Supplementary Online Content

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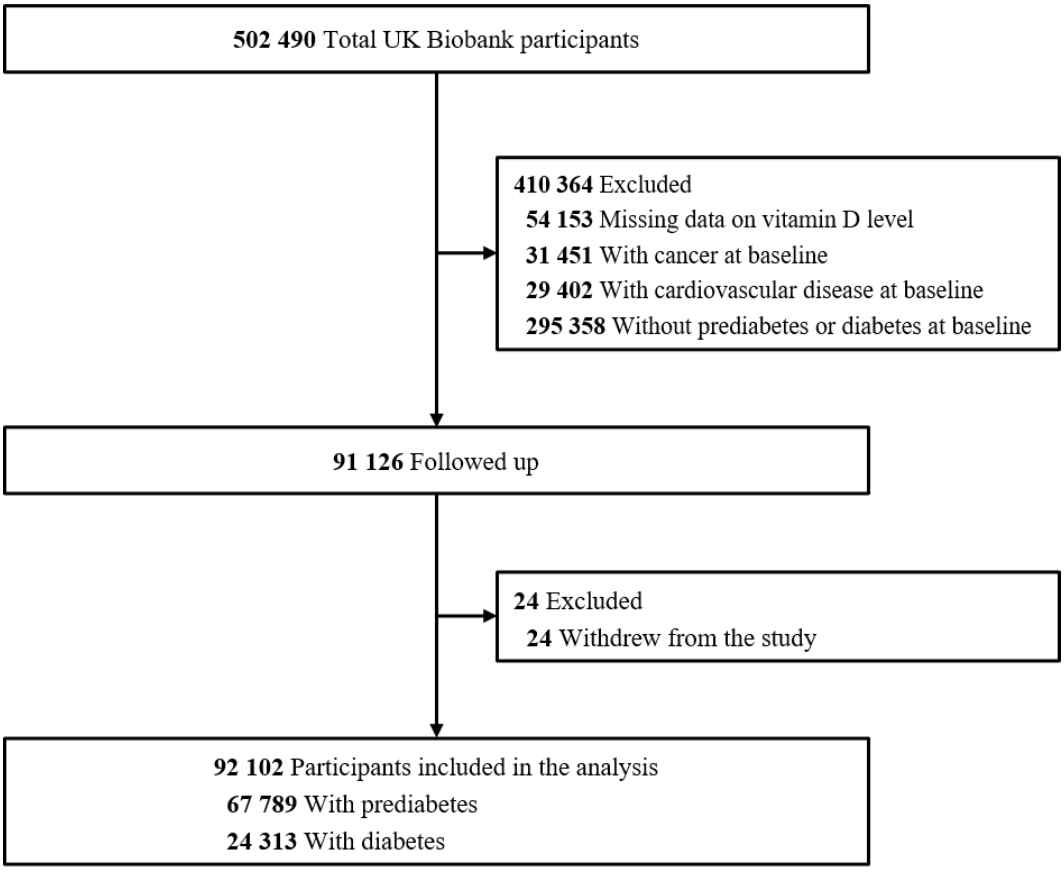

Supplementary Figure 1 Flowchart of participant enrolment.

Supplementary Table 1. Multivariable associations of serum 25(OH)D concentrations with cardiovascular risk factors among participants with prediabetes and diabetes

Cardiovascular risk factors	Model 1			Model 2		
	Regression coefficient β	Standard error	*P* value	Regression coefficient β	Standard error	*P* value
Prediabetes (N=67 789)						
Age	0.133	0.004	<0.001	0.105	0.004	<0.001
Body mass index (Kg/m^2)	-0.187	0.004	<0.001	-0.190	0.004	<0.001
Glycated haemoglobin (mmol/mol)	-0.097	0.004	<0.001	-0.072	0.004	<0.001
Fasting glucose (mmol/L)	0.031	0.004	<0.001	0.013	0.004	<0.001
Total cholesterol (mmol/L)	-0.079	0.004	<0.001	-0.092	0.004	<0.001
Triglycerides (mmol/L) *	-0.046	0.006	<0.001	-0.051	0.006	<0.001
HDL cholesterol (mmol/L)	0.100	0.004	<0.001	0.096	0.004	<0.001
LDL cholesterol (mmol/L)	-0.090	0.004	<0.001	-0.101	0.004	<0.001
Diabetes (N=24 311)						
Age	0.148	0.006	<0.001	0.126	0.006	<0.001
Body mass index (Kg/m^2)	-0.187	0.006	<0.001	-0.204	0.006	<0.001
Glycated haemoglobin (mmol/mol)	-0.140	0.006	<0.001	-0.130	0.007	<0.001
Fasting glucose (mmol/L)	-0.068	0.006	<0.001	-0.079	0.007	<0.001
Total cholesterol (mmol/L)	-0.085	0.006	<0.001	-0.099	0.006	<0.001
Triglycerides (mmol/L) *	-0.065	0.012	<0.001	-0.081	0.012	<0.001
HDL cholesterol (mmol/L)	0.109	0.006	<0.001	0.108	0.006	<0.001
LDL cholesterol (mmol/L)	-0.094	0.006	<0.001	-0.106	0.006	<0.001

* Log-transformed values.

