

SUPPLEMENTAL MATERIAL

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Supplemental Figure 5. Cumulative incidence of A. myocardial infarction and B. fatal coronary heart disease by prevalent coronary heart disease and diabetes (those with and without albuminuria) status

Supplemental Table 1. Baseline characteristics of REGARDS participants by presence and absence of insulin-use and albuminuria

Characteristics	Diabetes only‡			
	Insulin use n = 973	Non-insulin use n = 3,039	Albuminuria n = 1,131	No albuminuria n = 2, 881
Age, years, mean ± SD	65.0 ± 8.6	64.9 ± 8.7	65.7 ± 8.5	67.4 ± 8.2
Black, n (%)	698 (71.7)	1,775 (58.4)	753 (66.6)	1,720 (59.7)
Female, n (%)	560 (57.6)	1, 717 (56.5)	614 (54.3)	1, 663 (57.7)
Region, n (%)				
Stroke belt*	345 (35.5)	1,133 (37.3)	421 (37.2)	1,057 (36.7)
Stroke buckle†	232 (23.8)	656 (21.6)	245 (21.7)	643 (22.3)
Non-stroke belt or buckle	396 (40.7)	1,250 (41.1)	465 (41.1)	1,181 (41.0)
Annual household income <\$20,000, n (%)	295 (35.2)	713 (26.5)	349 (35.3)	659 (25.9)
Education ≤ High school, n (%)	490 (50.5)	1,393 (45.9)	568 (50.3)	1,315 (45.7)
Fasting blood glucose, mg/dL, mean ± SD	145.9 ± 73.6	136.5 ± 47.9	150.1 ± 68.2	134.3 ± 48.1
Diabetes treatment, n (%)				
No pharmacologic treatment	0 (0.0)	496 (16.3)	91 (8.0)	405 (14.1)
Oral medications	0 (0.0)	2,543 (83.7)	624 (55.2)	1,919 (66.6)
Insulin	514 (52.8)	0 (0.0)	243 (21.5)	271 (9.4)
Both oral medications and insulin	459 (47.2)	0 (0.0)	173 (15.3)	286 (9.9)
Systolic blood pressure, mm Hg, mean ± SD	133.9 ± 18.3	131.0 ± 16.4	137.2 ± 18.1	129.6 ± 16.0
Diastolic blood pressure, mm Hg, mean ± SD	76.9 ± 10.9	77.0 ± 9.8	78.5 ± 11.1	76.4 ± 9.7
Hypertension prevalence, n (%)	779 (80.2)	2,332 (76.7)	941 (83.2)	2, 170 (75.4)
Smoker, n (%)				
Current	118 (12.2)	430 (14.2)	186 (16.5)	362 (12.6)
Never	453 (46.7)	1,381 (45.6)	494 (43.8)	1, 340 (46.7)
Past	400 (41.2)	1,216 (40.2)	447 (39.7)	1,169 (40.7)
Total Cholesterol, mg/dL, mean ± SD	178.3 ± 40.5	184.0 ± 41.1	186.8 ± 44.7	181.0 ± 39.4

HDL-C, mg/dL, mean ± SD	49.0 ± 15.0	47.6 ± 13.9	47.2 ± 14.4	48.2 ± 14.1
LDL-C, mg/dL, mean ± SD	102.2 ± 34.6	106.6 ± 34.7	109.0 ± 37.9	104.2 ± 33.3
Triglycerides, mg/dL, mean ± SD	132.8 ± 93.1	150.3 ± 99.1	156.6 ± 119.2	142.1 ± 88.1
Other medication use, n (%)				
Aspirin	499 (51.3)	1,418 (46.7)	528 (46.7)	1,389 (48.3)
Statins	457 (47.0)	1,262 (41.5)	492 (43.5)	1,227 (42.6)
ACE inhibitors or ARBs	708 (72.8)	1,751 (57.6)	746 (66.0)	1,713 (59.5)
BMI, kg/m², mean ± SD	33.4 ± 7.3	32.2 ± 6.5	32.5 ± 6.8	32.5 ± 6.7
Physical activity, n (%)				
None	414 (43.1)	1,136 (37.9)	687 (45.6)	5,272 (31.2)
1-3 times per week	308 (32.1)	1,113 (37.2)	449 (29.8)	6,380 (37.8)
4+ times per week	238 (24.8)	746 (24.9)	258 (23.0)	726 (25.6)
C-reactive protein, mg/L, n (%)				
<1	175 (19.5)	588 (20.5)	183 (17.5)	580 (21.3)
1 to 3	248 (27.7)	883 (30.8)	291 (27.7)	840 (30.9)
>3	474 (52.8)	1,401 (48.8)	575 (54.8)	1,300 (47.8)
Estimated glomerular filtration rate, <60 mL/min/1.73 m², n (%)	229 (25.1)	352 (12.0)	290 (27.2)	291 (10.5)
Ratio of albumin to creatinine, ≥ 30 mg/g, n (%)	416 (42.8)	715 (23.5)	1,131 (100.0)	0 (0.0)

Abbreviations: REGARDS, Reasons for Geographic and Racial Differences in Stroke; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol

*Defined as the states of Alabama, Arkansas, Louisiana, Mississippi, Tennessee and the noncoastal regions of North Carolina, South Carolina and Georgia.

†Defined as the coastal regions of North Carolina, South Carolina and Georgia.

‡Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

The frequencies and percentages may not add up to the total sample size due to missing data.

