

Online Supplement

Original Research

25-Hydroxyvitamin D Deficiency Elevates the Risk of COPD Incidence and Mortality: A Large Population-Based Prospective Cohort Study

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Table S1. Baseline Characteristics of UK Biobank Participants based on COPD diagnosis

Characteristic	Total (N=328855)		COPD (N=13890)		Control (N=314965)		<i>p</i> value
	Means±SD	N(%)	Means±SD	N(%)	Means±SD	N(%)	
Age, yr	56.08±8.12		61.09±6.43		55.86±8.12		<0.001
<65	53.77±7.02	270923(82.38)	57.73±5.68	8871(63.87)	53.64±7.02	262052(83.2)	
≥65	66.88±1.48	57932(17.62)	67.01±1.50	5019(36.13)	66.87±1.48	52913(16.8)	
Sex							<0.001
Male		162045(49.28)		8073(58.12)		153972(48.89)	
Female		166810(50.72)		5817(41.88)		160993(51.11)	
BMI^b, kg/m²	27.35±4.73		28.44±5.60		27.31±4.68		<0.001
Underweight	17.64±0.79	1523(0.46)	17.44±0.94	176(1.27)	17.67±0.77	1347(0.43)	
Normal	22.83±1.52	106676(32.44)	22.67±1.64	3647(26.26)	22.83±1.51	103029(32.71)	
Overweight	27.24±1.40	141585(43.05)	27.37±1.41	5380(38.73)	27.24±1.40	136205(43.24)	
Obesity	33.84±3.85	79071(24.04)	34.57±4.39	4687(33.74)	33.79±3.81	74384(23.62)	
Smoking status							<0.001
Never		178845(54.38)		2361(17.00)		176484(56.03)	
Previous		115692(35.18)		6568(47.29)		109124(34.65)	
Current		34318(10.44)		4961(35.72)		29357(9.32)	
Alcohol intake							<0.001
Yes		306032(93.06)		12378(89.11)		314965(93.23)	
No		22823(6.94)		1512(10.89)		293654(6.77)	
Coffee intake							<0.001
Yes		258237(78.53)		10472(75.39)		247765(78.66)	
No		70618(21.47)		3418(24.61)		67200(21.34)	
Time spent outdoor, hours							0.019
In summer							
Yes		328164(99.79)		13848(99.7)		314316(99.79)	
No		691(0.21)		42(0.3)		649(0.21)	<0.001
In winter							
Yes		318172(96.75)		13338(96.03)		304834(96.78)	
No		10683(3.25)		552(3.97)		10131(3.22)	<0.001
Family income, pounds							
<18,000		71477(21.74)		6814(49.06)		64663(20.53)	
18,000-30,999		82815(25.18)		3886(27.98)		78929(25.06)	
31,000-51,999		86861(26.41)		2104(15.15)		84757(26.91)	
52,000-100,000		69110(21.02)		917(6.6)		68193(21.65)	

>100,000		18592(5.65)		169(1.22)		18423(5.85)	
sCa^e, mmol/L	2.38±0.09		2.37±0.1		2.38±0.09		<0.001
Low	2.16±0.05	6618(2.01)	2.15±0.07	416(2.99)	2.16±0.05	6202(1.97)	
Normal	2.38±0.09	321667(97.81)	2.38±0.09	13449(96.83)	2.38±0.09	308218(97.86)	
High	2.84±0.11	570(0.17)	2.85±0.14	25(0.18)	2.84±0.11	545(0.17)	
25(OH)D^d, nmol/L	48.77±21.05		45.79±21.78		48.91±21.00		<0.001
Deficiency	22.31±5.07	67797(20.62)	21.40±5.26	3792(27.3)	22.37±5.06	64005(20.32)	
Insufficiency	40.02±5.74	113576(34.54)	39.70±5.73	4621(33.27)	40.03±5.74	108955(34.59)	
Sufficiency	67.68±14.57	147482(44.84)	67.82±15.08	5477(39.43)	67.67±14.55	142005(45.09)	
Comorbidities, n (%)							<0.001
Hypertension		101872(30.98)		9009(64.86)		92863(29.48)	
CVD		33722(10.25)		4460(32.11)		29262(9.29)	
CKD		13934(4.24)		1847(13.3)		12087(3.84)	
DM		28446(8.65)		3313(23.85)		25133(7.98)	
Cancer		65356(19.87)		5067(36.48)		60289(19.14)	
Cirrhosis		1520(0.46)		213(1.53)		1307(0.41)	
Depression		20110(6.12)		2481(17.86)		17629(5.60)	

Abbreviations: SD, standard deviation; BMI, Body mass index; sCa, serum calcium; 25(OH)D, 25-hydroxyvitamin D; CVD, cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus;

^a Statistical significance was set at 2-sided $P \leq 0.05$.

