

Supplemental Materials

for

Safety Profile of Vitamin D Supplements Using Real-World Data from 445,493 Participants of the UK Biobank: Slightly Higher Hypercalcemia Prevalence but Neither Increased Risks of Kidney Stones nor Atherosclerosis

Table of Contents

Table S1. Complete list of baseline characteristics of the population analyzed (N=445,493).....	2
Table S2. Overviews of baseline characteristics for study population in the four analytical datasets	7
Table S3. Cross-sectional associations of vitamin D serum status and vitamin supplement use with hypercalcemia, subgroup analysis by age groups	9
Table S4. Cross-sectional associations of vitamin D serum status and vitamin supplement use with hypercalcemia, subgroup analysis by sex	10
Table S5. Cross-sectional associations of vitamin D serum status as well as vitamin supplement use with hypercalcemia, subgroup analyses by kidney function	11
Table S6. Longitudinal associations of vitamin D serum status and vitamin supplement use with kidney stones, subgroup analysis by age groups	12
Table S7. Longitudinal associations of vitamin D serum status as well as vitamin supplement use with kidney stones, subgroup analysis by sex.....	13
Table S8. Longitudinal associations of vitamin D serum status as well as vitamin supplement use with kidney stones, subgroup analyses by kidney function.....	14
Figure S1. Distribution of serum 25-hydroxyvitamin D concentration among regular vitamin D supplement users stratified by hypercalcemia status.....	15

Table S1. Complete list of baseline characteristics of the population analyzed (N=445,493)

Variables	N (%)^{a/} Median (IQR)
SOCIO-DEMOGRAPHIC/ -ECONOMIC FACTORS	
Age (years), median (IQR)	58 (50; 63)
Sex, n (%)	
Female	238,942 (53.6)
Male	206,551 (46.4)
Education (years), median (IQR)	11 (10; 17)
Townsend deprivation index (points), median (IQR)	-0.3 (-0.7; 0.4)
No. of individuals in household, n (%)	
1	81,563 (18.3)
2	206,572 (46.4)
3-4	130,470 (29.3)
≥ 5	23,885 (5.3)
Annual household income (£), n (%)	
< 18,000	85,742 (19.2)
18,000 - < 30,999	96,749 (21.7)
31,000- < 51,999	100,058 (22.5)
52,000 - < 100,000	78,640 (17.7)
≥ 100,000	21,000 (4.7)
LIFE-STYLE FACTORS	
Smoking, n (%)	
Never	244,481 (54.9)
Occasionally	63,247 (14.2)
Regularly	137,621 (30.9)
Alcohol consumption (g ethanol/d), n (%)	
Abstainer	137,944 (31.0)
Women 0 - < 20 / men 0 - < 40	178,258 (40.0)
Women 20 - < 40 / men 40 - < 60	75,677 (17.0)
Women ≥ 40 / men ≥ 60	53,614 (12.0)
Venturesome personality, n (%)	
No	313,093 (70.3)
Yes	115,706 (26.0)
Total physical activity (hours/day), n (%)	
≤ 1	63,786 (14.3)
≤ 2	140,699 (31.6)
> 2	142,047 (31.9)
Frequency of visiting friends/family, n (%)	
Almost daily	59,760 (13.4)
2-4 times/week	158,268 (35.5)
Once/week	136,111 (30.6)
Once every few months/rare	51,555 (11.6)
Oily fish consumption, n (%)	
Never/ less than once a week	195,508 (43.9)
At least once a week	247,484 (55.6)
Cereal consumption (bowls/week), n (%)	
Never	75,841 (17.0)
< 7	198,082 (44.5)
≥ 7	170,066 (38.2)

