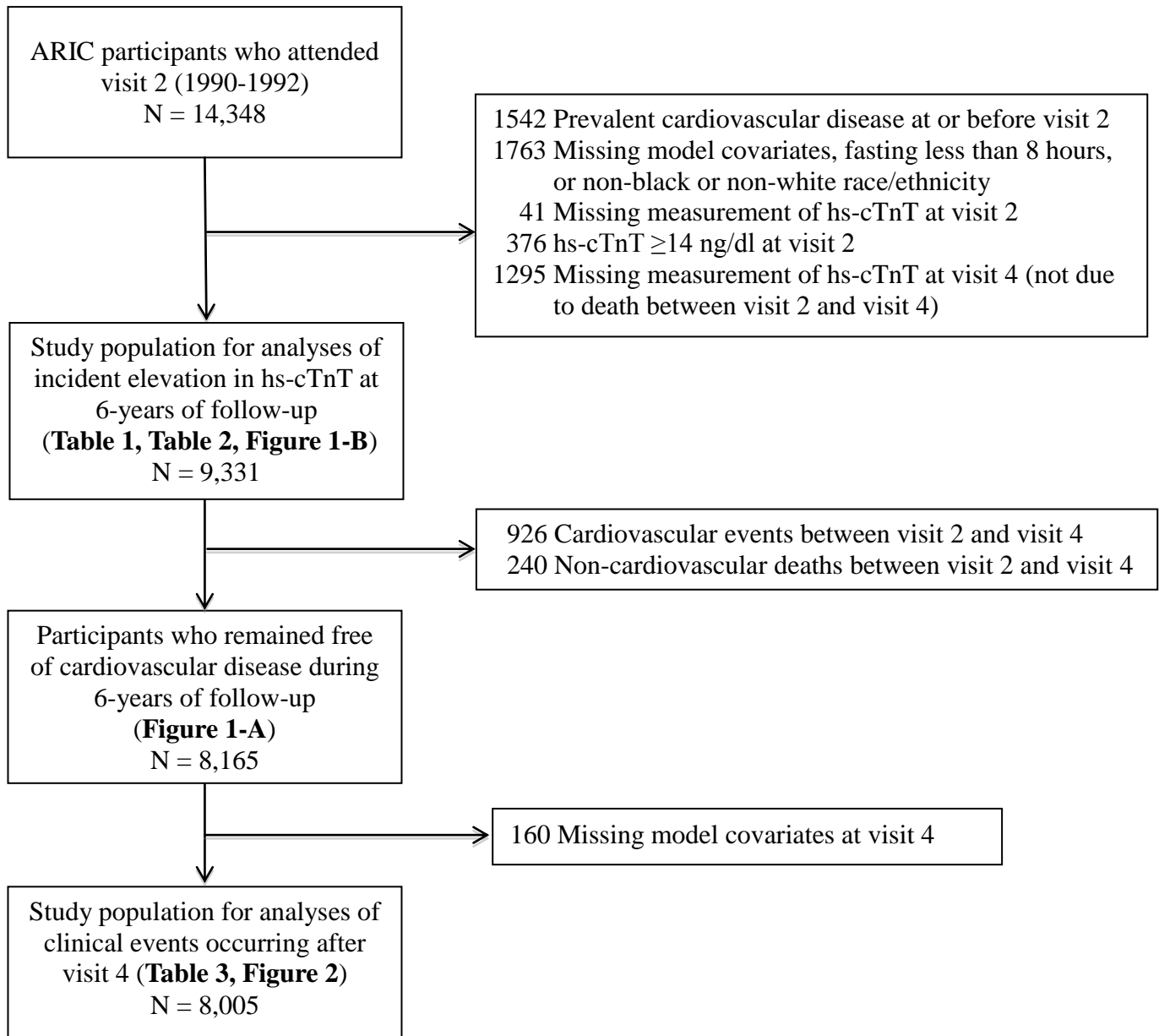**SUPPLEMENTAL MATERIAL**

Supplemental Figure 1. Flow diagram for selection of study population from the Atherosclerosis Risk in Communities (ARIC) Study cohort