^b BMI is calculated as weight in kilograms divided by height in meters squared. Underweight : BMI<18.5kg/m²; Normal :18.5-25kg/m²; Overweight: 25-30kg/m²; Obesity: BMI≥30kg/m².

^csCa categorized as 3 groups: Low: <2.2 mmol/L; Normal:2.2-2.75 mmol/L; High:>2.75 mmol/L.

^d25(OH)D was divided in to 3 categories. Deficiency: <30 nmol/L; Insufficiency: 30-50 nmol/L; Sufficiency: ≥50 nmol/L.

Table S2. Baseline Characteristics of UK Biobank Participants developing COPD within 15 years of follow-up

Characteristic	Total (N=327871)		COPD (N=12906)		Control (N=314965)		<i>p</i> value
	Means±SD	N(%)	Means±SD	N(%)	Means±SD	N(%)	
Age, yr	56.07±8.12	327871(100)	61.04±6.44	12906(3.94)	55.86±8.12	314965(96.06)	<0.001
<65	53.77±7.02	270328(82.45)	57.70±5.69	8276(64.13)	53.64±7.02	262052(83.2)	
≥65	66.89±1.48	57543(17.55)	67.01±1.50	4630(35.87)	66.88±1.48	52913(16.8)	
Sex							<0.001
Male		161493(49.26)		7521(58.28)		153972(48.89)	
Female		166378(50.74)		5385(41.72)		160993(51.11)	
BMI^b, kg/m²	27.35±4.72		28.34±5.54		27.31±4.68		<0.001
Underweight	17.65±0.79	1511(0.46)	17.46±0.94	164(1.27)	17.67±0.77	1347(0.43)	
Normal	22.83±1.52	106480(32.48)	22.68±1.63	3451(26.74)	22.84±1.51	103029(32.71)	
Overweight	27.24±1.40	141248(43.08)	27.37±1.41	5043(39.07)	27.24±1.40	136205(43.24)	
Obesity	33.84±3.84	78632(23.98)	34.51±4.35	4248(32.91)	33.80±3.81	74384(23.62)	
Ethnicity							<0.001
White		312962(95.46)		12584(97.51)		300378(95.37)	
Non-white		14156(4.32)		288(2.23)		13868(4.40)	
Smoking status							<0.001
Never		178649(54.49)		2165(16.78)		176484(56.03)	
Previous		115151(35.12)		6027(46.70)		109124(34.65)	
Current		34071(10.39)		4714(36.53)		29357(9.32)	
Alcohol intake							<0.001
Yes		305215(93.09)		11561(89.58)		314965(93.23)	
No		22656(6.91)		1345(10.42)		293654(6.77)	
Coffee intake							<0.001
Yes		257536(78.55)		9771(75.71)		247765(78.66)	
No		70335(21.45)		3135(24.29)		67200(21.34)	
Time spent outdoor, hours							
In summer							0.019
Yes		327185(99.79)		12869(99.71)		314316(99.79)	
No		686(0.21)		37(0.29)		649(0.21)	
In winter							<0.001
Yes		317243(96.76)		12409(96.15)		304834(96.78)	
No		10628(3.24)		497(3.85)		10131(3.22)	
Family income, pounds							<0.001