Variables	N (%) ^{a/} Median (IQR)
Processed meat intake, n (%)	
Never/ less than once a week	176,398 (39.6)
At least once a week	268,147 (60.2)
Milk consumption, n (%)	
Never/rarely	14,590 (3.3)
Occasionally/regularly	430,583 (96.7)
Spread consumption, n (%)	
Never/rarely	48,201 (10.8)
Butter	160,664 (36.1)
Margarine/others	235,855 (52.9)
Preferred bread type, n (%)	
White	113,435 (25.5)
Wholemeal/wholegrain/brown	316,220 (70.9)
DISEASES & DISEASE SYMPTOMS	
Diabetes, n (%)	
No	423,131 (94.9)
Yes	22,264 (5.1)
Stroke, n (%)	
No	439,410 (98.6)
Yes	5,984 (1.3)
CHD, n (%)	
No	424,553 (95.3)
Yes	20,841 (4.7)
COPD, n (%)	
No	443,907 (99.6)
Yes	1,487 (0.3)
Hypertension, n (%)	
No	325,480 (73.1)
Untreated hypertension	33,253 (7.5)
Treated hypertension	86,671 (19.5)
Asthma, n (%)	
No	393,732 (88.4)
Yes	51,662 (11.6)
Osteoporosis, n (%)	
No	434,431 (97.5)
Yes	10,963 (2.5)
Fracture in last 5 years, n (%)	
No	401,340 (90.1)
Yes	41,918 (9.4)
Arthritis, n (%)	
No	398,918 (89.5)
Yes	46,476 (10.4)
Gout, n (%)	
No	438,211 (98.4)
Yes	7,183 (1.6)
Parkinson, n (%)	
No	444,460 (99.8)
Yes	934 (0.2)
Depressed mood in last 2 weeks, n (%)	
≤ half the days	404,447 (90.8)

Variables	N (%)^{a/} Median (IQR)
> half the days	21,023 (4.7)
Tiredness/lethargy in last 2 weeks, n (%)	
≤ half the days	377,274 (84.7)
> half the days	54,403 (12.2)
Chronic fatigue syndrome, n (%)	
No	443,479 (99.5)
Yes	1,915 (0.4)
Hypothyroidism, n (%)	
No	423,940 (95.2)
Yes	21,454 (4.8)
Dementia, n (%)	
No	442,754 (99.4)
Yes	2,640 (0.6)
Cancer, n (%)	
No	410,621 (92.2)
Yes	33,570 (7.5)
Hyperparathyroidism, n (%)	
No	444,910 (99.9)
Yes	583 (0.1)
BIOMARKERS	
BMI (kg/m²), n (%)	
Underweight, < 18.5	2,285 (0.5)
Low normal weight, 18.5 - <20	8,188 (1.8)
High normal weight, 20 - < 25	137,420 (30.8)
Overweight: 25 - < 30	188,111 (42.2)
Obesity class I: 30 - < 35	77,278 (17.3)
Obesity class II: 35 - < 40	22,021 (4.9)
Obesity class III: ≥ 40	8,515 (1.9)
Waist circumference (cm), median (IQR)	90 (80; 99)
eGFR (ml/min/1.73 m²), n (%)	
≥ 90	264,715 (59.4)
< 90	180,237 (40.5)
HbA_{1c}, (%), n (%)	
< 6	411,465 (92.4)
6 - < 6.5	17,488 (3.9)
6.5 - < 7	6,204 (1.4)
7 - < 8	5,972 (1.3)
≥ 8	4,364 (1.0)
HDL cholesterol (mg/dl), n (%)	
< 40	89,800 (20.1)
≥ 40	355,693 (79.8)
SBP (mmHg), n (%)	
< 140	236,879 (53.2)
140 - < 160	140,521 (31.5)
160 - < 180	53,988 (12.1)
≥ 180	14,105 (3.2)
DBP (mmHg), n (%)	
< 90	339,609 (76.2)
90 - < 100	80,476 (18.1)
≥ 100	25,408 (5.7)