Model 1: adjusted for age, sex.

Model 2: included model 1 variables and additionally ethnicity (white, black, Asian, Chinese, mixed, or others), season of vitamin D assessment, vitamin D supplementation (yes or no).

Supplementary Table 2. Hazard ratios for incident type 2 diabetes among participants with prediabetes

	Serum 25(OH)D concentrations (nmol/L)				P_{trend}
	<25.0	**25.0–49.9**	**50.0–74.9**	**≥75.0**	
Prediabetes (N=67 789)	10 105	29 309	21 891	6 484	
T2DM events					
Number of events	1 211/10 105	2 674/29 309	1 458/21 891	341/6 484	5 684
Crude model	1.00	0.74 (0.70-0.80)	0.54 (0.50-0.58)	0.42 (0.37-0.47)	<0.001
Model 1	1.00	0.72 (0.67-0.77)	0.50 (0.47-0.54)	0.39 (0.35-0.44)	<0.001
Model 2	1.00	0.86 (0.81-0.93)	0.72 (0.67-0.78)	0.62 (0.55-0.71)	<0.001

Crude model: without adjustment.

Model 1: adjusted for age, sex.

Model 2: included model 1 variables and additionally ethnicity(white, black, Asian, Chinese, mixed, or others), household income(<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status(never, former, or current), drinking status(never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use(yes or no), cholesterol lowering medication(yes or no), aspirin use(yes or no), vitamin D supplementation (yes or no), LDL-c. For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [<53 mmol/mol], or ≥7.0% [≥53 mmol/mol]), insulin treatment (yes or no).

Supplementary Table 3. Hazard ratios for cardiovascular events according to subgroup among participants with prediabetes and diabetes

	Serum 25(OH)D concentrations (nmol/L)					
	<25.0	**25.0–49.9**	**50.0–74.9**	**≥75.0**	P_{trend}	$P_{interaction}$
Cardiovascular events						
Prediabetes (N=67 789)						
Age (years)						
≤ 60	1.00	0.89 (0.80-0.98)	0.88 (0.79-0.99)	0.80 (0.67-0.95)	0.01	0.34
> 60	1.00	0.86 (0.78-0.94)	0.84 (0.77-0.93)	0.80 (0.71-0.91)	0.002	
Sex						
Male	1.00	0.88 (0.81-0.97)	0.88 (0.80-0.97)	0.83 (0.73-0.94)	0.009	0.03
Female	1.00	0.79 (0.71-0.88)	0.76 (0.68-0.85)	0.72 (0.61-0.84)	<0.001	
Ethnicity						
White	1.00	0.83 (0.78-0.89)	0.83 (0.77-0.89)	0.78 (0.70-0.86)	<0.001	0.96
Non-white	1.00	0.96 (0.78-1.19)	0.70 (0.51-0.97)	1.01 (0.51-1.99)	0.11	
Smoking status						
Never	1.00	0.85 (0.77-0.95)	0.91 (0.81-1.02)	0.87 (0.75-1.02)	0.45	
Previous	1.00	0.90 (0.80-1.01)	0.83 (0.73-0.93)	0.79 (0.68-0.93)	<0.001	<0.001
Current	1.00	0.81 (0.71-0.92)	0.76 (0.65-0.89)	0.67 (0.52-0.85)	<0.001	
Drinking status						
Never	1.00	0.91 (0.72-1.15)	0.68 (0.50-0.91)	0.97 (0.64-1.48)	0.11	
Previous	1.00	0.88 (0.68-1.15)	0.95 (0.71-1.28)	0.62 (0.39-1.00)	0.19	0.84
Current	1.00	0.84 (0.78-0.90)	0.83 (0.77-0.89)	0.78 (0.70-0.86)	<0.001	
Hypertension						
Yes	1.00	0.91 (0.79-1.04)	0.95 (0.82-1.09)	0.88 (0.72-1.07)	0.42	0.12
No	1.00	0.82 (0.76-0.89)	0.79 (0.73-0.86)	0.75 (0.67-0.84)	<0.001	
BMI (Kg/m^2)						
< 30	1.00	0.87 (0.80-0.95)	0.84 (0.76-0.92)	0.78 (0.69-0.87)	<0.001	0.38
≥30	1.00	0.80 (0.73-0.89)	0.79 (0.71-0.88)	0.76 (0.63-0.91)	<0.001	
Diabetes (N=24 311)						
Age (years)						
≤ 60	1.00	0.88 (0.78-0.98)	1.02 (0.89-1.17)	0.83 (0.65-1.06)	0.67	0.04
> 60	1.00	0.90 (0.81-0.99)	0.76 (0.68-0.86)	0.81 (0.69-0.96)	<0.001	
Sex						

