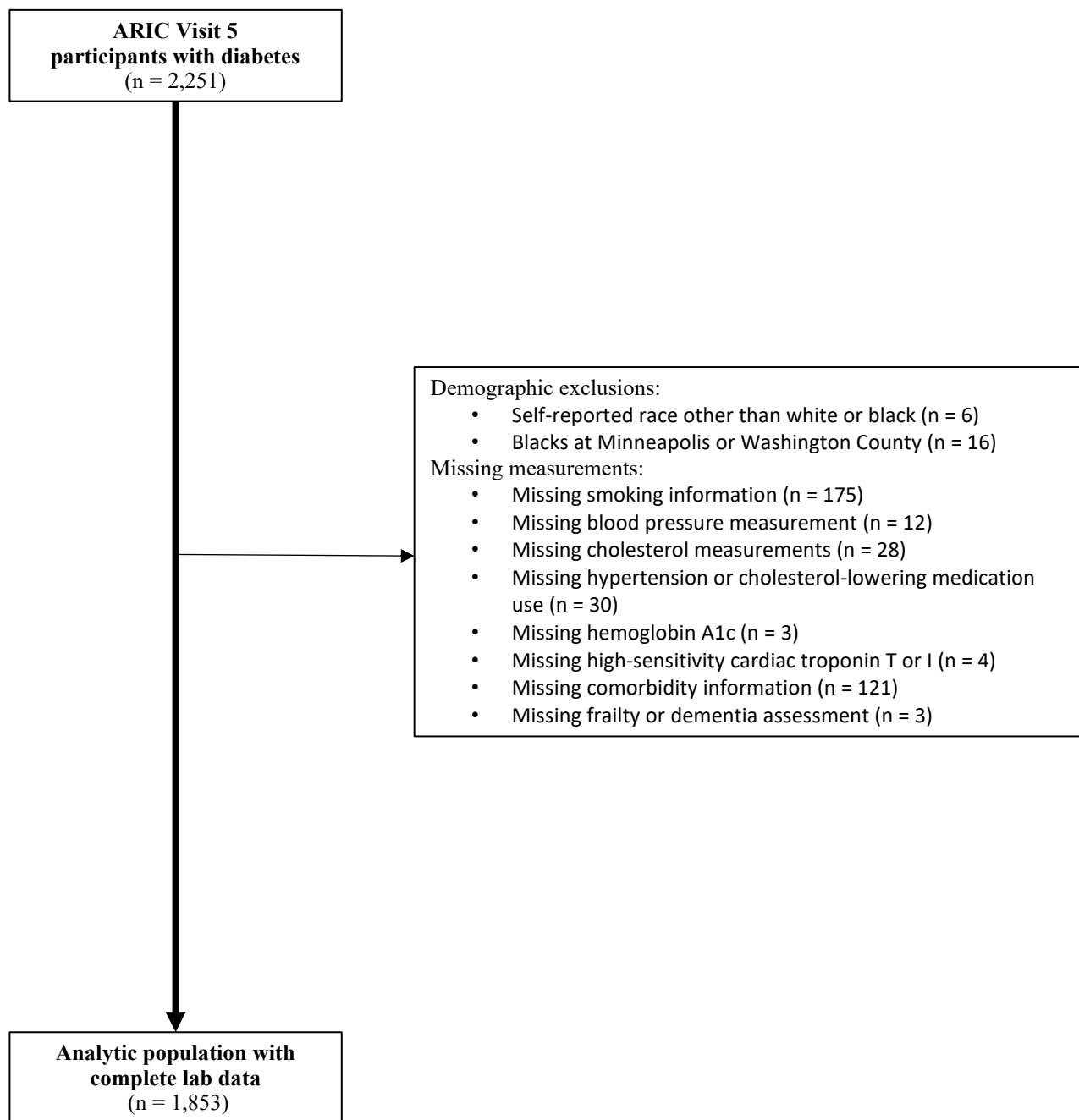


Supplementary Figure 1. Analytic population



SUPPLEMENTARY DATA

Supplementary Table 1. Baseline characteristics of older adults with diabetes according to hs-cTnI categories, the Atherosclerosis Risk in Communities (ARIC) Study, Visit 5 (2011-2013), N=1,738