Variables	N (%)^{a/} Median (IQR)
C-reactive protein (mg/L), n (%)	
< 1	177,546 (39.9)
≥ 1	267,947 (60.1)
FEV1 (L), median (IQR)	2.8 (2.3; 3.3)
Hand grip strength (Kg), median (IQR)	31 (24; 40)
GENERAL HEALTH	
Disability (%)	
No	416,119 (93.4)
Yes	25,799 (5.8)
General self-reported health, n (%)	
Excellent	73,626 (16.5)
Good	257,527 (57.8)
Fair	92,895 (20.9)
Poor	19,507 (4.4)
No of chronic diseases, median (IQR)	2 (1; 3)
No of drugs, median (IQR)	2 (0; 4)
Low-dose aspirin use, n (%)	
No	382,319 (85.8)
Yes	63,075 (14.2)
Lipid-lowering drugs use, n (%)	
No	365,816 (82.1)
Yes	79,585 (17.9)
Anti-depressants use, n (%)	
No	416,037 (93.4)
Yes	29,357 (6.6)
VITAMIN D SPECIFIC FACTORS	
Latitude of study center (per 1°), median (IQR)	53.0 (51.5; 53.8)
Month of attending the study center (month of blood draw)	
1	30,516 (6.8)
2	35,121 (7.9)
3	43,433 (9.7)
4	38,830 (8.7)
5	46,372 (10.4)
6	46,028 (10.3)
7	38,137 (8.6)
8	33,952 (7.6)
9	32,617 (7.3)
10	38,241 (8.6)
11	37,335 (8.4)
12	24,911 (5.6)
Time spent outdoors in summer (h/day), n (%)	
<1	18,616 (4.2)
1-2	130,269 (29.2)
3-4	138,749 (31.1)
5-6	84,309 (18.9)
≥ 7	48,338 (10.9)
Time spent outdoors in winter (h/day), n (%)	

Variables	N (%)^a
	Median (IQR)
<1	83,763 (18.8)
1-2	238,767 (53.6)
3-4	63,525 (14.3)
≥ 5	34,082 (7.6)
Skin color, n (%)	
Very fair	34,021 (7.6)
Fair	299,581 (67.2)
Olive	81,675 (18.3)
Brown	8,248 (1.9)
Black	12,428 (2.8)
Unknown	3,364 (0.8)
Ease of skin tanning, n (%)	
Very tanned	94,016 (21.1)
Moderately tanned	173,061 (38.8)
Mildly/occasionally tanned	91,909 (20.6)
Never tan, only burn	74,631 (16.8)
Sun screen/UV protection use, n (%)	
Never/rarely	44,849 (10.1)
Sometimes	148,262 (33.3)
Most of times	157,360 (35.3)
Always	91,671 (20.6)
Do not go out in sunshine	2,666 (0.6)
Solarium/sunlamp use (times per year), n (%)	
Never	399,596 (89.7)
< 1	21,586 (4.8)
1 - 6	10,720 (2.4)
7 - 12	4,624 (1.0)
> 12	4,390 (1.0)

Abbreviations: BMI: body mass index CHD: coronary heart disease, COPD: chronic obstructive pulmonary disease, DBP: diastolic blood pressure, eGFR: estimated Glomerular filtration rate, FEV1: Forced expiratory volume in 1-second, IQR: interquartile range, SBP: systolic blood pressure

^a Denominators in proportion calculations contain missing values.

Table S2. Overviews of baseline characteristics for study population in the four analytical datasets

