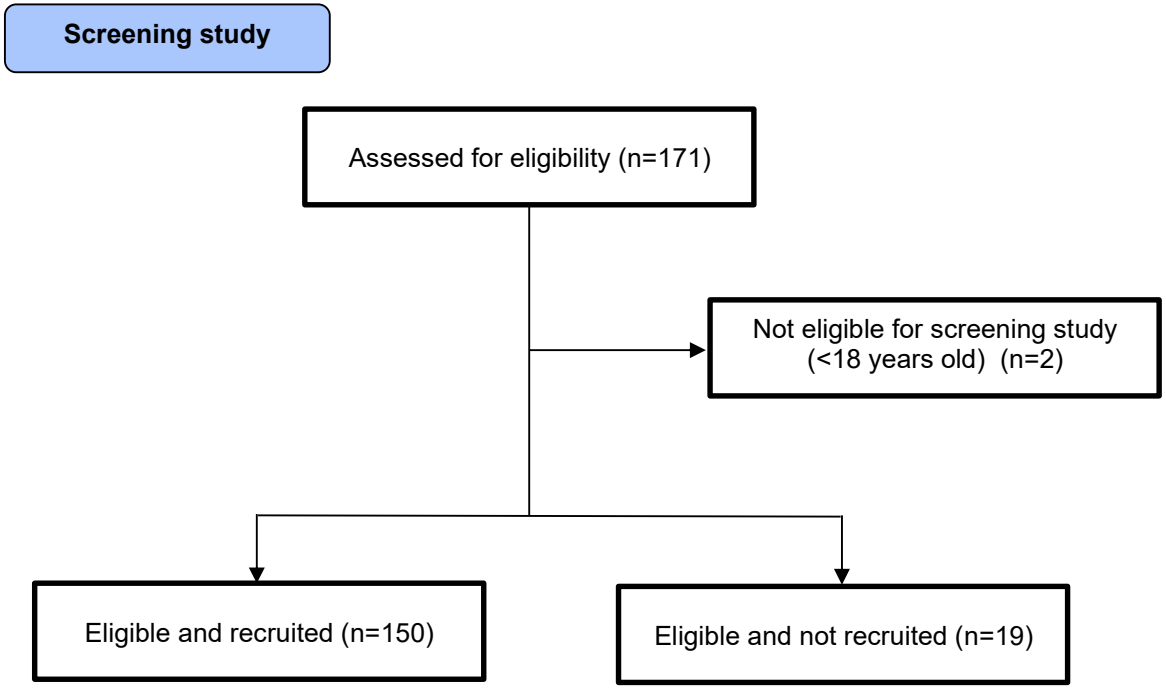
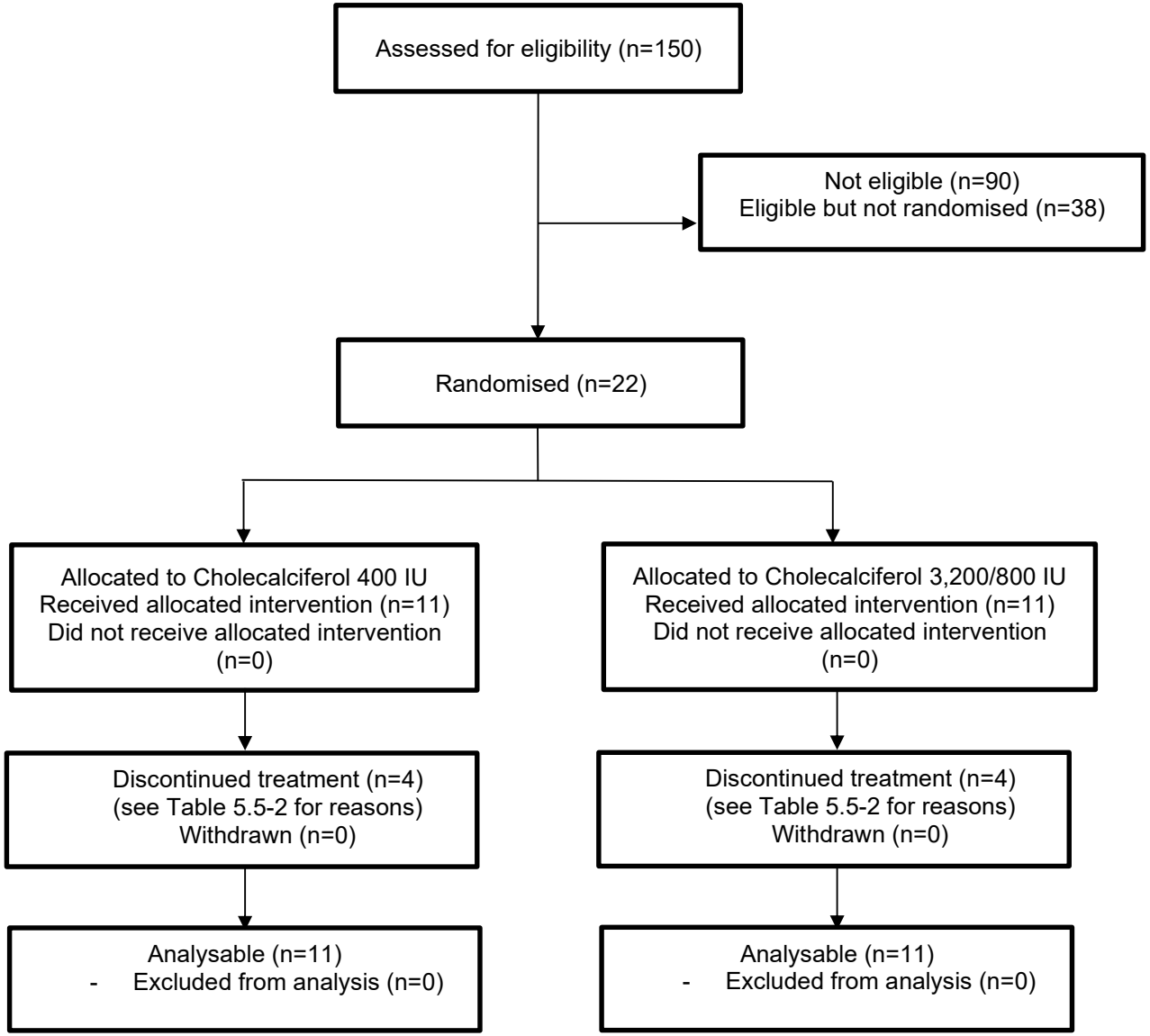
Participant Flow



