SUPPLEMENTARY MATERIAL

Table of Contents

Supplementary Methods – Flexible parametric survival models

We modelled the baseline log cumulative hazard function using a restricted cubic spline with two internal knots (placed at the 33rd and 67th percentiles of the uncensored log survival times). If the flexible parametric survival model (FPSM) included an interaction between randomisation group and time since randomisation, this was fitted as a restricted cubic spline with one internal knot, placed at the median of uncensored log survival times.

We used the model that included the interaction with time to produce a plot of the estimated hazard ratio (HR) and 95% confidence interval (CI) as a function of time since randomisation. The significance of the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction.

We used FPSMs to predict the difference in cause-specific standardised cumulative incidence, treating death without prior major cardiovascular event as a competing risk. For this analysis we used the user-written standsurv command in Stata with the competing risks models option. The cumulative incidence functions were standaridised to the distribution of age, sex, and state of residence at baseline in the entire cohort.

Supplementary Table 1. Codes used to identify major cardiovascular event.

Major cardiovascular event	Codes
	ICD-10-AM 9th edition (1 July 2015)
Myocardial infarction	I21, I22
Stroke	Hemorrhagic: I60, I61, I62 Ischemic: I63 Not specified as either hemorrhagic or ischemic: I64
	Australian Classification of Health Interventions (Block code)
Stent (coronary)	3830600, 3830601, 3830602, 3830603, 3830604, 3830605 (671)
Balloon (coronary)	3830000, 3830300, 3830001, 3830301 (370)
Artherectomy (coronary)	3830900, 3831200, 3831201, 3831500, 3831800, 3831801 (669)
Thromboectomy (coronary)	9021800, 9021801, 9021802, 9021803 (669)
Endarterectomy (open)	3850500 (669)
Coronary Artery Bypass Graft	3849700, 3849701, 3849702, 3849703, 3849704, 3849705, 3849706, 3849707, 3850000, 3850001, 3850301, 3850002, 3850300, 3850302, 3850003, 3850303, 3850004, 3850304, 3850005, 3850305, 9020100, 9020101, 9020102, 9020103 (672 – 679)
	Medicare Benefits Schedule
Stent (coronary)	38306
Balloon (coronary)	38300, 38303, 38309, 38312, 38315, 38318
Artherectomy (coronary)	38309, 38312, 38315, 38318
Endarterectomy (open)	38505
Coronary Artery Bypass Graft	38497, 38498, 38500, 38501, 38503, 38504

Supplementary Table 2a. Concordance between statin use from Pharmaceutical Benefits Scheme data and self-reported treatment for hypercholesterolaemia at baseline.

Self-reported treatment for hypercholesterolaemia	PBS claim for statins at baseline n (row %) No	Yes	Total	Did not consent to linkage with PBS
No	11 789 (90.2)	1288 (9.8)	13 077	1279
Yes	715 (11.3)	5625 (88.7)	6340	517
Missing	53 (72.6)	20 (27.4)	73	16
Total	12 557	6933		1812

[a] Anatomical Therapeutic Chemical code C10 in PBS data within 3 months of randomisation, or self-reported treatment for hypercholesterolaemia prior to randomisation. Abbreviation: PBS, Pharmaceutical Benefits Scheme.

Supplementary Table 2b. Concordance between cardiovascular drug use (other than statins) from Pharmaceutical Benefits Scheme data and self-reported treatment for hypertension at baseline.

Self-reported treatment for hypertension	PBS claim for cardiovascular drugs at baseline n (row %) No	Yes	Total	Did not consent to linkage with PBS
No	9563 (84.9)	1702 (15.1)	11265	1104
Yes	705 (8.6)	7454 (91.4)	8159	692
Missing	38 (57.6)	28 (42.4)	66	16
Total	10306	9184		1812

[a] Anatomical Therapeutic Chemical codes C01 – C09 in PBS data within 3 months of randomisation, or self-reported treatment for hypertension prior to randomisation.

Supplementary Table 3. Additional baseline characteristics according to randomisation group

Characteristic	N (%) Vitamin D (N = 10 658)	Placebo (N = 10 644)
Ancestry		
British/European	9733 (93.0)	9711 (92.9)
Australian/New Zealander	364 (3.5)	361 (3.5)
Asian	114 (1.1)	127 (1.2)
Indigenous	80 (0.8)	71 (0.7)
Mixed/other	179 (1.7)	186 (1.8)
Missing	*188*	*188*
Highest qualification obtained		
None	1098 (10.4)	1046 (10.0)
School or intermediate certificate	1798 (17.1)	1756 (16.7)
Higher school or leaving certificate	1435 (13.6)	1528 (14.5)
Apprenticeship or certificate	3453 (32.8)	3575 (34.0)
University degree or higher	2748 (26.1)	2602 (24.8)
Missing	*126*	*137*
Alcohol consumption (drinks/week)		
< 1	2488 (24.3)	2558 (25.0)
1 to 7	4539 (44.3)	4565 (44.6)
> 7 to 14	1930 (18.8)	1822 (17.8)
> 14	1289 (12.6)	1286 (12.6)
Missing	*412*	*413*
Smoking history		
Never	5823 (55.1)	5766 (54.7)
Ex-smoker	4340 (41.0)	4293 (40.7)
Current	411 (3.9)	484 (4.6)
Missing	*84*	*101*
Self-rated overall health		
Excellent or very good	5852 (55.9)	5791 (55.2)
Good	3738 (35.7)	3777 (36.0)
Fair or poor	885 (8.4)	914 (8.7)
Missing	*183*	*162*
Statin and/or cardiovascular drug use at baseline[a]		
No	4559 (42.8)	4680 (44.0)
Yes	6090 (57.2)	5957 (56.0)
Missing	*9*	*7*
Self-reported history of diabetes		
No	9717 (91.6)	9736 (91.8)
Yes	891 (8.4)	867 (8.2)
Missing	*50*	*41*

Characteristic	N (%) Vitamin D (N = 10 658)	Placebo (N = 10 644)
Self-reported history of stroke (including transient ischaemic attack)		
No	10 010 (94.5)	10 023 (94.7)
Yes	579 (5.5)	559 (5.3)
Missing	*69*	*62*
Self-reported history of coronary revascularisation		
No	9865 (93.0)	9827 (92.7)
Yes	741 (7.0)	775 (7.3)
Missing	*52*	*42*
Self-reported history of myocardial infarction		
No	10 036 (94.8)	10 019 (94.7)
Yes	554 (5.2)	562 (5.3)
Missing	*68*	*63*

[a] Anatomical Therapeutic Chemical codes C01 – C10 in Pharmaceutical Benefits Scheme data within 3 months of randomisation, or self-reported treatment for hypercholesterolaemia and/or hypertension prior to randomisation.

Supplementary Table 4. Effect of supplementation with vitamin D on incidence of major cardiovascular events. Predicted difference in cause-specific standardised cumulative incidence and time-varying hazard ratio at 2 and 5 years post-randomisation, and predicted overall hazard ratio.[a]

Years since randomisation	CIF Difference (95% CI)	Hazard Ratio (95% CI)
Major event		
2	-0.0017 (-0.0055 to 0.0021)	0.90 (0.80 to 1.02)
5	-0.0058 (-0.0122 to 0.0005)	0.88 (0.74 to 1.05)
Overall HR	..	0.91 (0.81 to 1.01)
Myocardial infarction		
2	-0.0011 (-0.0032 to 0.0011)	0.80 (0.65 to 0.98)
5	-0.0041 (-0.0078 to -0.0003)	0.76 (0.56 to 1.03)
Overall HR	..	0.81 (0.67 to 0.98)
Coronary revascularisation		
2	-0.0018 (-0.0050 to 0.0014)	0.87 (0.75 to 1.01)
5	-0.0046 (-0.0099 to 0.0006)	0.89 (0.71 to 1.11)
Overall HR	..	0.89 (0.78 to 1.01)
Stroke		
2	0.0006 (-0.0011 to 0.0023)	1.06 (0.83 to 1.35)
5	-0.0001 (-0.0034 to 0.0033)	0.86 (0.60 to 1.22)
Overall HR	..	0.99 (0.80 to 1.23)
Haemorrhagic stroke		
2	-0.0001 (-0.0009 to 0.0007)	1.16 (0.65 to 2.07)
5	-0.0001 (-0.0017 to 0.0015)	0.90 (0.44 to 1.81)
Overall HR	..	0.97 (0.63 to 1.50)
Ischaemic stroke		
2	0.0003 (-0.0010 to 0.0017)	1.07 (0.79 to 1.44)
5	0.0003 (-0.0024 to 0.0030)	0.94 (0.61 to 1.45)
Overall HR	..	1.03 (0.79 to 1.33)

[a] Estimates (comparing vitamin D to placebo) are from flexible parametric survival models that include randomisation group, age, sex, and state of residence at baseline. Time-varying estimates (i.e., estimates at 2 and 5 years post randomisation) were predicted using a model that also included an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). Cause-specific standardised cumulative incidence was estimated treating death (without prior cardiovascular event of interest) as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort.

Abbreviations: CI, confidence interval; CIF, cumulative incidence function; HR, hazard ratio

Supplementary Table 5. Exploratory analysis of major cardiovascular events– Effect modification by use of statins and/or cardiovascular drugs at baseline, and by self-reported history of cardiovascular events.

	n/N (%)			
	Vitamin D	**Placebo**	**HR (95% CI)[a]**	**P-value[b]**
All participants	637/10 658 (6.0)	699/10 644 (6.6)	0.91 (0.81 to 1.01)	
Using statins and/or cardiovascular drugs at baseline[c]				0.23
No	190/4559 (4.2)	195/4680 (4.2)	1.00 (0.82 to 1.22)	
Yes	446/6090 (7.3)	504/5957 (8.5)	0.86 (0.76 to 0.98)	
Self-reported history of cardiovascular events at baseline[d]				0.53
No	422/9180 (4.6)	471/9167 (5.1)	0.89 (0.78 to 1.01)	
Yes	210/1407 (14.9)	225/1416 (15.9)	0.95 (0.79 to 1.15)	

[a] Estimates (comparing vitamin D to placebo) are from flexible parametric survival models that include randomisation group, age, sex, and state of residence at baseline. The models producing stratified estimates included the characteristic of interest and an interaction between randomisation group and the characteristic of interest.
[b] P-value is for the interaction term, calculated using a likelihood ratio test.
[c] n=16 participants with missing data for statin and/or cardiovascular drug use were excluded from the stratified analysis
[d] Participants had a positive history of cardiovascular events at baseline if they reported having had a myocardial infarction, stroke, and/or coronary revascularisation prior to baseline. n=132 participants with missing data were excluded from this analysis.
Abbreviations: CI, confidence interval; HR, hazard ratio

Supplementary Table 6. Exploratory analysis – Effect modification of statin use at baseline and cardiovascular drug use at baseline on myocardial infarction and coronary revascularisation.

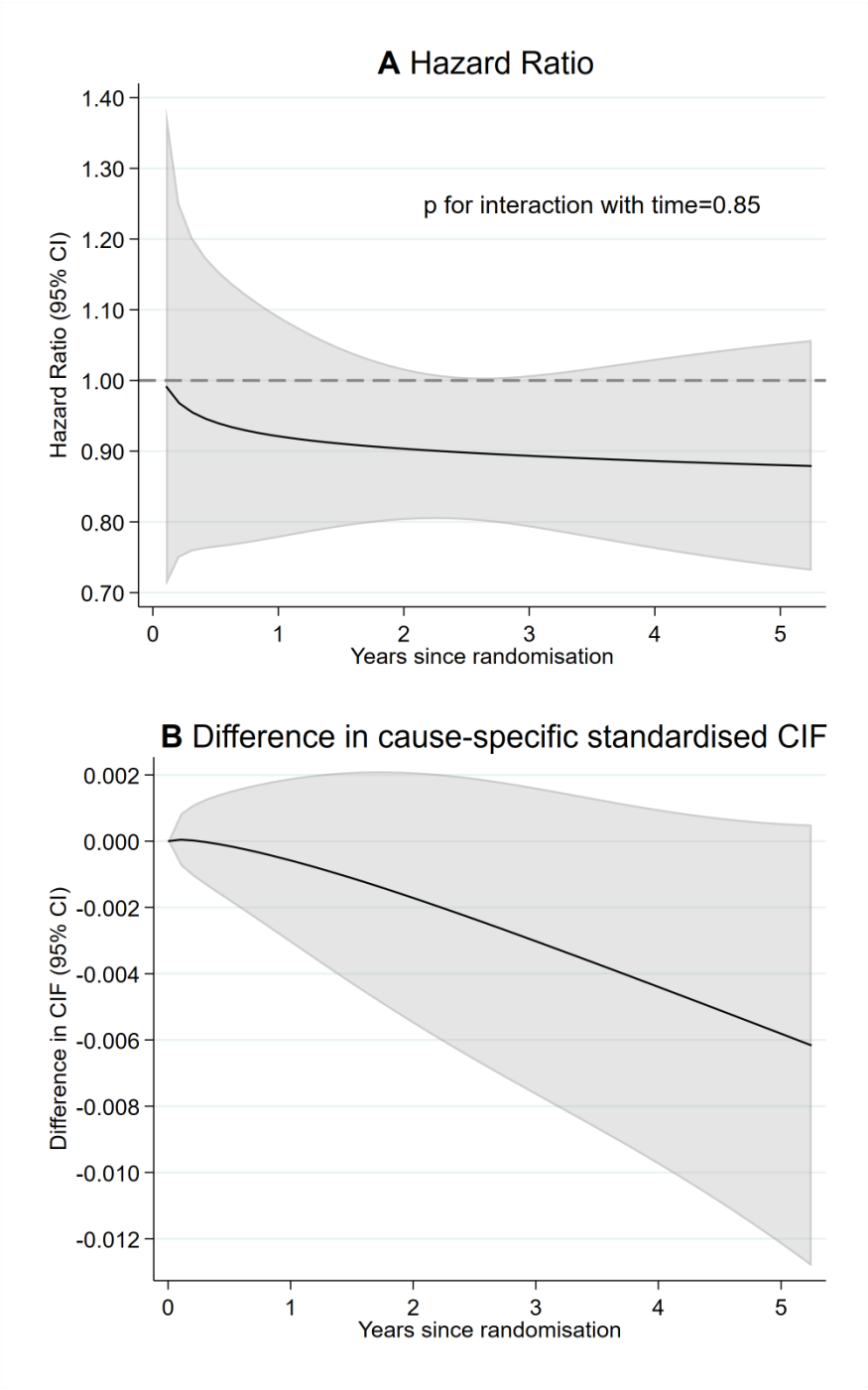
	n/N (%)			
	Vitamin D	**Placebo**	**HR (95% CI)[a]**	**P-value[b]**
Myocardial infarction				
All participants	194/10 658 (1.8)	238/10 644 (2.2)	0.81 (0.67 to 0.98)	
Using statins at baseline[c]				0.66
No	109/6880 (1.6)	130/6956 (1.9)	0.84 (0.65 to 1.09)	
Yes	85/3769 (2.3)	108/3681 (2.9)	0.77 (0.58 to 1.03)	
Using cardiovascular drugs at baseline[d]				0.75
No	80/5655 (1.4)	96/5755 (1.7)	0.84 (0.63 to 1.13)	
Yes	114/4994 (2.3)	142/4882 (2.9)	0.79 (0.62 to 1.01)	
Coronary revascularisation				
All participants	413/10 658 (3.9)	462/10 644 (4.3)	0.89 (0.78 to 1.01)	
Using statins at baseline[c]				0.68
No	201/6880 (2.9)	235/6956 (3.4)	0.86 (0.71 to 1.04)	
Yes	211/3769 (5.6)	227/3681 (6.2)	0.91 (0.75 to 1.10)	
Using cardiovascular drugs at baseline[d]				0.71
No	150/5655 (2.7)	166/5755 (2.9)	0.91 (0.73 to 1.14)	
Yes	262/4994 (5.2)	296/4882 (6.1)	0.87 (0.73 to 1.02)	