Variables	Dataset for analysis of			
	Hypercalcemia N=407,185	Kidney stone N= 439,189	PASI N=150,117	CIMT N=43,958
	N (%) ^a /Median (IQR)			
Sex, n (%)				
Female	216,671 (53.2)	237,079 (54.0)	80,118 (53.4)	22,710 (51.7)
Male	190,514 (46.8)	202,110 (46.0)	69,999 (46.6)	21,248 (48.3)
Age (years)				
Mean (SD)	56.5 (8.1)	56.4 (8.1)	56.7 (8.2)	55.1 (7.6)
Median (IQR)	58 (50; 63)	58 (50; 63)	58 (50; 63)	56 (49; 61)
BMI, n (%)				
< 18.5	2,092 (0.5)	2,268 (0.5)	768 (0.5)	195 (0.4)
18.5 - <25	132,408 (32.5)	144,148 (32.9)	49,001 (32.7)	17,241 (39.3)
25 - < 30	172,089 (42.3)	185,336 (42.2)	63,333 (42.2)	18,834 (42.8)
≥30	99,049 (24.3)	105,802 (24.1)	36,838 (24.5)	7631 (17.3)
Smoking, n (%)				
Never	223,218 (54.8)	241,248 (54.9)	83,003 (55.3)	26,626 (60.6)
Ever	183,833 (45.0)	197,799 (45.1)	67,050 (44.7)	17,327 (39.4)
Alcohol consumption ^b, n (%)				
Abstainer	126,017 (30.9)	135,739 (30.9)	49,074 (32.7)	10,442 (23.8)
Low	163,194 (40.1)	175,571 (40.0)	59,889 (39.9)	19,244 (43.8)
Medium	69,070 (17.0)	74,854 (17.0)	23,981 (16.0)	8,559 (19.5)
High	48,904 (12.0)	53,025 (12.1)	17,173 (11.4)	5,713 (13.0)
Hypertension, n (%)	109,824 (27.0)	117,488 (26.7)	40,838 (27.2)	8,554 (19.4)
Diabetes, n (%)	20,356 (5.1)	21,662 (4.9)	8,209 (5.5)	1,092 (2.5)
CHD, n (%)	19,089 (4.7)	20,311 (4.6)	6,774 (4.5)	1,051 (2.4)
eGFR (ml/min/1.73 m²), n (%)				
≥ 90	242,500 (59.6)	261,252 (59.5)	87,250 (58.1)	27,130 (61.7)
60-< 90	155,290 (38.1)	167,534 (38.1)	59,184 (39.4)	16,232 (36.9)
< 60	9,157 (2.2)	9,868 (2.2)	3,487 (2.3)	539 (1.2)
Hypercalcemia	6,325 (1.6)	-	-	-
Kidney stones during follow-up, n (%)	-	5,097 (1.2)	-	-
PASI, Median (IQR)	-	-	9.0 (6.9; 11.1)	-
Adversely high PASI ^c, n (%)	-	-	11,473 (7.6)	-
Average of mean CIMT, Median (IQR)	-	-	-	0.67 (0.60; 0.76)
Adversely high CIMT > 0.9 mm, n (%)	-	-	-	2,713 (6.2)
No. of chronic diseases, Median (IQR)	2 (1;3)	2 (1;3)	2 (1;3)	1 (0;2)
25(OH)D concentration (nmol/L), Median (IQR)	46.8 (32.3; 62.4)	46.9 (32.4; 62.5)	48.5 (33.7; 64.0)	48.1 (33.9; 63.4)
Vitamin D status, n (%)				
Deficiency (<30 nmol/L)	85,776 (21.1)	92,063 (21)	28,842 (19.2)	8091 (18.4)
Insufficiency (30- <50 nmol/L)	140,013 (34.4)	150,657 (34.3)	49,880 (33.2)	15,327 (34.9)
Sufficiency (50 - < 100 nmol/L)	175,302 (43.1)	189,875 (43.2)	68,827 (45.8)	19,844 (45.1)
High status (≥ 100 nmol/L)	6,094 (1.5)	6,594 (1.5)	2,568 (1.7)	696 (1.6)
Regular vitamin supplement use, n (%)				
No	306,849 (75.4)	330,625 (75.3)	112,249 (74.8)	32,925 (74.9)
Multivitamins +/-minerals	82,793 (20.3)	89,638 (20.4)	30,863 (20.6)	9,246 (21.0)
Vitamin D	17,543 (4.3)	18,926 (4.3)	7,005 (4.7)	1,787 (4.1)

Abbreviations: 25(OH)D: 25-hydroxyvitamin D, BMI: body mass index, CHD: coronary heart disease, CIMT: carotid intima-medial thickness, eGFR: estimated glomerular filtration rate, IQR: interquartile range, PASI: pulse wave arterial stiffness index, SD: standard deviation.