Supplemental Table 2. Incidence rates and adjusted hazard ratios and 95% confidence intervals for coronary heart disease events, myocardial infarction and fatal coronary heart disease according to severity of diabetes (insulin use and albuminuria separately) and prevalent coronary heart disease status at baseline

	Prevalent CHD only§		Diabetes only		
		<i>Insulin use</i>	<i>Non-insulin use</i>	<i>Albuminuria</i>	<i>No albuminuria</i>
CHD					
Number of events	332	88	160	106	142
Person-years of follow up	16,654	5,084	16,908	5,811	16,182
Incidence rate (95% CI)*	19.9 (17.8, 22.0)	17.3 (13.7, 20.9)	9.5 (8.0, 10.9)	18.2 (14.8, 21.7)	8.8 (7.3, 10.2)
Hazard Ratio (95% CI)†	1.0 (Reference)	1.15 (0.90, 1.47)	0.62 (0.51, 0.75)	1.15 (0.92, 1.44)	0.58 (0.47, 0.71)
Hazard Ratio (95% CI)‡	1.0 (Reference)	0.91 (0.71, 1.17)	0.57 (0.47, 0.69)	0.90 (0.71, 1.13)	0.59 (0.48, 0.72)
MI					
Number of events	238	60	124	78	106
Person-years of follow up	16,654	5,084	16,908	5,811	16,182
Incidence rate (95% CI)*	14.3 (12.5, 16.1)	11.8 (8.8, 14.8)	7.3 (6.0, 8.6)	13.4 (10.4, 16.4)	6.6 (5.3, 8.0)
Hazard Ratio (95% CI)†	1.0 (Reference)	1.16 (0.87, 1.55)	0.69 (0.55, 0.86)	1.24 (0.95, 1.61)	0.63 (0.49, 0.79)
Hazard Ratio (95% CI)‡	1.0 (Reference)	0.92 (0.68, 1.25)	0.64 (0.51, 0.80)	0.98 (0.75, 1.28)	0.64 (0.50, 0.81)
Fatal CHD					
Number of events	132	34	52	37	49
Person-years of follow up	16,654	5,084	16,908	5,811	16,182
Incidence rate (95% CI)*	7.9 (6.6, 9.3)	6.7 (4.4, 8.9)	3.1 (2.2, 3.9)	6.4 (4.3, 8.4)	3.0 (2.2, 3.9)
Hazard Ratio (95% CI)†	1.0 (Reference)	1.05 (0.71, 1.55)	0.49 (0.36, 0.69)	0.96 (0.66, 1.40)	0.49 (0.35, 0.69)
Hazard Ratio (95% CI)‡	1.0 (Reference)	0.80 (0.54, 1.21)	0.44 (0.32, 0.62)	0.71 (0.49, 1.05)	0.50 (0.35, 0.70)

Abbreviations: CHD, coronary heart disease; MI, myocardial infarction; CHD only; prevalent coronary heart disease; CI, confidence interval

*Per 1,000 person years

†Adjusted for age (continuous), race (categorical), sex (categorical) and region of residence (categorical) for the overall models.

‡Adjusted for model 1 covariates, income (categorical) and education (categorical), systolic and diastolic blood pressure (continuous), hypertension (hypertensive based on SBP, DBP and self-reported use of antihypertensive medications) (categorical), cigarette smoking (categorical), total cholesterol (continuous),

HDL cholesterol (continuous), triglycerides (continuous) and use of other medications (aspirin; statins; ACE inhibitors or ARBs) (categorical), BMI (continuous), physical activity (categorical), C-reactive protein (categorical), estimated glomerular filtration rate (categorical), urinary albumin to creatinine ratio (categorical) with the exclusion of urinary albumin to creatinine ratio (categorical) for models with diabetes severity based on presence of albuminuria as the exposure. §CHD was assessed using ECG evidence of MI or self-report of MI or revascularization. ||Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Supplemental Table 3. Incidence rates and adjusted hazard ratios and 95% confidence intervals for total coronary heart disease events according to diabetes and prevalent coronary heart disease status at baseline, stratified by age

Age < 65 years				
	Prevalent CHD only§	Diabetes only 	Diabetes and prevalent CHD	Neither diabetes nor prevalent CHD
CHD				
Number of events	80	98	86	186
Person-years of follow up	5,567	11,210	3,009	55,173
Incidence rate (95% CI)*	14.4 (11.2, 17.5)	8.7 (7.0, 10.4)	28.6 (22.6, 34.6)	3.4 (2.9, 3.9)
Hazard Ratio (95% CI)†	1.0 (Reference)	0.68 (0.51, 0.92)	2.01 (1.48, 2.73)	0.27 (0.21, 0.36)
Hazard Ratio (95% CI)‡	1.0 (Reference)	0.61 (0.45, 0.82)	1.53 (1.12, 2.10)	0.32 (0.24, 0.41)
Age ≥ 65 years				
	Prevalent CHD only§	Diabetes only 	Diabetes and prevalent CHD	Neither diabetes nor prevalent CHD
CHD				
Number of events	252	150	186	347
Person-years of follow up	11,087	10,783	4,694	44,675
Incidence rate (95% CI)*	22.7 (19.9, 25.5)	13.9 (11.7, 16.1)	39.6 (33.9, 45.3)	7.8 (7.0, 8.6)
Hazard Ratio (95% CI)†	1.0 (Reference)	0.74 (0.60, 0.91)	1.89 (1.56, 2.29)	0.41 (0.35, 0.48)
Hazard Ratio (95% CI)‡	1.0 (Reference)	0.65 (0.52, 0.80)	1.51 (1.24, 1.85)	0.45 (0.38, 0.53)
P for difference in hazard ratios by age		0.74	0.95	0.03

Abbreviations: CHD, coronary heart disease events; MI, myocardial infarction; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease; CI, confidence interval

*Per 1,000 person years

†Adjusted for age (continuous), race (categorical), sex (categorical) and region of residence (categorical).

