Supplemental Table 1. Effects of Vitamin D_3 vs Placebo on the Change in Each Outcome Associated with Baseline Participant Characteristics

	PTH (pg/mL)		Total 1,25(OH)$_2$D (pg/mL)		Total 25(OH)D (ng/mL)		Urine Calcium/creatinine (mg/g)	
Variable	**Difference in change (95% CI)[1]**	**p-value**	**Difference in change (95% CI)[1]**	**P-value**	**Difference in change (95% CI)[1]**	**P-value**	**Difference in change (95% CI)[1]**	**P-value**
Age (per decade)	2 (-2, 6)	0.327	2 (-2, 5)	0.399	1 (-1, 2)	0.512	-2 (-22, 19)	0.862
Sex								
Female	Ref	0.558	Ref	0.700	Ref	0.798	Ref	0.913
Male	2 (-5, 8)		1 (-5, 7)		0 (-3, 2)		-2 (-29, 26)	
Race/ethnicity								
White	Ref	0.285	Ref	0.008	Ref	0.917	Ref	0.591
Black	1 (-7, 8)		6 (-1, 13)		1 (-3, 4)		-17 (-49, 15)	
Hispanic	7 (-3, 17)		8 (0, 15)		-1 (-5, 4)		0 (-42, 43)	
Chinese	5 (-2, 13)		-8 (-12, -4)		0 (-4, 4)		-24 (-73, 25)	
BMI (kg/m^2)								
< 25	Ref	0.132	Ref	0.030	Ref	0.615	Ref	0.697
25 - <30	1 (-6, 8)		4 (-3, 12)		-2 (-6, 1)		-3 (-39, 32)	
30 - <35	-9 (-18, 0)		11 (4, 18)		-1 (-4, 3)		-23 (-63, 18)	
≥ 35	-8 (-20, 4)		5 (-3, 13)		-2 (-6, 2)		-12 (-48, 24)	
eGFR (per 10 mL/min/1.73m^2)	-2 (-3, 0)	0.071	0 (-2, 2)	0.947	0 (-1, 1)	0.789	2 (-7, 11)	0.677
Bioavailable 25(OH)D (per 1 ng/mL decrement)	-4 (-7, -1)	0.009	1 (-2, 3)	0.586	2 (1, 3)	0.001	6 (-4, 16)	0.210
25(OH)D (ng/mL)								
< 20	-14 (-24, -3)		0 (-8, 7)		6 (2, 9)		11 (-23, 45)	
20 – <30	1 (-6, 7)		5 (-2, 13)		5 (2, 8)		14 (-18, 46)	
≥ 30	Ref	0.022	Ref	0.282	Ref	<0.001	Ref	0.677
Per 10 ng/mL decrement	-4 (-8, -1)	0.011	1 (-2, 3)	0.575	2 (1, 4)	0.002	10 (-2, 22)	0.101
VDBP (per 1 SD increment)	0 (-3, 3)	0.936	1 (-3, 4)	0.740	0 (-2, 1)	0.407	-1 (-14, 12)	0.878
VDMR tertiles								
Tertile 1	-10 (-18, -2)		1 (-6, 8)		5 (1, 8)		-1 (-38, 35)	
Tertile 2	-1 (-8, 5)		-1 (-8, 7)		3 (0, 6)		9 (-21, 39)	

Tertile 3	Ref	0.062	Ref	0.900	Ref	0.033	Ref	0.802
Per 1 SD decrement	-3 (-7, 0)	0.055	1 (-2, 4)	0.555	2 (0, 3)	0.026	-2 (-16, 11)	0.724

PTH, parathyroid hormone; $1,25(OH)_2D$, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; BMI, body mass index; eGFR, estimated glomerular filtration rate; VDBP, vitamin D binding protein; VDMR, vitamin D metabolite ratio (24,25-dihydroxyvitamin D_3 to $25(OH)D_3$).

[1]Differences in change in each outcome after 16-weeks of treatment comparing vitamin D_3 with placebo, adjusted for age, sex, race/ethnicity, BMI, eGFR and season at baseline exam, and accounts for missing data using multiple imputation.