	Percentile range	hs-cTnI categories				
		<40th	40th to <55th	55th to <70th	70th to <85th	≥85th
N		727	270	281	296	279
Visit 5 age, mean (SD)		74.0 (4.5)	76.0 (4.7)	75.5 (5.0)	77.4 (5.6)	76.9 (5.6)
Male		239 (32.9%)	102 (37.8%)	138 (49.1%)	147 (49.7%)	168 (60.2%)
Black race		187 (25.7%)	81 (30.0%)	96 (34.2%)	83 (28.0%)	120 (43.0%)
Current smoker		42 (5.8%)	14 (5.2%)	18 (6.4%)	11 (3.7%)	22 (7.9%)
Blood pressure						
Systolic		127.5 (16.5)	129.5 (18.5)	132.0 (20.5)	134.1 (19.6)	132.8 (20.9)
Diastolic		65.4 (10.2)	64.7 (10.1)	65.7 (10.8)	64.7 (11.7)	63.6 (11.9)
Hypertension medication use		541 (74.4%)	218 (80.7%)	247 (87.9%)	259 (87.5%)	245 (87.8%)
Total cholesterol, mmol/L, mean (SD)		4.5 (1.0)	4.5 (1.0)	4.2 (1.1)	4.3 (1.1)	4.3 (1.1)
HDL-Cholesterol, mmol/L, mean (SD)		1.3 (0.3)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)
Cholesterol-lowering medication use		491 (67.5%)	181 (67.0%)	214 (76.2%)	210 (70.9%)	202 (72.4%)
ADA Comorbidities						
Coronary heart disease		76 (10.5%)	45 (16.7%)	60 (21.4%)	83 (28.0%)	99 (35.5%)
Heart failure		87 (12.0%)	56 (20.7%)	68 (24.2%)	100 (33.8%)	119 (42.7%)
Stroke		22 (3.0%)	14 (5.2%)	16 (5.7%)	23 (7.8%)	23 (8.2%)
Arthritis		496 (68.2%)	202 (74.8%)	198 (70.5%)	222 (75.0%)	210 (75.3%)
Cancer		162 (22.3%)	56 (20.7%)	70 (24.9%)	73 (24.7%)	76 (27.2%)
Chronic Kidney Disease, Stage 3+		206 (28.3%)	131 (48.5%)	140 (49.8%)	183 (61.8%)	179 (64.2%)
Depression		20 (2.8%)	8 (3.0%)	11 (3.9%)	7 (2.4%)	13 (4.7%)
Emphysema or COPD		54 (7.4%)	20 (7.4%)	14 (5.0%)	23 (7.8%)	30 (10.8%)
History of hospitalized fall		22 (3.0%)	8 (3.0%)	10 (3.6%)	13 (4.4%)	15 (5.4%)
History of severe hypoglycemia		7 (1.0%)	11 (4.1%)	8 (2.8%)	15 (5.1%)	15 (5.4%)
Hypertension		573 (78.8%)	229 (84.8%)	253 (90.0%)	267 (90.2%)	256 (91.8%)