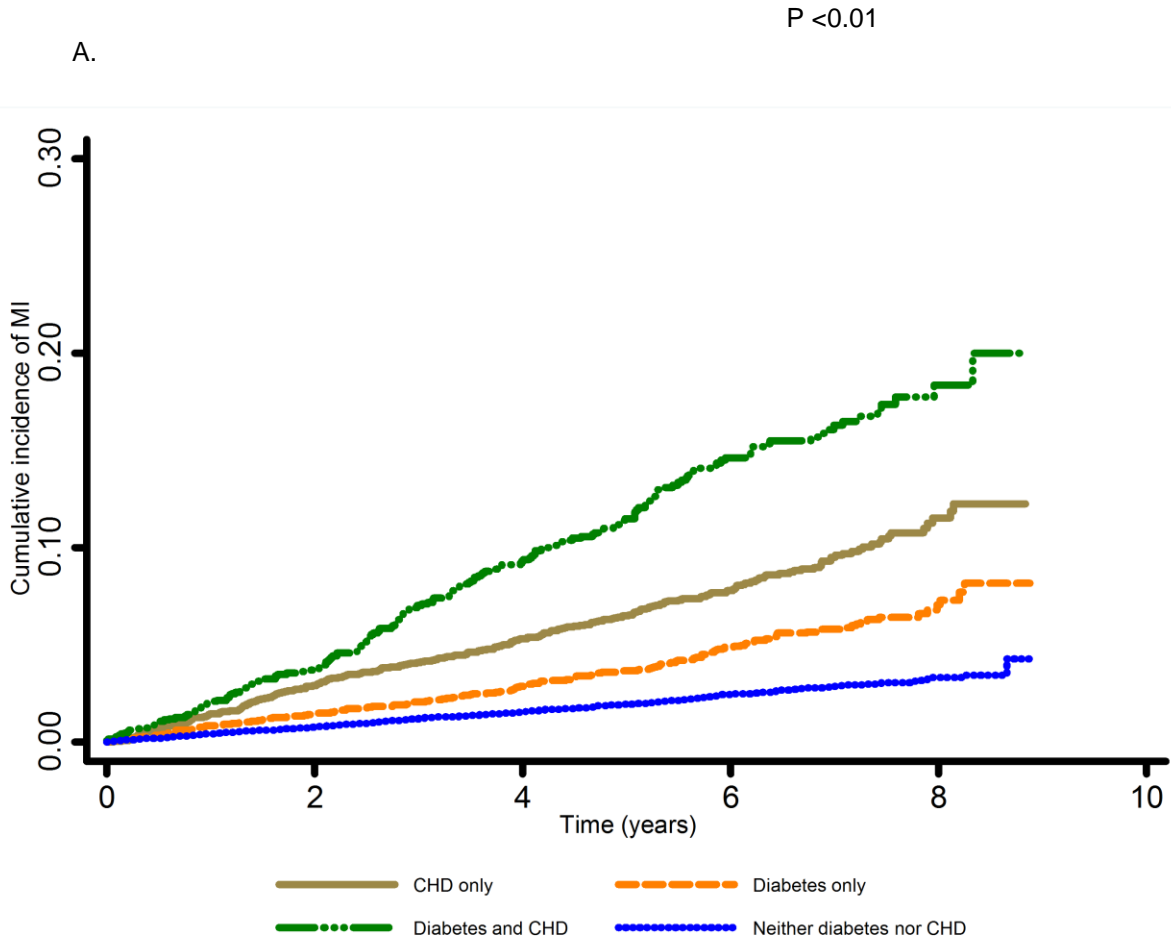
‡Adjusted for model 1 covariates, income (categorical) and education (categorical), systolic and diastolic blood pressure (continuous), hypertension (hypertensive based on SBP, DBP and self-reported use of antihypertensive medications) (categorical), cigarette smoking (categorical), total cholesterol (continuous), HDL cholesterol (continuous), triglycerides (continuous) and use of other medications (aspirin; statins; ACE inhibitors or ARBs) (categorical), BMI (continuous), physical activity (categorical), C-reactive protein (categorical), estimated glomerular filtration rate (categorical), urinary albumin to creatinine ratio (categorical).

§CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

||Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

P for omnibus interaction test = 0.04

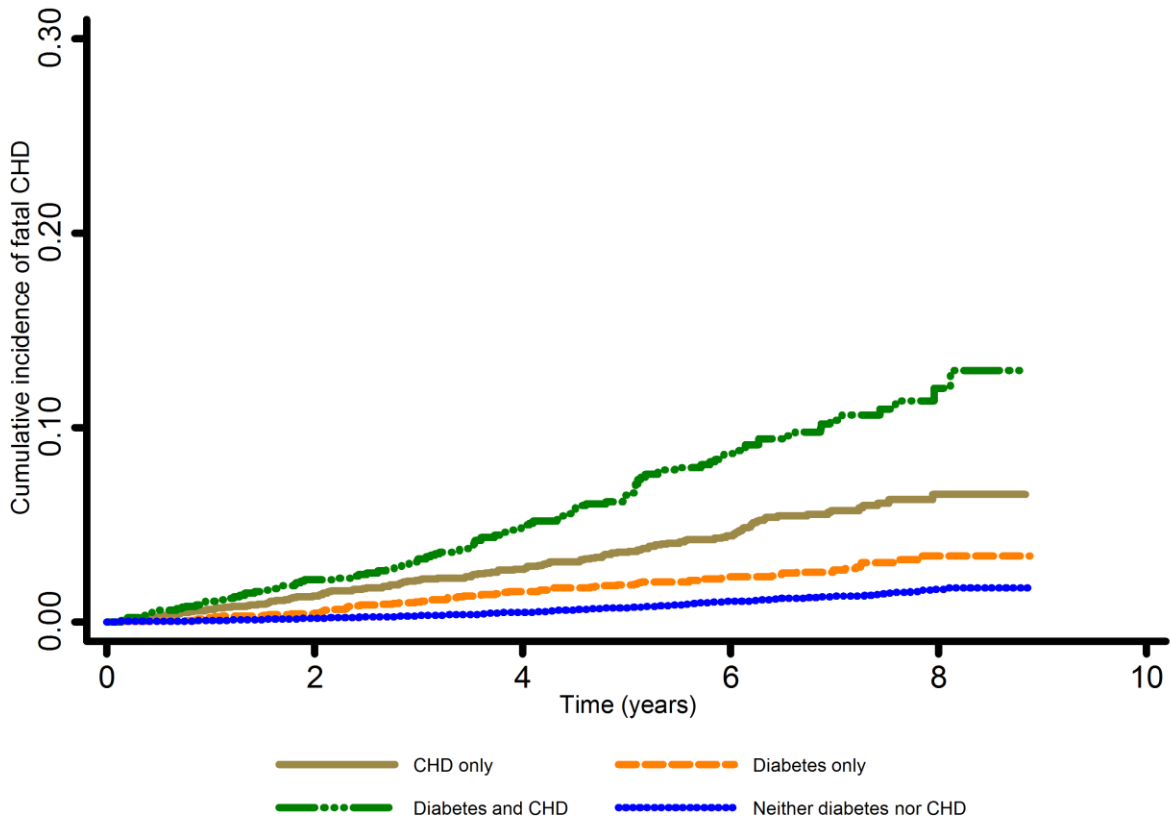
Supplemental Figure 1. Cumulative incidence of A. myocardial infarction and B. fatal coronary heart disease by prevalent coronary heart disease and diabetes status