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┌─────────────────────────────┐
│ ARIC participants who attended │
│     visit 2 (1990-1992)      │
│        N = 14,348            │
└─────────────────────────────┘
          │          ┌──────────────────────────────────────────────────────┐
          │          │ 1542 Prevalent cardiovascular disease at or before visit 2 │
          │          │ 1763 Missing model covariates, fasting less than 8 hours,  │
          │          │        or non-black or non-white race/ethnicity           │
          │ ────────▶│   41 Missing measurement of hs-cTnT at visit 2            │
          │          │  376 hs-cTnT ≥14 ng/dl at visit 2                          │
          │          │ 1295 Missing measurement of hs-cTnT at visit 4 (not due   │
          │          │        to death between visit 2 and visit 4)              │
          ▼          └──────────────────────────────────────────────────────┘
┌─────────────────────────────┐
│ Study population for analyses of │
│ incident elevation in hs-cTnT at │
│     6-years of follow-up     │
│ (Table 1, Table 2, Figure 1-B) │
│        N = 9,331             │
└─────────────────────────────┘
          │          ┌──────────────────────────────────────────────────────┐
          │ ────────▶│ 926 Cardiovascular events between visit 2 and visit 4    │
          │          │ 240 Non-cardiovascular deaths between visit 2 and visit 4 │
          ▼          └──────────────────────────────────────────────────────┘
┌─────────────────────────────┐
│ Participants who remained free  │
│ of cardiovascular disease during │
│     6-years of follow-up     │
│        (Figure 1-A)          │
│        N = 8,165            │
└─────────────────────────────┘
          │          ┌──────────────────────────────────────────┐
          │ ────────▶│ 160 Missing model covariates at visit 4     │
          ▼          └──────────────────────────────────────────┘
┌─────────────────────────────┐
│ Study population for analyses of │
│ clinical events occurring after │
│ visit 4 (Table 3, Figure 2)  │
│        N = 8,005            │
└─────────────────────────────┘
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Supplemental Table 1. Cross-tabulation of categories of highly sensitive cardiac troponin T (hs-cTnT) at two visits, 6 years apart (visit 2 in 1990-1992 and visit 4 in 1996-1998), among persons with hs-cTnT <14 ng/L (not elevated) at baseline (visit 2, 1990-1992) and remained free of cardiovascular disease during the 6-year follow-up period

		Hs-cTnT at visit 4 (1996-1998)				
		<5 ng/L (not detectable)	5-8 ng/L	9-13 ng/L	≥14 ng/L (elevated)	*Total*
Hs-cTnT at visit 2 (1990-1992)	<5 ng/L (not detectable)	*3,727* 64.6%	*1,616* 27.9%	*356* 6.2%	*78* 1.3%	*5,771* 100%
	5-8 ng/L	*522* 28.3%	*733* 39.7%	*444* 24.1%	*145* 7.9%	*1,844* 100%
	9-13 ng/L	*26* 4.7%	*131* 23.8%	*221* 40.2%	*172* 31.3%	*550* 100%
	Total	*4,275* 52.4%	*2,474* 30.3%	*1,021* 12.5%	*395* 4.8%	*8,165* 100%

Values are *N* and row percentages.

Supplemental Table 2. Adjusted* risk ratios (95% confidence intervals) for the association of pre-diabetes and diabetes with incident elevated (≥14 ng/L) highly sensitive cardiac troponin T (hs-cTnT), cardiovascular events, or death during the 6 year follow-up period according to diagnostic categories of pre-diabetes and diabetes defined by hemoglobin A1c (HbA1c) or fasting glucose at baseline (visit 2, 1990-1992), N=9,331