Supplemental Table 2. Associations of Baseline 25-Hydroxyvitamin D Categories with Change in Parathyroid Hormone (pg/mL) Among Participants Assigned to Vitamin D_3

			Unadjusted Model	Adjusted Model[1]	
Variable	**N**	**Change in PTH from baseline, mean (95% CI)**	**Difference in change in PTH (95% CI)[2]**	**Difference in change in PTH (95% CI)[2]**	**P-value**
25(OH)D (ng/mL)					<0.001
<12	20	-19 (-34, -5)	-19 (-26, -11)	-19 (-26, -12)	
12 – <20	59	-8 (-11, -4)	-7 (-11, -3)	-7 (-12, -3)	
20 – <30	144	-3 (-5, -1)	-2 (-5, 1)	-3 (-6, 1)	
≥ 30	230	-1 (-2, 1)	Ref	Ref	

25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone.

[1]Adjusted for age, sex, race/ethnicity, BMI, eGFR and season at baseline exam.
[2]Modeled estimates account for missing data using multiple imputation.

Supplemental Table 3. Associations of Baseline Characteristics with Change in Serum Total 1,25-Dihydroxyvitamin D Concentration (pg/mL) Among Participants Assigned to Vitamin D_3

			Unadjusted Model	Adjusted Model[1]	
Variable	**N**	**Change in total $1,25(OH)_2D$ from baseline, mean (95% CI)[2]**	**Difference in change in total $1,25(OH)_2D$ (95% CI)[3]**	**Difference in change in total $1,25(OH)_2D$ (95% CI)[3]**	**P-value**
Age (per decade)	499		0 (-2, 2)	0 (-2, 2)	0.785
Sex					
Female	272	2 (0, 4)	Ref	Ref	0.412
Male	227	1 (-1, 3)	-1 (-4, 2)	-1 (-4, 2)	
Race/ethnicity					
White	169	3 (0, 5)	Ref	Ref	0.279
Black	184	3 (0, 5)	0 (-3, 4)	0 (-3, 4)	
Hispanic	82	1 (-3, 5)	-1 (-6, 3)	-2 (-6, 3)	
Chinese	64	-2 (-6, 2)	-4 (-9, 0)	-5 (-10, 0)	
BMI (kg/m^2)					
< 25	127	1 (-2, 4)	Ref	Ref	0.876
25 - <30	189	1 (-1, 4)	0 (-3, 4)	0 (-4, 3)	
30 - <35	107	2 (-1, 5)	1 (-3, 5)	0 (-4, 5)	
≥ 35	76	4 (0, 7)	3 (-2, 7)	1 (-4, 7)	
eGFR (per 10 $mL/min/1.73m^2$)	499		0 (-1, 1)	0 (-1, 1)	0.817
Bioavailable 25(OH)D (per 1 ng/mL decrement)	499		0 (-1, 1)	0 (-1, 1)	0.714
25(OH)D (ng/mL)					
< 20	79	3 (-1, 7)	2 (-3, 6)	2 (-3, 6)	
20 – <30	144	2 (-1, 4)	0 (-3, 3)	0 (-3, 4)	
≥ 30	230	1 (-1, 4)	Ref	Ref	0.731
Per 10 ng/mL decrement	499		0 (-1, 2)	1 (-1, 2)	0.441
VDBP (per 1 SD increment)	499		1 (-1, 2)	1 (0, 3)	0.117
VDMR tertiles[4]					
Tertile 1	149	3 (0, 5)	0 (-3, 4)	0 (-4, 4)	
Tertile 2	155	0 (-2, 3)	-3 (-6, 1)	-2 (-6, 1)	
Tertile 3	149	3 (0, 5)	Ref	Ref	0.323
Per 1 SD decrement	499		0 (-1, 2)	0 (-1, 2)	0.664

$1,25(OH)_2D$, 1,25-dihydroxyvitamin D; BMI, body mass index; eGFR, estimated glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; VDBP, vitamin D binding protein; VDMR, vitamin D metabolite ratio (24,25-dihydroxyvitamin D_3 to $25(OH)D_3$).