^a Denominators in proportion calculations contain missing values.

^b Alcohol consumption: Low: Women > 0-19.99 grams of ethanol per day (g/d) or men > 0-39.99 g/d; Medium: Women 20-39.99 g/d or men 40-59.99 g/d; High: Women \geq 40g/d or men \geq 60 g/d.

^c Based on calculated age specific cut-off values.

Table S3. Cross-sectional associations of vitamin D serum status and vitamin supplement use with hypercalcemia, subgroup analysis by age groups

Vitamin D exposure	Age, 40 - 59 years ^a			Age, 60 - 69 years ^b			p-interaction ^c
	N=231,560			N=175,625			
	N _{total}	N _{case} (%)	OR (95%CI)	N _{total}	N _{case} (%)	OR (95%CI)	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency (<30)	55,930	676(1.2)	0.94(0.84,1.05)	29,846	538(1.8)	0.95(0.85,1.06)	0.93
Insufficiency (30-<50)	81,079	1,060(1.3)	1.00(0.92,1.10)	58,934	1,084(1.8)	0.96(0.89,1.05)	0.97
Sufficiency (50-<100)	91,177	1,237(1.4)	Ref	84,125	1,634(1.9)	Ref	-
High status (≥100)	3,374	37(1.1)	0.80(0.58,1.12)	2,720	59(2.2)	1.13(0.87,1.48)	0.36
Vitamin supplement use							
Non-users	175,023	2,141(1.2)	Ref	131,826	2,329(1.8)	Ref	-
Multivitamin user	48,331	679(1.4)	1.12(1.02,1.22)	34,462	695(2.0)	1.10(1.01,1.20)	0.21
Vitamin D user	8,206	190(2.3)	1.55(1.33,1.82)	9,337	291(3.1)	1.39(1.22,1.58)	0.26

Abbreviations: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, HR: hazard ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

All covariates were adjusted in the model (see the legend of Table 2)

^a including as small minority of study participants aged 37-39 years (n=6)

^b including as small minority of study participants aged 70-73 years (n=1,947)

^c Age was considered as continuous variable when calculating interaction terms.

Table S4. Cross-sectional associations of vitamin D serum status and vitamin supplement use with hypercalcemia, subgroup analysis by sex

Vitamin D exposure	Female			Male			p-interaction
	N _{total}	N _{case} (%)	OR (95%CI)	N _{total}	N _{case} (%)	OR (95%CI)	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency (<30)	45,362	794 (1.8)	0.89 (0.81, 0.98)	40,414	420 (1.0)	1.02 (0.88, 1.17)	<.001
Insufficiency (30-<50)	74,311	1,492 (2.0)	0.96 (0.90, 1.03)	65,702	652 (1.0)	1.00 (0.90, 1.12)	0.19
Sufficiency (50-<100)	93,904	2,065 (2.2)	Ref	81,398	806 (1.0)	Ref	-
High status (≥100)	3,094	67 (2.2)	1.02 (0.79, 1.31)	3,000	29 (1.0)	0.93 (0.64, 1.36)	0.97
Vitamin supplement use							
Non-users	154,733	2,983 (1.9)	Ref	152,116	1,487 (1.0)	Ref	-
Multivitamin user	49,521	1,017 (2.1)	1.10 (1.02, 1.18)	33,272	357 (1.1)	1.14 (1.01, 1.28)	0.63
Vitamin D user	12,417	418 (3.4)	1.50 (1.34, 1.67)	5,126	63 (1.2)	1.20 (0.93, 1.56)	0.59

Abbreviation: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, HR: hazard ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

All covariates were adjusted in the model (see the legend of Table 2)