Feasibility study



Baseline Characteristics

Characteristic	Screening study	Feasibility trial	
		Cholecalciferol 400 IU	Cholecalciferol 3,200/800 IU
Patients recruited, n	150	11	11
Sex, n (%)			
Male	70 (46.7 %)	6 (54.5 %)	6 (54.5 %)
Female	80 (53.3 %)	5 (45.5 %)	5 (45.5 %)
Age (years)			
Mean (SD)	42.7 (16.7)	37 (15.1)	38.2 (17.5)
Median (IQR)	39 (28-56)	33 (23-53)	30 (24-56)
Range	18-81	18-59	19-69
Ethnicity, n (%)			
English/Welsh/Scottish/Northern Irish/British	116 (77.3 %)	8 (72.7 %)	8 (72.7 %)
Any other white background	3 (2 %)	0 (0.0%)	1 (9.1 %)
White and Black Caribbean	2 (1.3 %)	1 (9.1 %)	1 (9.1 %)
Indian	9 (6 %)	1 (9.1 %)	0 (0.0%)
Pakistani	7 (4.7 %)	0 (0.0%)	0 (0.0%)
Bangladeshi	2 (1.3 %)	0 (0.0%)	0 (0.0%)
Any other Asian background	5 (3.3 %)	0 (0.0%)	1 (9.1 %)
African	1 (0.7 %)	0 (0.0%)	0 (0.0%)
Caribbean	2 (1.3 %)	1 (9.1 %)	0 (0.0%)
Any other Black/African/Caribbean background	3 (2 %)	0 (0.0%)	0 (0.0%)
Crohn's disease status, n (%)			
In remission	36 (24 %)	2 (18.2 %)	4 (36.4 %)
Active (receiving treatment)	114 (76 %)	9 (81.8 %)	7 (63.6 %)
Current medication, n (%)			
Over-the-counter vitamin D, fish oil or multivitamin supplementation	49 (32.7 %)	4 (36.4 %)	1 (9.1 %)
Vitamin D-containing supplementation prescribed by a healthcare professional	31 (20.7 %)	0 (0.0%)	0 (0.0%)
Bisphosphonates	1 (0.7 %)	0 (0.0%)	0 (0.0%)
Barbiturates (e.g. Amylobarbitone, Butobarbitone, Methyl Phenobarbitone, Pentobarbitone, Quinalbarbitone)	1 (0.7 %)	0 (0.0%)	0 (0.0%)
None	71 (47.3 %)	7 (63.6 %)	10 (90.9 %)

