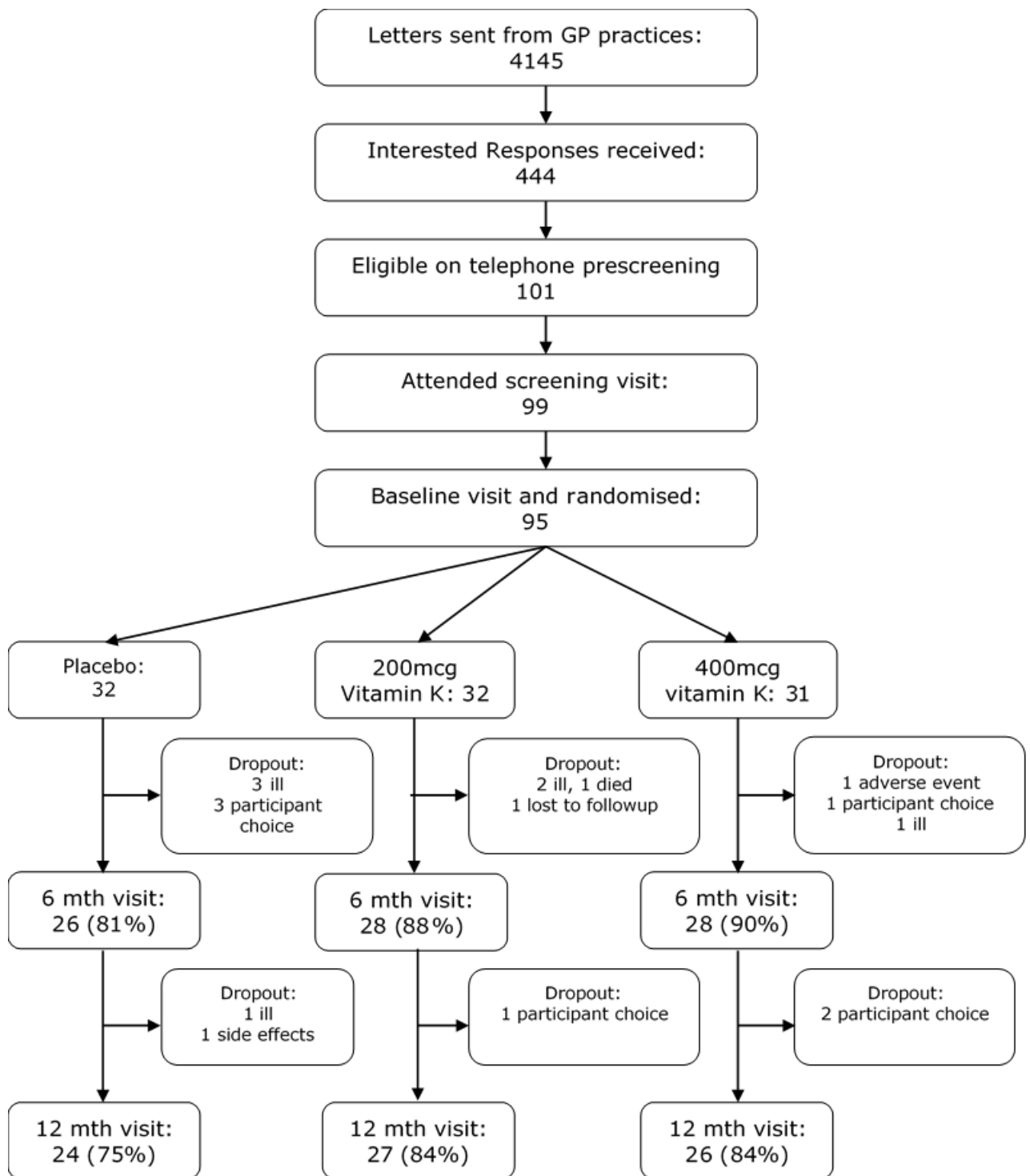


Participant flow



Baseline characteristics

	Placebo (n=32)	Vitamin K 200mcg (n=32)	Vitamin K 400mcg (n=31)
Mean age (SD) (years)	75.0 (6.9)	74.7 (7.4)	75.1 (6.5)
Female sex (%)	18 (56)	21 (66)	19 (61)
Median number of falls in last year (IQR)	3 (2-7)	3 (2-6)	3 (2-4)
Uses walking aid (%)	21 (66)	15 (47)	12 (39)
Previous myocardial infarction (%)	2 (6)	1 (3)	1 (3)
Chronic heart failure (%)	0 (0)	1 (3)	0 (0)
Parkinsonian syndrome (%)	0 (0)	0 (0)	0 (0)
Previous stroke (%)	2 (6)	2 (6)	3 (10)
Hypertension (%)	17 (53)	15 (47)	18 (58)
Diabetes mellitus (%)	6 (19)	1 (3)	8 (26)
Peripheral neuropathy (%)	4 (13)	1 (3)	2 (6)
Previous fragility fracture (%)	8 (25)	14 (44)	12 (39)
Osteoarthritis (%)	15 (47)	19 (59)	18 (58)
Chronic obstructive pulmonary disease (%)	4 (13)	7 (22)	6 (19)
Cataracts (%)	9 (28)	15 (47)	12 (39)
Retinopathy (%)	2 (6)	1 (3)	3 (10)
Median number of medications (IQR)	5 (4-8)	6 (3-10)	6 (4-9)
ACEi/ARB (%)	14 (44)	12 (38)	12 (39)
Other antihypertensive or antianginal (%)	13 (41)	14 (44)	15 (48)
Vitamin D or analog (%)	4 (13)	12 (38)	12 (39)
Bisphosphonate (%)	1 (3)	5 (16)	5 (16)
Antidepressant (%)	8 (25)	8 (25)	7 (23)
Hypnotic (%)	5 (16)	0 (0)	1 (3)
Opioid (%)	13 (41)	10 (31)	8 (26)
Mean body mass index (kg/m ²) (SD)	29.7 (4.7)	29.4 (5.1)	30.8 (7.9)

Outcome measures