[a] Estimates (comparing vitamin D to placebo) are from flexible parametric survival models that include randomisation group, age, sex, and state of residence at baseline. Models producing stratified estimates included the characteristic of interest and an interaction between randomisation group and the characteristic.
[b] P-value is for the interaction term, calculated using a likelihood ratio test.
[c] n=16 participants with missing data for statins were excluded from the stratified analysis
[d] n=16 participants with missing data for cardiovascular drugs were excluded from the stratified analysis
Abbreviations: CI, confidence interval; HR, hazard ratio

Supplementary Table 7. Cross-tabulation of statin use and cardiovascular drug use at baseline.

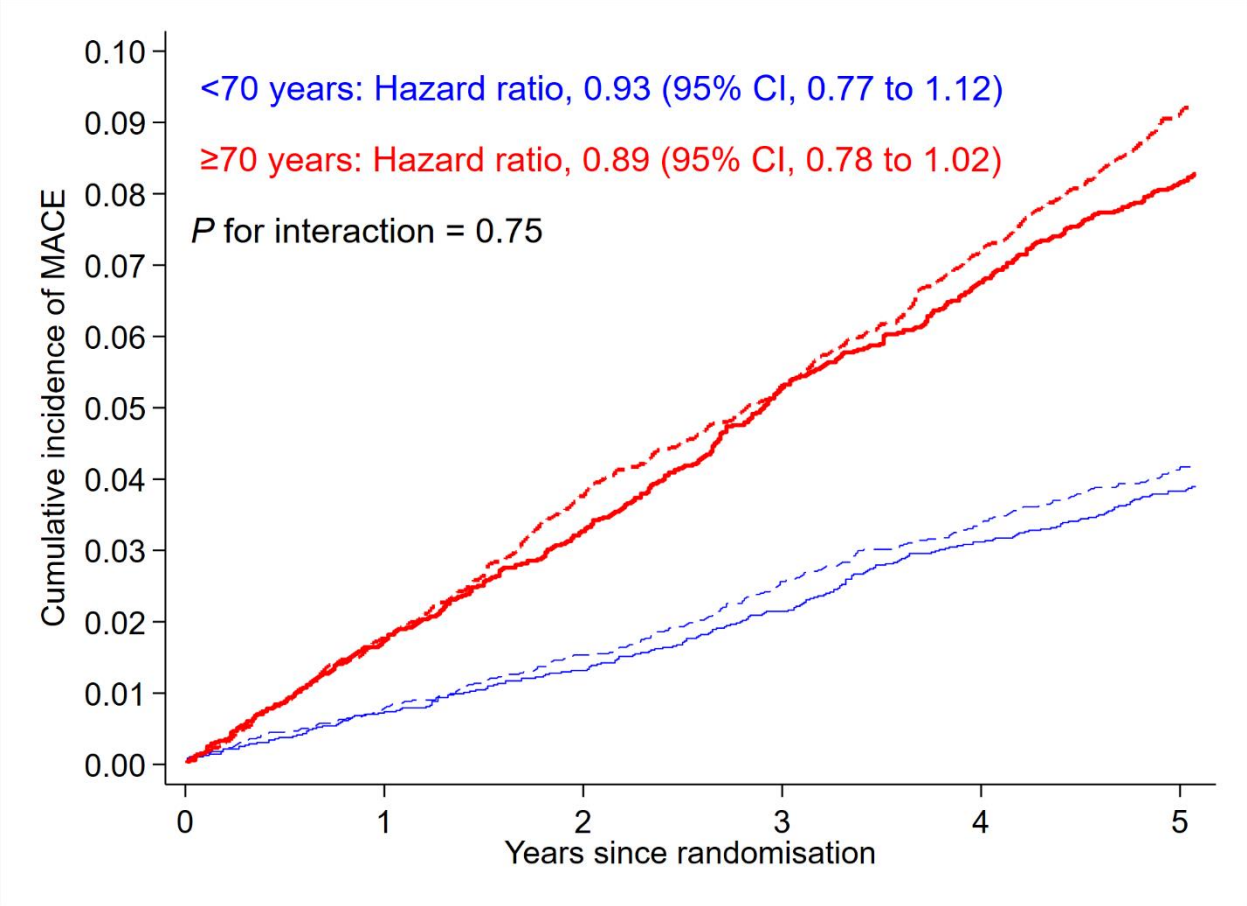
n (row %) (column %)	Statins at baseline		
Cardiovascular drugs at baseline	No	Yes	Total
No	9239 (81.0) (66.8)	2171 (19.0) (29.1)	11 410
Yes	4597 (46.5) (33.2)	5279 (53.5) (70.9)	9 876
Total	13 836	7 450	21 286[a]

[a] Medication data were missing for n=16 participants.



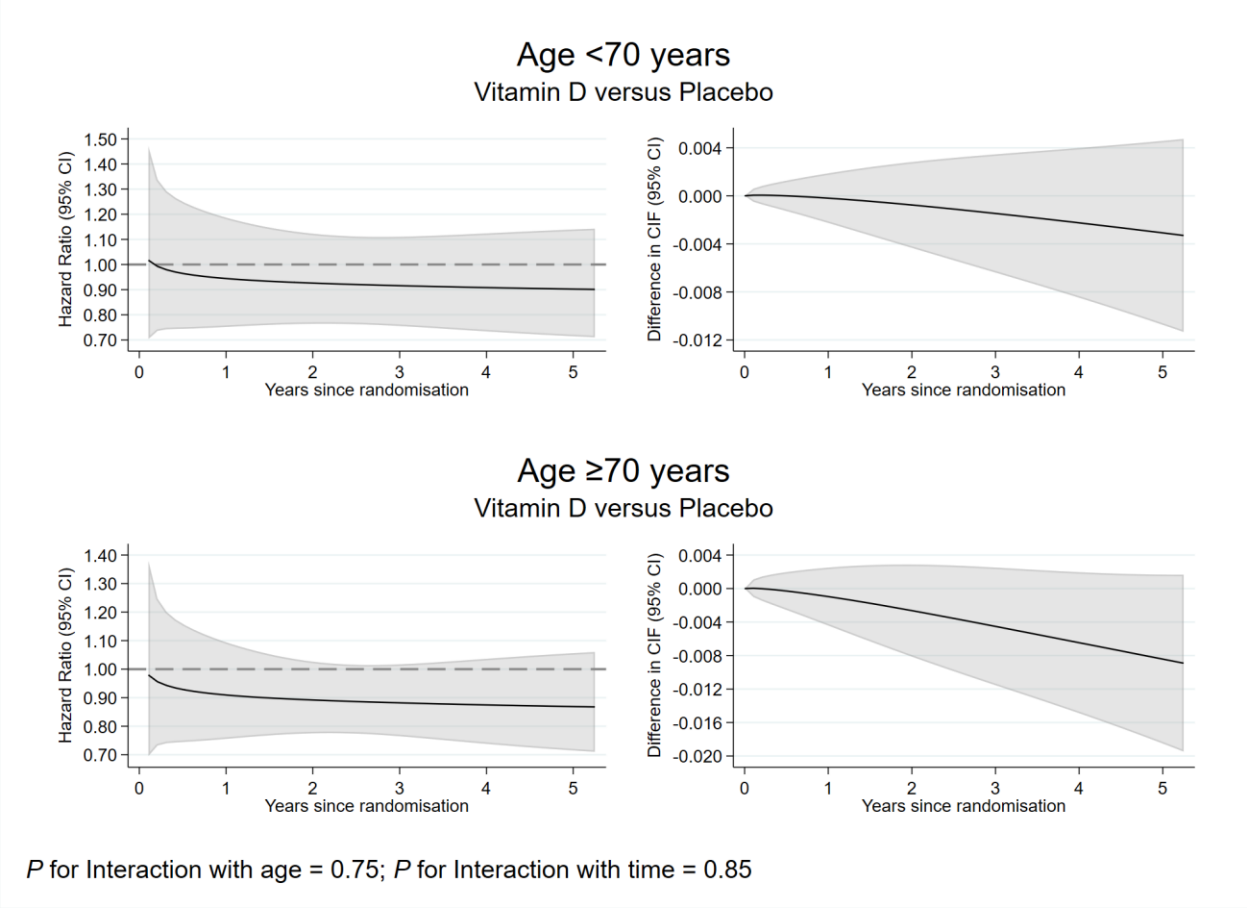
Supplementary Figure 1. Effect of vitamin D supplementation on incidence of major cardiovascular events. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



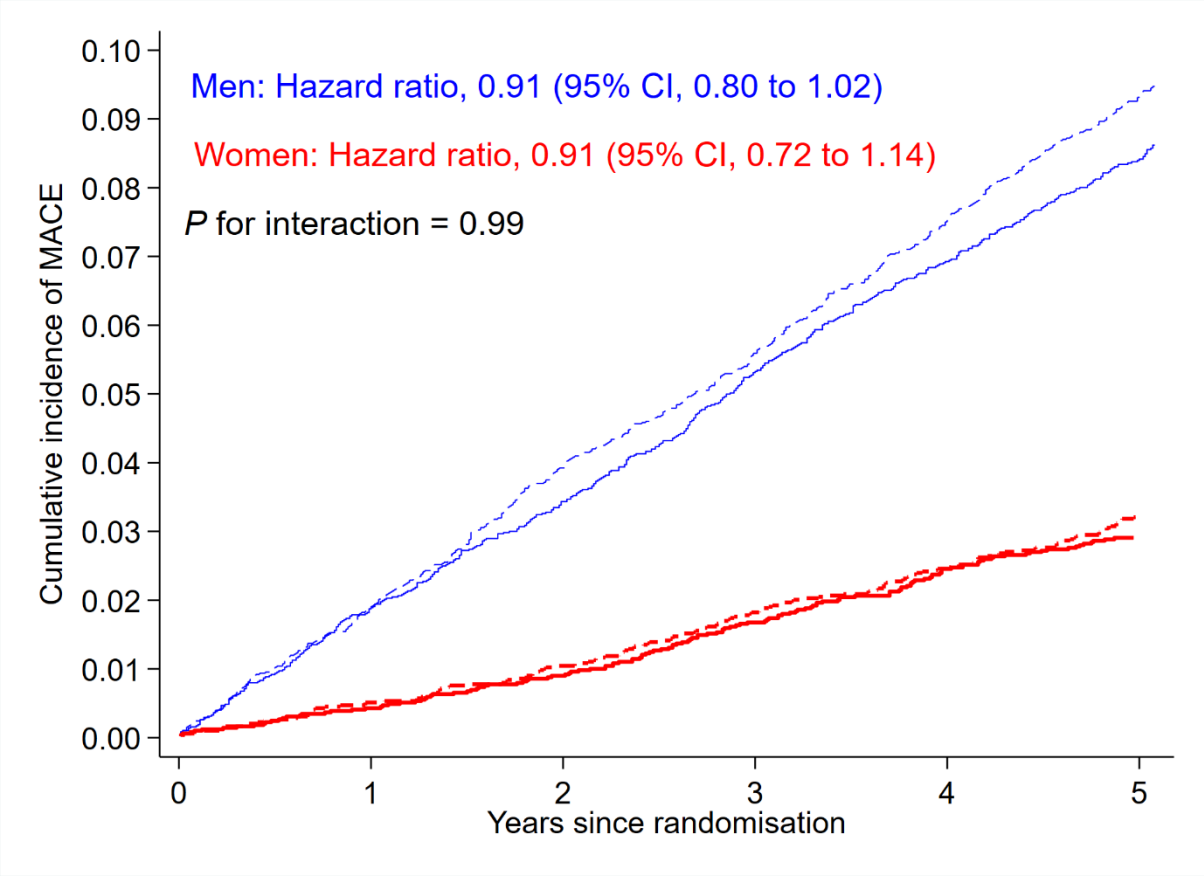
Supplementary Figure 2. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by age at baseline (<70 years, thin blue lines; ≥70 years, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, age, sex, state of residence, and an interaction between randomisation group and age. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. Abbreviation: CI, confidence interval; MACE, major cardiovascular event.