SUPPLEMENTARY DATA

Incontinence	76 (10.5%)	39 (14.4%)	34 (12.1%)	42 (14.2%)	43 (15.4%)
Geriatric syndromes					
Dementia	15 (2.1%)	13 (4.8%)	15 (5.3%)	23 (7.8%)	27 (9.7%)
Frailty	41 (5.6%)	18 (6.7%)	31 (11.0%)	58 (19.6%)	44 (15.8%)
hs-cTnI, ng/L, median (Q1, Q3)	2.1 (1.6, 2.5)	3.4 (3.2, 3.7)	4.5 (4.2, 4.9)	6.7 (6.0, 7.8)	16.7 (11.5, 27.3)
hs-cTnT, ng/L, median (Q1, Q3)	9.0 (6.0, 12.0)	11.0 (9.0, 16.0)	13.0 (10.0, 19.0)	16.5 (12.0, 22.0)	26.0 (16.0, 40.0)
Hemoglobin A1c, %, mean(SD)	6.5 (1.0)	6.6 (1.0)	6.7 (1.0)	6.7 (1.2)	6.8 (1.3)
Diabetes medication use					
No medication	335 (46.1%)	119 (44.1%)	102 (36.3%)	119 (40.2%)	98 (35.1%)
Oral(s) only	327 (45.0%)	116 (43.0%)	124 (44.1%)	121 (40.9%)	111 (39.8%)
Insulin only	30 (4.1%)	13 (4.8%)	22 (7.8%)	25 (8.4%)	43 (15.4%)
Insulin and oral(s)	35 (4.8%)	22 (8.1%)	33 (11.7%)	31 (10.5%)	27 (9.7%)

Abbreviations: COPD – chronic obstructive pulmonary disease; hs-cTnI – high-sensitivity cardiac troponin I; hs-cTnT – high-sensitivity cardiac troponin T

SUPPLEMENTARY DATA

Supplementary Table 2. Baseline characteristics of older adults with diabetes according to hs-cTnT categories, the Atherosclerosis Risk in Communities (ARIC) Study, Visit 5 (2011-2013), N=1,738