NB: RMS sway outcome not collected or included in statistical analysis plan

1. Sway measures, eyes open

Timepoint and analysis		Unadjusted scores (SD or IQR)			200mcg vs placebo		400mcg vs placebo		400mcg vs 200mcg	
		Placebo	Vitamin K 200mcg	Vitamin K 400mcg	Treatment effect (95%CI)*	P	Treatment effect (95% CI)*	P	Treatment effect (95% CI)*	P
A-P sway	Baseline	2.74 (1.01)	2.95 (0.88)	2.93 (1.21)	-0.09 (-0.53 to 0.35)	0.69	0.19 (-0.25 to 0.63)	0.40	0.28 (-0.15 to 0.70)	0.20
	6 mths	2.84 (1.35)	3.01 (1.33)	2.67 (1.22)						
	12 mths	2.75 (1.38)	2.51 (1.02)	2.88 (1.20)						
M-L (cm)	Baseline	2.38 (1.40)	2.09 (0.95)	2.41 (1.31)	-0.10 (-0.68 to 0.49)	0.74	-0.08 (-0.64 to 0.49)	0.79	0.02 (-0.53 to 0.58)	0.94
	6 mths	2.54 (1.76)	2.17 (1.35)	2.26 (1.81)						
	12 mths	2.48 (2.03)	2.10 (1.57)	2.50 (1.84)						
Median 95% ellipse (cm ²)	Baseline	2.81 [1.75-7.95]	3.44 [2.11-5.80]	3.36 [1.70-9.40]	-0.02** (-0.15 to 0.10)	0.71	-0.04** (-0.16 to 0.09)	0.55	-0.01** (-0.13 to 0.10)	0.81
	6 mths	3.27 [1.86-5.72]	3.83 [1.77-6.54]	2.57 [1.27-6.23]						
	12 mths	2.76 [1.62-5.24]	2.94 [1.37-4.36]	3.33 [1.75-7.83]						
Median Path length (cm)	Baseline	69 [62-89]	64 [58-77]	67 [57-93]	-0.02** (-0.06 to 0.02)	0.32	-0.02** (-0.06 to 0.02)	0.34	0.00** (-0.04 to 0.04)	0.97
	6 mths	67 [59-85]	64 [55-79]	65 [60-91]						
	12 mths	71 [61-75]	66 [56-70]	66 [56-96]						