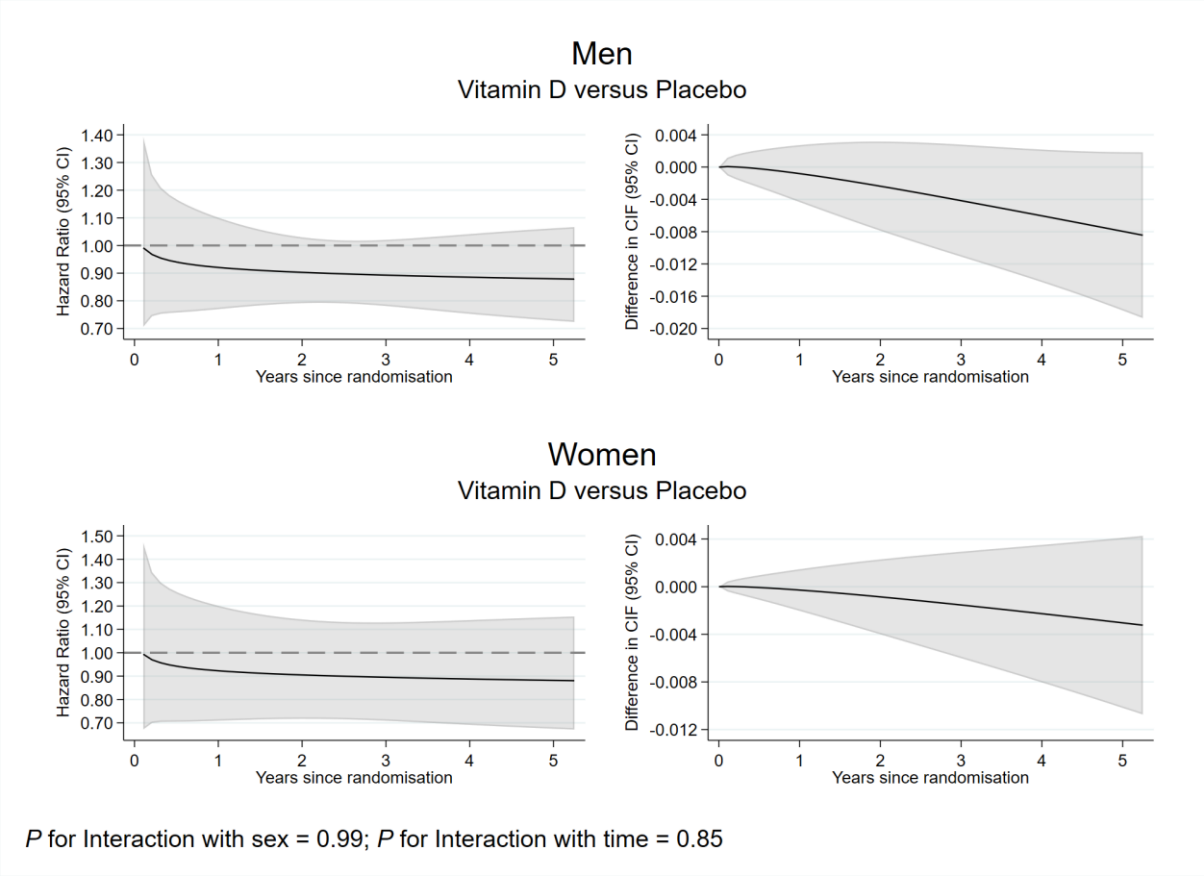
Supplementary Figure 3. Effect of vitamin D supplementation on incidence of major cardiovascular events according to age at randomisation. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, state of residence, an interaction between randomisation group and age, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



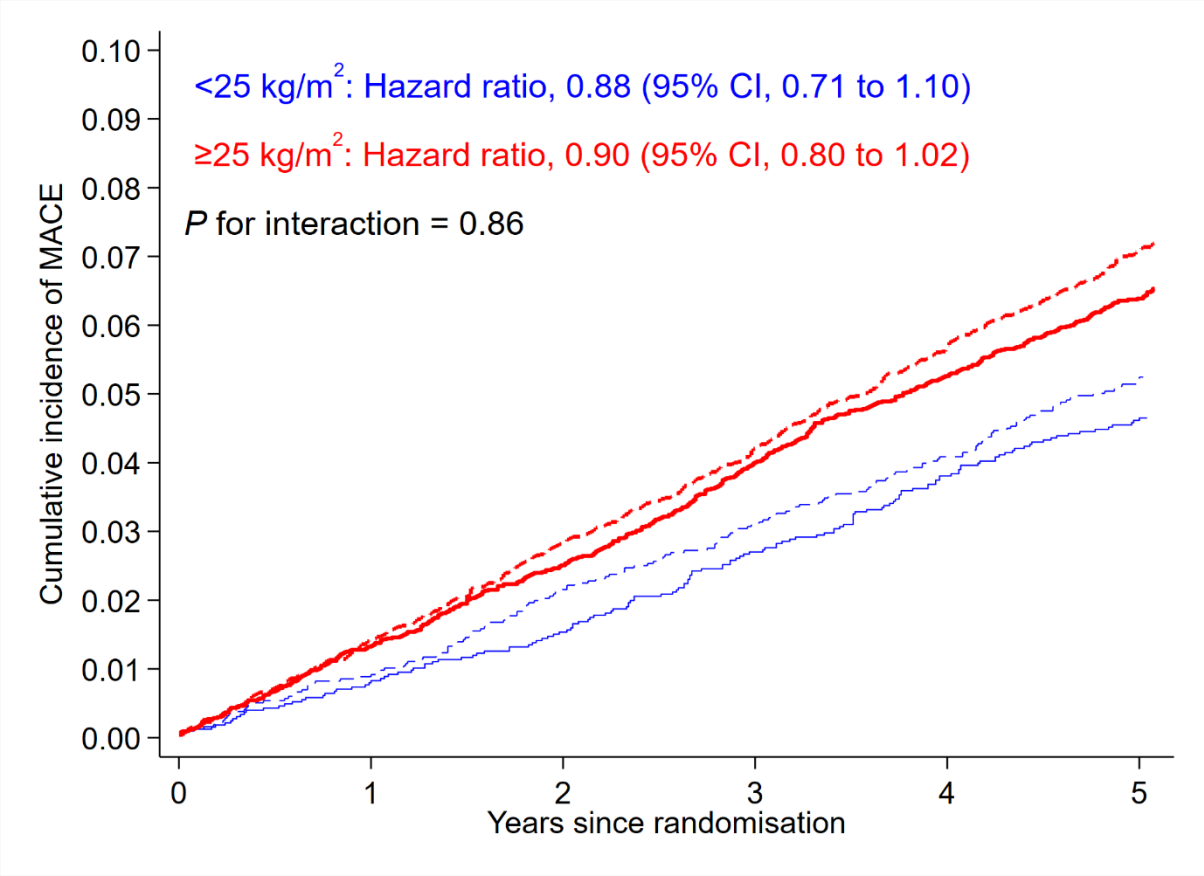
Supplementary Figure 4. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by sex (men, thin blue lines; women, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, age, sex, state of residence, and an interaction between randomisation group and sex. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. Abbreviation: CI, confidence interval; MACE, major cardiovascular event.



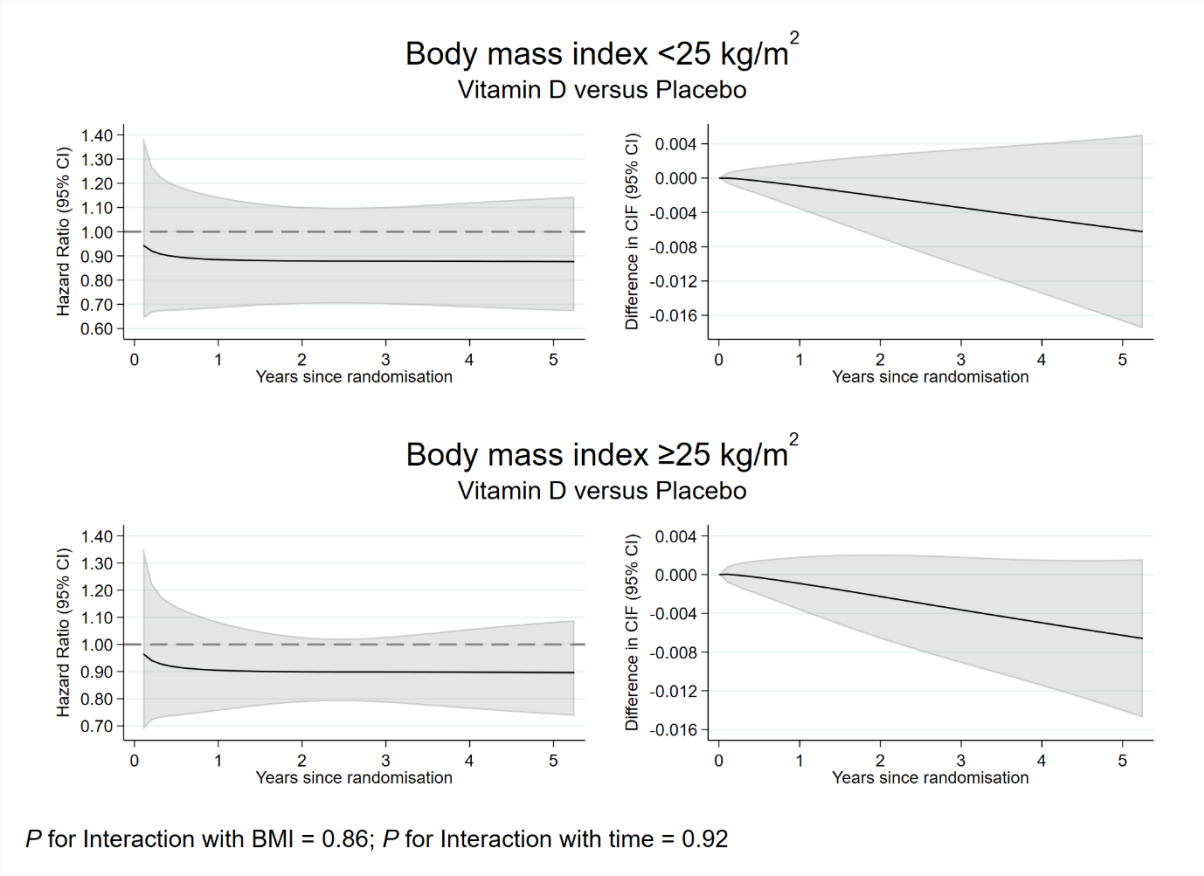
Supplementary Figure 5. Effect of vitamin D supplementation on incidence of major cardiovascular events according to sex. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, state of residence, an interaction between randomisation group and sex, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



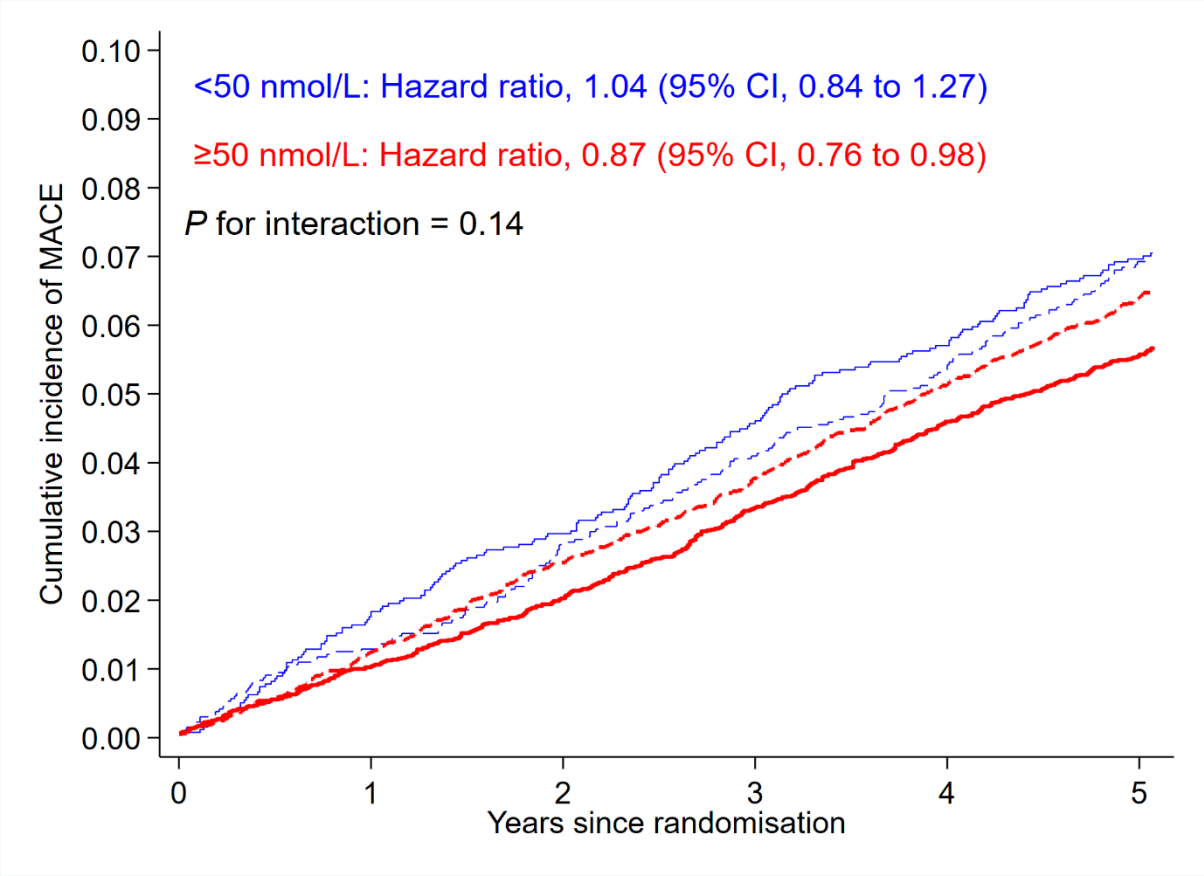
Supplementary Figure 6. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by body mass index at baseline (<25 kg/m^2, thin blue lines; ≥25 kg/m^2, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, BMI, age, sex, state of residence, and an interaction between randomisation group and BMI. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. N=119 participants were excluded from the analysis due to missing BMI. Abbreviation: BMI, body mass index; CI, confidence interval; MACE, major cardiovascular event.



