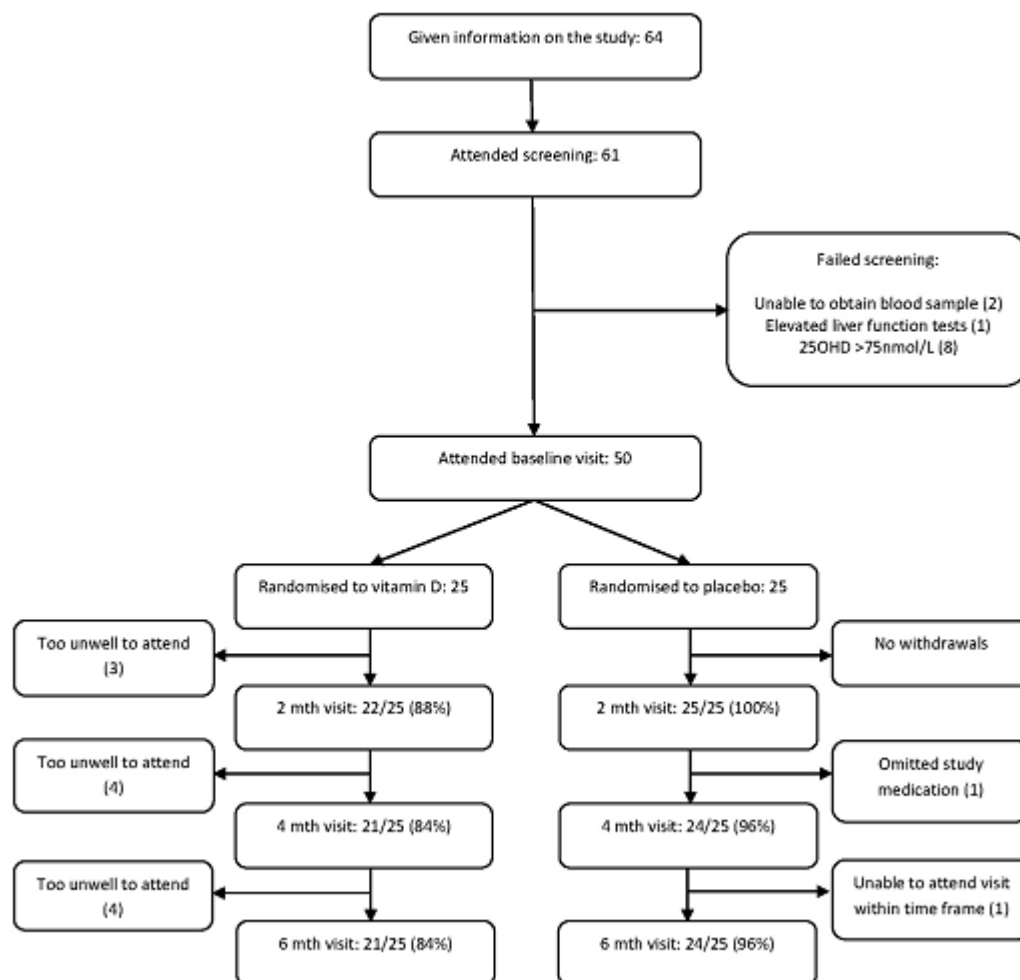


## Participant Flow



## Baseline characteristics

	Vitamin D (n=25)	Placebo (n=25)
Mean age (SD)	48.1 (12.0)	50.7 (13.1)
Male sex (%)	7 (28)	5 (20)
Current smoker (%)	4 (16)	6 (24)
Body mass index (Kg/m <sup>2</sup> ) (SD)	28.8 (7.9)	29.8 (5.4)
Previous cancer (%)	1 (4)	1 (4)
Previous diagnosis of vascular disease (%)	1 (4)	3 (12)
Previous diagnosis of diabetes mellitus (%)	3 (12)	1 (4)
Statin use (%)	2 (4)	4 (8)
Antiplatelet use (%)	0 (0)	3 (6)
Antihypertensive use (%)	4 (16)	5 (20)
Median number of medications [IQR]	2 [4]	4 [4]
Serum creatinine (umol/L) (SD)	68 (12)	71 (10)
Mean adjusted serum calcium (mmol/L) (SD)	2.27 (0.06)	2.31 (0.08)
Mean 25OHD (nmol/L) (SD)	44 (15)	48 (20)
Mean 1,25OHD (pmol/L) (SD)	48 (17)	43 (19)
Mean PTH (pmol/L) (SD)	6.0 (2.6)	5.0 (2.0)
Mean systolic blood pressure (mmHg) (SD)	125 (17)	132 (18)
Mean diastolic blood pressure (mmHg) (SD)	76 (10)	81 (12)
Mean pulse rate (beats/min) (SD)	70 (11)	70 (9)
Mean total cholesterol (mmol/L) (SD)	5.2 (1.2)	5.7 (1.3)
Mean LDL cholesterol (mmol/L) (SD)	3.2 (0.9)	3.6 (1.2)
Mean HDL cholesterol (mmol/L) (SD)	1.5 (0.5)	1.2 (0.3)
Mean triglycerides (mmol/L) (SD)	1.2 (0.7)	2.0 (0.8)
Median HOMA-IR (IQR)	2.6 (3.0)	2.2 (3.7)
Mean brachial artery FMD (%) (SD)	7.7 (3.1)	6.5 (2.9)
Mean pulse wave velocity (m/s) (SD)	7.3 (2.6)	8.3 (1.9)