* Treatment effects adjusted for age, sex, baseline A-P sway, baseline value of variable under test, and trial centre

** Between-group comparison of Log10 of outcome

Bold: Primary outcome. A-P: Anteroposterior. M-L: Mediolateral

2. Sway measures, Eyes closed

		Unadjusted scores (SD) or [IQR]			200mcg vs placebo		400mcg vs placebo		400mcg vs 200mcg	
		Placebo	Vitamin K 200mcg	Vitamin K 400mcg	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p
A-P (cm)	Baseline	3.79 (1.35)	3.74 (1.14)	3.89 (2.18)	-0.11 (-0.46 to 0.24)	0.54	-0.36 (-0.71 to -0.01)	0.05	-0.25 (-0.60 to 0.09)	0.15
	6 mths	3.83 (1.49)	3.76 (1.34)	3.66 (1.34)						
	12 mths	3.82 (1.56)	3.60 (0.88)	3.45 (1.16)						
M-L (cm)	Baseline	2.67 (1.67)	2.49 (0.99)	3.78 (2.57)	-0.45 (-0.97 to 0.07)	0.09	-0.44 (-0.96 to 0.09)	0.10	0.01 (-0.52 to 0.54)	0.96
	6 mths	2.55 (1.37)	2.33 (1.00)	3.18 (2.10)						
	12 mths	3.12 (2.07)	2.45 (1.19)	2.60 (1.53)						
Median 95% ellipse (cm ²)	Baseline	5.20 [2.15-8.26]	5.03 [2.73-8.79]	6.20 [2.61-13.15]	-0.02** (-0.13 to 0.09)	0.75	-0.06** (-0.17 to 0.05)	0.28	-0.04** (-0.15 to 0.07)	0.44
	6 mths	5.26 [2.46-10.23]	5.02 [2.78-8.50]	4.70 [2.70-11.04]						
	12 mths	4.85 [1.94-13.26]	4.70 [2.90-7.92]	5.18 [2.20-8.30]						
Median Path length (cm)	Baseline	91 [75-119]	84 [73-100]	77 [64-115]	-0.01** (-0.05 to 0.02)	0.53	-0.03** (-0.06 to 0.01)	0.11	-0.02** (-0.05 to 0.02)	0.32
	6 mths	89 [70-108]	83 [70-94]	78 [70-147]						
	12 mths	96 [73-132]	79 [66-92]	81 [63-108]						

* Treatment effects adjusted for age, sex, baseline A-P sway, baseline value of variable under test, and trial centre

** Between-group comparison of Log10 of outcome

A-P: Anteroposterior. M-L: Mediolateral

3. Physical performance and balance measures

		Unadjusted scores (SD) or [IQR]			200mcg vs placebo		400mcg vs placebo		400mcg vs 200mcg	
		Placebo	Vitamin K 200mcg	Vitamin K 400mcg	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p
SPPB	Baseline	7.7 (2.3)	7.4 (2.6)	7.1 (2.7)	-0.2 (-1.1 to 0.7)	0.63	-0.4 (-1.3 to 0.5)	0.37	-0.2 (-1.1 to 0.7)	0.66
	6 mths	8.0 (2.7)	7.8 (2.7)	7.2 (2.8)						
	12 mths	7.9 (3.0)	7.8 (2.7)	6.7 (3.1)						
Median TUAG (s)	Baseline	12.9 [9.7-17.1]	14.2 [9.2-21.3]	14.1 [9.4-20.4]	0.021** (-0.034 to 0.076)	0.44	0.034 ** (-0.022 to 0.090)	0.23	0.012** (-0.041 to 0.066)	0.64
	6 mths	9.9 [8.5-16.2]	11.7 [8.4-18.1]	12.9 [8.4-17.9]						
	12 mths	11.2 [9.1-17.2]	12.5 [8.9-19.0]	13.3 [9.6-18.7]						
Median Berg balance score	Baseline	50 [45-53]	48 [42-53]	48 [44-54]	0.009** (-0.009 to 0.028)	0.31	-0.002** (-0.021 to 0.016)	0.80	-0.012** (-0.030 to 0.006)	0.20
	6 mths	51 [38-53]	52 [46-54]	47 [42-54]						
	12 mths	52 [41-54]	50 [47-54]	49 [40-54]						