Table S5. Cross-sectional associations of vitamin D serum status as well as vitamin supplement use with hypercalcemia, subgroup analyses by kidney function

Vitamin D exposure	eGFR < 60 ml/min/1.73m ²		eGFR 60-<90 ml/min/1.73m ²		eGFR ≥ 90 ml/min/1.73m ²		p-interaction
	N _{case} (%)	OR (95%CI) ^a	N _{case} (%)	OR (95%CI) ^a	N _{case} (%)	OR (95%CI) ^a	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency	42 (2.2)	0.64 (0.43; 0.96)	469 (1.7)	0.97 (0.86; 1.10)	701 (1.2)	0.95 (0.86; 1.06)	0.72
Insufficiency	103 (3.3)	1.03 (0.78; 1.37)	892 (1.7)	0.96 (0.88; 1.05)	1,146 (1.4)	1.00 (0.92; 1.09)	0.27
Sufficiency	130 (3.3)	Ref	1,338 (1.8)	Ref	1,394 (1.4)	Ref	-
High status	5 (2.3)	0.67 (0.26; 1.70)	43 (1.7)	0.93 (0.68; 1.27)	47 (1.4)	1.05 (0.78; 1.42)	0.75
Vitamin supplement use							
Non-users	216 (3.0)	Ref	1,961 (1.7)	Ref	2,284 (1.3)	Ref	-
Multivitamin user	44 (3.1)	1.00 (0.71; 1.41)	588 (2.0)	1.15 (1.04; 1.26)	736 (1.4)	1.08 (0.99; 1.18)	0.21
Vitamin D user	20 (4.3)	1.09 (0.66; 1.79)	193 (2.9)	1.35 (1.15; 1.58)	268 (2.6)	1.59 (1.39; 1.82)	0.15

Abbreviation: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, eGFR: estimated Glomerular filtration rate, OR: odds ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

^aModel adjusted for all covariates (see legend of Table 2)

Table S6. Longitudinal associations of vitamin D serum status and vitamin supplement use with kidney stones, subgroup analysis by age groups

Vitamin D exposure	Age, 40 - 59 years ^a			Age, 60 - 69 years ^b			p-interaction ^c
	N=250,696			N=188,493			
	N _{total}	N _{case} (%)	HR (95%CI)	N _{total}	N _{case} (%)	HR (95%CI)	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency (<30)	60,077	713 (1.2)	1.07 (0.95, 1.20)	31,986	459 (1.4)	1.07 (0.94, 1.21)	0.75
Insufficiency (30-<50)	87,610	1,024 (1.2)	1.13 (1.03, 1.24)	63,047	835 (1.3)	1.09 (0.99, 1.20)	0.35
Sufficiency (50-<100)	99,329	954 (1.0)	Ref	90,546	1,040 (1.2)	Ref	-
High status (≥100)	3,680	35 (1.0)	1.00 (0.71, 1.40)	2,914	37 (1.3)	1.06 (0.76, 1.47)	0.78
Vitamin supplement use							
Non-users	189,248	2,167 (1.2)	Ref	141,377	1,813 (1.3)	Ref	-
Multivitamin user	52,564	486 (0.9)	0.89 (0.81, 0.99)	37,074	439 (1.3)	1.04 (0.93,1.16)	0.06
Vitamin D user	8,884	73 (0.8)	0.77 (0.61, 0.98)	10,042	119 (1.2)	1.10 (0.91,1.34)	0.12

Abbreviation: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, HR: hazard ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

All covariates were adjusted in the model (see the legend of Table 2)

^a including as small minority of study participants aged 37-39 years (n=5)

^b including as small minority of study participants aged 70-73 years (n=2,088)

^c Age was considered as continuous variable when calculating interaction terms.