		Incident elevation in hs-cTnT		Cardiovascular event		Death	
	N	**Events**	**RR (95% CI)**	**Events**	**RR (95% CI)**	**Events**	**RR (95% CI)**
HbA1c diagnostic criteria							
< 5.7 % (no diabetes)	6,333	214	1 (reference)	437	1 (reference)	136	1 (reference)
5.7 – 6.4% (pre-diabetes)	2,172	116	1.38 (1.07-1.77)	293	1.42 (1.20-1.69)	77	1.29 (0.95-1.75)
Diabetes (≥ 6.5% or diagnosis)	826	65	2.46 (1.77-3.42)	196	2.85 (2.28-3.55)	27	1.51 (0.95-2.39)
p-value for trend†			*<0.001*		*<0.001*		*0.040*
Fasting glucose diagnostic criteria							
< 100 mg/dL (no diabetes)	3,751	104	1 (reference)	260	1 (reference)	83	1 (reference)
100 – 125 mg/dL (pre-diabetes)	4,536	211	1.08 (0.84-1.39)	456	1.03 (0.87-1.22)	124	1.08 (0.80-1.45)
Diabetes (≥ 126 mg/dL or diagnosis)	1,044	80	1.92 (1.37-2.68)	210	1.91 (1.53-2.40)	33	1.32 (0.84-2.07)
p-value for trend†			*0.001*		*<0.001*		*0.274*

Abbreviations: RR, risk ratio; HbA1c, hemoglobin A1c; hs-cTnT, cardiac troponin T measured with a high sensitivity assay.

*Adjusted for age (years), race-center (whites-Washington County; whites-Minneapolis; blacks-Jackson; blacks-Forsyth County, whites-Forsyth County), sex (male or female), body mass index (kg/m2), C-reactive protein (mg/L), smoking (current; former; never), mean systolic blood pressure (mm Hg), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), estimated glomerular filtration rate (mL/min/1.73m^2), current use of hypertension medication (yes or no), current lipid-lowering medication use (yes or no), alcohol use (current; former; never) and left ventricular hypertrophy (yes or no).

†p-values for linear trend were obtained by numbering the categories 1 through 3 and including this categorical variable as a linear term in the model.

Supplemental Table 3. Adjusted* risk ratios (95% confidence intervals) for the association of pre-diabetes and diabetes with 6-year incident elevated (≥14 ng/L) highly sensitive cardiac troponin T (hs-cTnT) according to diagnostic categories of pre-diabetes and diabetes defined by hemoglobin A1c (HbA1c) or fasting glucose at baseline (visit 2, 1990-1992) stratified by race group (black or white)

Whites

	Incident elevated hs-cTnT (≥ 14 ng/L) N = 7,381		
	N	Events	RR (95% CI)
HbA1c diagnostic criteria			
< 5.7 % (no diabetes)	5,520	189	1 (reference)
5.7 – 6.4% (pre-diabetes)	1,387	76	1.37 (1.02-1.83)
Diabetes (≥ 6.5% or diagnosis)	474	45	2.58 (1.76-3.77)
p-value for trend†			*<0.001*
Fasting glucose diagnostic criteria			
< 100 mg/dl (no diabetes)	3,155	88	1 (reference)
100 – 125 mg/dl (pre-diabetes)	3,558	167	1.06 (0.80-1.40)
Diabetes (≥ 126 mg/dl or diagnosis)	668	55	1.78 (1.21-2.63)
p-value for trend†			*0.017*

Blacks

	Incident elevated hs-cTnT (≥ 14 ng/L) N = 1,950		
	N	Events	RR (95% CI)
HbA1c diagnostic criteria			
< 5.7 % (no diabetes)	813	25	1 (reference)
5.7 – 6.4% (pre-diabetes)	785	40	1.33 (0.77-2.31)
Diabetes (≥ 6.5% or diagnosis)	352	20	2.05 (1.03-4.08)
p-value for trend†			*0.047*
Fasting glucose diagnostic criteria			
< 100 mg/dl (no diabetes)	596	16	1 (reference)
100 – 125 mg/dl (pre-diabetes)	978	44	1.22 (0.66-2.26)
Diabetes (≥ 126 mg/dl or diagnosis)	376	25	2.25 (1.09-4.63)
p-value for trend†			*0.030*

NOTE: p-values for race interaction with diabetes status: 0.271 for HbA1c criteria; 0.956 for fasting glucose criteria.

*Adjusted for age (years), race-center (whites-Washington County; whites-Minneapolis; blacks-Jackson; blacks-Forsyth County, whites-Forsyth County), sex (male or female), body mass index (kg/m2), C-reactive protein (mg/L), smoking (current; former; never), mean systolic blood pressure (mm Hg), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), estimated glomerular filtration rate (mL/min/1.73m^2), current use of hypertension medication (yes or no), current lipid-lowering medication use (yes or no), alcohol use (current; former; never) and left ventricular hypertrophy (yes or no).