* Treatment effects adjusted for age, sex, baseline A-P sway, baseline value of variable under test, and trial centre

** Between-group comparison of Log10 of outcome

SPPB: Short physical performance battery. TUAG: Timed Up And Go

4. Blood pressure and markers of vitamin K activity

		Unadjusted scores (SD)			Vitamin K 200mcg vs placebo		Vitamin K 400mcg vs placebo		Vitamin K 400mcg vs 200mcg	
		Placebo	Vitamin K 200mcg	Vitamin K 400mcg	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p	Treatment effect (95% CI)*	p
SBP (mmHg)	Baseline	150 (18)	149 (20)	142 (18)	4.8 (-2.5 to 12.0)	0.20	0.9 (-6.5 to 8.3)	0.80	-3.8 (-11.0 to 3.4)	0.29
	6 mths	141 (18)	144 (20)	137 (14)						
	12 mths	145 (15)	149 (15)	143 (22)						
DBP (mmHg)	Baseline	77 (9)	76 (11)	76 (9)	1.0 (-2.4 to 4.5)	0.54	1.3 (-2.1 to 4.8)	0.45	0.3 (-3.1 to 3.6)	0.87
	6 mths	73 (10)	73 (10)	73 (7)						
	12 mths	75 (9)	74 (8)	76 (10)						
SBP postural drop (mmHg)	Baseline	13 (15)	15 (15)	14 (16)	1.5 (-5.1 to 8.2)	0.64	-0.7 (-7.4 to 6.1)	0.84	-2.2 (-8.7 to 4.3)	0.50
	6 mths	16 (16)	18 (14)	15 (17)						
	12 mths	16 (15)	18 (16)	15 (17)						
DBP postural drop (mmHg)	Baseline	3 (7)	1 (6)	2 (8)	-1.7 (-4.9 to 1.5)	0.29	-1.3 (-4.5 to 2.0)	0.43	0.4 (-2.7 to 3.5)	0.79
	6 mths	6 (8)	3 (7)	2 (8)						
	12 mths	5 (8)	2 (7)	3 (9)						
Dp-ucMGP (pmol/L)	Baseline	849 (316)	859 (300)	885 (342)	-196 (-315 to -77)	0.002	-261 (-381 to -141)	<0.001	-64 (-178 to 84)	0.26
	12 mths	855 (331)	659 (296)	485 (338)						

* Treatment effects adjusted for age, sex, baseline A-P sway, baseline value of variable under test, and trial centre

Dp-ucMGP :Desphospho-undercarboxylated Matrix Gla Protein. SBP: Systolic blood pressure. DBP: Diastolic blood pressure

5. Falls

	Placebo	Vitamin K 200mcg	Vitamin K 400mcg
Median number of falls (IQR)	3 (1-6)	4 (1-7)	2 (0-4)
Falls per 1000 days (IQR)	8.3 (3.0 – 16.7)	11.1 (2.6 - 19.4)	5.6 (0 – 12.1)
Adjusted falls rate* (per 1000 days) (95% CI)	11.5 (7.5 to 17.8)	15.0 (9.8 to 23.0)	10.6 (7.0 to 16.0)

*adjusted for age, sex, site, falls in last year, baseline anteroposterior sway and number of falls in previous year