Known conditions, n (%)			
Renal disease or other kidney stones	5 (3.3 %)	0 (0.0%)	0 (0.0%)
Underlying liver disease	3 (2 %)	0 (0.0%)	0 (0.0%)
Hypersensitivity to vitamin D supplement or any of trial medication excipients	1 (0.7 %)	0 (0.0%)	0 (0.0%)
None	142 (94.7 %)	11 (100 %)	11 (100 %)
Sun exposure, n (%)			
Has the patient visited a warm/sunny country in the last three months?			
Yes	27 (18 %)	0 (0.0%)	2 (18.2 %)
No	122 (81.3 %)	11 (100 %)	9 (81.8 %)
Missing	1 (0.7 %)	0 (0.0%)	0 (0.0%)
If the patient is exposed to sunshine does their skin normally…			
tan or darken easily?	64 (42.7 %)	5 (45.5 %)	6 (54.5 %)
go red then tan?	49 (32.7 %)	3 (27.3 %)	3 (27.3 %)
burn?	36 (24 %)	3 (27.3 %)	2 (18.2 %)
Missing	1 (0.7 %)	0 (0.0%)	0 (0.0%)
Would the patient normally use a sun lotion with sun protection factor (SPF) if they are exposed to sunshine? Yes	120 (80 %)	9 (81.8 %)	10 (90.9 %)
No	30 (20 %)	2 (18.2 %)	1 (9.1 %)
What SPF would they normally use?			
Mean (SD)	38.2 (12.9)	36.9 (11)	37.2 (17.3)
Median (IQR)	45 (30-50)	30 (30-50)	50 (30-50)
Range	5-50	25-50	5-50
Missing	38 (25.3 %)	3 (27.3 %)	2 (18.2 %)
In the sunshine is the patient most likely to wear…			
Shorts and a short-sleeve top	91 (60.7 %)	6 (54.5 %)	6 (54.5 %)
Long trousers/skirt and a short-sleeve top	31 (20.7 %)	2 (18.2 %)	3 (27.3 %)
Keep arms and legs covered	22 (14.7 %)	3 (27.3 %)	1 (9.1 %)
Keep whole body completely covered	6 (4 %)	0 (0.0%)	1 (9.1 %)