[1]Adjusted for age, sex, race/ethnicity, BMI, eGFR and season at baseline exam.
[2]Change from baseline after 16 weeks of vitamin D_3 summarized over all participants (N = 499) using multiple imputation. The mean (95% CI) among all vitamin D_3 participants was 2 (0, 3) pg/mL.
[3]Modeled estimates account for missing data using multiple imputation.
[4]Tertile cut points are based on the entire study population.

Supplemental Table 4. Associations of Baseline Characteristics with Change in Serum Total 25-Hydroxyvitamin D Concentration (ng/mL) Among Participants Assigned to Vitamin D_3

			Unadjusted Model	Adjusted Model[1]	
Variable	**N**	**Change in total 25(OH)D from baseline, mean (95% CI)[2]**	**Difference in change in total 25(OH)D (95% CI)[3]**	**Difference in change in total 25(OH)D (95% CI)[3]**	**P-value**
Age (per decade)	499		1 (0, 2)	0 (-1, 2)	0.740
Sex					
Female	272	11 (9, 12)	Ref	Ref	0.773
Male	227	10 (9, 12)	0 (-2, 1)	0 (-1, 2)	
Race/ethnicity					
White	169	11 (9, 13)	Ref	Ref	0.238
Black	184	11 (10, 13)	1 (-2, 3)	1 (-1, 3)	
Hispanic	82	9 (7, 10)	-2 (-4, 1)	-2 (-4, 1)	
Chinese	64	11 (9, 13)	0 (-3, 3)	0 (-3, 3)	
BMI (kg/m^2)					
< 25	127	12 (10, 13)	Ref	Ref	0.513
25 - <30	189	10 (9, 12)	-1 (-4, 1)	-1 (-4, 1)	
30 - <35	107	11 (9, 13)	-1 (-3, 2)	-1 (-4, 2)	
≥ 35	76	9 (8, 11)	-2 (-5, 1)	-2 (-6, 1)	
eGFR (per 10 mL/min/1.73m^2)	499		0 (-1, 0)	-1 (-1, 0)	0.095
Bioavailable 25(OH)D (per 1 ng/mL decrement)	499		3 (3, 4)	4 (3, 4)	<0.001
25(OH)D (ng/mL)					
< 20	79	17 (15, 19)	10 (7, 12)	11 (9, 14)	<0.001
20 – <30	144	12 (10, 14)	4 (2, 6)	6 (4, 7)	
≥ 30	230	8 (7, 9)	Ref	Ref	
Per 10 ng/mL decrement	499		4 (3, 4)	4 (4, 5)	<0.001
VDBP (per 1 SD increment)	499		0 (-1, 1)	0 (-1, 1)	0.371
VDMR tertiles[4]					
Tertile 1	149	14 (13, 15)	6 (4, 8)	7 (5, 9)	
Tertile 2	155	10 (9, 11)	2 (0, 4)	2 (0, 5)	
Tertile 3	149	8 (6, 10)	Ref	Ref	<0.001
Per 1 SD decrement	499		3 (2, 4)	3 (2, 4)	<0.001

BMI, body mass index; eGFR, estimated glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; VDBP, vitamin D binding protein; VDMR, vitamin D metabolite ratio (24,25-dihydroxyvitamin D_3 to 25(OH)D_3).

[1]Adjusted for age, sex, race/ethnicity, BMI, eGFR and season at baseline exam.
[2]Change from baseline after 16 weeks of vitamin D_3 summarized over all participants (N = 499) using multiple imputation. The mean (95% CI) among all vitamin D_3 participants was 11 (10, 11) ng/mL.
[3]Modeled estimates account for missing data using multiple imputation.
[4]Tertile cut points are based on the entire study population.