Male	1.00	0.86 (0.78-0.95)	0.78 (0.70-0.87)	0.84 (0.72-0.99)	<0.001	0.91
Female	1.00	0.91 (0.80-1.03)	0.90 (0.77-1.04)	0.70 (0.55-0.89)	0.01	
Ethnicity						
White	1.00	0.91 (0.83-0.99)	0.84 (0.76-0.92)	0.82 (0.71-0.94)	<0.001	0.56
Non-white	1.00	0.78 (0.64-0.94)	0.89 (0.67-1.18)	0.91 (0.44-1.86)	0.17	
Smoking status						
Never	1.00	0.93 (0.82-1.05)	0.82 (0.71-0.94)	0.93 (0.76-1.15)	0.04	
Previous	1.00	0.86 (0.76-0.98)	0.84 (0.74-0.97)	0.78 (0.64-0.95)	0.02	0.16
Current	1.00	0.82 (0.68-0.98)	0.80 (0.63-1.01)	0.51 (0.32-0.81)	0.003	
Drinking status						
Never	1.00	0.99 (0.79-1.25)	0.94 (0.69-1.28)	0.86 (0.46-1.63)	0.62	
Previous	1.00	0.88 (0.67-1.14)	0.88 (0.65-1.21)	0.95 (0.59-1.53)	0.65	0.58
Current	1.00	0.86 (0.79-0.94)	0.80 (0.73-0.89)	0.78 (0.68-0.90)	<0.001	
Hypertension						
Yes	1.00	0.87 (0.76-0.99)	0.81 (0.70-0.95)	0.73 (0.58-0.92)	0.003	0.44
No	1.00	0.88 (0.80-0.97)	0.83 (0.74-0.92)	0.85 (0.72-1.00)	0.005	
BMI (Kg/m^2)						
< 30	1.00	0.82 (0.72-0.93)	0.72 (0.62-0.82)	0.70 (0.58-0.84)	<0.001	0.03
≥30	1.00	0.90 (0.81-0.99)	0.87 (0.77-0.98)	0.86 (0.70-1.04)	0.03	

Adjusted for age, sex, ethnicity (white, black, Asian, Chinese, mixed, or others), household income (<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status (never, former, or current), drinking status (never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use (yes or no), cholesterol lowering medication (yes or no), aspirin use (yes or no), vitamin D supplementation (yes or no), LDL-c. In the stratified analyses, the stratified variables were not included in the model. For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [<53 mmol/mol], or ≥7.0% [≥53 mmol/mol]), insulin treatment (yes or no).

Supplementary Table 4. Hazard ratios for CVD mortality according to subgroup among participants with prediabetes and diabetes