Weekly food frequency, n (%)				
Oily fish (salmon, sardines, herring, mackerel, tuna)				
	0	72 (48 %)	5 (45.5 %)	4 (36.4 %)
	1-2	67 (44.7 %)	6 (54.5 %)	6 (54.5 %)
	3-4	9 (6 %)	0 (0.0%)	1 (9.1 %)
	5+	2 (1.3 %)	0 (0.0%)	0 (0.0%)
Red meat				
	0	61 (40.7 %)	3 (27.3 %)	4 (36.4 %)
	1-2	71 (47.3 %)	5 (45.5 %)	6 (54.5 %)
	3-4	16 (10.7 %)	2 (18.2 %)	1 (9.1 %)
	5+	2 (1.3 %)	1 (9.1 %)	0 (0.0%)
Liver or offal				
	0	148 (98.7 %)	11 (100 %)	10 (90.9 %)
	1-2	1 (0.7 %)	0 (0.0%)	1 (9.1 %)
	5+	1 (0.7 %)	0 (0.0%)	0 (0.0%)
Eggs including the yolk				
	0	39 (26 %)	2 (18.2 %)	1 (9.1 %)
	1-2	53 (35.3 %)	6 (54.5 %)	5 (45.5 %)
	3-4	36 (24 %)	3 (27.3 %)	2 (18.2 %)
	5+	21 (14 %)	0 (0.0%)	3 (27.3 %)
	Missing	1 (0.7 %)	0 (0.0%)	0 (0.0%)
Foods that are labelled as fortified with vitamin D				
(breakfast cereal, spread, etc.)	0	102 (68 %)	10 (90.9 %)	10 (90.9 %)
	1-2	15 (10 %)	0 (0.0%)	1 (9.1 %)
	3-4	10 (6.7 %)	0 (0.0%)	0 (0.0%)
	5+	23 (15.3 %)	1 (9.1 %)	0 (0.0%)
Current smoker, n (%)	Yes	22 (14.7 %)	2 (18.2 %)	1 (9.1 %)
	No	128 (85.3 %)	9 (81.8 %)	10 (90.9 %)
Vitamin D level (nmol/L), n (%)				
	Mean (SD)	48.3 (25)	31 (8.5)	27.4 (11.7)
	Median (IQR)	46 (31-62)	35 (20-36)	26 (15-38)
	Range	11-185	16-40	12-47
	Missing	1 (0.7 %)	0 (0.0%)	0 (0.0%)
	Deficient (<25)	26 (17.3 %)	3 (27.3 %)	5 (45.5 %)
	Insufficient (25-<50)	53 (35.3 %)	8 (72.7 %)	6 (54.5 %)
	Normal (≥50)	70 (46.7 %)	0 (0.0%)	0 (0.0%)
	Missing	1 (0.7 %)	0 (0.0%)	0 (0.0%)

Additional baseline characteristics for feasibility trial

Characteristic	Cholecalciferol 400 IU	Cholecalciferol 3,200/800 IU
Height (cm)		
Mean (SD)	172.5 (10.6)	172.5 (10.6)
Median (IQR)	172 (164-178.4)	177 (166-179.5)
Range	153.6-193	151.5-185
Weight (kg)		
Mean (SD)	71.6 (17.6)	77.8 (11.9)
Median (IQR)	67.5 (60.6-75.3)	74 (66.3-92.5)
Range	53.9-119.7	64.7-94.5

Outcome Measures

Outcomes: Screening study

Prevelance of vitamin D deficiency

Month	Number of patients recruited	Number of patients with vitamin D deficiency*	Prevalence (%)
SEP2019	12	3	25%
OCT2019	33	13	39.4%
NOV2019	23	11	47.8%
DEC2019	12	8	66.7%
JAN2020	17	9	52.9%
NOV2020	13	9	69.2%
DEC2020	40	27	67.5%
Total	**150**	**80**	**53.3%**

* Defined as 25(OH) vitamin D <50 nmol/L.

Vitamin D levels	Number of patients
Deficient (<25 nmol/L)	27 (18%)
Insufficient (25-<50 nmol/L)	53 (35.3%)
Normal (≥50 nmol/L)	70 (46.7%)

Outcomes: Feasibility Study

Consent rate – overall 47.1%

Compliance rate; Taking vitamin D supplement: Assessment of compliance (self-reported by patients on CRF)

Week 12

Timepoint	Quantity of tablets	Number of patients that reported taking tablets (%)	
		Cholecalciferol 400 IU	Cholecalciferol 3,200/800 IU
Prior to COVID-19 pandemic		(N=5)	(N=6)
	All	0 (0 %)	2 (33.3 %)
	Most	0 (0 %)	1 (16.7 %)
	Some	1 (20 %)	1 (16.7 %)
	None	1 (20 %)	0(0.0%)
	Missing	3 (60 %)	2 (33.3 %)
During COVID-19 pandemic		(N=6)	(N=5)
	All	2 (33.3 %)	2 (40 %)
	Most	4 (66.7 %)	2 (40 %)
	Some	0 (0 %)	1 (20 %)
	None	0 (0 %)	0(0.0%)
	Missing	0 (0 %)	0 (0 %)
Overall		(N=11)	(N=11)
	All	2 (18.2 %)	4 (36.4 %)
	Most	4 (36.4 %)	3 (27.3 %)
	Some	1 (9.1 %)	2 (18.2 %)
	None	1 (9.1 %)	0(0.0%)
	Missing	3 (27.3 %)	2 (18.2 %)

