 (-1.14 to -0.73)	<0.001
Log [TRACP-5b (mIU/mL)]	-0.88 (1.10)	-0.76 (1.38)	-0.18 (-0.53 to 0.18)	0.32
Log [PTH (pmol/L)]	2.46 (0.76)	2.48 (0.69)	-0.05 (-0.20 to 0.10)	0.50
Phosphate (mmol/L)	1.19 (0.19)	1.19 (0.21)	0.01 (-0.05 to 0.07)	0.83
Calcium (mmol/L)	2.33 (0.11)	2.32 (0.12)	0.01 (-0.02 to 0.04)	0.61
Log [Fetuin (ng/ml)]	7.14 (0.33)	7.22 (0.31)	0.01 (-0.07 to 0.09)	0.81
Log [FGF-23 (RU/ml)]	5.33 (0.71)	5.34 (0.83)	-0.10 (-0.28 to 0.07)	0.23
Log [25OHD (nmol/L)]	3.84 (0.63)	3.75 (0.54)	0.04 (-0.09 to 0.17)	0.57
Log 1,25OHD	4.18 (0.51)	4.14 (0.38)	0.06 (-0.08 to 0.19)	0.39
Log [Urine P/Cr ratio]	3.85 (1.12)	3.76 (1.54)	-0.02 (-0.49 to 0.46)	0.95

*Adjusted for age, sex, eGFR, site and baseline values

Adverse events

Number of participants* with adverse events by System Order Class (SOC)

	Vitamin K (n=95)	Placebo (n=94)
Blood and lymphatic (%)	3 (3)	4 (4)
Cardiac (%)	5 (5)	4 (4)
Congenital and genetic (%)	1 (1)	0 (0)
Ear and labyrinth (%)	0 (0)	1 (1)
Endocrine (%)	0 (0)	1 (1)
Eye (%)	0 (0)	1 (1)
Gastrointestinal (%)	13 (14)	12 (13)
General (%)	2 (2)	1 (1)
Hepatobiliary (%)	1 (1)	3 (3)
Immune system (%)	0 (0)	1 (1)
Infections and infestations (%)	29 (31)	30 (32)
Injury, poisoning and procedural complications (%)	19 (20)	14 (15)
Investigations (%)	3 (3)	9 (10)
Metabolism and nutrition (%)	9 (9)	4 (4)
Musculoskeletal (%)	8 (8)	13 (14)
Neoplasms (%)	2 (2)	1 (1)
Nervous system (%)	5 (5)	10 (11)
Psychiatric (%)	0 (0)	2 (2)
Renal and urinary (%)	9 (9)	6 (6)
Reproductive and breast (%)	0 (0)	1 (1)
Respiratory (%)	4 (4)	6 (6)
Skin (%)	11 (12)	4 (4)
Surgical/medical procedures (%)	11 (12)	9 (10)
Vascular (%)	3 (3)	3 (3)
Any event (%)	69 (72)	68 (72)
Deaths (%)	2 (3)	1 (1)
Commenced renal replacement therapy** (%)	1 (1)	1 (1)

*All 189 randomised individuals included in adverse event analysis

**Haemodialysis, peritoneal dialysis or renal transplant