

Atrial Fibrillation in an African-American Cohort: the Jackson Heart Study

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**Abstract**

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While many risk factors for atrial fibrillation (AF) are more prevalent among African Americans (AAs) than whites, AF incidence appears to be lower. Data from the Jackson Heart Study (JHS), a community-based cohort study of cardiovascular disease among 5,306 AAs were used to investigate incident AF. Using participant characteristic data ascertained at baseline and incident AF identified through hospital surveillance, study electrocardiogram, and Medicare claims, we determined age- and sex-specific AF incidence rates, studied associations of demographic and cardiovascular risk factors with AF, and compared age- and sex-specific AF incidence rates in JHS to those of AA participants in the Cardiovascular Health Study (CHS) and Multi-Ethnic Study of Atherosclerosis (MESA). Cox proportional hazards models were used to determine the association of risk factors with incident AF. Age- and sex-specific AF incidence rates in

JHS were broadly similar to those among AAs in CHS and MESA. In a multivariable model, hypertension, higher BMI in the obese range, and history of myocardial infarction were associated with incident AF. The associations of risk factors with AF observed in JHS reinforce the importance of efforts to control blood pressure and body weight for the prevention of AF.

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## INTRODUCTION

Though the burden of AF is well-characterized among white Americans, less is understood about AF in African Americans (AA). In an early publication from the Multi-Ethnic Study of Atherosclerosis (MESA), AA participants had a 49% lower risk of incident AF compared with whites, though the number of AF cases among AAs at the time of that analysis was small (n=64) (1). The Atherosclerosis Risk in Communities (ARIC) study has also investigated AF incidence among AAs, finding a 41% lower risk of incident AF diagnosis for AAs compared with whites (2). ARIC has a larger pool of incident AF cases in AA than MESA (n=143, as of 2009), and has contributed greatly to AF research in AAs (3). However, the ARIC cohort was recruited over 25 years ago, between 1987 and 1989, at a time when the prevalence of AF risk factors among AAs likely differed compared with more recent times. Obesity and diabetes are more prevalent in recent years, while current smoking is less common now than in the 1980s.

To provide additional information about incident AF in a more contemporary cohort of AAs, we used data from the Jackson Heart Study (JHS). Our aims were (1) to identify incident AF among JHS participants and describe the methods of AF event ascertainment, (2) to compare age and sex-specific AF incidence in JHS with that of AA participants in the Cardiovascular Health Study (CHS) and the Multi-Ethnic Study of Atherosclerosis (MESA), and (3) to describe associations of demographic, anthropometric, cardiovascular, and electrocardiographic risk factors with AF incidence in AAs.

## METHODS

## Study population

The Jackson Heart Study (JHS) is a community-based cohort study of cardiovascular disease in AA that enrolled 5,306 residents from the Jackson, MS, metropolitan area who completed a baseline examination between 2000 and 2004. After this initial assessment, participants were examined at two additional in-person follow-up study visits (2005-2008 and 2009-2013). The ARIC study also has a field center in Jackson, MS. JHS participants were recruited from living ARIC participants (22%), community volunteers (30%), from a random sample of the community (17%), and from the families of ARIC participants (31%). Details of the JHS design, methods, and recruitment are published elsewhere (4, 5).

## Baseline examination

At the baseline examination, participants reported their age, smoking status, health insurance status, educational achievement, current medication use, and history of hypertension and myocardial infarction (5). A history of heart failure was reported at the second examination in 2005-2008. The baseline examination included a blood draw in the fasting state and measurement of height and weight, forced expiratory volume in one second (FEV<sub>1</sub>), and sitting blood pressure with a random zero sphygmomanometer. Cardiac rhythm, PR interval, and evidence of past MI were assessed on a 12-lead resting electrocardiogram (ECG; Marquette MAC/PC digital ECG recorder) that was read at the Electrocardiographic Reading Center (ECGRC) at the University of Minnesota in accordance with the Minnesota Code Classification system (6). Fasting plasma glucose was measured and glucose status was categorized as normal (fasting



glucose < 100 mg/dL or HbA1c < 5.7% with no use of diabetic medications), impaired (fasting glucose  $\geq$  100 and < 126 mg/dL or HbA1c  $\geq$  5.7 and < 6.5% with no use of diabetic medications), or diabetes (use of diabetes medication, fasting glucose  $\geq$  126 mg/dL, or HbA1c  $\geq$  6.5%). Hypertension was defined as a blood pressure of  $\geq$  140 mmHg systolic or  $\geq$  90 mmHg diastolic or current use of antihypertensive medication. BMI was calculated from height and weight.