	Serum 25(OH)D concentrations (nmol/L)					
	<25.0	**25.0–49.9**	**50.0–74.9**	**≥75.0**	P_{trend}	$P_{interaction}$
CVD mortality						
Prediabetes (N=67 789)						
Age (years)						
≤ 60	1.00	0.71 (0.52-0.96)	0.81 (0.58-1.15)	0.44 (0.23-0.84)	0.05	0.56
> 60	1.00	0.64 (0.51-0.81)	0.58 (0.45-0.74)	0.44 (0.31-0.63)	<0.001	
Sex						
Male	1.00	0.67 (0.53-0.84)	0.62 (0.49-0.80)	0.42 (0.28-0.62)	<0.001	0.87
Female	1.00	0.62 (0.46-0.84)	0.59 (0.43-0.82)	0.47 (0.29-0.79)	0.003	
Ethnicity						
White	1.00	0.61 (0.51-0.74)	0.57 (0.47-0.70)	0.41 (0.30-0.55)	<0.001	0.02
Non-white	1.00	1.31 (0.52-3.27)	1.75 (0.58-5.30)	2.47 (0.30-20.91)	0.25	
Smoking status						
Never	1.00	0.90 (0.64-1.26)	0.76 (0.53-1.09)	0.63 (0.37-1.07)	0.04	0.25
Previous	1.00	0.52 (0.38-0.72)	0.57 (0.41-0.80)	0.38 (0.22-0.63)	0.003	
Current	1.00	0.64 (0.47-0.88)	0.65 (0.46-0.93)	0.43 (0.24-0.79)	0.005	
Drinking status						
Never	1.00	0.61 (0.29-1.28)	0.57 (0.24-1.38)	0.99 (0.33-2.98)	0.71	0.31
Previous	1.00	0.80 (0.41-1.56)	0.62 (0.27-1.43)	0.36 (0.08-1.65)	0.12	
Current	1.00	0.64 (0.52-0.77)	0.61 (0.49-0.75)	0.41 (0.30-0.57)	<0.001	
Hypertension						
Yes	1.00	0.81 (0.52-1.26)	0.92 (0.58-1.47)	0.66 (0.33-1.31)	0.50	0.08
No	1.00	0.61 (0.50-0.75)	0.55 (0.44-0.69)	0.39 (0.28-0.56)	<0.001	
BMI (Kg/m^2)						
< 30	1.00	0.67 (0.53-0.86)	0.60 (0.47-0.78)	0.43 (0.30-0.62)	<0.001	0.79
≥30	1.00	0.60 (0.45-0.81)	0.60 (0.44-0.83)	0.41 (0.22-0.76)	0.002	
Diabetes (N=24 311)						
Age (years)						
≤ 60	1.00	0.57 (0.42-0.78)	0.71 (0.48-1.03)	0.93 (0.51-1.67)	0.29	0.05
> 60	1.00	0.70 (0.55-0.89)	0.43 (0.32-0.57)	0.51 (0.33-0.78)	<0.001	
Sex						

Male	1.00	0.60 (0.48-0.74)	0.39 (0.30-0.52)	0.54 (0.36-0.80)	<0.001	0.11
Female	1.00	0.72 (0.50-1.04)	0.76 (0.49-1.16)	0.65 (0.32-1.30)	0.19	
Ethnicity						
White	1.00	0.62 (0.51-0.76)	0.44 (0.34-0.56)	0.54 (0.38-0.76)	<0.001	0.26
Non-white	1.00	0.65 (0.37-1.15)	1.05 (0.48 -2.28)	0.87 (0.11-6.64)	0.73	
Smoking status						
Never	1.00	0.73 (0.54-0.99)	0.54 (0.37-0.79)	0.90 (0.54-1.51)	0.07	
Previous	1.00	0.70 (0.51-0.96)	0.48 (0.33-0.69)	0.49 (0.29-0.85)	<0.001	0.06
Current	1.00	0.50 (0.33-0.74)	0.57 (0.34-0.95)	0.38 (0.14-1.08)	0.008	
Drinking status						
Never	1.00	1.29 (0.65-2.53)	1.23 (0.52-2.91)	0.68 (0.08-5.37)	0.88	
Previous	1.00	0.51 (0.28-0.92)	0.37 (0.17-0.83)	0.51 (0.15-1.78)	0.03	0.17
Current	1.00	0.61 (0.50-0.75)	0.46 (0.35-0.59)	0.56 (0.39-0.81)	<0.001	
Hypertension						
Yes	1.00	0.58 (0.43-0.80)	0.40 (0.26-0.60)	0.51 (0.28-0.90)	<0.001	0.49
No	1.00	0.68 (0.53-0.86)	0.53 (0.40-0.71)	0.62 (0.41-0.96)	<0.001	
BMI (Kg/m^2)						
< 30	1.00	0.58 (0.43-0.79)	0.38 (0.26-0.54)	0.41 (0.25-0.68)	<0.001	0.12
≥30	1.00	0.66 (0.52-0.84)	0.53 (0.39-0.73)	0.72 (0.44-1.15)	0.002	

Adjusted for age, sex, ethnicity (white, black, Asian, Chinese, mixed, or others), household income (<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status (never, former, or current), drinking status (never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use (yes or no), cholesterol lowering medication (yes or no), aspirin use (yes or no), vitamin D supplementation (yes or no), LDL-c. In the stratified analyses, the stratified variables were not included in the model. For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [<53 mmol/mol], or ≥7.0% [≥53 mmol/mol]), insulin treatment (yes or no).