†p-values for linear trend were obtained by numbering the categories 1 through 3 and including this categorical variable as a linear term in the model.

Supplemental Table 4. Adjusted* hazard ratios (95% confidence intervals) for the association of visit 2 (1990-1992) diabetes status and 6-year incident elevated (≥14 ng/L) highly sensitive cardiac troponin T (hs-cTnT) with incident coronary heart disease (CHD), heart failure and all-cause mortality (N=8,005)

Visit 4 hs-cTnT	HbA1c diagnostic criteria	N	CHD		Heart Failure		Death	
			Events	HR (95%CI)	Events	HR (95%CI)	Events	HR (95%CI)
hs-cTnT <14 ng/L	No diabetes (< 5.7%)	5,477	540	1 (reference)	370	1 (reference)	831	1 (reference)
	Pre-diabetes (5.7-6.4 %)	1,642	228	1.34 (1.14-1.58)	193	1.32 (1.10-1.59)	380	1.30 (1.15-1.48)
	Diabetes (diagnosis or ≥ 6.5 %)	506	109	2.31 (1.86-2.88)	115	2.49 (1.99-3.12)	150	1.71 (1.43-2.06)
hs-cTnT ≥14 ng/L	No diabetes (< 5.7%)	207	38	1.61 (1.15-2.26)	48	3.21 (2.35-4.39)	77	2.07 (1.62-2.64)
	Pre-diabetes (5.7-6.4 %)	110	34	2.92 (2.04-4.17)	36	4.30 (3.01-6.14)	56	2.61 (1.97-3.45)
	Diabetes (diagnosis or ≥ 6.5 %)	63	24	3.84 (2.52-5.84)	28	6.37 (4.27-9.51)	39	4.36 (3.14-6.07)
	Fasting glucose diagnostic criteria							
hs-cTnT <14 ng/L	No diabetes (< 100 mg/dl)	3,263	284	1 (reference)	224	1 (reference)	492	1 (reference)
	Pre-diabetes (100-125 mg/dl)	3,678	455	1.13 (0.97-1.31)	315	1.01 (0.85-1.20)	671	1.05 (0.93-1.19)
	Diabetes (diagnosis or ≥ 126 mg/dl)	684	138	1.98 (1.60-2.46)	139	2.10 (1.68-2.63)	198	1.62 (1.36-1.93)
hs-cTnT ≥14 ng/L	No diabetes (< 100 mg/dl)	99	19	1.86 (1.16-2.98)	24	3.32 (2.16-5.12)	41	2.28 (1.64-3.15)
	Pre-diabetes (100-125 mg/dl)	206	50	2.12 (1.55-2.90)	56	3.36 (2.47-4.58)	86	2.16 (1.70-2.75)
	Diabetes (diagnosis or ≥ 126 mg/dl)	75	27	3.50 (2.33-5.26)	32	5.42 (3.67-7.99)	45	3.66 (2.67-5.03)

Abbreviations: CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; HbA1c, hemoglobin A1c; Hs-cTnT, cardiac troponin T measured with a high sensitivity assay.

*Adjusted for age (years), race-center (whites-Washington County; whites-Minneapolis; blacks-Jackson; blacks-Forsyth County, whites-Forsyth County), sex (male or female), body mass index (kg/m2), C-reactive protein (mg/L), smoking (current; former; never), mean systolic blood pressure (mm Hg), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), estimated glomerular filtration rate (mL/min/1.73m^2), current use of hypertension medication (yes or no), current lipid-lowering medication use (yes or no), alcohol use (current; former; never) and left ventricular hypertrophy (yes or no).