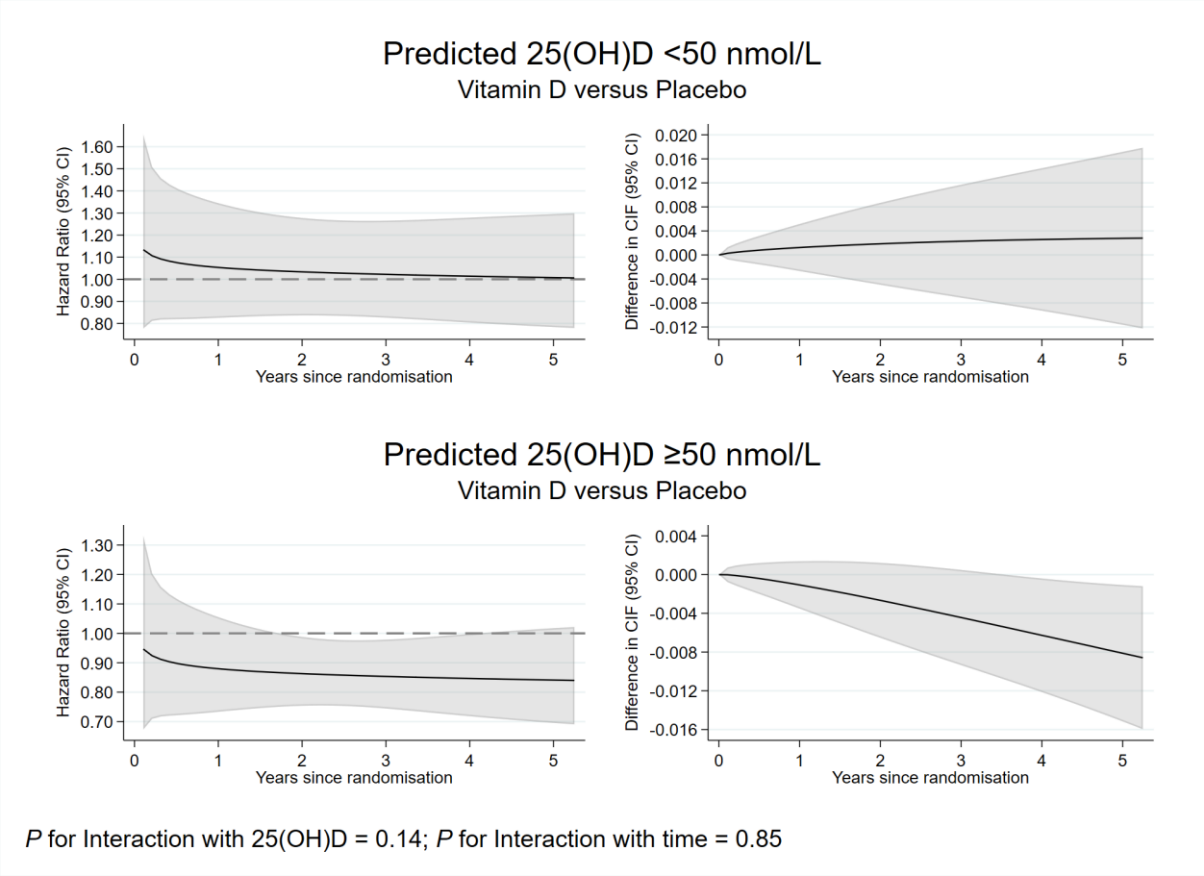
Supplementary Figure 7. Effect of vitamin D supplementation on incidence of major cardiovascular events according to body mass index at baseline. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, BMI, age, sex, state of residence, an interaction between randomisation group and BMI, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. N=119 participants were excluded from the analysis due to missing BMI.
Abbreviations: BMI, body mass index; CI, confidence interval; CIF, cumulative incidence function.



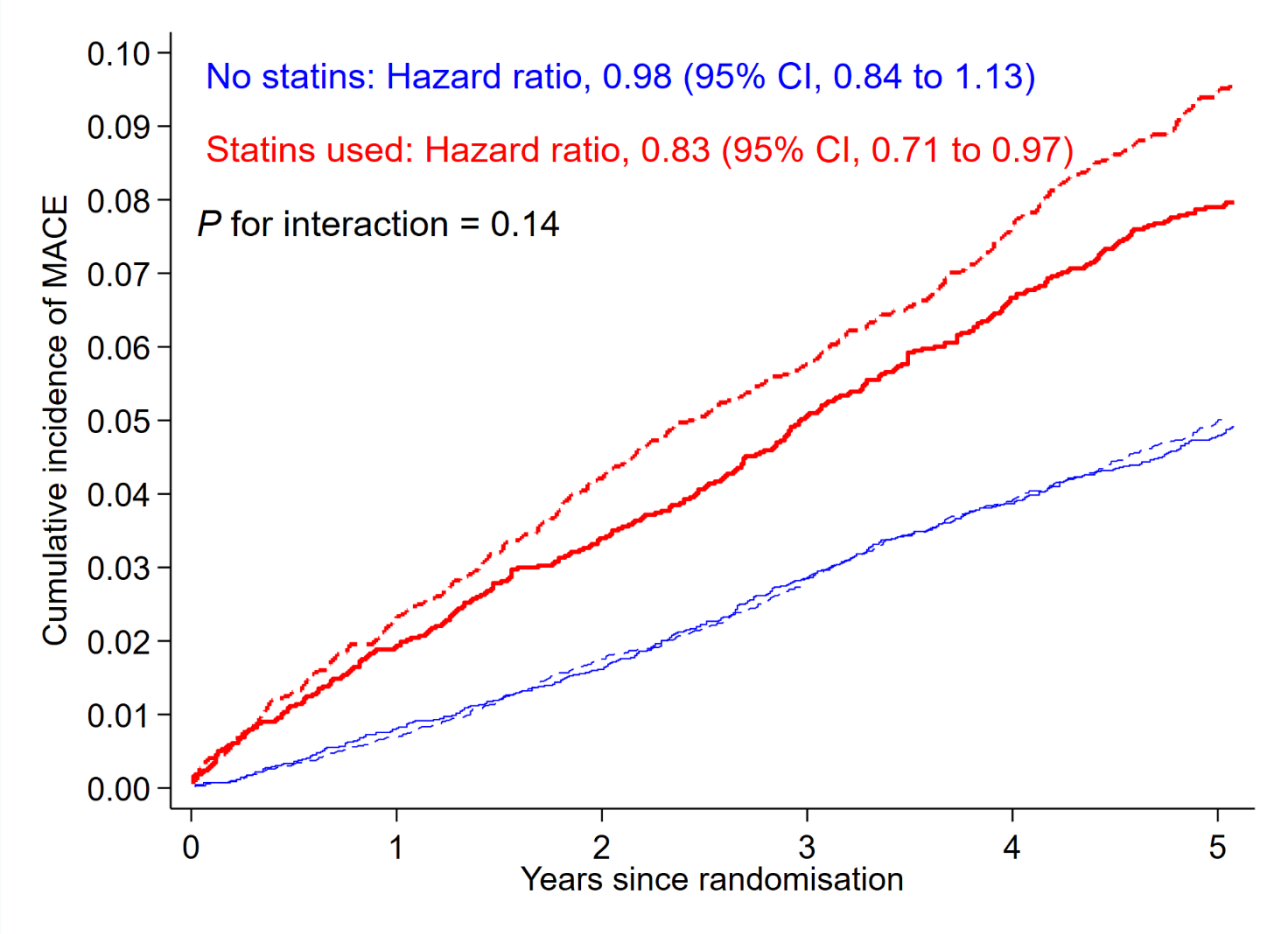
Supplementary Figure 8. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by predicted deseasonalised baseline 25(OH)D concentration (<50 nmol/L, thin blue lines; ≥50 nmol/L, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, predicted 25(OH)D concentration, age, sex, state of residence, and an interaction between randomisation group and predicted 25(OH)D concentration. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. Abbreviation: CI, confidence interval; MACE, major cardiovascular event.



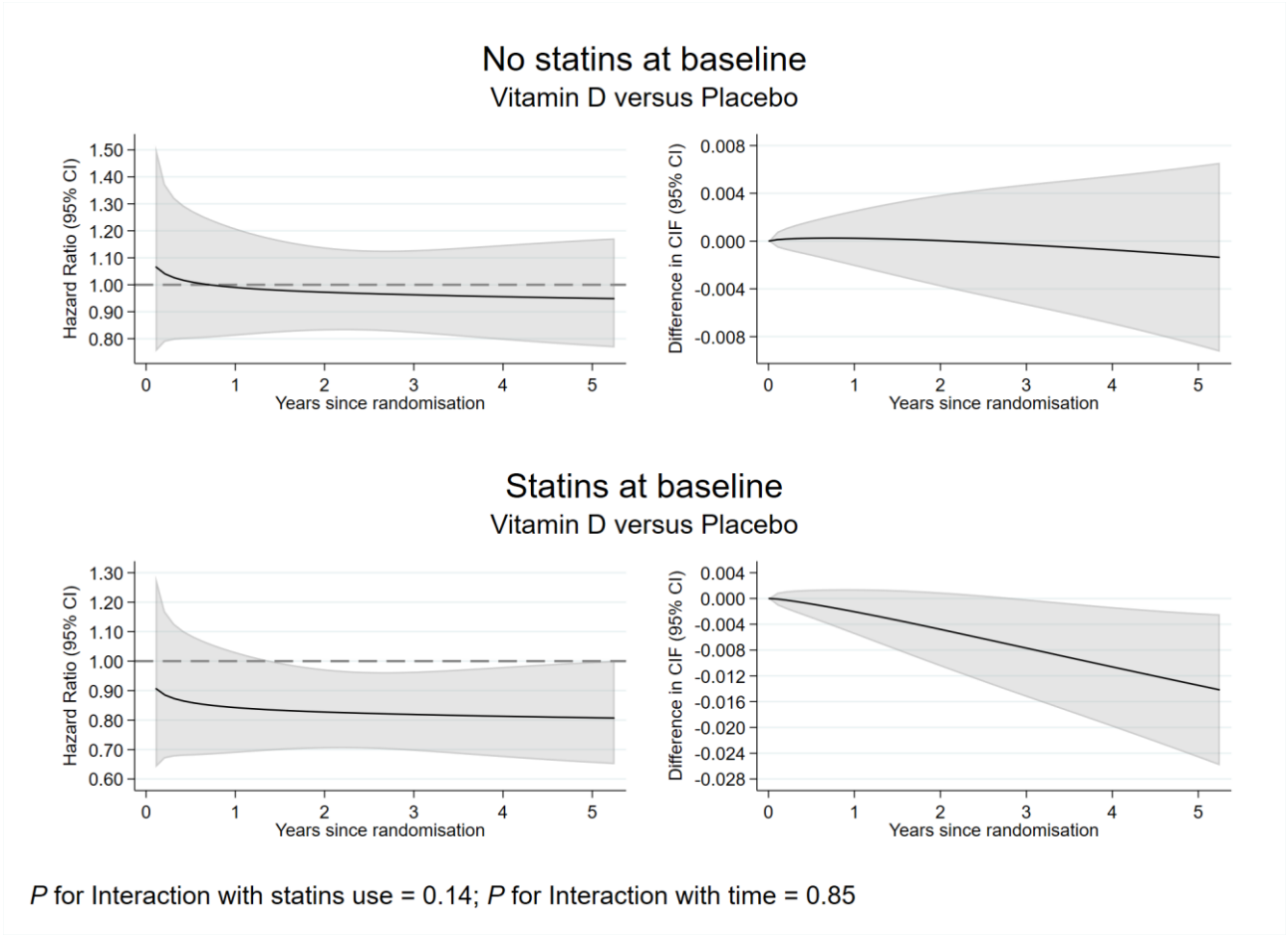
Supplementary Figure 9. Effect of vitamin D supplementation on incidence of major cardiovascular events according to predicted deseasonlised baseline 25(OH)D concentration. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, predicted 25(OH)D concentration, age, sex, state of residence, an interaction between randomisation group and predicted 25(OH)D concentration, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