Week 24

Timepoint	Quantity of tablets	Number of patients that reported taking tablets (%)	
		Cholecalciferol 400 IU	Cholecalciferol 3,200/800 IU
Prior to COVID-19 pandemic		(N=5)	(N=6)
	All	0 (0 %)	0 (0 %)
	Most	0 (0 %)	0 (0 %)
	Some	0(0.0%)	0 (0 %)
	None	0(0.0%)	0 (0 %)
	Missing	5 (100 %)	6 (100 %)
During COVID-19 pandemic		(N=6)	(N=5)
	All	1 (16.7 %)	1 (20 %)
	Most	5 (83.3 %)	2 (40 %)
	Some	0(0.0%)	1 (20 %)
	None	0(0.0%)	1 (20 %)
	Missing	0 (0 %)	0 (0 %)
Overall		(N=11)	(N=11)
	All	1 (9.1 %)	1 (9.1 %)
	Most	5 (45.5 %)	2 (18.2 %)
	Some	0(0.0%)	1 (9.1 %)
	None	0(0.0%)	1 (9.1 %)
	Missing	5 (45.5 %)	6 (54.5 %)

Outcomes for the assessment of efficacy in a future trial

Primary Outcome for the assessment of efficacy in a future trial - IBDQ

Domain		Cholecalciferol 400 IU		Cholecalciferol 3,200/800 IU	
		Eligibility	**Week 24**	**Eligibility**	**Week 24**
Bowel systems	Total (n)	9*	6*	11	4*
	Mean (SD)	52.1 (15.3)	52.0 (10.4)	55.6 (8.1)	51.3 (15.2)
	Median (IQR)	60.0 (44.0-65.0)	50.5 (43.0-64.0)	59.0 (50.0-62.0)	51.0 (41.0-61.5)
	Range	29.0-67.0	40.0-64.0	41.0-67.0	33.0-70.0
	Missing/Not valid	2	5	0	7
Emotional health	Total (n)	10*	6*	11	4*
	Mean (SD)	56.8 (18.4)	54.5 (14.3)	58.4 (15.4)	63.0 (19.6)
	Median (IQR)	62.0 (34.0-73.0)	49.5 (43.0-67.0)	61.0 (48.0-69.0)	66.5 (47.0-79.0)
	Range	28.0-78.0	41.0-77.0	32.0-83.0	39.0-80.0
	Missing/Not valid	1	5	0	7
Systemic systems	Total (n)	11	6*	11	4*
	Mean (SD)	21.2 (7.2)	24.5 (5.6)	19.6 (7.4)	22.3 (8.5)
	Median (IQR)	23.0 (15.0-29.0)	24.5 (19.0-30.0)	18.0 (13.0-25.0)	22.0 (15.0-29.5)
	Range	11.0-29.0	18.0-31.0	8.0-34.0	14.0-31.0
	Missing/Not valid	0	5	0	7
Social function	Total (n)	10*	6*	11	4*
	Mean (SD)	28.5 (9.4)	27.2 (7.1)	32.1 (5.8)	27.3 (9.3)
	Median (IQR)	33.5 (23.0-35.0)	26.5 (20.0-35.0)	34.0 (32.0-35.0)	29.5 (20.0-34.5)
	Range	6.0-35.0	20.0-35.0	15.0-35.0	15.0-35.0
	Missing/Not valid	1	5	0	7
Total IBDQ score	Total (n)	10*	6*	11	4*
	Mean (SD)	159.4 (46.4)	158.2 (33.9)	165.4 (32.4)	163.8 (47.7)
	Median (IQR)	178.3 (114.6-188.0)	155.0 (128.0-179.0)	171.0 (148.6-186.0)	161.5 (123.0-204.5)
	Range	74.0-209.00	126.0-206.0	106.0-219.0	119.0-213.0
	Missing/Not valid	1	5	0	7

Secondary outcomes for the assessment of efficacy in a future trial - Quality of life (EQ-5D-5L)