Mean augmentation index (%) (SD)	16 (13)	27 (10)
Median C-reactive protein (mg/l) (IQR)	0.6 (3.2)	2.7 (4.6)
Mean IL-6 (pg/ml) (SD)	1.6 (0.8)	2.5 (1.8)
Mean TNF alpha (pg/ml) (SD)	1.5 (0.7)	1.9 (0.8)
Mean d-ROMS (U.Carr) (SD)	389 (99)	473 (143)
Mean BAP (umol/L) (SD)	2128 (407)	1815 (480)
Piper Behavioural (SD)	6.6 (1.8)	8.0 (1.3)
Piper Affective (SD)	7.4 (1.6)	7.8 (1.6)
Piper Sensory (SD)	6.3 (1.9)	7.5 (1.5)
Piper Cognitive (SD)	5.1 (1.5)	6.1 (1.4)
Piper fatigue score total (SD)	6.3 (1.6)	7.3 (1.2)

25OHD: 25-hydroxyvitamin D; 1,25OHD: 1,25-hydroxyvitamin D; PTH: Parathyroid hormone; FMD: Flow-mediated dilatation of the brachial artery; LDL: Low density lipoprotein; HDL: High density lipoprotein; HOMA-IR: Homeostasis model assessment – insulin resistance; IL-6: Interleukin 6; TNF: Tumor necrosis factor; d-ROMS: derivatives of Reactive Oxygen Metabolites; BAP: Biological Antioxidant Potential

## Outcome measures

### Primary outcome measures

		Vitamin D (SD)	Placebo (SD)	Adjusted treatment effect (95% CI)*	p
Pulse wave velocity (m/s)	2 mths	7.2 (2.5)	8.5 (1.7)	-0.2 (-0.7 to 0.3)	0.44
	6 mths	6.9 (2.4)	8.1 (1.4)	0.0 (-0.6 to 0.6)	0.93

\*adjusted for baseline outcome measure values

### Secondary outcome measures

		Vitamin D (SD)	Placebo (SD)	Adjusted treatment effect (95% CI)*	p
Augmentation index (%)	2 mths	15 (12)	25 (9)	2 (-1 to 6)	0.16
	6 mths	15 (12)	25 (10)	1 (-4 to 6)	0.60
Systolic blood pressure (mmHg)	2 mths	123 (17)	130 (16)	-2 (-10 to 6)	0.59
	6 mths	124 (17)	133 (15)	-2 (-10 to 5)	0.55
Diastolic blood pressure (mmHg)	2 mths	76 (8)	83 (9)	-5 (-9 to 0)	0.04
	6 mths	75 (9)	82 (10)	-2 (-7 to 2)	0.34
Pulse (beats/min)	2 mths	74 (12)	76 (14)	-3 (-9 to 4)	0.40
	6 mths	74 (13)	73 (11)	1 (-5 to 6)	0.78
FMD (%)	2 mths	7.4 (2.6)	6.1 (2.8)	0.9 (-0.4 to 2.2)	0.17
	6 mths	7.4 (2.5)	6.9 (3.4)	0.1 (-1.6 to 1.7)	0.93
25OHD (nmol/L)	2 mths	55 (18)	44 (21)	15 (7 to 22)	0.001
	6 mths	64 (21)	44 (22)	22 (10 to 34)	0.001
1,25OHD (pmol/L)	2 mths	53 (19)	36 (17)	14 (5 to 23)	0.003
	6 mths	56 (22)	35 (24)	18 (5 to 31)	0.008
Adjusted serum calcium (mmol/L)	2 mths	2.30 (0.09)	2.29 (0.08)	0.03 (-0.02 to 0.08)	0.23
	6 mths	2.31 (0.07)	2.30 (0.09)	0.04 (-0.01 to 0.09)	0.10
PTH (pmol/L)	2 mths	7.0 (5.9)	6.4 (3.3)	0.4 (-1.9 to 2.8)	0.72