<18,000		70863(21.61)		6200(48.04)		64663(20.53)	
18,000-30,999		82590(25.19)		3661(28.37)		78929(25.06)	
31,000-51,999		86766(26.46)		2009(15.57)		84757(26.91)	
52,000-100,000		69069(21.07)		876(6.79)		68193(21.65)	
>100,000		18583(5.67)		160(1.24)		18423(5.85)	
sCa^c, mmol/L	2.38±0.09		2.37±0.10		2.38±0.09		<0.001
Low	2.16±0.05	6582(2.01)	2.15±0.07	380(2.94)	2.16±0.05	6202(1.97)	
Normal	2.38±0.09	320719(97.82)	2.38±0.09	12501(96.86)	2.38±0.09	308218(97.86)	
High	2.84±0.11	570(0.17)	2.86±0.14	25(0.19)	2.84±0.11	545(0.17)	
25(OH)D^d, nmol/L	48.79±21.05		46.00±21.85		48.91±21		<0.001
Deficiency	22.32±5.07	67500(20.59)	21.45±5.25	3495(27.08)	22.37±5.06	64005(20.32)	
Insufficiency	40.02±5.74	113232(34.54)	39.76±5.74	4277(33.14)	40.03±5.74	108955(34.59)	
Sufficiency	67.68±14.57	147139(44.88)	67.91±15.19	5134(39.78)	67.68±14.55	142005(45.09)	
Comorbidities^e, n (%)							<0.001
Hypertension		101187(30.86)		8324(64.5)		92863(29.48)	
CVD		33298(10.16)		4036(31.27)		29262(9.29)	
CKD		13810(4.21)		1723(13.35)		12087(3.84)	
DM		28146(8.58)		3013(23.35)		25133(7.98)	
Cancer		65005(19.83)		4716(36.54)		60289(19.14)	
Cirrhosis		1513(0.46)		206(1.60)		1307(0.41)	
Depression		19908(6.07)		2279(17.66)		17629(5.60)	

Abbreviations: SD, standard deviation; BMI, Body mass index; sCa, serum calcium; 25(OH)D, 25-hydroxyvitamin D; CVD, cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus;

^a Statistical significance was set at 2-sided $P \leq 0.05$.

^b BMI is calculated as weight in kilograms divided by height in meters squared. Underweight : BMI<18.5kg/m²; Normal :18.5-25kg/m²; Overweight: 25-30kg/m²; Obesity: BMI≥30kg/m².

^csCa categorized as 3 groups: Low: <2.2 mmol/L; Normal:2.2-2.75 mmol/L; High:> 2.75 mmol/L

^d25(OH)D was divided in to 3 categories. Deficiency: <30 nmol/L; Insufficiency: 30-50 nmol/L; Sufficiency: ≥50 nmol/L.

Table S3. Association of 25(OH)D level with COPD prevalence by Endocrine Society Clinical Practice Guideline

25(OH)D, nmol/L	OR	95%CI	<i>p</i> value
Model 1^a			<0.001
Normal	Ref		
Insufficiency	0.987	0.927-1.050	0.674
Deficiency	1.249	1.178-1.323	<0.001
Model 2^b			<0.001
Normal	Ref		
Insufficiency	0.997	0.936-1.061	0.916
Deficiency	1.360	1.283-1.442	<0.001
Model 3^c			<0.001
Normal	Ref		
Insufficiency	1.019	0.955-1.087	0.568
Deficiency	1.164	1.094-1.239	<0.001
Model 4^d			
Normal	Ref		
Insufficiency	1.031	0.965-1.102	0.365
Deficiency	1.169	1.097-1.245	<0.001

Abbreviations: OR, Odds Ratio; 95%CI, 95% Confidence Interval.

a Calculated by means of a Logistic regression analysis with no adjustment.

b Adjusted by age, sex, ethnicity, area(rural or urban) and family income.

c Adjusted for model 2 plus BMI, lifestyle (coffee take, alcohol take, smoking status, sCa, sun exposure and vitamin D supplement) and lipids(Triglycerides, Cholesterol, LDL and HDL).

d Adjusted for model 3 plus comorbidities (hypertension, CVD, CKD, DM, cancer, cirrhosis, and depression).

Table S4. Association of vitamin D level with COPD risk and COPD-specific mortality by Endocrine Society Clinical Practice Guideline

Vit D, nmol/L	Model 1 ^a		Model 2 ^b		Model 3 ^c		Model 4 ^d	
	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value	HR (95%CI)	<i>p</i> value
COPD incidence								
Normal	Ref		Ref		Ref		Ref	
Insufficiency	1.015(0.839-1.228)	0.878	1.031(0.852-1.247)	0.756	1.125(0.930-1.363)	0.226	1.146(0.947-1.388)	0.162
Deficiency	1.766(1.484-2.103)	<0.001	2.006(1.684-2.389)	<0.001	1.734(1.451-2.073)	<0.001	1.724(1.442-2.062)	<0.001
COPD-specific mortality								
Normal	Ref		Ref		Ref		Ref	
Insufficiency	1.095(0.894-1.342)	0.379	1.109(0.891-1.337)	0.398	1.198(0.977-1.470)	0.083	1.198(0.977-1.470)	0.083
Deficiency	1.558(1.293-1.878)	<0.001	1.647(1.366-1.986)	<0.001	1.654(1.366-2.004)	<0.001	1.654(1.366-2.004)	<0.001

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval.