Table S7. Longitudinal associations of vitamin D serum status as well as vitamin supplement use with kidney stones, subgroup analysis by sex

Vitamin D exposure	Female			Male			p-interaction
	N _{total}	N _{case} (%)	HR (95%CI)	N _{total}	N _{case} (%)	HR (95%CI)	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency (<30)	49,295	455 (0.9)	1.18 (1.02, 1.35)	42,768	717 (1.7)	1.02 (0.91, 1.13)	0.02
Insufficiency (30-<50)	81,292	657 (0.8)	1.15 (1.03, 1.29)	69,365	1,202 (1.7)	1.09 (1.01, 1.19)	0.54
Sufficiency (50-<100)	103,117	685 (0.7)	Ref	86,758	1,309 (1.5)	Ref	-
High status (≥100)	3,375	28 (0.8)	1.23 (0.84, 1.80)	3219	44 (1.4)	0.93 (0.69, 1.26)	0.19
Vitamin supplement use							
Non-users	169,252	1,333 (0.8)	Ref	161,373	2,647 (1.6)	Ref	-
Multivitamin user	54,301	374 (0.7)	0.91 (0.81, 1.02)	35,337	551 (1.6)	0.99 (0.90, 1.09)	0.21
Vitamin D user	13,526	118 (0.9)	1.05 (0.87, 1.28)	5400	74 (1.4)	0.82 (0.65, 1.03)	0.08

Abbreviation: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, HR: hazard ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

All covariates were adjusted in the model (see the legend of Table 2)

Table S8. Longitudinal associations of vitamin D serum status as well as vitamin supplement use with kidney stones, subgroup analyses by kidney function

Vitamin D exposure	eGFR < 60 ml/min/1.73m ²		eGFR 60-<90 ml/min/1.73m ²		eGFR ≥ 90 ml/min/1.73m ²		p-interaction
	N _{case} (%)	HR (95%CI) ^a	N _{case} (%)	HR (95%CI) ^a	N _{case} (%)	HR (95%CI) ^a	
Vitamin D serum status, (25[OH]D, nmol/L)							
Deficiency	49 (2.4)	1.57 (0.99, 2.50)	382 (1.3)	1.01 (0.88, 1.17)	740 (1.2)	1.09 (0.98, 1.22)	0.18
Insufficiency	57 (1.7)	1.27 (0.86, 1.89)	664 (1.2)	1.01 (0.91, 1.12)	1,136 (1.3)	1.18 (1.08, 1.29)	0.21
Sufficiency	52 (1.2)	Ref	866 (1.1)	Ref	1,071 (1.0)	Ref	-
High status	4 (1.7)	1.42 (0.50, 4.06)	36 (1.3)	1.11 (0.79, 1.56)	32 (0.9)	0.92 (0.64, 1.31)	0.23
Vitamin supplement use							
Non-users	132 (1.7)	Ref	1,535 (1.2)	Ref	2,307 (1.2)	Ref	-
Multivitamin user	20 (1.3)	0.86 (0.53, 1.40)	351 (1.1)	1.03 (0.91, 1.15)	553 (1.0)	0.92 (0.84, 1.01)	0.37
Vitamin D user	10 (2.0)	1.42 (0.73, 2.76)	62 (0.9)	0.85 (0.66, 1.10)	119 (1.1)	0.99 (0.82, 1.19)	0.60

Abbreviation: 25(OH)D: 25-hydroxyvitamin D, CI: confidence interval, eGFR: estimated Glomerular filtration rate, OR: odds ratio, Ref: reference.

Bold print: statistically significant (p<0.05).