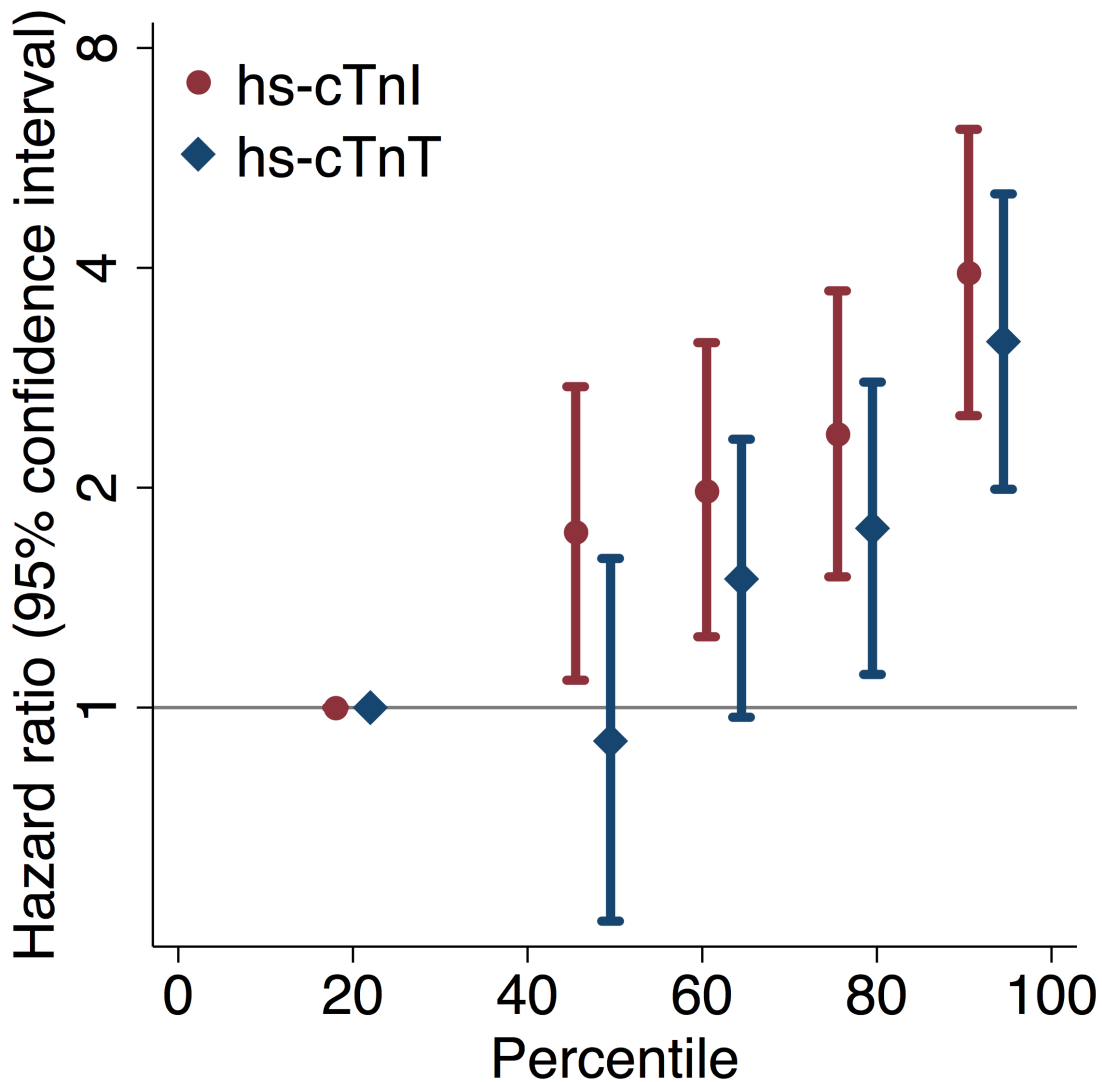
	Percentile range	hs-cTnT categories				
		<40th	40th to <55th	55th to <70th	70th to <85th	≥85th
N		741	228	319	286	279
Visit 5 age, mean (SD)		73.8 (4.3)	75.7 (4.8)	76.1 (5.3)	76.7 (5.1)	78.1 (5.6)
Male		192 (25.9%)	87 (38.2%)	153 (48.0%)	169 (59.1%)	193 (69.2%)
Black race		204 (27.5%)	73 (32.0%)	103 (32.3%)	88 (30.8%)	99 (35.5%)
Current smoker		52 (7.0%)	11 (4.8%)	13 (4.1%)	16 (5.6%)	15 (5.4%)
Blood pressure						
Systolic		129.4 (17.8)	132.0 (19.4)	130.1 (18.6)	131.1 (19.7)	130.8 (20.2)
Diastolic		66.1 (10.2)	65.3 (11.2)	65.5 (11.1)	63.8 (10.3)	62.1 (11.8)
Hypertension medication use		574 (77.5%)	182 (79.8%)	268 (84.0%)	246 (86.0%)	240 (86.0%)
Total cholesterol, mmol/L, mean (SD)		4.5 (1.1)	4.5 (1.0)	4.3 (1.0)	4.2 (1.0)	4.2 (1.2)
HDL-Cholesterol, mmol/L, mean (SD)		1.3 (0.3)	1.3 (0.3)	1.2 (0.3)	1.2 (0.3)	1.1 (0.3)
Cholesterol-lowering medication use		493 (66.5%)	159 (69.7%)	224 (70.2%)	209 (73.1%)	213 (76.3%)
ADA Comorbidities						
Coronary heart disease		81 (10.9%)	42 (18.4%)	59 (18.5%)	78 (27.3%)	103 (36.9%)
Heart failure		104 (14.0%)	51 (22.4%)	68 (21.3%)	78 (27.3%)	129 (46.2%)
Stroke		24 (3.2%)	5 (2.2%)	23 (7.2%)	19 (6.6%)	27 (9.7%)
Arthritis		521 (70.3%)	155 (68.0%)	232 (72.7%)	205 (71.7%)	215 (77.1%)
Cancer		145 (19.6%)	52 (22.8%)	82 (25.7%)	71 (24.8%)	87 (31.2%)
Chronic Kidney Disease, Stage 3+		210 (28.3%)	93 (40.8%)	158 (49.5%)	169 (59.1%)	209 (74.9%)
Depression		24 (3.2%)	5 (2.2%)	8 (2.5%)	9 (3.1%)	13 (4.7%)
Emphysema or COPD		50 (6.7%)	16 (7.0%)	21 (6.6%)	22 (7.7%)	32 (11.5%)
History of hospitalized fall		20 (2.7%)	9 (3.9%)	12 (3.8%)	12 (4.2%)	15 (5.4%)
History of severe hypoglycemia		10 (1.3%)	8 (3.5%)	8 (2.5%)	9 (3.1%)	21 (7.5%)
Hypertension		602 (81.2%)	195 (85.5%)	275 (86.2%)	256 (89.5%)	250 (89.6%)