Domain	Level	Cholecalciferol 400 IU		Cholecalciferol 3,200/800 IU	
		Eligibility n (%)	Week 24 n (%)	Eligibility n (%)	Week 24 n (%)
Mobility	No problem	9 (81.8%)	4 (36.4%)	9 (81.8%)	2 (18.2%)
	Slight problems	0 (0.0%)	0 (0.0%)	2 (18.2%)	2 (18.2%)
	Moderate problems	1 (9.1%)	2 (18.2%)	0 (0.0%)	0 (0.00%)
	Severe problems	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.00%)
	Missing	0 (0.0%)	5 (45.5%)	0 (0.0%)	7 (63.6%)
Self-care	No problem	10 (90.9%)	5 (45.5%)	9 (81.8%)	4 (36.4%)
	Slight problems	1 (9.1%)	1 (9.1%)	2 (18.2%)	0 (0.0%)
	Missing	0 (0.0%)	5 (45.5%)	0 (0.0%)	7 (63.6%)
Usual activities	No problem	6 (54.5%)	3 (27.3%)	6 (54.5%)	2 (18.2%)
	Slight problems	3 (27.3%)	1 (9.1%)	4 (36.4%)	2 (18.2%)
	Moderate problems	1 (9.1%)	1 (9.1%)	1 (9.1%)	0 (0.0%)
	Severe problems	1 (9.1%)	1 (9.1%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	5 (45.5%)	0 (0.0%)	7 (63.6%)
Pain/discomfort	No problem	4 (36.4%)	2 (18.2%)	4 (36.4%)	1 (9.1%)
	Slight problems	5 (45.5%)	1 (9.1%)	4 (36.4%)	2 (18.2%)
	Moderate problems	0 (0.0%)	2 (18.2%)	3 (27.3%)	1 (9.1%)
	Severe problems	0 (0.0%)	1 (9.1%)	0 (0.0%)	0 (0.0%)
	Extreme problems	2 (18.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	5 (45.5%)	0 (0.0%)	7 (63.6%)
Anxiety/depression	No problem	3 (27.3%)	2 (18.2%)	3 (27.3%)	3 (27.3%)
	Slight problems	5 (45.5%)	1 (9.1%)	5 (45.5%)	0 (0.0%)
	Moderate problems	2 (18.2%)	2 (18.2%)	2 (18.2%)	1 (9.1%)
	Severe problems	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)
	Extreme problems	1 (9.1%)	1 (9.1%)	0 (0.0%)	0 (0.0%)
	Missing	0 (0.0%)	5 (45.5%)	0 (0.0%)	7 (63.6%)

Crohn's Disease Activity Index (CDAI)

	Cholecalciferol 400 IU			Cholecalciferol 3,200/ 800 IU		
	Eligibility n (%)	**12-week follow-up n (%)**	**24-week follow-up n (%)**	**Eligibility n (%)**	**12-week follow-up n (%)**	**24-week follow-up n (%)**
Category n (%) Indicative of remission (<150) Mild disease (150-220) Moderate (221-450) Missing	 8 (72.7%) 1 (9.1%) 2 (18.2%) 0 (0.0%)	 4 (36.4%) 1 (9.1%) 3 (27.3%) 3 (27.3 %)	 4 (36.4%) 1 (9.1%) 1 (9.1%) 5 (4b 5.5 %)	 7 (63.6%) 3 (27.3%) 1 (9.1%) 0 (0.0%)	 8 (72.7 %) 1 (9.1%) 0 (0.0%) 2 (18.2 %)	 4 (36.4 %) 1 (9.1%) 0 (0.0%) 6 (54.5 %)
Total (n)	11	8	6	11	9	5
Mean (SD)	114.2 (108.7)	156.9 (102.2)	116.0 (72.9)	109.2 (86.2)	63.6 (59.2)	105.4 (74.7)
Median (IQR)	106.0 (28.0-174.0)	140.0 (76.0-244.0)	89.0 (69.0-159.0)	92.0 (31.0-186.0)	75.0 (10.0-99.0)	113.0 (73.0-142.0)
Range	5.0-365.0	24.0-311.0	47.0-243.0	12.0-273.0	0.0-163.0	0.0-199.0
Missing (n)	0	3	5	0	2	6