Supplementary Table 5. Hazard ratios for all-cause mortality according to subgroup among participants with prediabetes and diabetes

	Serum 25(OH)D concentrations (nmol/L)					
	<25.0	**25.0–49.9**	**50.0–74.9**	**≥75.0**	P_{trend}	$P_{interaction}$
All-cause mortality						
Prediabetes (N=67 789)						
Age (years)						
≤ 60	1.00	0.75 (0.65-0.85)	0.67 (0.58-0.78)	0.65 (0.52-0.81)	<0.001	0.36
> 60	1.00	0.83 (0.75-0.93)	0.70 (0.63-0.79)	0.71 (0.62-0.83)	<0.001	
Sex						
Male	1.00	0.77 (0.69-0.86)	0.63 (0.56-0.71)	0.66 (0.57-0.78)	<0.001	0.99
Female	1.00	0.78 (0.69-0.88)	0.70 (0.61-0.80)	0.66 (0.54-0.80)	<0.001	
Ethnicity						
White	1.00	0.76 (0.70-0.83)	0.65 (0.59-0.71)	0.65 (0.57-0.73)	<0.001	0.73
Non-white	1.00	0.75 (0.53-1.04)	0.53 (0.31-0.92)	0.84 (0.30-2.32)	0.03	
Smoking status						
Never	1.00	0.82 (0.71-0.95)	0.76 (0.65-0.89)	0.79 (0.64-0.97)	0.01	
Previous	1.00	0.76 (0.66-0.87)	0.63 (0.54-0.73)	0.67 (0.55-0.81)	<0.001	0.03
Current	1.00	0.80 (0.69-0.92)	0.64 (0.54-0.77)	0.56 (0.44-0.73)	<0.001	
Drinking status						
Never	1.00	0.77 (0.56-1.05)	0.53 (0.36-0.78)	0.89 (0.54-1.48)	0.05	
Previous	1.00	0.84 (0.62-1.12)	0.67 (0.47-0.95)	0.61 (0.36-1.02)	0.01	0.74
Current	1.00	0.77 (0.70-0.84)	0.66 (0.60-0.72)	0.65 (0.57-0.74)	<0.001	
Hypertension						
Yes	1.00	0.73 (0.60-0.89)	0.75 (0.60-0.93)	0.67 (0.50-0.91)	0.02	0.61
No	1.00	0.78 (0.71-0.86)	0.64 (0.58-0.71)	0.66 (0.58-0.75)	<0.001	
BMI (Kg/m^2)						
< 30	1.00	0.78 (0.70-0.87)	0.62 (0.55-0.70)	0.63 (0.55-0.73)	<0.001	0.08
≥30	1.00	0.75 (0.66-0.86)	0.73 (0.63-0.85)	0.73 (0.58-0.93)	0.001	
Diabetes (N=24 311)						
Age (years)						
≤ 60	1.00	0.65 (0.56-0.77)	0.63 (0.52-0.77)	0.68 (0.49-0.93)	<0.001	0.65
> 60	1.00	0.80 (0.71-0.91)	0.60 (0.52-0.70)	0.61 (0.50-0.75)	<0.001	
Sex						

Male	1.00	0.74 (0.66-0.84)	0.58 (0.50-0.66)	0.61 (0.50-0.75)	<0.001	0.89
Female	1.00	0.69 (0.58-0.81)	0.60 (0.49-0.73)	0.56 (0.41-0.76)	<0.001	
Ethnicity						
White	1.00	0.71 (0.64-0.78)	0.56 (0.50-0.63)	0.58 (0.48-0.68)	<0.001	0.07
Non-white	1.00	0.80 (0.58-1.08)	0.80 (0.50-1.27)	0.97 (0.35-2.69)	0.31	
Smoking status						
Never	1.00	0.74 (0.63-0.86)	0.65 (0.54-0.78)	0.69 (0.52-0.91)	<0.001	
Previous	1.00	0.78 (0.67-0.91)	0.59 (0.49-0.70)	0.63 (0.49-0.81)	<0.001	0.04
Current	1.00	0.66 (0.54-0.82)	0.54 (0.41-0.71)	0.41 (0.24-0.68)	<0.001	
Drinking status						
Never	1.00	1.09 (0.79-1.51)	0.81 (0.52-1.26)	0.67 (0.28-1.59)	0.23	
Previous	1.00	0.62 (0.46-0.83)	0.46 (0.32-0.67)	0.44 (0.24-0.81)	<0.001	0.52
Current	1.00	0.71 (0.64-0.80)	0.59 (0.52-0.67)	0.61 (0.51-0.73)	<0.001	
Hypertension						
Yes	1.00	0.64 (0.54-0.76)	0.56 (0.45-0.68)	0.55 (0.40-0.74)	<0.001	0.47
No	1.00	0.78 (0.69-0.87)	0.60 (0.53-0.69)	0.63 (0.51-0.77)	<0.001	
BMI (Kg/m^2)						
< 30	1.00	0.65 (0.56-0.76)	0.51 (0.43-0.60)	0.51 (0.41-0.64)	<0.001	0.24
≥30	1.00	0.78 (0.69-0.88)	0.63 (0.54-0.74)	0.66 (0.51-0.86)	<0.001	

Adjusted for age, sex, ethnicity (white, black, Asian, Chinese, mixed, or others), household income (<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status (never, former, or current), drinking status (never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use (yes or no), cholesterol lowering medication (yes or no), vitamin D supplementation (yes or no), aspirin use (yes or no), LDL-c. In the stratified analyses, the stratified variables were not included in the model. For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [<53 mmol/mol], or ≥7.0% [≥53 mmol/mol]), insulin treatment (yes or no).