Supplemental Table 5. Associations of Baseline Characteristics with Change in Urine Calcium Excretion Among Participants Assigned to Vitamin D_3

			Unadjusted Model	Adjusted Model[1]	
Variable	**N**	**Change in urine calcium excretion from baseline, mean (95% CI)[2]**	**Difference in change in urine calcium excretion (95% CI)[3]**	**Difference in change in urine calcium excretion (95% CI)[3]**	**P-value**
Age (per decade)	499		5 (-4, 15)	5 (-6, 17)	0.338
Sex					
Female	272	13 (2, 24)	Ref	Ref	
Male	227	3 (-5, 11)	-10 (-25, 5)	-10 (-25, 5)	0.197
Race/ethnicity					
White	169	10 (-4, 24)	Ref	Ref	0.974
Black	184	8 (-2, 17)	-2 (-20, 16)	-1 (-19, 17)	
Hispanic	82	10 (-5, 24)	0 (-22, 22)	-1 (-23, 22)	
Chinese	64	6 (-20, 32)	-4 (-28, 20)	-6 (-31, 19)	
BMI (kg/m^2)					
< 25	127	13 (-2, 28)	Ref	Ref	0.648
25 - <30	189	11 (-3, 24)	-3 (-22, 16)	-3 (-23, 17)	
30 - <35	107	7 (-4, 18)	-7 (-28, 15)	-7 (-30, 16)	
≥ 35	76	-2 (-15, 11)	-15 (-40, 9)	-16 (-43, 11)	
eGFR (per 10 mL/min/1.73m^2)	499		0 (-5, 4)	1 (-4, 6)	0.687
Bioavailable 25(OH)D (per 1 ng/mL decrement)	499		3 (-3, 9)	4 (-2, 10)	0.186
25(OH)D (ng/mL)					
< 20	79	8 (-4, 21)	3 (-19, 24)	8 (-14, 31)	
20 – <30	144	13 (0, 26)	8 (-9, 24)	10 (-7, 28)	
≥ 30	230	6 (-6, 17)	Ref	Ref	0.483
Per 10 ng/mL decrement	499		2 (-5, 9)	4 (-3, 12)	0.282
VDBP (per 1 SD increment)	499		-5 (-12, 3)	-4 (-12, 4)	0.345
VDMR tertiles[4]					
Tertile 1	149	12 (1, 24)	5 (-12, 24)	9 (-11, 28)	0.661
Tertile 2	155	6 (-8, 20)	0 (-19, 18)	2 (-17, 22)	
Tertile 3	149	7 (-7, 20)	Ref	Ref	
Per 1 SD decrement	499		0 (-7, 8)	1 (-6, 9)	0.721

BMI, body mass index; eGFR, estimated glomerular filtration rate; 25(OH)D, 25-hydroxyvitamin D; VDBP, vitamin D binding protein; VDMR, vitamin D metabolite ratio (24,25-dihydroxyvitamin D_3 to 25(OH)D_3).

[1]Adjusted for age, sex, race/ethnicity, BMI, eGFR and season at baseline exam.
[2]Change in spot urine calcium to creatinine ratio (mg/g) from baseline after 16 weeks of vitamin D_3 summarized over all participants (N = 499) using multiple imputation. The mean (95% CI) among all vitamin D_3 participants was 9 (1, 16) mg/g.
[3]Modeled estimates account for missing data using multiple imputation.
[4]Tertile cut points are based on the entire study population.

Supplemental Table 6. Adverse Events

Outcome by Organ System	**Placebo (N = 167), N (%)**	**Vitamin D_3 (N = 499), N (%)**
Cardiac disorders	1 (1)	5 (1)
Gastrointestinal disorders	6 (4)	22 (4)
General disorders and administration site conditions	1 (1)	8 (2)
Immune system disorders	2 (1)	8 (2)
Metabolism and nutrition disorders	1 (1)	2 (<1)
Musculoskeletal, connective tissue and bone disorders	2 (1)	5 (1)
Neoplasms benign, malignant and unspecified	0 (0)	1 (<1)
Psychiatric disorders	1 (1)	0 (0)
Renal and urinary tract disorders	2 (1)	1 (<1)
Respiratory, thoracic and mediastinal disorders	0 (0)	2 (<1)
Unknown	0 (0)	1 (<1)

Supplemental Figure 1. Participant Flow in the Multi-Ethnic Study of Atherosclerosis Individualized Response to Vitamin D Treatment Trial