^a Calculated by means of a Cox proportional hazards analysis with no adjustment.

^b Adjusted by age, sex, ethnic and area(rural or urban)and family income.

^c Adjusted for model 2 plus BMI, lifestyle (coffee take, alcohol take, smoking status, sCa, sun exposure and vitamin D supplement), lipids(Triglycerides, Cholesterol, LDL and HDL).

^d Adjusted for model 3 plus underlying diseases (hypertension, CVD, CKD, DM, cancer, cirrhosis, and depression).

Table S5. Stratified Analysis of Association between 25(OH)D level and COPD incidence

		cut-offs of the US-American Institute of Medicine ^a			Endocrine Society Clinical Practice Guideline ^b		
		HR (95%CI)	<i>p</i> value	<i>p</i> for interaction	HR (95%CI)	<i>p</i> value	<i>p</i> for interaction
Total population	Normal	Ref			Ref		
	Insufficiency	1.358(1.207-1.527)	<0.001		1.146(0.947-1.388)	0.162	
	Deficiency	1.874(1.659-2.117)	<0.001		1.724(1.442-2.062)	<0.001	
				0.032			0.038
Vitamin D supplement	No	Ref			Ref		
	Normal	1.322(1.146-1.525)	<0.001		1.055(0.829-1.342)	0.663	
	Insufficiency	1.867(1.617-2.155)	<0.001		1.611(1.290-2.011)	<0.001	
	Deficiency						
	Yes	Ref			Ref		
	Normal	0.824(0.425-1.600)	0.568		0.943(0.470-1.892)	0.869	
		2.073(0.098-4.163)	0.440		0.739(0.377-1.449)	0.379	
Gender	Male			0.013			0.001
	Normal	Ref			Ref		
	Insufficiency	1.399(1.205-1.601)	<0.001		1.116(0.889-1.402)	0.342	
	Deficiency	1.919(1.652-2.230)	<0.001		1.720(1.390-2.127)	<0.001	
	Female	Ref			Ref		
	Normal	1.291(1.045-1.593)	0.018		1.196(0.838-1.706)	0.324	
		1.743(1.410-2.154)	<0.001		1.700(1.218-2.373)	0.002	
Age	≥65years			0.473			0.436
	Normal	Ref			Ref		
	Insufficiency	1.248(1.055-1.476)	0.010		1.012(0.787-1.302)	0.926	
	Deficiency	1.933(1.618-2.310)	<0.001		1.496(1.179-1.899)	0.001	
	<65years						
	Normal	Ref			Ref		
	Insufficiency	1.462(1.238-1.727)	<0.001		1.329(0.989-1.786)	0.059	
	Deficiency	1.855(1.567-2.197)	<0.001		2.021(1.535-2.661)	<0.001	
	Never			0.020			0.112
		Ref			Ref		
	Normal	1.112(0.988-1.252)	0.079		1.027(0.884-1.194)	0.724	
	Insufficiency	1.062(0.963-1.171)	0.231		1.101(0.951-1.275)	0.197	

Smoking status	Precious				
	Normal	Ref		Ref	
	Insufficiency	1.056(0.995-1.120)	0.072	1.016(0.930-1.109)	0.729
	Deficiency	1.238(1.151-1.331)	<0.001	1.135(1.042-1.236)	0.004
	Current				
	Normal	Ref		Ref	
	Insufficiency	1.053(0.980-1.133)	0.159	0.994(0.887-1.115)	0.923
	Deficiency	1.257(1.173-1.347)	<0.001	1.133(1.020-1.260)	0.020

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval.

Calculated by means of a Cox proportional hazards analysis with adjustment by Model 4 included age, sex, ethnic, area, BMI, lifestyle (coffee take, alcohol take, smoking status, sCa, sun exposure, vitamin D supplement), lipids (Triglycerides, Cholesterol, LDL and HDL), family income and comorbidities

^a 25(OH) D sufficiency ≥ 20 ng/mL (50 nmol/L); Vitamin D insufficiency between 12-20 ng/mL (30-50 nmol/L) and Vitamin D deficiency < 12 ng/mL (30 nmol/L)

^b 25(OH) D sufficiency ≥ 30 ng/mL (75 nmol/L); Vitamin D insufficiency between 21-29 ng/mL (50-75 nmol/L) and Vitamin D deficiency < 20 ng/mL (50 nmol/L)