Abbreviations: MI, myocardial infarction; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
 Exposure groups: CHD only, Diabetes only, Diabetes and CHD, Neither diabetes nor CHD.
 CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.
 Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.
 Outcome: Y-axis

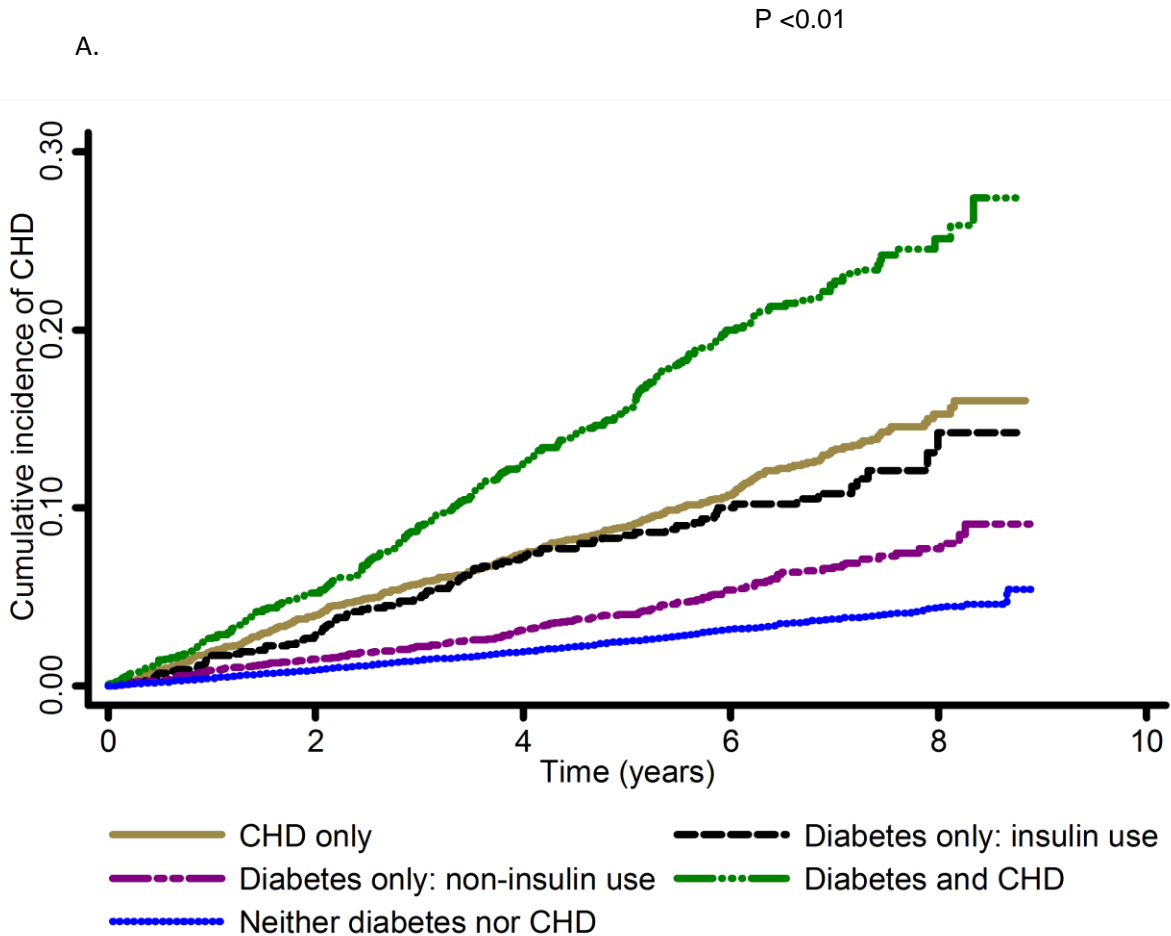
B.

P <0.01



Abbreviations: Fatal CHD, fatal coronary heart disease; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
Exposure groups: CHD only, Diabetes only, Diabetes and CHD, Neither diabetes nor CHD.
CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.
Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.
Outcome: Y-axis

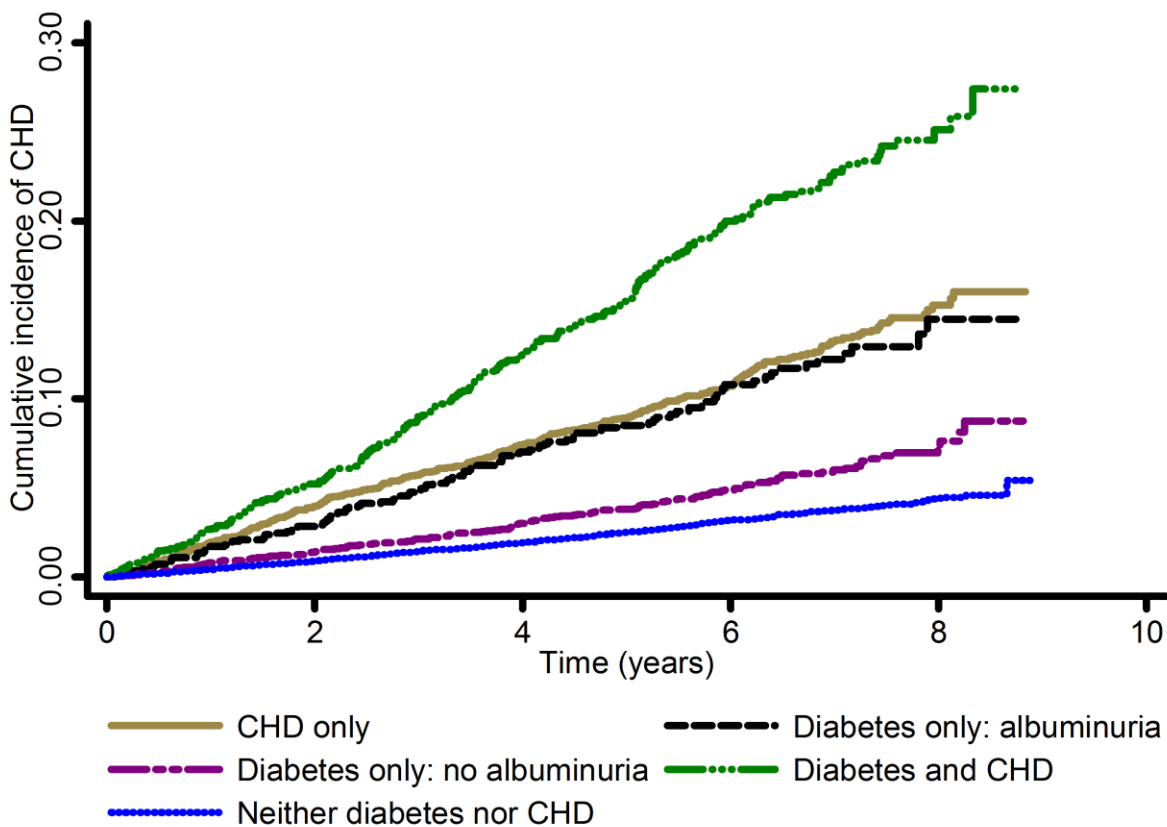
Supplemental Figure 2. Cumulative incidence of coronary heart disease by A. prevalent coronary heart disease and diabetes (insulin users and non-insulin users) status and B. prevalent coronary heart disease and diabetes (those with and without albuminuria) status