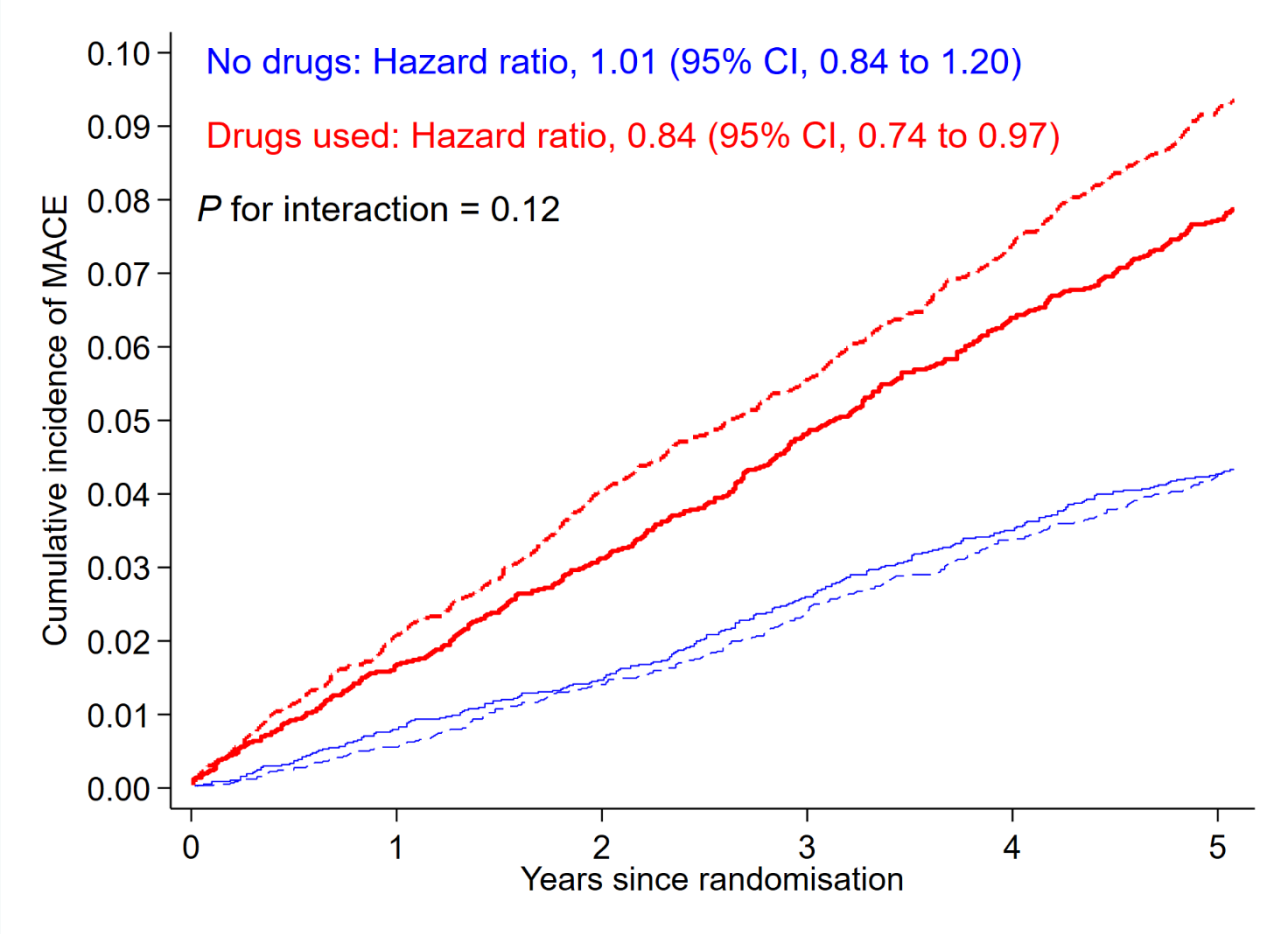
Supplementary Figure 10. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by use of statins at baseline (no statins, thin blue lines; statins used, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, statin use, age, sex, state of residence, and an interaction between randomisation group and statin use. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. N=16 participants were excluded from the analysis due to missing statins data. Abbreviation: CI, confidence interval; MACE, major cardiovascular event.



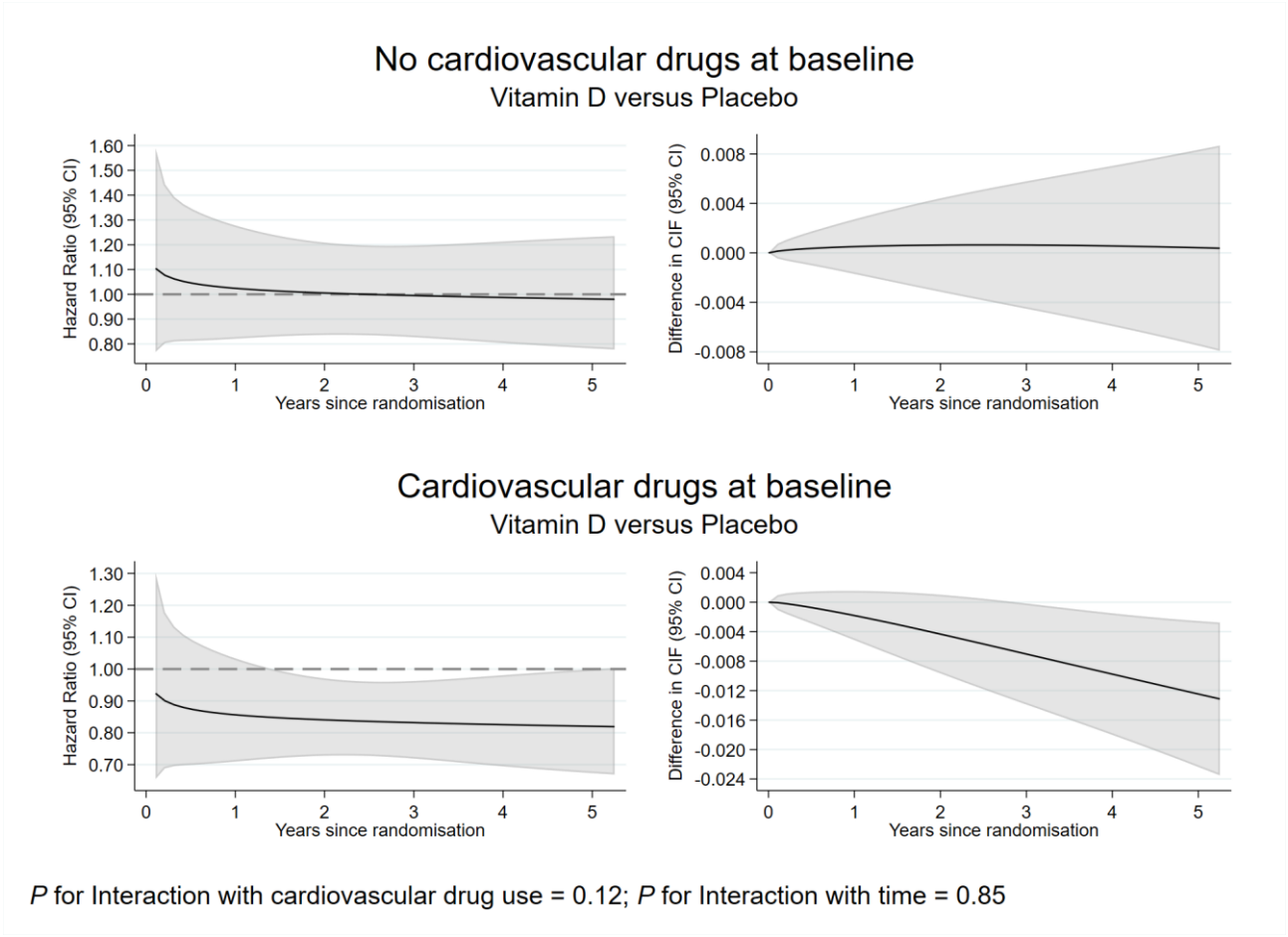
Supplementary Figure 11. Effect of vitamin D supplementation on incidence of major cardiovascular events according to statin use at baseline. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, statin use, age, sex, state of residence, an interaction between randomisation group and statin use, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. N=16 participants were excluded from the analysis due to missing statins data. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



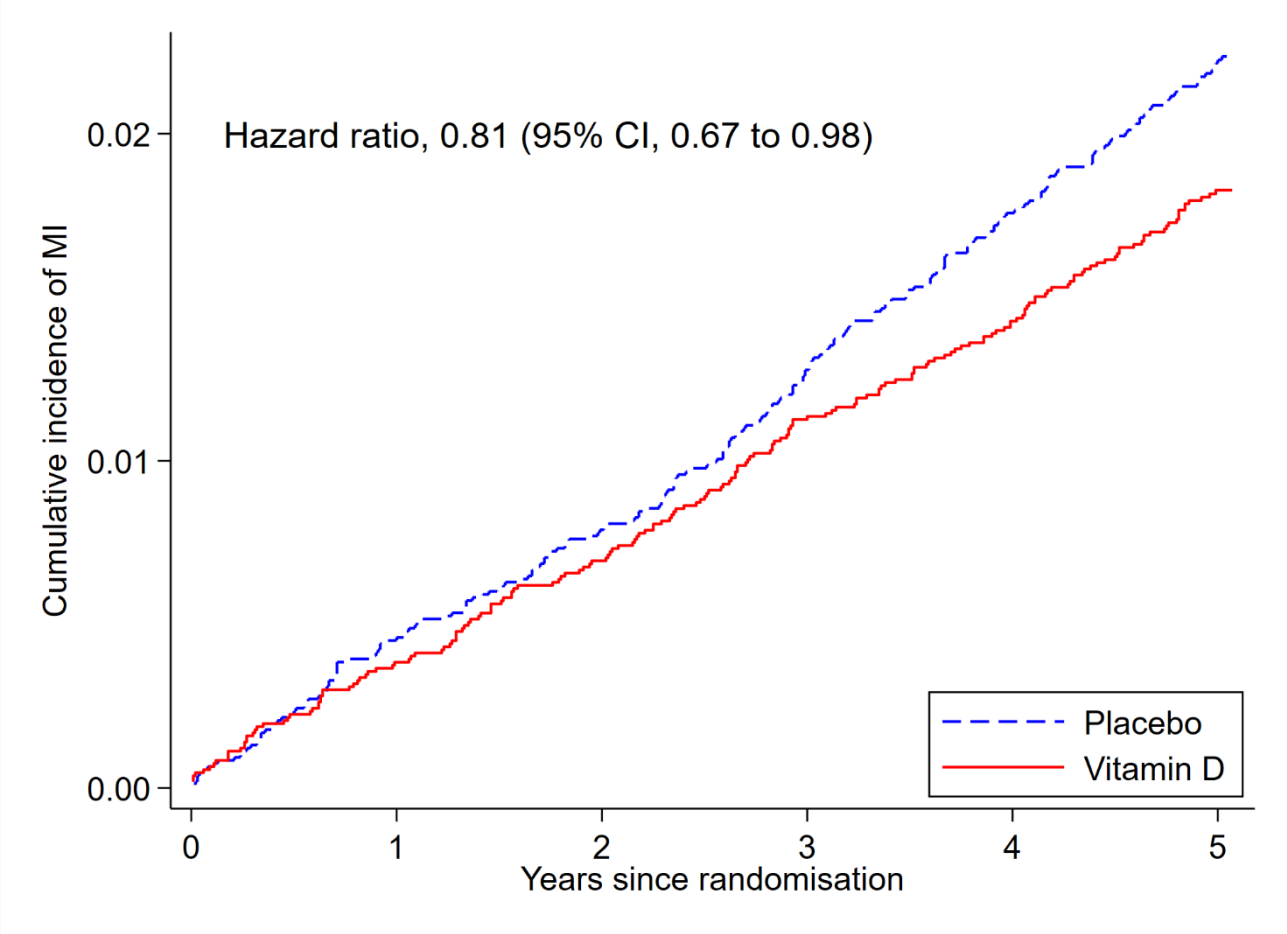
Supplementary Figure 12. Cause-specific cumulative incidence of major cardiovascular events according to randomisation group (vitamin D, solid line; placebo, dashed line) and time since randomisation, stratified by cardiovascular drug use (other than statins) at baseline (no cardiovascular drugs, thin blue lines; cardiovascular drugs used, thick red lines).

Curves estimated using Aalen-Johansen methods, treating death without prior major cardiovascular event as a competing risk. The hazard ratios (vitamin D versus placebo) were estimated using a flexible parametric survival model that included randomisation group, cardiovascular drug use, age, sex, state of residence, and an interaction between randomisation group and cardiovascular drug use. P value for the interaction is from a likelihood ratio test comparing models with and without the interaction term. N=16 participants were excluded from the analysis due to missing cardiovascular drug data. Abbreviation: CI, confidence interval; MACE, major cardiovascular event.