^aModel adjusted for all covariates (see legend of Table 2)

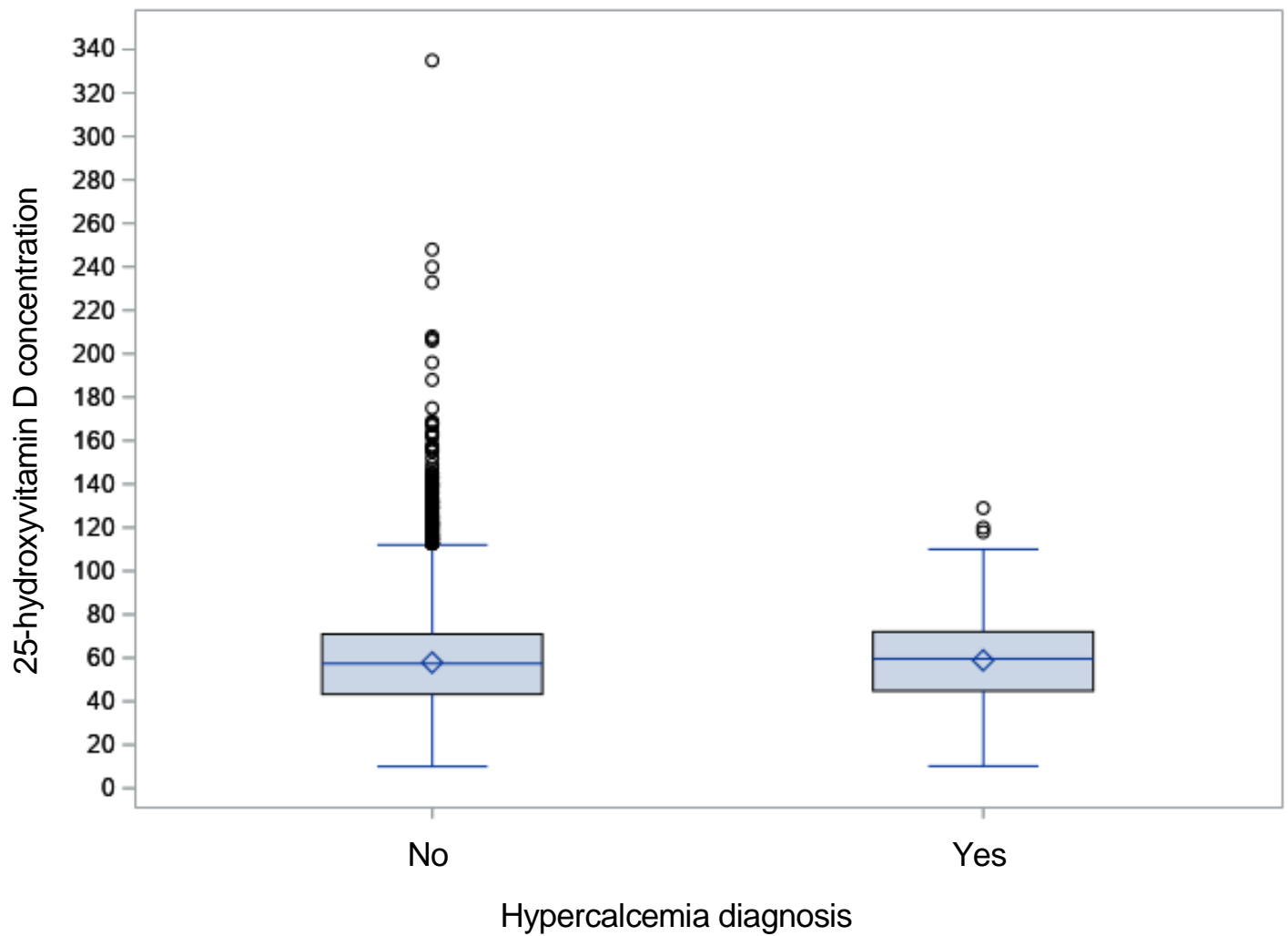


Figure S1. Distribution of serum 25-hydroxyvitamin D concentration among regular vitamin D supplement users stratified by hypercalcemia status

Notes: The sample sizes are as follows: $n_{\text{(total)}}=17,543$, $n_{\text{(without hypercalcemia)}}=17,062$, $n_{\text{(with hypercalcemia)}}=481$. The Wilcoxon rank sum test for comparing the median 25-hydroxyvitamin D levels in the groups result was $p=0.14$.