Supplementary Table 6. Hazard ratios for outcomes according to serum 25(OH)D concentrations in prediabetes stratified by progression to T2DM

	Number of participants	Serum 25(OH)D concentrations (nmol/L)					
		<25.0	25.0–49.9	50.0–74.9	≥75.0	P_{trend}	$P_{interaction}$
Cardiovascular events		1 238/10 105	3 182/29 309	2 345/21 891	656/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.82 (0.72-0.94)	0.89 (0.76-1.04)	0.74 (0.57-0.95)	0.08	0.18
No	62 105	1.00	0.87 (0.81-0.94)	0.85 (0.78-0.92)	0.82 (0.74-0.92)	<0.001	
CVD mortality		186/10 105	389/29 309	273/21 891	74 /6 484		
Progression to T2DM							
Yes	5 684	1.00	0.93 (0.58-1.49)	1.01 (0.59-1.73)-	0.70 (0.28-1.74)	0.69	0.43
No	62 105	1.00	0.63 (0.52-0.76)	0.55 (0.45-0.67)	0.49 (0.36-0.65)	<.0.001	
All-cause mortality		810/10 105	1 976/29 309	1 328/21 891	420/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.93 (0.74-1.16)	0.89 (0.69-1.15)	0.81 (0.55-1.20)	0.27	0.08
No	62 105	1.00	0.75 (0.69-0.82)	0.63 (0.57-0.69)	0.65 (0.57-0.73)	<0.001	
Coronary heart disease		910/10 105	2 343/29 309	1 728/21 891	472/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.90 (0.77-1.05)	0.97 (0.82-1.17)	0.67 (0.49-0.90)	0.13	0.16
No	62 105	1.00	0.87 (0.80-0.96)	0.86 (0.79-0.95)	0.85 (0.75-0.96)	0.02	
Heart failure		322/10 105	753/29 309	544/21 891	142/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.84 (0.65-1.07)	0.78 (0.58-1.04)	0.58 (0.35-0.96)	0.02	0.22
No	62 105	1.00	0.76 (0.65-0.89)	0.77 (0.65-0.91)	0.71 (0.56-0.89)	0.01	
Stroke		243/10 105	609/29 309	461/21 891	140/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.56 (0.40-0.79)	0.78 (0.54-1.12)	1.05 (0.63-1.77)	0.69	0.70
No	62 105	1.00	0.88 (0.74-1.04)	0.79 (0.66-0.95)	0.75 (0.59-0.96)	0.007	
Ischemic stroke		164/10 105	403/29 309	306/21 891	93/6 484		
Progression to T2DM							
Yes	5 684	1.00	0.56 (0.38-0.84)	0.81 (0.52-1.24)	1.06 (0.57-1.95)	0.63	0.60
No	62 105	1.00	0.85 (0.69-1.04)	0.77 (0.61-0.96)	0.75 (0.56-1.00)	0.02	
Hemorrhagic stroke		78/10 105	179/29 309	131/21 891	40/6 484		
Progression to T2DM							

Yes	5 684	1.00	0.43 (0.23-0.81)	0.48 (0.23-1.00)	0.74 (0.27-2.07)	0.30	0.34
No	62 105	1.00	0.85 (0.63-1.15)	0.76 (0.55-1.05)	0.69 (0.45-1.07)	0.06	

Adjusted for age, sex, ethnicity (white, black, Asian, Chinese, mixed, or others), household income (<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status (never, former, or current), drinking status (never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use (yes or no), cholesterol lowering medication (yes or no), vitamin D supplementation (yes or no), aspirin use (yes or no), LDL-c. For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [<53 mmol/mol], or ≥7.0% [≥53mmol/mol]), insulin treatment (yes or no).