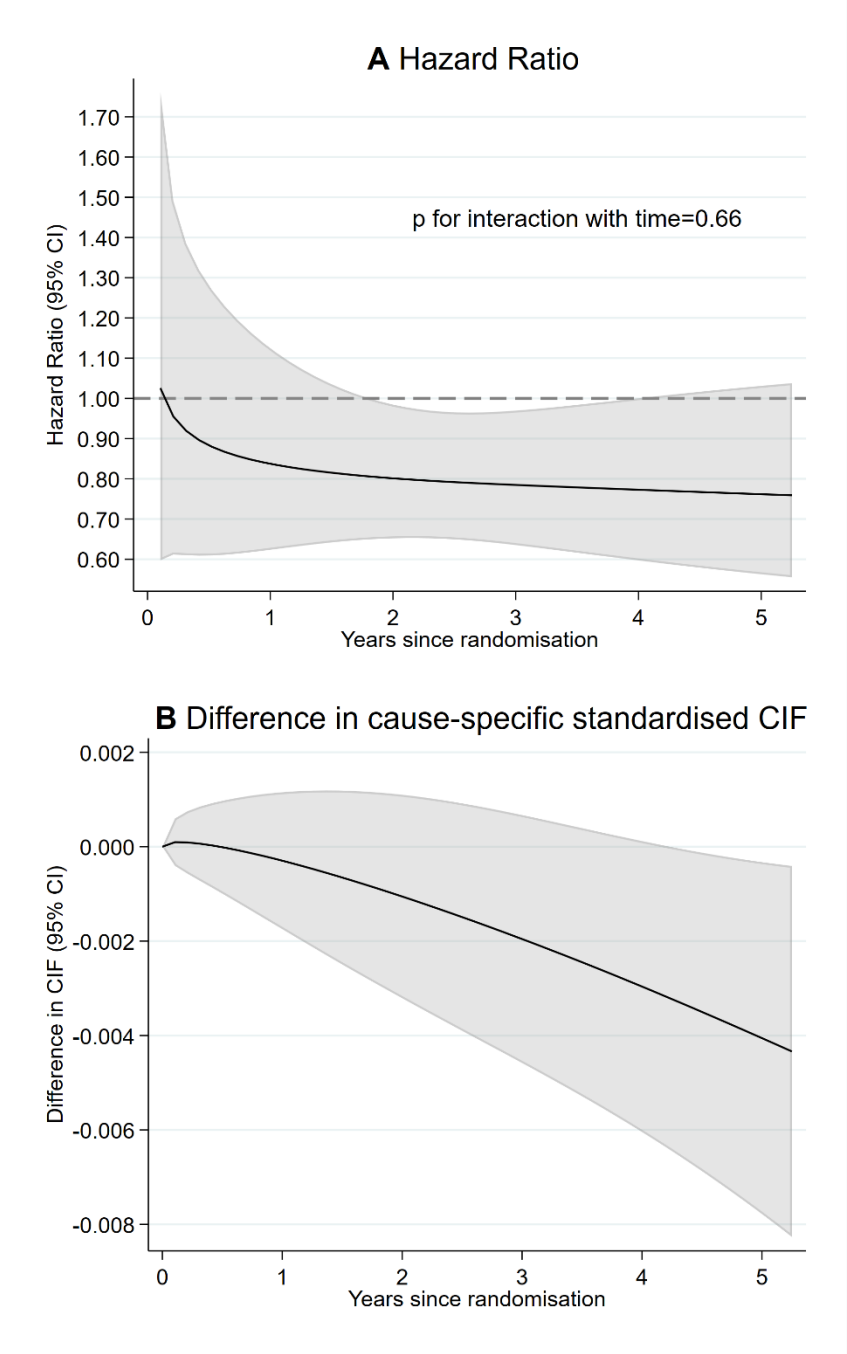
Supplementary Figure 13. Effect of vitamin D supplementation on incidence of major cardiovascular events according to cardiovascular drug use (other than statins) at baseline. Plots on the left hand side show the time-varying hazard ratio. Plots on the right hand side show the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, cardiovascular drug use, age, sex, state of residence, an interaction between randomisation group and cardiovascular drug use, and an interaction between randomisation group and time since randomisation. P values for interactions are from likelihood ratio tests that compared models with and without the interaction term of interest. Cause-specific standardised cumulative incidence was estimated treating death without prior major cardiovascular event as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. N=16 participants were excluded from the analysis due to missing cardiovascular drug data. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



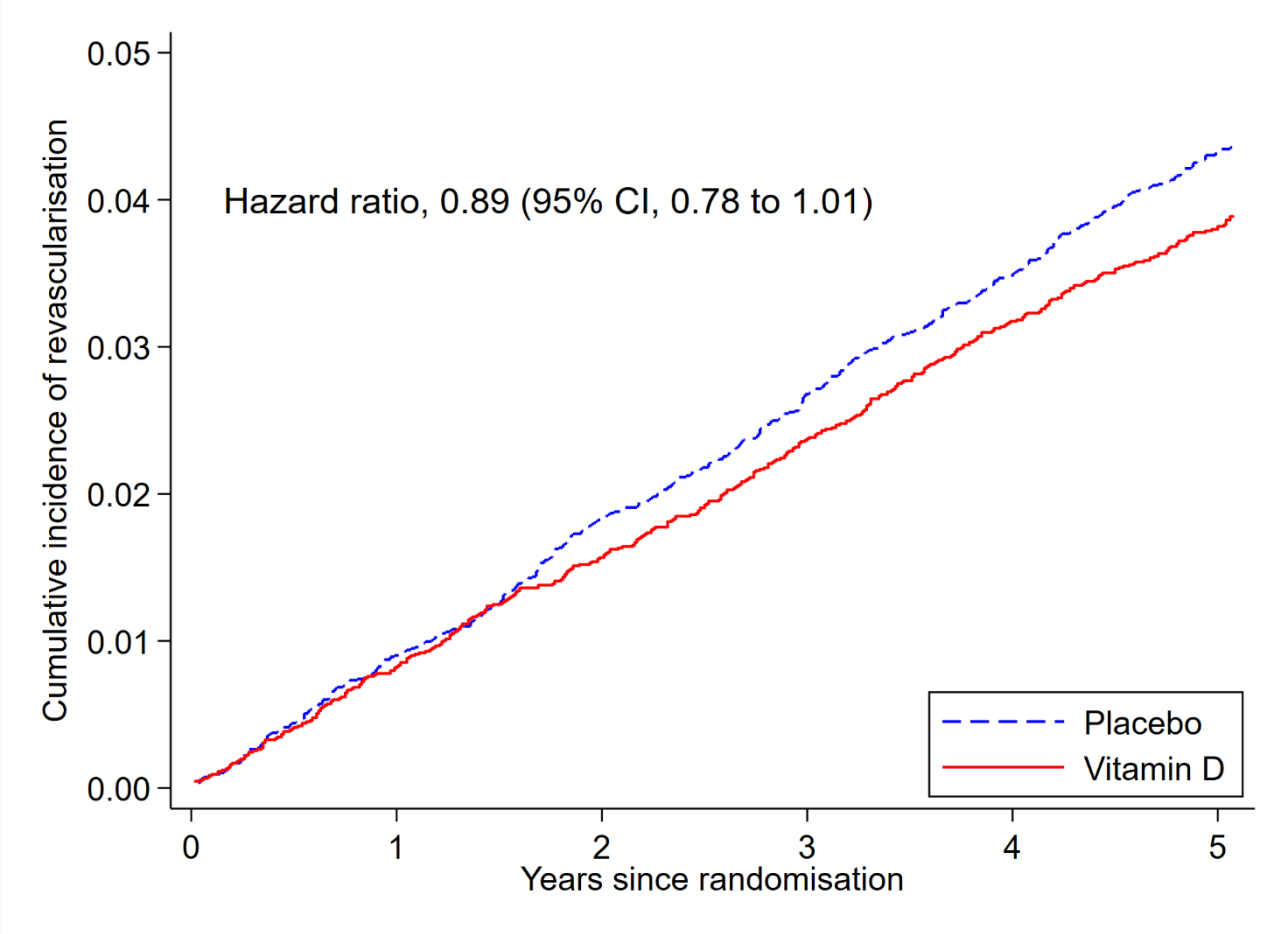
Supplementary Figure 14. Cause-specific cumulative incidence of myocardial infarction according to randomisation group and time since randomisation.

Curves estimated using Aalen-Johansen methods, treating death without prior myocardial infarction as a competing risk. The hazard ratio (vitamin D versus placebo) was estimated using a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline. Abbreviations: CI, confidence interval; MI, myocardial infarction.



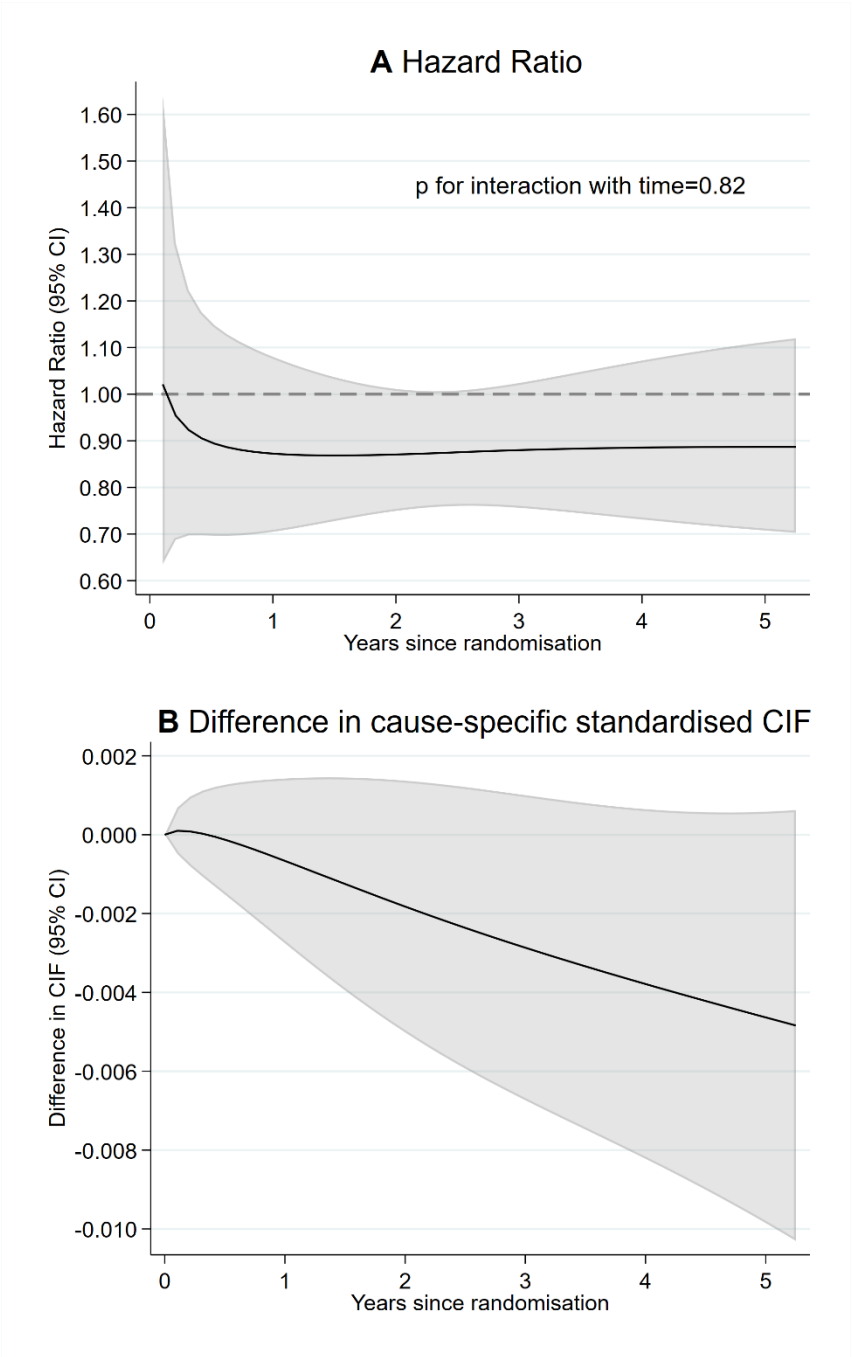
Supplementary Figure 15. Effect of vitamin D supplementation on incidence of myocardial infarction. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior myocardial infarction as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



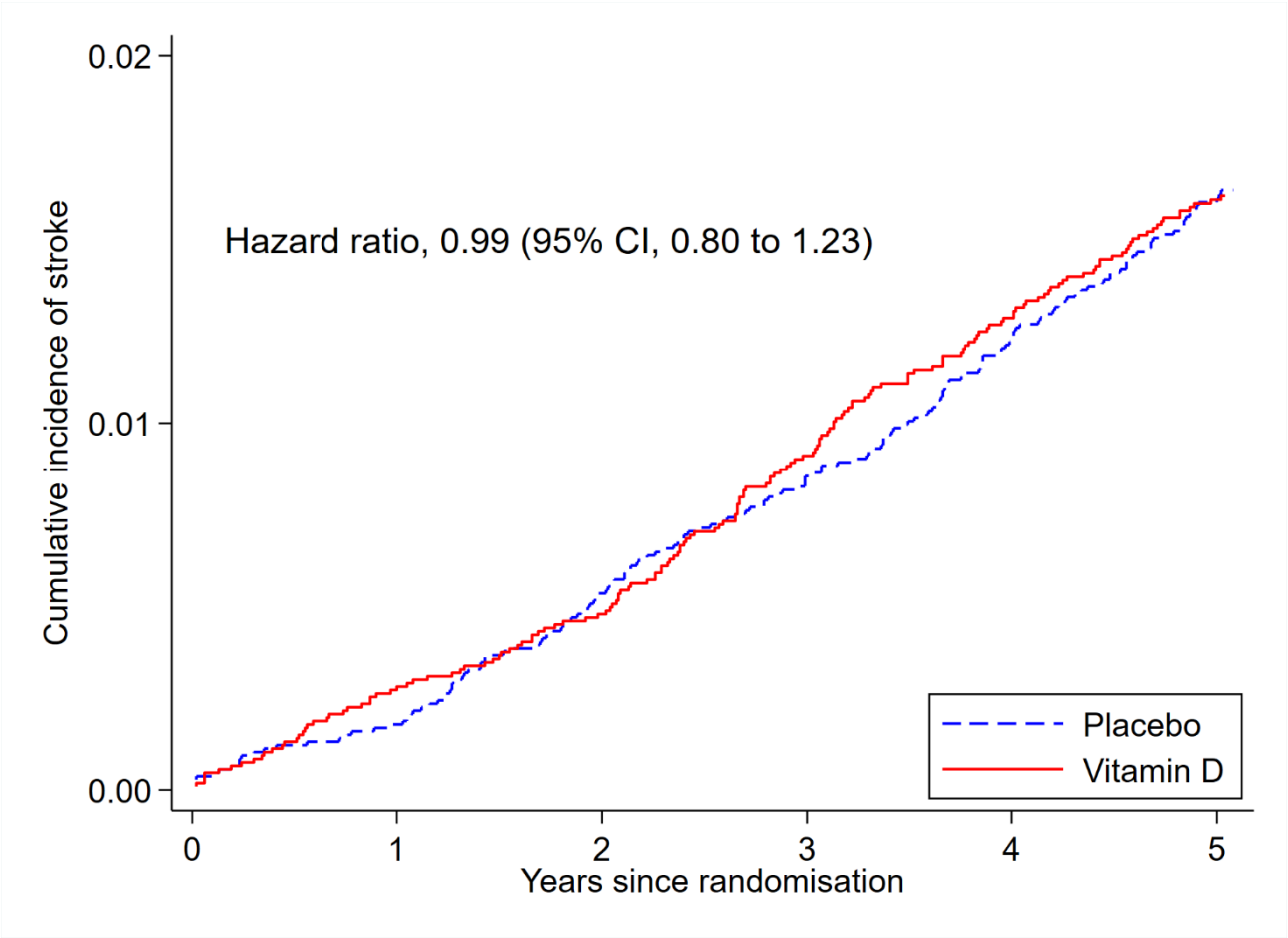
Supplementary Figure 16. Cause-specific cumulative incidence of coronary revascularisation according to randomisation group and time since randomisation.