Table S6. Stratified Analysis of Association between 25(OH) D level and COPD-specific death

		cut-offs of the US-American Institute of Medicine ^a			Endocrine Society Clinical Practice Guideline ^b		
		HR (95%CI)	<i>p</i> value	<i>p</i> for interaction	HR (95%CI)	<i>p</i> value	<i>p</i> for interaction
Total population	Normal	Ref			Ref		
	Insufficiency	1.327(1.171-1.504)	<0.001		1.198(0.977-1.470)	0.083	
	Deficiency	1.598(1.406-1.816)	<0.001		1.654(1.366-2.004)	<0.001	
Vitamin D supplement	No			0.131			0.342
	Normal	Ref			Ref		
	Insufficiency	1.303(1.119-1.516)	0.001		1.194(0.923-1.546)	0.178	
	Deficiency	1.641(1.412-1.908)	<0.001		1.663(1.311-2.109)	<0.001	
	Yes						
	Normal	Ref			Ref		
Gender	Insufficiency	1.215(0.573-2.573)	0.612		1.017(0.474-2.181)	0.966	
	Deficiency	1.658(0.745-3.687)	0.215		1.406(0.640-3.087)	0.396	
	Male			0.001			0.001
	Normal	Ref			Ref		
	Insufficiency	1.289(1.106-1.503)	<0.001		1.160(0.908-1.481)	0.236	
	Deficiency	1.572(1.341-1.842)	0.001		1.570(1.249-1.973)	<0.001	
Age	Female						
	Normal	Ref			Ref		
	Insufficiency	1.381(1.108-1.721)	0.004		1.261(0.864-1.840)	0.229	
	Deficiency	1.564(1.254-1.951)	<0.001		1.754(1.229-2.503)	0.002	
	≥65years			0.305			0.248
	Normal	Ref			Ref		
Age	Insufficiency	1.293(1.083-1.544)	0.005		1.156(0.878-1.520)	0.302	
	Deficiency	1.630(1.354-1.963)	<0.001		1.594(1.227-2.070)	<0.001	
	<65years						
	Normal	Ref			Ref		
	Insufficiency	1.355(1.133-1.621)	<0.001		1.328(0.973-1.812)	0.074	
	Deficiency	1.587(1.326-1.898)	<0.001		1.803(1.354-2.402)	<0.001	
Age	Never			0.161			0.430
	Normal	Ref			Ref		
	Insufficiency	1.499(0.942-2.388)	0.088		0.947(0.455-1.973)	0.885	
	Deficiency	2.254(1.368-3.715)	0.001		1.681(0.849-3.329)	0.136	

Smoking status	Precious				
	Normal	Ref		Ref	
	Insufficiency	1.382(1.170-1.632)	<0.001	1.045(0.807-1.354)	0.737
	Deficiency	1.759(1.479-2.091)	<0.001	1.655(1.296-2.114)	<0.001
	Current				
	Normal	Ref		Ref	
	Insufficiency	1.320(1.104-1.577)	0.002	1.352(0.992-1.843)	0.056
	Deficiency	2.065(1.721-2.477)	<0.001	1.913(1.435-2.549)	<0.001

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval.

Calculated by means of a Cox proportional hazards analysis with adjustment by Model 4 included age, sex, ethnicity, area, BMI,lifestyle (coffee take, alcohol take, smoking status, serum calcium, sun exposure, vitamin D supplement), lipids(Triglycerides, Cholesterol, LDL and HDL),family income and comorbidities.

^a 25(OH) D sufficiency $\geq$ 20ng/mL(50nmol/L); insufficiency between12-20ng/mL(30-50nmol/L) and deficiency<12ng/mL(30nmol/L)

^b 25(OH) D sufficiency $\geq$ 30ng/mL(75nmol/L); insufficiency between21-29ng/mL(50-75nmol/L) and deficiency<20ng/mL(50nmol/L)

Table S7. Association of vitamin D level with COPD-specific death in Patients with COPD Comorbidities