Supplementary Table 7. Hazard ratios for outcomes according to serum 25(OH)D concentrations in prediabetes and diabetes after excluding participants who experienced an outcome event within the first two years of follow-up

	Serum 25(OH)D concentrations (nmol/L)				P_{trend}
	<25.0	**25.0–49.9**	**50.0–74.9**	**≥75.0**	
Prediabetes (N=66 666)	9 929	28 791	21 561	6 385	
Cardiovascular events					
Number of events	1 095/9 929	2 769/28 791	2 078/21 561	581/6 385	6 523
Crude model	1.00	0.86 (0.80-0.92)	0.86 (0.80-0.93)	0.81 (0.74-0.90)	<0.001
Model 1	1.00	0.77 (0.72-0.83)	0.72 (0.67-0.77)	0.66 (0.59-0.73)	<0.001
Model 2	1.00	0.83 (0.77-0.89)	0.83 (0.77-0.89)	0.78 (0.70-0.87)	<0.001
CVD mortality					
Number of events	154/9 929	308/28 791	221/21 561	51/6 385	734
Crude model	1.00	0.69 (0.57-0.83)	0.66 (0.54-0.81)	0.52 (0.38-0.71)	<0.001
Model 1	1.00	0.59 (0.49-0.72)	0.52 (0.42-0.63)	0.39 (0.28-0.54)	<0.001
Model 2	1.00	0.65 (0.53-0.79)	0.60 (0.48-0.74)	0.45 (0.33-0.62)	<0.001
All-cause mortality					
Number of events	739/9 929	1 776/28 791	1 207/21 561	380/6 385	4 102
Crude model	1.00	0.82 (0.76-0.90)	0.75 (0.68-0.82)	0.80 (0.71-0.90)	<0.001
Model 1	1.00	0.71 (0.66-0.78)	0.59 (0.54-0.65)	0.61 (0.54-0.69)	<0.001
Model 2	1.00	0.76 (0.70-0.83)	0.65 (0.59-0.71)	0.65 (0.57-0.74)	<0.001
Coronary heart disease					
Number of events	795/9 929	1 995/28 791	1 506/21 561	412/6 385	4 708
Crude model	1.00	0.86 (0.79-0.93)	0.86 (0.79-0.94)	0.80 (0.71-0.90)	0.001
Model 1	1.00	0.78 (0.72-0.85)	0.74 (0.68-0.81)	0.66 (0.59-0.75)	<0.001
Model 2	1.00	0.84 (0.77-0.91)	0.85 (0.78-0.93)	0.79 (0.70-0.90)	0.002
Heart failure					
Number of events	287/9 929	690/28 791	493/21 561	125/6 385	1 595
Crude model	1.00	0.82 (0.72-0.94)	0.78 (0.68-0.90)	0.67 (0.54-0.83)	<0.001
Model 1	1.00	0.70 (0.61-0.80)	0.60 (0.52-0.70)	0.50 (0.41-0.62)	<0.001
Model 2	1.00	0.79 (0.69-0.91)	0.77 (0.66-0.89)	0.67 (0.54-0.83)	<0.001
Stroke					
Number of events	217/9 929	536/28 791	415/21 561	130/6 385	1 298

Crude model	1.00	0.85 (0.72-0.99)	0.87 (0.74-1.03)	0.93 (0.74-1.15)	0.63
Model 1	1.00	0.73 (0.63-0.86)	0.69 (0.59-0.82)	0.71 (0.57-0.89)	0.002
Model 2	1.00	0.78 (0.66-0.91)	0.75 (0.64-0.89)	0.77 (0.62-0.97)	0.03
Ischemic stroke					
Number of events	148/9 929	354/28 791	273/21 561	86/6 385	861
Crude model	1.00	0.82 (0.68-0.99)	0.84 (0.69-1.03)	0.90 (0.69-1.17)	0.52
Model 1	1.00	0.71 (0.58-0.86)	0.66 (0.54-0.81)	0.68 (0.52-0.89)	0.004
Model 2	1.00	0.74 (0.61-0.90)	0.73 (0.59-0.89)	0.76 (0.58-1.00)	0.06
Hemorrhagic stroke					
Number of events	67/9 929	162/28 791	117/21 561	38/6 385	384
Crude model	1.00	0.83 (0.62-1.10)	0.80 (0.59-1.07)	0.87 (0.59-1.30)	0.41
Model 1	1.00	0.73 (0.55-0.97)	0.65 (0.48-0.88)	0.70 (0.47-1.05)	0.04
Model 2	1.00	0.77 (0.58-1.03)	0.69 (0.50-0.94)	0.70 (0.47-1.06)	0.06
Diabetes (N=23 649)	4 749	10 681	6 399	1 820	
Cardiovascular events					
Number of events	874/4 749	1 769/10 681	996/6 399	263/1 820	3 622
Crude model	1.00	0.88 (0.81-0.96)	0.82 (0.75-0.90)	0.76 (0.66-0.87)	<0.001
Model 1	1.00	0.79 (0.73-0.85)	0.68 (0.62-0.75)	0.62 (0.54-0.71)	<0.001
Model 2	1.00	0.88 (0.81-0.95)	0.83 (0.75-0.91)	0.79 (0.68-0.91)	<0.001
CVD mortality					
Number of events	161/4 749	249/10 681	113/6 399	39/1 820	559
Crude model	1.00	0.68 (0.56-0.83)	0.51 (0.40-0.65)	0.63 (0.44-0.89)	<0.001
Model 1	1.00	0.59 (0.48-0.72)	0.41 (0.32-0.52)	0.48 (0.34-0.68)	<0.001
Model 2	1.00	0.65 (0.53-0.80)	0.49 (0.38-0.63)	0.61 (0.42-0.87)	<0.001
All-cause mortality					
Number of events	587/4 749	1 083/10 681	546/6 399	161/1 820	2 357
Crude model	1.00	0.81 (0.73-0.90)	0.68 (0.61-0.76)	0.71 (0.59-0.84)	<0.001
Model 1	1.00	0.70 (0.63-0.78)	0.54 (0.48-0.60)	0.54 (0.45-0.64)	<0.001
Model 2	1.00	0.74 (0.67-0.82)	0.58 (0.51-0.66)	0.59 (0.49-0.71)	<0.001
Coronary heart disease					
Number of events	653/4 749	1 348/10 681	759/6 399	191/1 820	2 666
Crude model	1.00	0.90 (0.82-0.99)	0.84 (0.76-0.94)	0.74 (0.63-0.87)	<0.001
Model 1	1.00	0.81 (0.74-0.90)	0.71 (0.64-0.79)	0.62 (0.52-0.72)	<0.001