Abbreviations: CHD, coronary heart disease; CHD only, prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
 Exposure groups: CHD only, Diabetes only: insulin use, Diabetes only: non-insulin use, Diabetes and CHD, Neither diabetes nor CHD
 CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.
 Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.
 Outcome: Y-axis

P < 0.01

B.



Abbreviations: CHD, coronary heart disease; CHD only, prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
Exposure groups: CHD only, Diabetes only: albuminuria, Diabetes only: no albuminuria, Diabetes and CHD, Neither diabetes nor CHD.

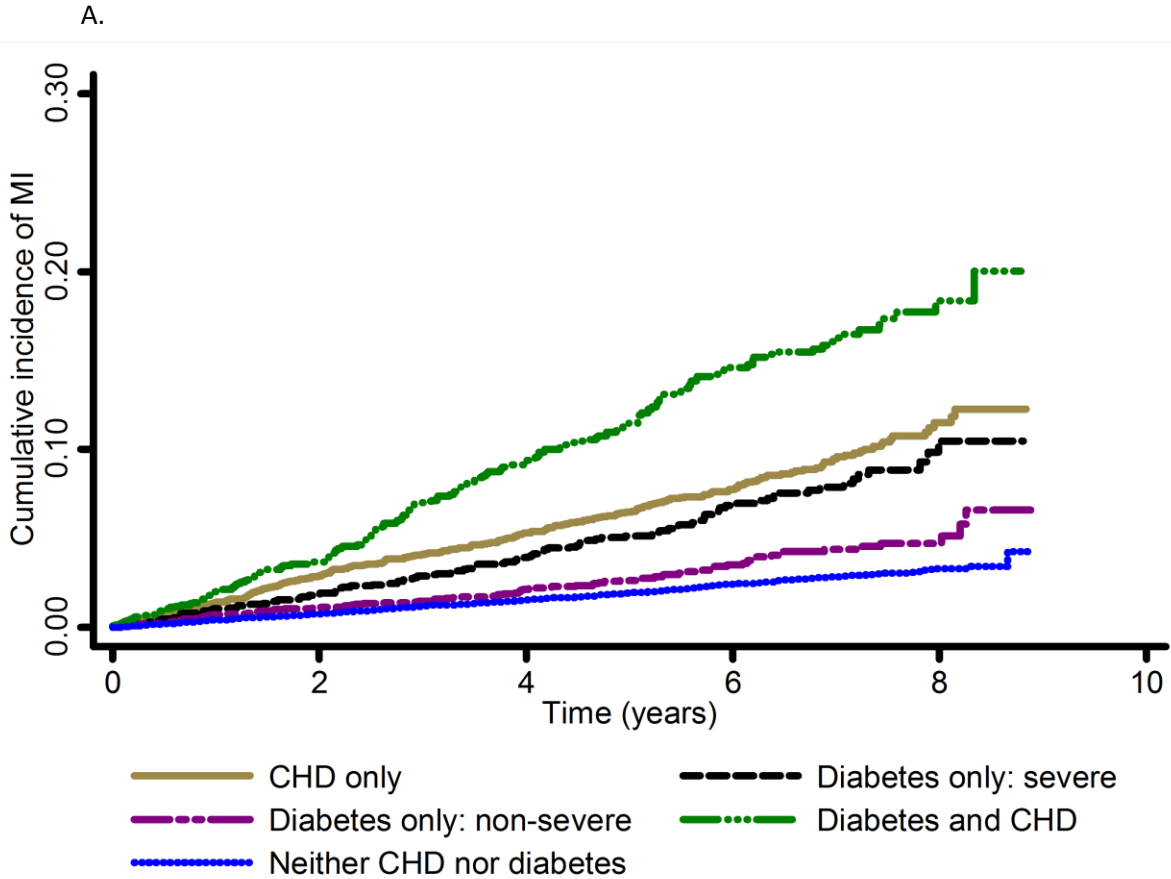
CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Outcome: Y-axis

Supplemental Figure 3. Cumulative incidence of A. myocardial infarction and B. fatal coronary heart disease by prevalent coronary heart disease and diabetes (insulin use and/or albuminuria) status