Supplemental Table 5. Adjusted* hazard ratios (95% confidence intervals) for the association of visit 2 (1990-1992) diabetes status and 6-year incident elevated (≥14 ng/L) highly sensitive cardiac troponin T (hs-cTnT) with incident coronary heart disease (CHD), heart failure and all-cause mortality, stratified by race group (black or white)

<u>**Whites**</u>

Visit 4 hs-cTnT	HbA1c diagnostic criteria	N	Events	CHD HR (95%CI)	Events	Heart Failure HR (95%CI)	Events	Death HR (95%CI)
hs-cTnT <14 ng/L	No diabetes (< 5.7%)	4,804	492	1 (reference)	314	1 (reference)	732	1 (reference)
	Pre-diabetes (5.7-6.4 %)	1,039	168	1.37 (1.14-1.64)	123	1.35 (1.09-1.67)	248	1.29 (1.11-1.50)
	Diabetes (diagnosis or ≥ 6.5 %)	286	77	2.51 (1.95-3.23)	64	2.41 (1.82-3.19)	97	1.81 (1.45-2.25)
hs-cTnT ≥14 ng/L	No diabetes (< 5.7%)	182	34	1.61 (1.13-2.30)	42	3.30 (2.36-4.62)	68	2.10 (1.62-2.72)
	Pre-diabetes (5.7-6.4 %)	75	22	2.61 (1.69-4.04)	22	4.06 (2.60-6.33)	40	2.84 (2.05-3.93)
	Diabetes (diagnosis or ≥ 6.5 %)	45	18	3.61 (2.23-5.86)	21	6.25 (3.94-9.93)	30	4.27 (2.93-6.23)

<u>**Blacks**</u>

Visit 4 hs-cTnT	HbA1c diagnostic criteria	N	Events	CHD HR (95%CI)	Events	Heart Failure HR (95%CI)	Events	Death HR (95%CI)
hs-cTnT <14 ng/L	No diabetes (< 5.7%)	673	48	1 (reference)	56	1 (reference)	99	1 (reference)
	Pre-diabetes (5.7-6.4 %)	603	60	1.24 (0.84-1.83)	70	1.15 (0.80-1.64)	132	1.27 (0.97-1.67)
	Diabetes (diagnosis or ≥ 6.5 %)	220	32	1.80 (1.12-2.89)	51	2.37 (1.59-3.54)	53	1.57 (1.10-2.23)
hs-cTnT ≥14 ng/L	No diabetes (< 5.7%)	25	4	1.86 (0.65-5.29)	6	2.63 (1.10-6.27)	9	1.93 (0.95-3.91)
	Pre-diabetes (5.7-6.4 %)	35	12	4.01 (2.01-7.97)	14	4.25 (2.26-8.00)	16	2.18 (1.25-3.80)
	Diabetes (diagnosis or ≥ 6.5 %)	18	6	4.40 (1.80-10.80)	7	5.19 (2.24-12.03)	9	4.62 (2.27-9.43)

NOTE: p-value for race interactions with diabetes-hs-cTnT elevation status (4-category variable): 0.832 for CHD, 0.954 for HF, and 0.912 for all-cause mortality.

Abbreviations: CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; HbA1c, hemoglobin A1c; Hs-cTnT, cardiac troponin T measured with a high sensitivity assay.

*Adjusted for age (years), race-center (whites-Washington County; whites-Minneapolis; blacks-Jackson; blacks-Forsyth County, whites-Forsyth County), sex (male or female), body mass index (kg/m2), C-reactive protein (mg/L), smoking (current; former; never), mean systolic blood pressure (mm Hg), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), estimated glomerular filtration rate (mL/min/1.73m^2), current use of hypertension medication (yes or no), current lipid-lowering medication use (yes or no), alcohol use (current; former; never) and left ventricular hypertrophy (yes or no).

Supplemental Table 6. Adjusted* hazard ratios (95% confidence intervals) for the association of visit 2 (1990-1992) diabetes status and 6-year incident elevated (≥14 ng/L) highly sensitive cardiac troponin T (hs-cTnT) at visit 4 (1996-1998) with incident coronary heart disease (CHD), heart failure and all-cause mortality (N=7,847)