Blood test results

Blood test		Cholecalciferol 400 IU			Cholecalciferol 3,200/800 IU		
		Eligibility	12-week follow-up	24-week follow-up	Eligibility	12-week follow-up	24-week follow-up
25(OH) vitamin D (nmol/L)	Total (n)	10	8	6	11	9	5
	Mean (SD)	29.6 (11.4)	34.6 (15.7)	63.5 (23.1)	23.5 (9.3)	75.2 (25.5)	65.0 (13.6)
	Median (IQR)	31.0 (17.0-35.0)	31.0 (26.0-38.5)	70.0 (37.0-76.0)	23.0 (15.0-32.0)	74.0 (66.0-87.0)	66.0 (65.0-68.0)
	Range	13.00-48.00	17.0-69.0	35.0-93.0	12.0-38.0	28.0-121.0	44.0-82.0
	Missing (n)	1	3	5	0	2	6
Corrected calcium (mmol/L)	Total (n)	11	8	6	11	9	5
	Mean (SD)	2.32 (0.08)	2.30 (0.05)	2.33 (0.07)	2.33 (0.08)	2.3 (0.1)	2.4 (0.1)
	Median (IQR)	2.31 (2.25-2.40)	2.29 (2.28-2.33)	2.33 (2.27-2.36)	2.31 (2.27-2.37)	2.29 (2.27-2.34)	2.37 (2.35-2.38)
	Range	2.21-2.44	2.21-2.39	2.24-2.45	2.19-2.51	2.22-2.39	2.22-2.44
	Missing (n)	0	3	5	0	2	6
Parathyroid hormone (pmol/L)	Total (n)	11	8	6	11	9	5
	Mean (SD)	6.9 (3.9)	8.9 (7.4)	5.2 (1.8)	8.2 (2.8)	8.1 (3.3)	6.5 (2.9)
	Median (IQR)	6.2 (4.7-8.1)	6.7 (4.5-9.7)	5.4 (3.4-6.8)	7.6 (6.4-10.1)	7.4 (5.8-9.8)	5.8 (5.3-7.7)
	Range	2.4-16.7	3.3-26.0	2.9-7.5	5.0-13.8	4.8-14.4	2.9-10.7
	Missing (n)	0	3	5	0	2	6
Vitamin D metabolites (nmol/L)	Total (n)	10	7	4	11	8	5
	Mean (SD)	29.7 (11.8)	34.2 (18.9)	68.5 (14.7)	22.9 (13.4)	60.3 (23.8)	58.7 (16.2)
	Median (IQR)	31.6 (23.4-40.2)	32.9 (23.5-35.4)	67.1 (57.7-79.4)	16.5 (12.0-28.7)	68.2 (45.7-74.1)	56.8 (55.0-67.5)
	Range	10.9-46.7	15.4-73.8	52.6-87.3	10.6-53.1	21.4-85.4	35.4-79.0
	Missing (n)	1	4	7	0	3	6

Adverse Events

. There have been no SAEs

AE description	Cholecalciferol 400 IU		Cholecalciferol 3,200/800 IU		Total number of events	Total number of patients (%)
	Number of events	Number of patients (%)	Number of events	Number of patients (%)		
Groin cyst	1	1 (9.1%)	0	0 (0.0%)	1	1 (4.5%)
Tooth infection/root canal	1	1 (9.1%)	0	0 (0.0%)	1	1 (4.5%)
Watery Diarrhoea	1	1 (9.1%)	0	0 (0.0%)	1	1 (4.5%)
Nausea	0	0 (0.0%)	1	1 (9.1%)	1	1 (4.5%)
Rash	0	0 (0.0%)	1	1 (9.1%)	1	1 (4.5%)
Sinus infection	0	0 (0.0%)	1	1 (9.1%)	1	1 (4.5%)
Throat infection	0	0 (0.0%)	1	1 (9.1%)	1	1 (4.5%)
Tooth infection	1	1 (9.1%)	0	0 (0.0%)	1	1 (4.5%)
Total	4	3 (27.3%)	4	3 (27.3%)	8	6 (27.3%)