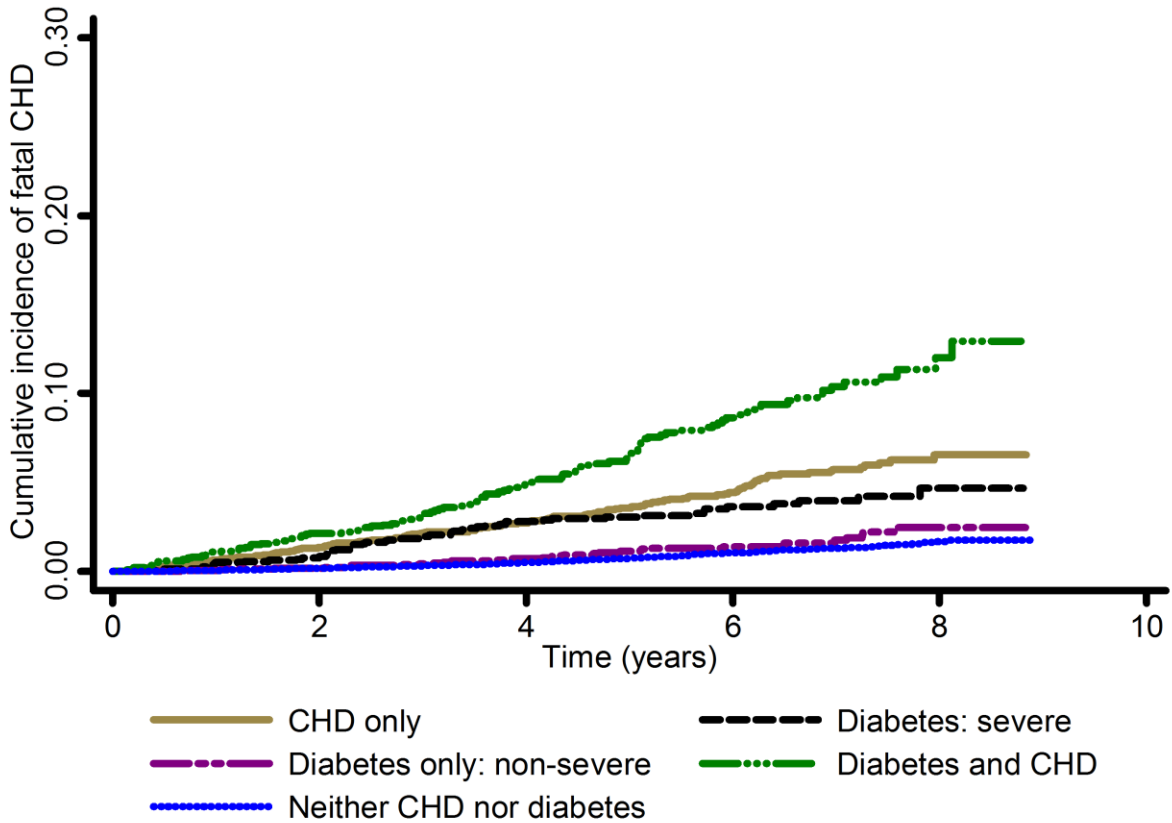
P <0.01



Abbreviations: CHD, coronary heart disease; CHD only, prevalent coronary heart disease; Diabetes only: severe, diabetes with insulin and/or albuminuria; Diabetes only: non-severe, diabetes with neither insulin nor albuminuria; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
 Exposure groups: CHD only, Diabetes only: severe, Diabetes only: non-severe, Diabetes and CHD, Neither diabetes nor CHD
 CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.
 Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.
 Outcome: Y-axis

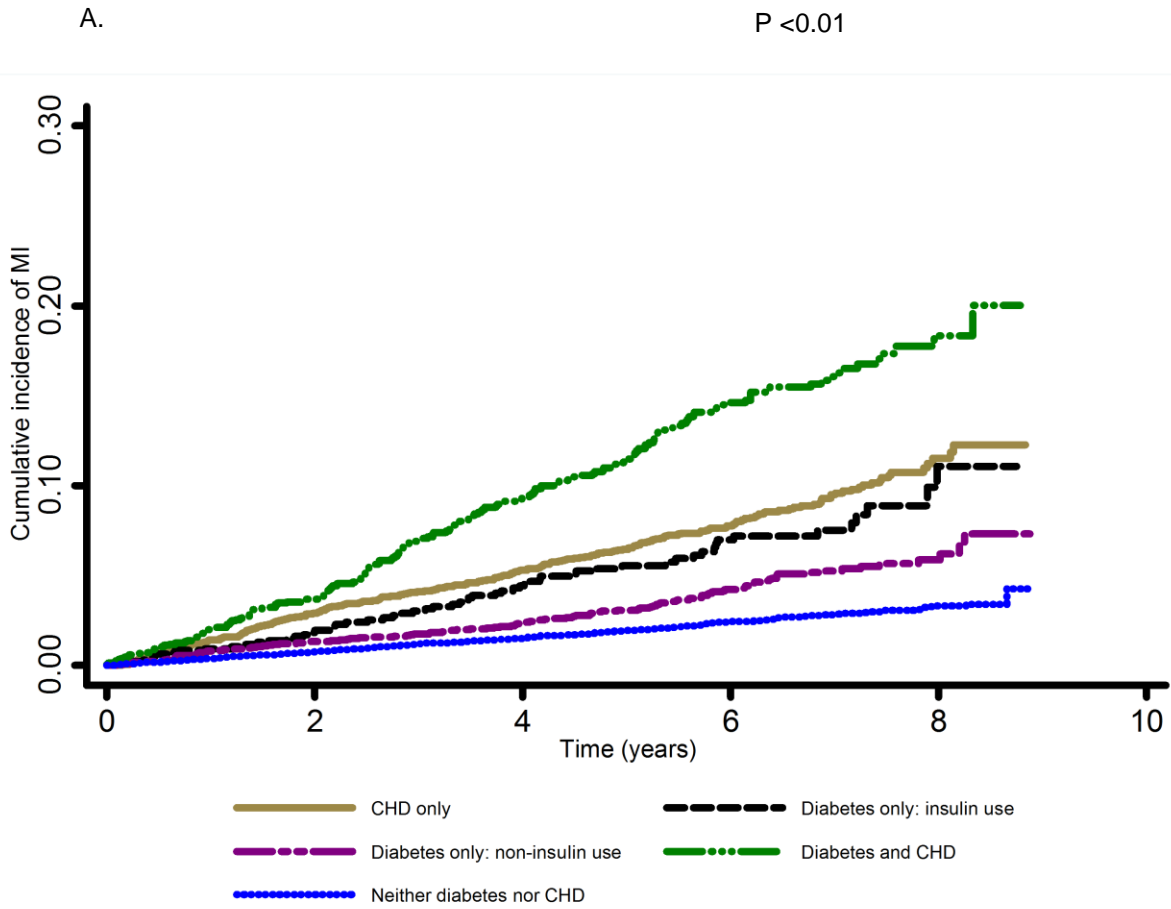
B.