Curves estimated using Aalen-Johansen methods, treating death without prior coronary revascularisation as a competing risk. The hazard ratio (vitamin D versus placebo) was estimated using a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline. Abbreviation: CI, confidence interval.



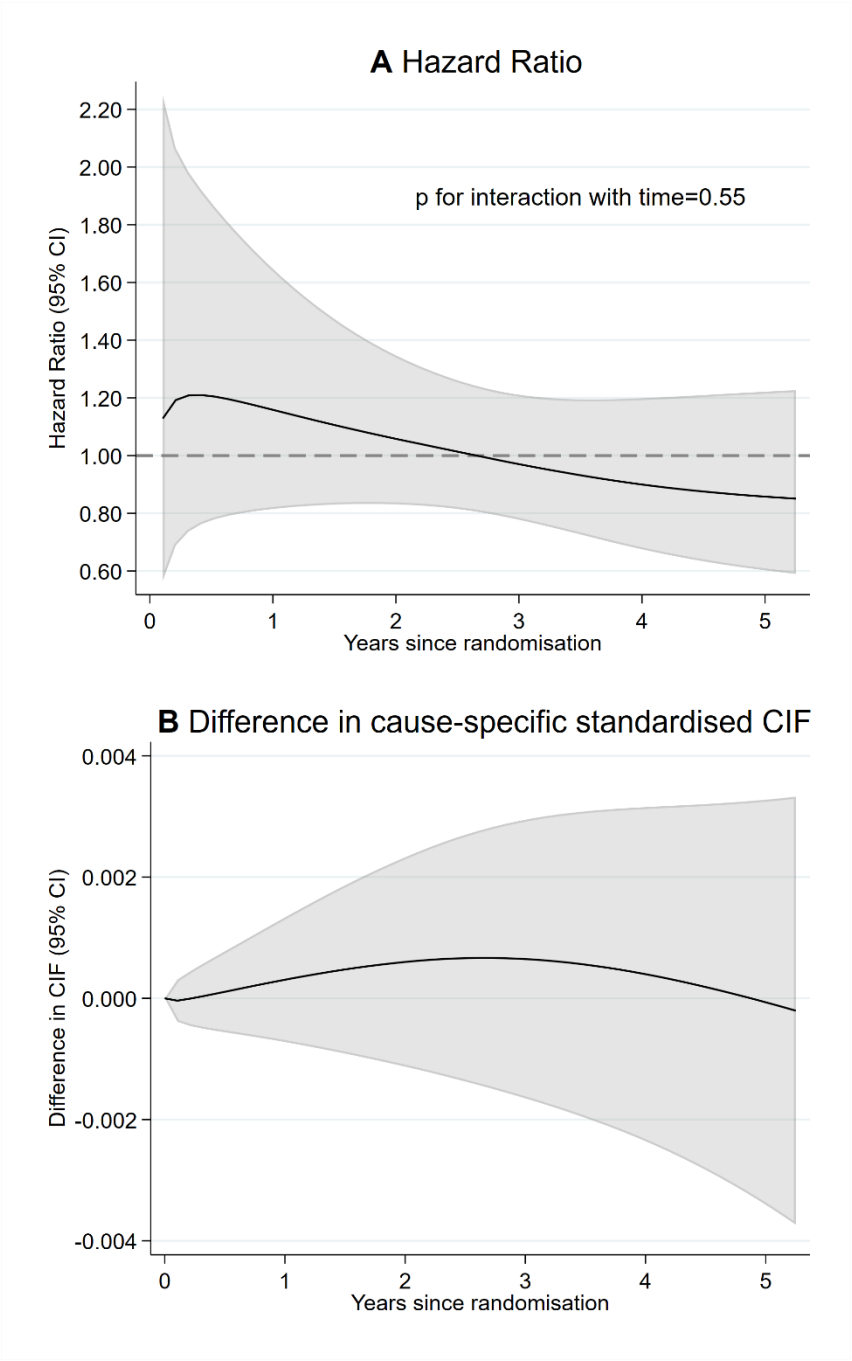
Supplementary Figure 17. Effect of vitamin D supplementation on incidence of coronary revascularisation. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior coronary revascularisation as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



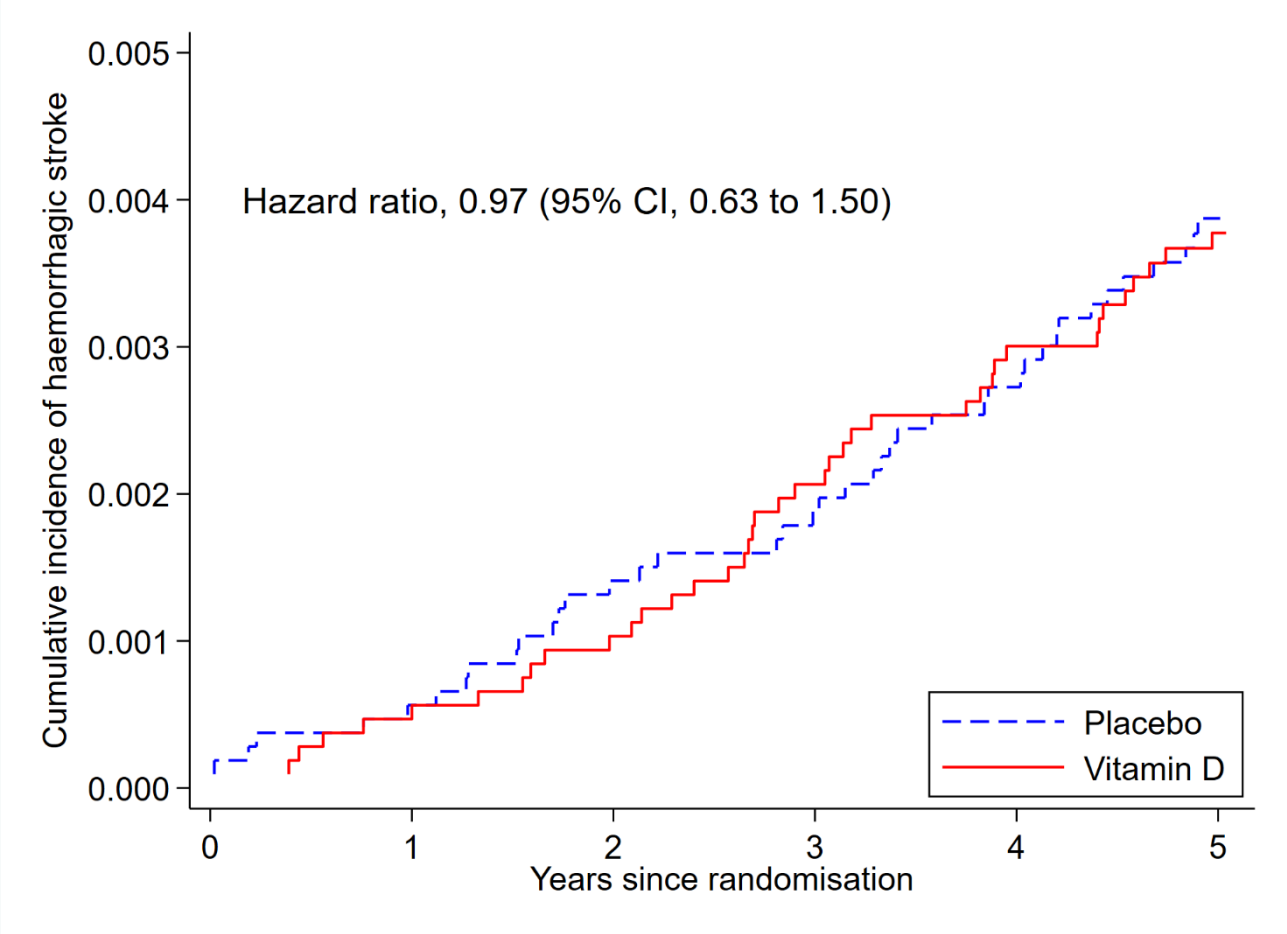
Supplementary Figure 18. Cause-specific cumulative incidence of stroke according to randomisation group and time since randomisation.

Curves estimated using Aalen-Johansen methods, treating death without prior stroke as a competing risk. The hazard ratio (vitamin D versus placebo) was estimated using a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline. Abbreviation: CI, confidence interval.



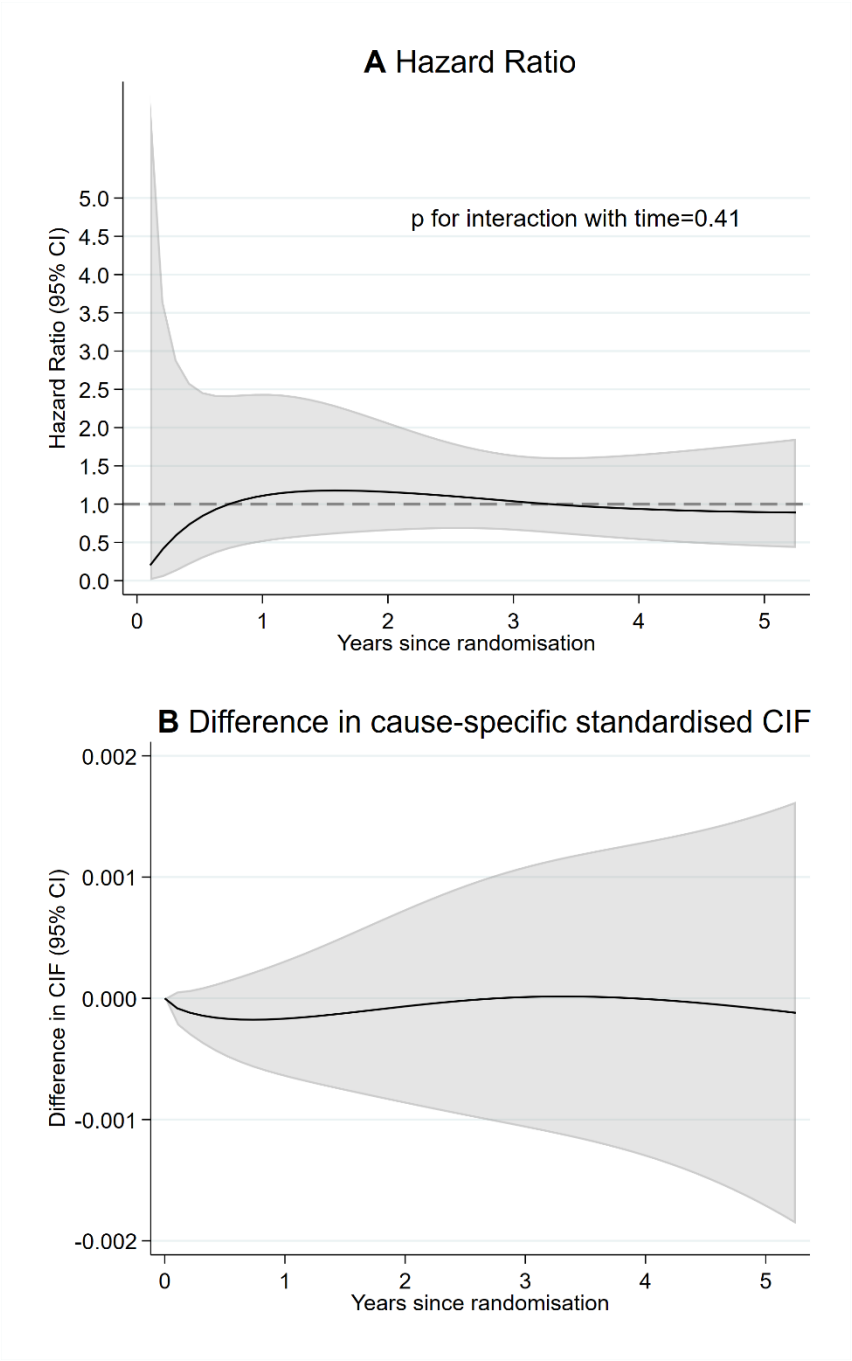
Supplementary Figure 19. Effect of vitamin D supplementation on incidence of stroke. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior stroke as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