Vit D, nmol/L	cut-offs of the US-American Institute of Medicine ^a			Endocrine Society Clinical Practice Guideline ^b		
	HR (95%CI)	<i>p</i> value	<i>p</i> for interaction	HR (95%CI)	<i>p</i> value	<i>p</i> for interaction
Total participants						
Normal	Ref			Ref		
Insufficiency	1.327(1.171-1.504)	<0.001		1.198(0.977-1.470)	0.083	
Deficiency	1.598(1.406-1.816)	<0.001		1.654(1.366-2.004)	<0.001	
DM			0.080			0.057
Normal	Ref			Ref		
Insufficiency	1.011(0.791-1.293)	0.928		1.424(0.892-2.276)	0.139	
Deficiency	1.416(1.106-1.812)	<0.001		1.567(1.005-2.443)	0.048	
Depression			0.047			0.042
Normal	Ref			Ref		
Insufficiency	1.881(1.404-2.519)	<0.001		1.925(1.121-3.307)	0.018	
Deficiency	1.924(1.430-2.590)	<0.001		3.097(1.867-5.138)	<0.001	
CHD			0.349			0.202
Normal	Ref			Ref		
Insufficiency	1.213(1.002-1.467)	0.047		1.132(0.834-1.532)	0.428	
Deficiency	1.632(1.340-1.987)	<0.001		1.512(1.315-2.014)	0.005	
Cancer			0.348			0.447
Normal	Ref			Ref		
Insufficiency	1.300(1.092-1.547)	0.003		1.216(0.920-1.608)	0.169	
Deficiency	1.657(1.379-1.990)	<0.001		1.665(1.280-2.165)	<0.001	

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval. Calculated by means of a Cox proportional hazards analysis with adjustment by Model 4 included age, sex, ethnicity, area, BMI, lifestyle (coffee take, alcohol take, smoking status, serum calcium, sun exposure, vitamin D supplement), lipids (Triglycerides, Cholesterol, LDL and HDL), family income and comorbidities.

^a Vitamin D sufficiency $\geq$ 20ng/mL (50nmol/L); Vitamin D insufficiency between 12-20ng/mL (30-50nmol/L) and Vitamin D deficiency < 12ng/mL (30nmol/L)

^b Vitamin D sufficiency $\geq$ 30ng/mL (75nmol/L); Vitamin D insufficiency between 21-29ng/mL (50-75nmol/L) and Vitamin D deficiency < 20ng/mL (50nmol/L)

Table S8. Association of vitamin D level with COPD outcomes using age, BMI, sCa as continuous variables and categorical variables

		cut-offs of the US-American Institute of Medicine ^a				Endocrine Society Clinical Practice Guideline ^b			
		categorical variables		continuous variables		categorical variables		continuous variables	
		HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value	HR (95%CI)	p value
COPD prevalence	Normal	Ref		Ref		Ref		Ref	
	Insufficiency	1.071(1.026-1.119)	0.002	1.083(1.037-1.132)	<0.001	1.031(0.965-1.102)	0.365	1.018(0.953-1.088)	0.592
	Deficiency	1.266(1.206-1.330)	<0.001	1.277(1.216-1.342)	<0.001	1.169(1.097-1.245)	<0.001	1.186(1.112-1.264)	<0.001
COPD incidence	Normal	Ref		Ref		Ref		Ref	
	Insufficiency	1.358(1.207-1.527)	<0.001	1.278(1.221-1.338)	<0.001	1.146(0.947-1.388)	0.162	1.002(0.941-1.067)	0.950
	Deficiency	1.874(1.659-2.117)	<0.001	1.915(1.816-2.217)	<0.001	1.724(1.442-2.062)	<0.001	1.744(1.677-1.816)	<0.001
specific mortality	Normal	Ref		Ref		Ref		Ref	
	Insufficiency	1.327(1.171-1.504)	<0.001	1.376(1.223-1.548)	<0.001	1.198(0.977-1.470)	0.083	1.122(0.927-1.358)	0.239
	Deficiency	1.598(1.406-1.816)	<0.001	1.665(1.475-2.011)	<0.001	1.654(1.366-2.004)	<0.001	1.768(1.478-2.116)	<0.001

Abbreviations: HR, Hazard Ratio; 95%CI, 95% Confidence Interval.

Calculated by means of a Cox proportional hazards analysis with adjustment by Model 4 included age, sex, ethnicity, area, BMI, lifestyle (coffee take, alcohol take, smoking status, sCa, sun exposure, vitamin D supplement), lipids (Triglycerides, Cholesterol, LDL and HDL), family income and comorbidities.

^a 25(OH) D sufficiency ≥ 20 ng/mL (50 nmol/L); insufficiency between 12-20 ng/mL (30-50 nmol/L) and deficiency < 12 ng/mL (30 nmol/L)

^b 25(OH) D sufficiency ≥ 30 ng/mL (75 nmol/L); insufficiency between 21-29 ng/mL (50-75 nmol/L) and deficiency < 20 ng/mL (50 nmol/L)