P < 0.01



Abbreviations: CHD, coronary heart disease; CHD only, prevalent coronary heart disease; Diabetes only: severe, diabetes with insulin and/or albuminuria; Diabetes only: non-severe, diabetes with neither insulin nor albuminuria; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
Exposure groups: CHD only, Diabetes only: severe, Diabetes only: non-severe, Diabetes and CHD, Neither diabetes nor CHD
CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.
Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.
Outcome: Y-axis

Supplemental Figure 4. Cumulative incidence of A. myocardial infarction and B. fatal coronary heart disease by prevalent coronary heart disease and diabetes (insulin users and non-insulin users) status



Abbreviations: MI, myocardial infarction; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease

Exposure groups: CHD only, Diabetes only: insulin use, Diabetes only: non-insulin use, Diabetes and CHD, Neither diabetes nor CHD

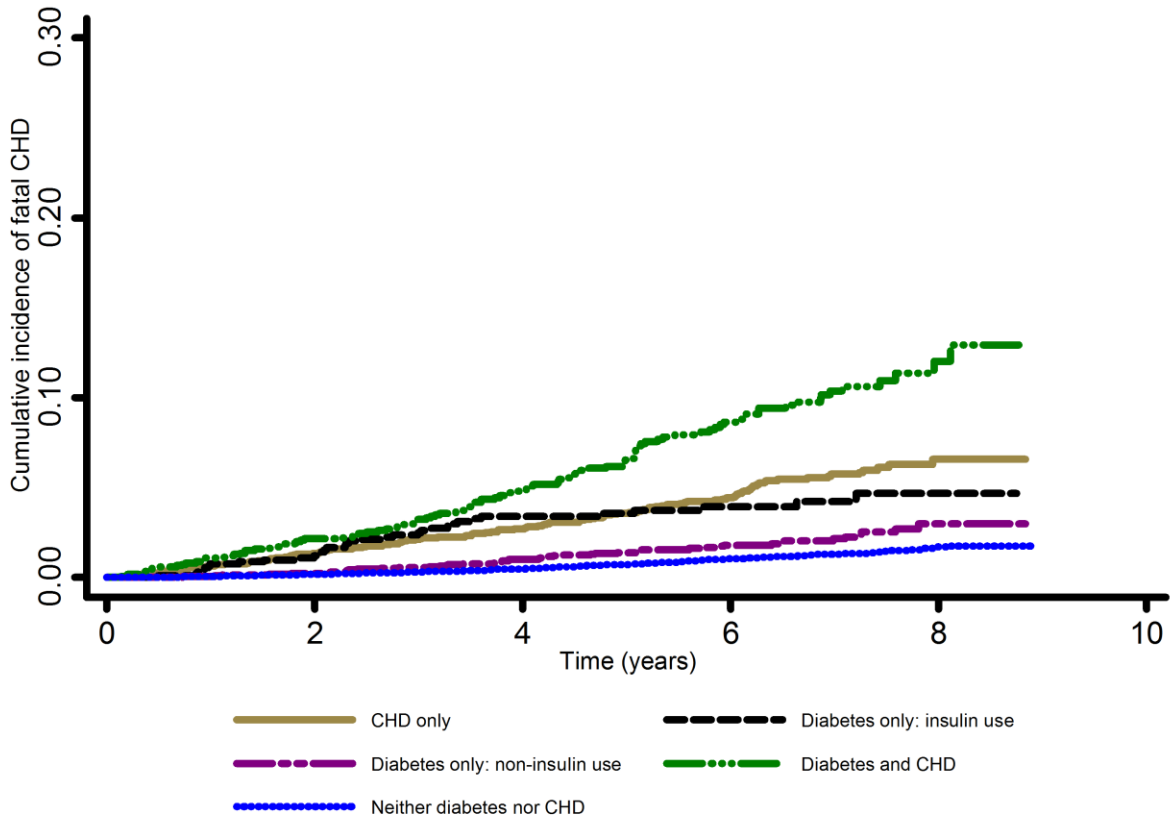
CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Outcome: Y-axis

P < 0.01

B.