SUPPLEMENTARY DATA

Incontinence	79 (10.7%)	27 (11.8%)	42 (13.2%)	38 (13.3%)	48 (17.2%)
Geriatric syndromes					
Dementia	20 (2.7%)	11 (4.8%)	16 (5.0%)	15 (5.2%)	31 (11.1%)
Frailty	39 (5.3%)	22 (9.6%)	28 (8.8%)	49 (17.1%)	54 (19.4%)
hs-cTnl, ng/L, median (Q1, Q3)	2.5 (1.8, 3.6)	3.6 (2.5, 5.1)	4.0 (2.7, 5.7)	5.3 (3.6, 8.3)	10.0 (5.3, 20.9)
hs-cTnT, ng/L, median (Q1, Q3)	7.0 (5.0, 9.0)	11.0 (11.0, 12.0)	14.0 (13.0, 15.0)	20.0 (18.0, 22.0)	35.0 (29.0, 47.0)
Hemoglobin A1c, %, mean(SD)	6.4 (1.0)	6.6 (1.1)	6.6 (1.1)	6.8 (1.2)	6.8 (1.3)
Diabetes medication use					
No medication	363 (49.0%)	101 (44.3%)	125 (39.2%)	94 (32.9%)	90 (32.3%)
Oral(s) only	313 (42.2%)	100 (43.9%)	145 (45.5%)	131 (45.8%)	110 (39.4%)
Insulin only	29 (3.9%)	10 (4.4%)	22 (6.9%)	25 (8.7%)	47 (16.8%)
Insulin and oral(s)	36 (4.9%)	17 (7.5%)	27 (8.5%)	36 (12.6%)	32 (11.5%)

Abbreviations: COPD – chronic obstructive pulmonary disease; hs-cTnl – high-sensitivity cardiac troponin I; hs-cTnT – high-sensitivity cardiac troponin T

Supplementary Figure 2. Hazard ratios (95% confidence interval) of the association of hs-cTnI and hs-cTnT percentile categories with all-cause mortality among those without prevalent cardiovascular disease (N = 1,212), adjusted for age, male sex, race-center, current smoking, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, and hemoglobin A1c.



SUPPLEMENTARY DATA

Supplementary Table 3. Sensitivity specificity likelihood ratios (LR) positive predictive value (PPV) and negative predictive value (NPV) associated with representative hs-cTnI and hs-cTnT cutpoints at the 90th, 95th, and 99th percentile in the ARIC cohort with diabetes (N= 1,853).

	Cutpoint	Sensitivity	Specificity	LR+	LR-	PPV	NPV
hs-cTnI	12.9 ng/L	22%	93%	3.4	0.8	49%	80%
	23.0 ng/L	11%	97%	3.5	0.9	51%	79%
	67.9 ng/mL	2%	99%	3.1	1.0	47%	79%
hs-cTnT	30.0 ng/L	27%	94%	4.5	0.8	57%	82%
	41.0 ng/L	15%	98%	6.5	0.9	65%	80%
	76.0 ng/mL	4%	99.7%	12.9	1.0	76%	78%

SUPPLEMENTARY DATA

Supplementary Table 4. Percent (95% confidence interval) reclassified based on addition of hs-cTnI or hs-cTnT to base models for all-cause mortality.