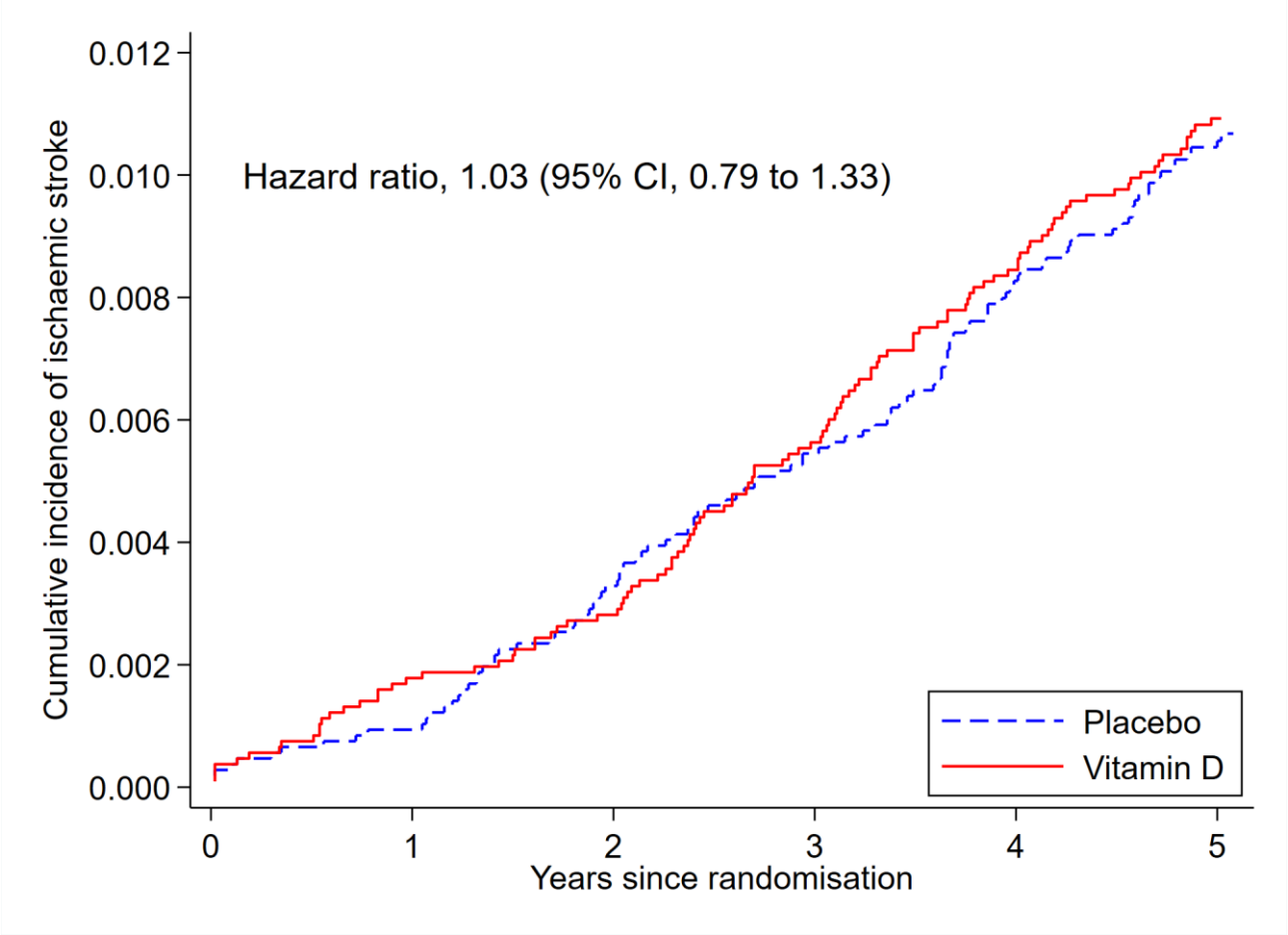
Supplementary Figure 20. Cause-specific cumulative incidence of haemorrhagic stroke according to randomisation group and time since randomisation.

Curves estimated using Aalen-Johansen methods, treating death without prior haemorrhagic stroke as a competing risk. The hazard ratio (vitamin D versus placebo) was estimated using a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline. Abbreviation: CI, confidence interval.



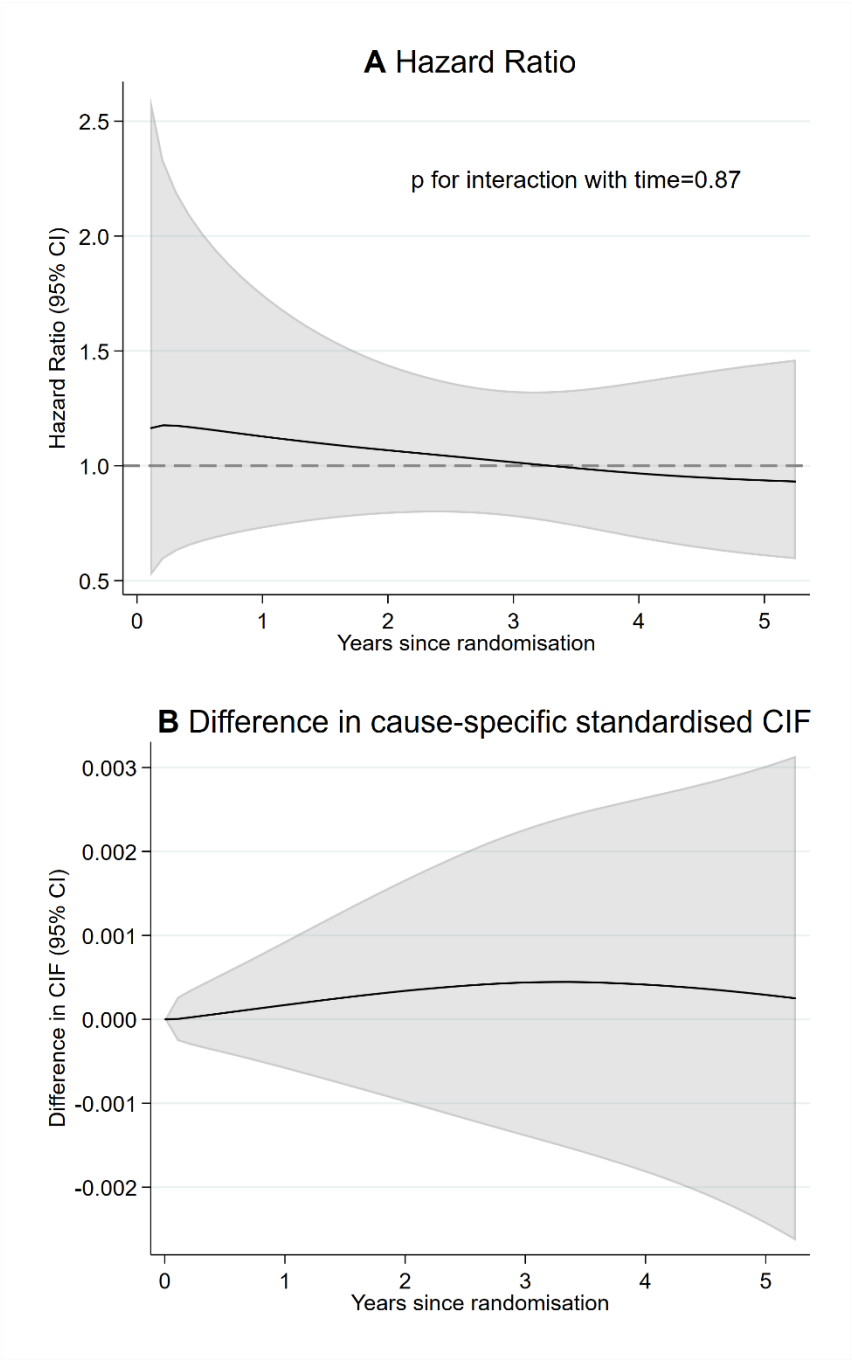
Supplementary Figure 21. Effect of vitamin D supplementation on incidence of haemorrhagic stroke. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior haemorrhagic stroke as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



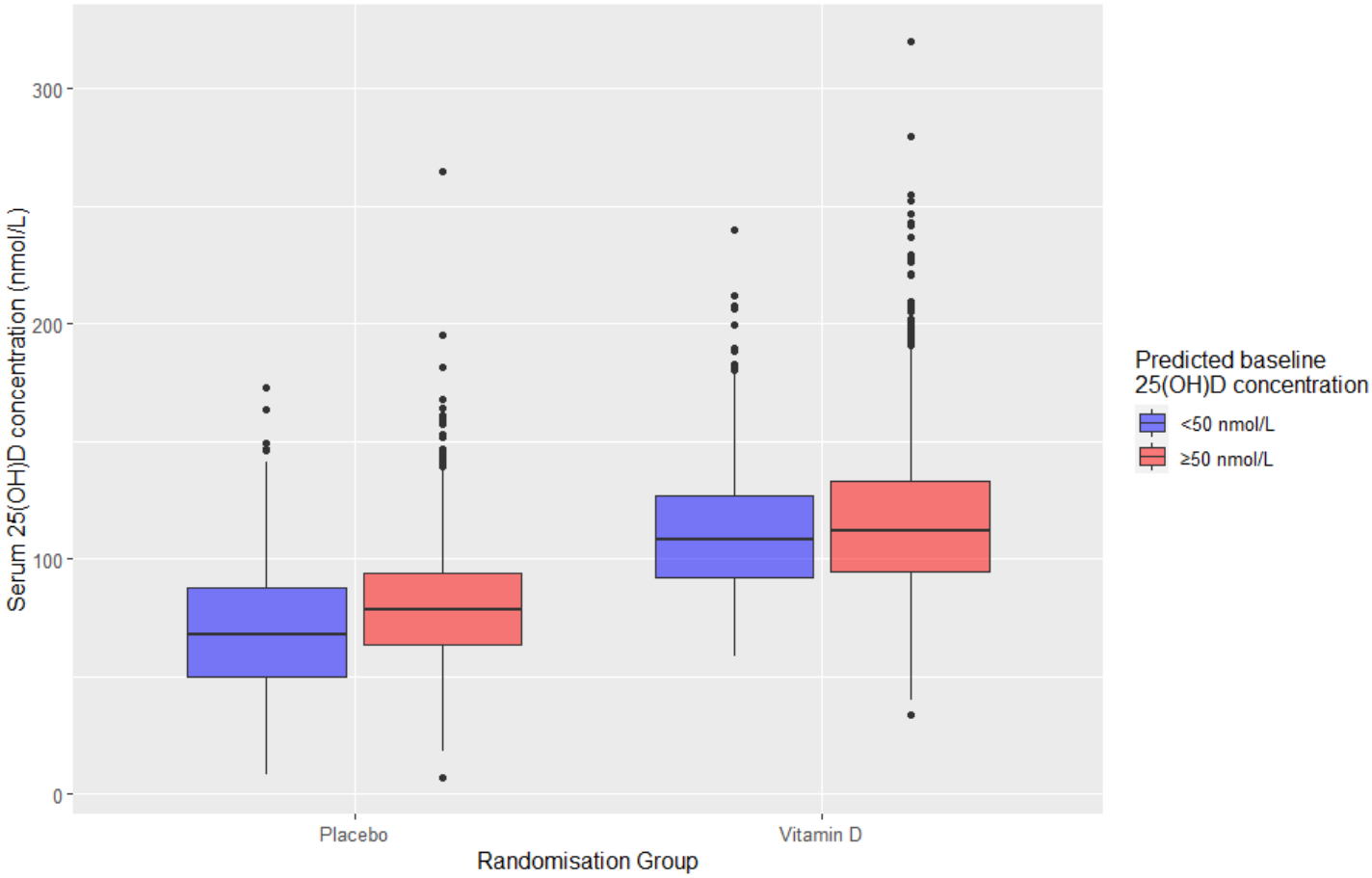
Supplementary Figure 22. Cause-specific cumulative incidence of ischaemic stroke according to randomisation group and time since randomisation.

Curves estimated using Aalen-Johansen methods, treating death without prior ischaemic stroke as a competing risk. The hazard ratio (vitamin D versus placebo) was estimated using a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline. Abbreviation: CI, confidence interval.



Supplementary Figure 23. Effect of vitamin D supplementation on incidence of ischaemic stroke. Panel A shows the time-varying hazard ratio and panel B shows the difference in cause-specific standardised cumulative incidence functions.

Estimates (comparing vitamin D and placebo) are from a flexible parametric survival model that included randomisation group, age, sex, and state of residence at baseline, and an interaction between randomisation group and time since randomisation, fitted as a restricted cubic spline with one internal knot (placed at the median of uncensored log survival times). The p-value for the interaction with time was assessed using a likelihood ratio test that compared models with and without the interaction term. Cause-specific standardised cumulative incidence was estimated treating death without prior ischaemic stroke as a competing risk, and probabilities were standardised to the distribution of age, sex, and state of residence at baseline in the entire cohort. Abbreviations: CI, confidence interval; CIF, cumulative incidence function.



Supplementary Figure 24. Measured 25(OH)D concentration during the trial according to predicted baseline 25(OH)D concentration and randomisation group.

Within each randomisation group, data for participants predicted to have 25(OH)D concentration <50 nmol/L are presented on the left hand side (in blue), and data for participants predicted to have 25(OH)D concentration ≥50 nmol/L are presented on the right hand side (in red).