6. Mean resource use and costs per patient incurred between baseline and 1 year follow-up (complete case analysis n=75)

Resource use item	Placebo, n=23			200mcg Vitamin K, n=26			400mcg Vitamin K, n=26		
	Resource users, n (%)	Mean resource use (SD)	Mean cost, £ (SD)	Resource users, n (%)	Mean resource use (SD)	Mean cost, £ (SD)	Resource users, n (%)	Mean resource use (SD)	Mean cost, £ (SD)
NHS hospital care									
Length of stay days	2 (9)	1.65 (7.30)	570.30 (2518.56)	2 (8)	1.58 (6.91)	544.32 (2387.83)	4 (15)	1.58 (5.27)	544.32 (1819.13)
Accident & Emergency visits	3 (13)	0.17 (0.49)	25.74 (72.67)	6 (23)	0.31 (0.62)	45.54 (91.42)	6 (23)	0.23 (0.43)	34.15 (63.59)
Day case visits	0 (0)	0.00 (0.00)	0.00 (0.00)	2 (8)	0.15 (0.54)	113.17 (399.80)	4 (15)	0.27 (0.72)	198.05 (532.81)
Outpatient visits	8 (35)	0.43 (0.66)	52.10 (79.38)	9 (35)	0.38 (0.57)	46.09 (68.44)	11 (42)	0.42 (0.50)	50.70 (60.38)
Day hospital visits	1 (4)	0.04 (0.21)	5.75 (27.57)	1 (4)	0.08 (0.39)	10.17 (51.86)	2 (8)	0.08 (0.27)	10.17 (35.93)
NHS primary care									
GP visits	11 (48)	1.09 (1.86)	41.30 (70.55)	19 (73)	1.27 (1.15)	48.23 (43.73)	13 (50)	0.96 (1.31)	36.54 (49.81)
District nurse visits	5 (22)	0.35 (0.88)	12.85 (32.67)	2 (8)	0.12 (0.43)	4.26 (15.93)	6 (23)	0.92 (2.47)	34.09 (91.01)
Physiotherapist visits	3 (13)	0.48 (1.41)	24.88 (73.35)	5 (19)	0.38 (1.06)	20.00 (55.20)	5 (19)	0.54 (1.17)	28.01 (61.08)
Occupational therapist visits	1 (4)	0.35 (1.67)	25.06 (120.20)	0 (0)	0.00 (0.00)	0.00 (0.00)	2 (8)	0.15 (0.61)	11.09 (44.15)
Speech therapist visits		0.00 (0.00)			0.00 (0.00)			0.00 (0.00)	
Social care									
Day centre visits	1 (4)	0.04 (0.21)	2.74 (13.14)	1 (4)	0.04 (0.20)	2.42 (12.36)	1 (4)	0.04 (0.20)	2.42 (12.36)
Home help/care visits	2 (9)	0.22 (0.85)	3.31 (12.94)	3 (12)	2.46 (8.40)	37.44 (127.71)	6 (23)	2.31 (7.93)	35.10 (120.59)
Mean Total Costs £ (SD)			764 (2819)			902¹ (2436)			1044² (1977)
						896³ (2436)			1033⁴ (1977)
<p>1. Includes 1 year Vitamin K2 price = £29.94 (over the counter product, "Vitamaze"; price for 180 tablets, 6 month's supply, 200mcg per tablet = £14.97; source: https://www.amazon.co.uk/Certified-Strength-Menaquinone-magnesium-stearate/dp/B01N7NI8ZV).</p> <p>2. Includes 1 year Vitamin K2 price = £59.88 (as above, assuming tablet taken twice daily).</p> <p>3. Includes 1 year Vitamin K2 price = £24.03 (NHS Tariff price, Phytomenadione 1 mg capsules, price for 12 capsules = £3.95. Calculation based on price for 1 year supply of 200mcg daily = 0.2 * (3.95/12) *365; https://bnfc.nice.org.uk/medicinal-forms/phytomenadione.html</p> <p>4. Includes 1 year Vitamin K2 price = £48.06 (as above.; calculation based on price for 1 year supply of 400mcg daily = 0.4 * (3.95/12) *365.</p>									

Adverse events

Event by MedDRA System Organ Class	Placebo	Vitamin K 200 mcg	Vitamin K 400 mcg	Total
Blood and lymphatic system	1	1	1	3
Cardiac	0	0	1	1
Ear and labyrinth	0	1	1	2
Endocrine	0	0	1	1
Gastrointestinal	2	7	1	10
Other	1	1	2	4
Hepatobiliary	2	0	0	2
Infections	16	20	18	54
Injury	5	14	8	27
Investigations	0	0	1	1
Metabolic	1	0	0	1
Musculoskeletal	5	7	6	18
Neoplasia	0	1	1	2
Nervous system	5	5	2	12
Psychiatric	0	0	1	1
Renal and urinary	2	1	0	3
Reproductive system and breast	1	2	0	3
Respiratory	2	1	1	4
Skin	1	3	1	5
Vascular	0	2	3	5
TOTAL	44	66	49	159
Deaths	0	1	0	0