Visit 4 hs-cTnT	Visit 2 diabetes status - HbA1c diagnostic criteria	Incident diabetes (visit 3 or 4)	N	CHD Events	CHD HR (95%CI)	Heart Failure Events	Heart Failure HR (95%CI)	Death Events	Death HR (95%CI)
hs-cTnT <14 ng/L	No diabetes (< 5.7%)	No	5,312	512	1 (reference)	357	1 (reference)	794	1 (reference)
		Yes	59	12	2.00 (1.12-3.55)	6	1.57 (0.70-3.54)	16	2.41 (1.47-3.98)
	Pre-diabetes (5.7-6.4 %)	No	1,467	196	1.31 (1.11-1.56)	163	1.24 (1.02-1.50)	330	1.27 (1.11-1.45)
		Yes	134	26	1.95 (1.30-2.91)	23	2.23 (1.45-3.43)	39	1.97 (1.42-2.74)
	Diabetes (diagnosis or ≥ 6.5 %)	-	502	109	2.38 (1.91-2.98)	115	2.51 (2.00-3.15)	150	1.76 (1.46-2.12)
hs-cTnT ≥14 ng/L	No diabetes (< 5.7%)	No	196	35	1.61 (1.14-2.29)	44	3.21 (2.32-4.43)	72	2.11 (1.64-2.71)
		Yes	5	3	5.04 (1.60-15.84)	1	2.36 (0.33-16.92)	2	1.89 (0.47-7.59)
	Pre-diabetes (5.7-6.4 %)	No	92	29	3.08 (2.10-4.52)	30	4.70 (3.20-6.91)	45	2.69 (1.98-3.66)
		Yes	17	5	2.82 (1.16-6.86)	6	3.17 (1.40-7.18)	11	2.61 (1.43-4.77)
	Diabetes (diagnosis or ≥ 6.5 %)	-	63	24	3.95 (2.60-6.02)	28	6.40 (4.29-9.56)	39	4.46 (3.20-6.21)
	Fasting glucose diagnostic criteria								
hs-cTnT <14 ng/L	No diabetes (< 100 mg/dl)	No	3,170	274	1 (reference)	219	1 (reference)	472	1 (reference)
		Yes	27	3	1.10 (0.35-3.45)	2	1.09 (0.27-4.41)	5	1.72 (0.71-4.17)
	Pre-diabetes (100-125 mg/dl)	No	3,470	414	1.09 (0.93-1.27)	285	0.96 (0.80-1.15)	615	1.04 (0.92-1.17)
		Yes	127	26	1.99 (1.32-3.01)	19	1.78 (1.10-2.87)	39	1.97 (1.41-2.76)
	Diabetes (diagnosis or ≥ 126 mg/dl)	-	680	138	2.01 (1.62-2.50)	139	2.09 (1.67-2.62)	198	1.67 (1.40-1.99)
hs-cTnT ≥14 ng/L	No diabetes (< 100 mg/dl)	No	95	19	1.95 (1.22-3.13)	22	3.25 (2.07-5.10)	39	2.28 (1.64-3.19)
		Yes	1	0	-	1	6.13 (0.83-45.03)	1	9.72 (1.34-70.49)
	Pre-diabetes (100-125 mg/dl)	No	186	43	2.10 (1.51-2.92)	50	3.47 (2.51-4.78)	77	2.29 (1.78-2.94)
		Yes	16	7	3.11 (1.46-6.63)	4	2.10 (0.77-5.70)	7	1.61 (0.76-3.42)
	Diabetes (diagnosis or ≥ 126 mg/dl)	-	75	27	3.54 (2.35-5.33)	32	5.38 (3.65-7.94)	45	3.74 (2.72-5.13)

Abbreviations: CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; HbA1c, hemoglobin A1c; Hs-cTnT, cardiac troponin T measured with a high sensitivity assay.

*Adjusted for age (years), race-center (whites-Washington County; whites-Minneapolis; blacks-Jackson; blacks-Forsyth County, whites-Forsyth County), sex (male or female), body mass index (kg/m2), C-reactive protein (mg/L), smoking (current; former; never), mean systolic blood pressure (mm Hg), LDL-cholesterol (mg/dL), HDL-cholesterol (mg/dL), triglycerides (mg/dL), estimated glomerular filtration rate (mL/min/1.73m^2), current use of hypertension medication (yes or no), current lipid-lowering medication use (yes or no), alcohol use (current; former; never) and left ventricular hypertrophy (yes or no).