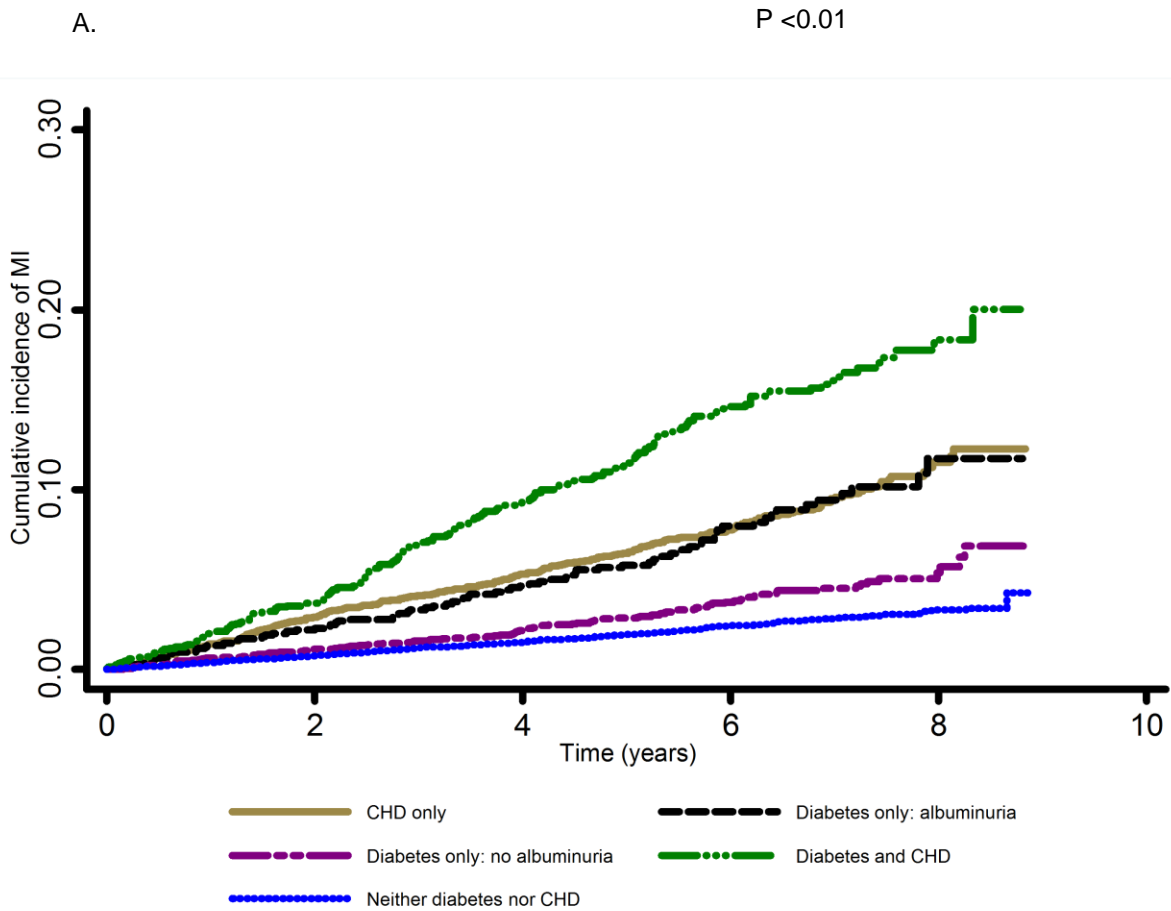
Abbreviations: Fatal CHD, fatal coronary heart disease; CHD only, prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
Exposure groups: CHD only, Diabetes only: insulin use, Diabetes only: non-insulin use, Diabetes and CHD, Neither diabetes nor CHD

CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Outcome: Y-axis

Supplemental Figure 5. Cumulative incidence of A. myocardial infarction and B. fatal coronary heart disease by prevalent coronary heart disease and diabetes (those with and without albuminuria) status



Abbreviations: MI, myocardial infarction; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
 Exposure groups: CHD only, Diabetes only: albuminuria, Diabetes only: no albuminuria, Diabetes and CHD, Neither diabetes nor CHD.

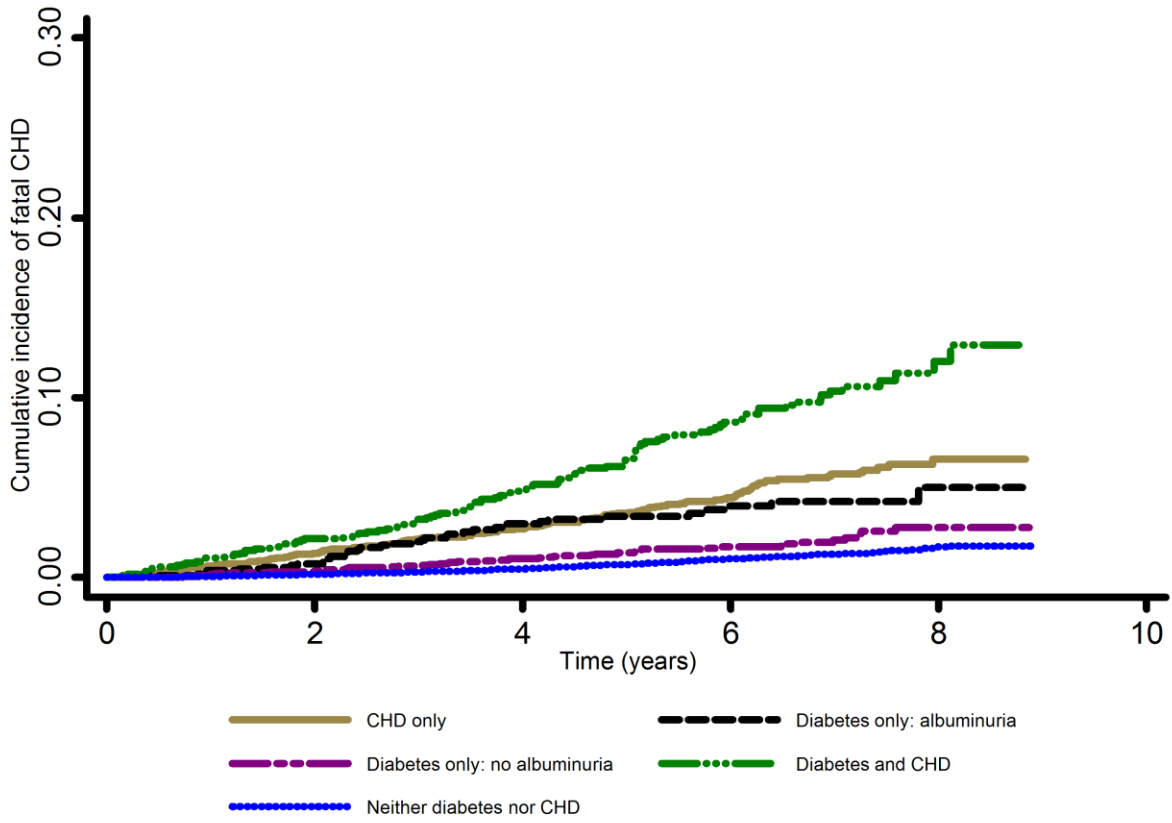
CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Outcome: Y-axis

P < 0.01

B.



Abbreviations: Fatal CHD, fatal coronary heart disease; CHD only; prevalent coronary heart disease; diabetes and CHD, diabetes and prevalent coronary heart disease; neither diabetes nor CHD, neither diabetes nor prevalent coronary heart disease
Exposure groups: CHD only, Diabetes only: albuminuria, Diabetes only: no albuminuria, Diabetes and CHD, Neither diabetes nor CHD.

CHD was assessed using ECG evidence of MI or self-report of MI or revascularization.

Diabetes was defined as blood glucose (fasting ≥ 126 mg/dL or non-fasting ≥ 200 mg/dL) or self-reported use of diabetes medication.

Outcome: Y-axis