	Died		Did not die		Weighted NRI (compared to base model)
	Increased Predicted Risk	Decreased Predicted Risk	Increased Predicted Risk	Decreased Predicted Risk	
Base Model*	-	-	-	-	-
+ comorbidity burden (≥3 comorbidities)	17.3 (15.5, 19.0)	5.3 (4.3, 6.3)	42.1 (39.8, 44.5)	35.2 (33.0, 37.4)	0.06 (0.001, 0.11)
+ hs-cTnI ≥ 85th percentile	7.7 (6.5, 9.0)	14.8 (13.3, 16.4)	15.4 (13.8, 17.1)	61.9 (59.6, 64.2)	0.39 (0.34, 0.44)
+ log ₂ (hs-cTnI)	11.3 (9.9, 12.7)	11.3 (9.8, 12.7)	25.3 (23.3, 27.2)	52.1 (49.8, 54.4)	0.30 (0.24, 0.35)
+ hs-cTnT ≥ 85th percentile	9.0 (7.6, 10.3)	13.6 (12.1, 15.1)	20.6 (18.8, 22.3)	56.8 (54.6, 59.0)	0.31 (0.26, 0.36)
+ log ₂ (hs-cTnT)	12.5 (11.0, 13.9)	10.1 (8.7, 11.4)	27.7 (25.7, 29.7)	49.6 (47.4, 52.0)	0.26 (0.21, 0.32)

* Age, male sex, race-center, current smoking, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, and hemoglobin A1c

SUPPLEMENTARY DATA

Supplementary Table 5. Percent (95% confidence interval) reclassified based on addition of hs-cTnI or hs-cTnT to base models with comorbidity burden for all-cause mortality

	Died		Did not die		Weighted NRI
	Increased Predicted Risk	Decreased Predicted Risk	Increased Predicted Risk	Decreased Predicted Risk	
Base Model* with comorbidity burden (≥3 comorbidities)	-	-	-	-	-
+ hs-cTnI ≥ 85th percentile	7.6 (6.4, 8.8)	14.9 (13.4, 16.5)	18.8 (17.0, 20.6)	58.6 (56.3, 60.9)	0.32 (0.26, 0.37)
+ log2(hs-cTnI)	11.2 (9.8, 12.6)	11.4 (10.0, 12.8)	27.3 (25.3, 29.3)	50.0 (47.7, 52.3)	0.24 (0.19, 0.30)
+ hs-cTnT ≥ 85th percentile	9.3 (7.9, 10.6)	13.3 (11.8, 14.8)	25.5 (23.6, 27.4)	51.9 (49.6, 54.1)	0.22 (0.16, 0.27)
+ log2(hs-cTnT)	12.4 (10.9, 13.8)	10.2 (8.9, 11.5)	29.4 (27.3, 31.5)	47.9 (45.6, 50.3)	0.23 (0.18, 0.29)
Base Model* with comorbidity burden (≥3 comorbidities or dementia or frailty)	-	-	-	-	-
+ hs-cTnI ≥ 85th percentile	7.6 (6.3, 8.8)	15.0 (13.3, 16.7)	18.8 (17.1, 20.6)	58.5 (56.3, 60.7)	0.32 (0.27, 0.36)
+ log2(hs-cTnI)	11.1 (9.7, 12.5)	11.5 (10.1, 12.9)	27.4 (25.3, 29.4)	50.0 (47.6, 52.3)	0.24 (0.18, 0.29)
+ hs-cTnT ≥ 85th percentile	9.1 (7.8, 10.5)	13.4 (11.9, 15.0)	25.0 (23.2, 26.9)	52.3 (50.0, 54.6)	0.22 (0.17, 0.27)
+ log2(hs-cTnT)	12.3 (10.8, 13.8)	10.3 (8.9, 11.6)	29.4 (27.3, 31.5)	47.9 (45.6, 50.3)	0.23 (0.17, 0.28)

* Age, male sex, race-center, current smoking, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, and hemoglobin A1c

Supplementary Figure 3. Hazard ratios (95% confidence interval) of all-cause mortality associated with cross-categories of high hs-cTnI or high hs-cTnT and high comorbidity burden or dementia or frailty, adjusted for age, male sex, race-center, smoking, systolic blood pressure, diastolic blood pressure, anti-hypertensive medication use, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, and hemoglobin A1c