	6 mths	5.8 (3.2)	7.8 (4.6)	-2.4 (-4.1 to -0.7)	0.006
Total cholesterol (mmol/L)	2 mths	5.1 (1.3)	5.5 (1.1)	0.0 (-0.3 to 0.4)	0.82
	6 mths	4.8 (1.1)	5.7 (1.2)	-0.3 (-0.8 to 0.1)	0.10
LDL cholesterol (mmol/L)	2 mths	2.9 (0.9)	3.4 (1.1)	-0.1 (-0.4 to 0.2)	0.55
	6 mths	2.8 (0.8)	3.6 (1.2)	-0.2 (-0.6 to 0.2)	0.31
HDL cholesterol (mmol/L)	2 mths	1.4 (0.5)	1.2 (0.3)	0.0 (-0.1 to 0.1)	0.72
	6 mths	1.3 (0.4)	1.3 (0.3)	-0.1 (-0.2 to 0.0)	0.14
Triglycerides (mmol/L)	2 mths	1.4 (0.9)	2.1 (1.0)	0.0 (-0.4 to 0.5)	0.90
	6 mths	1.4 (0.8)	1.9 (0.9)	0.2 (-0.2 to 0.5)	0.31
Median HOMA-IR [IQR]	2 mths	1.1 [3.2]	3.9 [5.4]	-2.7 (-5.8 to 0.4)	0.09
	6 mths	1.9 [2.9]	2.2 [4.2]	-0.3 (-2.4 to 1.7)	0.75
Median C-reactive protein (mg/L) [IQR]	2 mths	0.7 [8.3]	2.1 [9.4]	0.0 (-4.0 to 4.0)	0.98
	6 mths	0.9 [5.8]	1.8 [2.8]	0.4 (-1.1 to 1.9)	0.60
IL-6 (pg/ml)	2 mths	2.4 (1.8)	2.7 (1.9)	0.2 (-0.7 to 1.1)	0.66
	6 mths	2.4 (1.9)	2.1 (1.1)	0.7 (-0.2 to 1.6)	0.11
TNF-alpha (mg/ml)	2 mths	1.7 (0.8)	1.9 (0.8)	0.2 (-0.4 to 0.0)	0.06
	6 mths	1.5 (0.6)	2.1 (1.2)	-0.3 (-0.8 to 0.3)	0.28
d-ROMS (U.Carr)	6 mths	377 (134)	448 (72)	-32 (-93 to 29)	0.30
BAP (umol/L)	6 mths	2046 (349)	2113 (579)	-146 (-471 to 179)	0.37

\*adjusted for baseline outcome measure values

FMD: Flow-mediated dilatation of the brachial artery. 25OHD: 25-hydroxyvitamin D; 1,25OHD: 1,25-hydroxyvitamin D; PTH: Parathyroid hormone. LDL: Low density lipoprotein; HDL: High density lipoprotein; HOMA-IR: Homeostasis model assessment – insulin resistance; IL-6: Interleukin 6; TNF: Tumor necrosis factor; d-ROMS: derivatives of Reactive Oxygen Metabolites; BAP: Biological Antioxidant Potential.

	Vitamin D (SD)	Placebo (SD)	Adjusted treatment effect (95% CI)*	p
<i>Piper fatigue scale</i>				
Behavioural	6.7 (1.6)	7.5 (2.2)	0.1 (-1.1 to 1.3)	0.88

Affective	7.6 (1.4)	7.5 (2.2)	0.3 (-0.6 to 1.3)	0.48
Sensory	6.5 (1.5)	7.1 (2.2)	-0.1 (-1.2 to 1.0)	0.85
Cognitive	5.5 (1.1)	5.9 (1.7)	0.1 (-0.8 to 1.0)	0.85
Piper total	6.6 (1.1)	7.0 (1.9)	0.2 (-0.8 to 1.2)	0.73
<i>Hospital anxiety and depression score</i>				
Anxiety	5.7 (4.0)	5.0 (4.4)	0.4 (-0.9 to 1.8)	0.53
Depression	5.7 (3.1)	7.6 (4.6)	-1.0 (-2.6 to 0.5)	0.18

\*adjusted for baseline outcome measure values

## Adverse events

	Vitamin D	Placebo
Infection	14	9
Musculoskeletal	2	2
Gastrointestinal	6	12
Dermatological	0	1
Cardiovascular	1	2
New cancer	2	0
Hypercalcemia	0	0
Ureteric colic	0	0
Other	8	13
TOTAL:	33	39
Deaths	0	0
Hospitalisations	1	0