Model 2	1.00	0.91 (0.83-1.00)	0.86 (0.77-0.96)	0.78 (0.66-0.92)	0.001
Heart failure					
Number of events	284/4 749	519/10 681	287/6 399	75/1 820	1 133
Crude model	1.00	0.80 (0.69-0.92)	0.73 (0.62-0.86)	0.67 (0.52-0.87)	<0.001
Model 1	1.00	0.68 (0.59-0.79)	0.57 (0.48-0.67)	0.51 (0.39-0.65)	<0.001
Model 2	1.00	0.78 (0.67-0.91)	0.74 (0.62-0.88)	0.72 (0.55-0.93)	0.002
Stroke					
Number of events	163/4 749	311/10 681	178/6 399	57/1 820	676
Crude model	1.00	0.84 (0.69-1.01)	0.80 (0.65-0.99)	0.90 (0.67-1.22)	0.20
Model 1	1.00	0.74 (0.61-0.89)	0.64 (0.52-0.80)	0.71 (0.52-0.96)	0.002
Model 2	1.00	0.82 (0.68-0.99)	0.77 (0.62-0.96)	0.88 (0.64-1.21)	0.16
Ischemic stroke					
Number of events	107/4 749	238/10 681	140/6 399	35/1 820	509
Crude model	1.00	0.98 (0.78-1.23)	0.96 (0.74-1.23)	0.84 (0.57-1.23)	0.41
Model 1	1.00	0.86 (0.68-1.08)	0.77 (0.60-1.00)	0.66 (0.45-0.97)	0.02
Model 2	1.00	0.98 (0.77-1.23)	0.95 (0.73-1.24)	0.86 (0.58-1.27)	0.46
Hemorrhagic stroke					
Number of events	38/4 749	70/10 681	34/6 399	15/1 820	144
Crude model	1.00	0.81 (0.55-1.20)	0.65 (0.41-1.04)	1.02 (0.56-1.85)	0.42
Model 1	1.00	0.71 (0.48-1.06)	0.53 (0.33-0.84)	0.80 (0.44-1.47)	0.10
Model 2	1.00	0.73 (0.49-1.09)	0.56 (0.35-0.91)	0.86 (0.46-1.60)	0.19

Crude model: without adjustment.

Model 1: adjusted for age, sex.

Model 2: included model 1 variables and additionally ethnicity (white, black, Asian, Chinese, mixed, or others), household income (<£18 000, £18 000-£30 999, £31 000-£51 999, £52 000-£100 000, or >£100 000), season of vitamin D assessment, body mass index, smoking status (never, former, or current), drinking status (never, former, or current), physical activity, prevalent hypertension (yes or no), antihypertensive drug use (yes or no), cholesterol lowering medication (yes or no), aspirin use (yes or no), LDL-c, vitamin D supplementation (yes or no). For participants with diabetes, adjusted for variables in model 2 and additionally HbA1c levels (<7.0% [53 mmol/mol], or ≥7.0% [≥53 mmol/mol]), insulin treatment (yes or no).