#### AF ascertainment

Incident AF cases were identified from three sources: JHS study ECGs, hospital discharge diagnosis code surveillance, and, for participants enrolled in fee-for-service Medicare, from Medicare claims data. During a participant's third examination (2009-2013), a 12-lead resting ECG was performed and read at the Epidemiological Cardiology Research Center (EPICARE) at Wake Forest University. Hospitals in the Jackson, MS, area reported hospital discharge diagnosis *International Classification of Diseases, Ninth Revision* (ICD-9) codes for all JHS participants, providing "hospital surveillance" to identify events between participant visits. For those enrolled in fee-for-service Medicare, claims data included inpatient services covered under Medicare Part A, institutional outpatient services covered under Medicare Part B, carrier claims for physician services covered under Medicare Part B, and home health claims. If the diagnosis of AF or atrial flutter occurred during hospitalization for coronary artery bypass or cardiac valve surgery, it was not included as an AF case. However, a subsequent diagnosis of AF or atrial flutter unrelated to cardiac surgery among those who previously developed cardiac surgery-related AF was considered an incident AF

case and is included in our analysis. For both hospital surveillance and fee-for-service Medicare data, ICD-9 diagnosis codes of 427.31 or 427.32 (indicating atrial fibrillation and atrial flutter, respectively) in any position were considered evidence of AF.

Up to date information on incident AF from the Multi-Ethnic Study of Atherosclerosis (MESA) and the Cardiovascular Health Study (CHS) were obtained so that AF incidence in African American participants of those studies could be compared with AF incidence in JHS. MESA is a large multicenter observational study of 6,814 men and women (1,891 AA) recruited beginning in 2000 from six clinics in the US, and designed to study subclinical cardiovascular disease. CHS is a multicenter study of cardiovascular disease in 5,888 participants (911 AA) 65 years of age or older at recruitment beginning in 1989 and followed until the present. AF incidence in JHS was not compared to AF incidence in ARIC because about a fifth of the JHS participants are also ARIC participants. Methods of AF ascertainment in both MESA and CHS are very similar to those in JHS, involving study ECGs, hospital discharge diagnosis code surveillance, and Medicare claims data, and are detailed elsewhere (7, 8).

### Statistical analysis

Continuous data are presented as mean (standard deviation, SD) and categorical data are presented as frequencies (percentages). Data were missing for less than 5% of participants for all variables except FEV<sub>1</sub>, which was missing in 6.2% of participants. For participants with missing values in any covariate of interest, values were imputed using multiple-imputation by chained equations (9). Among participants without prevalent AF at baseline, person-years at risk for incident AF were calculated beginning

from the date of the baseline examination until the first diagnosis of AF, death, loss to follow-up, or the end of follow-up (December 31, 2012). Age- and sex-specific AF incidence rates were calculated as the number of cases of AF divided by the number of person-years in each age and sex category.

We identified 12 potential risk factors for AF from the existing literature (10-15) and examined individual models for each risk factor adjusted for age and sex. In addition, we fit a multivariable Cox proportional hazards model. We used splines to investigate non-linear associations between suspected risk factors and AF log hazard. Based on change in the hazard ratio (HR) of interest, we found evidence for a nonlinear association for BMI with AF, but no evidence for nonlinearity for other characteristics. In evaluating the associations of risk factors with incident AF from the multivariable model, a two-sided P value significance threshold of  $0.05/15 = 0.003$  was used to account for multiple comparisons. Because information on incident heart failure was collected only following the second JHS visit (2005-2008), we conducted a secondary multivariable analysis adding heart failure as a risk factor, in which participants began accruing time at risk for incident AF at the date of their second study visit. For this analysis, values from visit 2 were used when possible. When these data were unavailable, visit 1 measurements were used.

## RESULTS

Among the 5,306 JHS participants, 5,235 were free of prevalent AF at baseline. In total 3,327 women and 1,908 men were included in our analysis, with an average age of 55 and 54 years, respectively. In the overall cohort, the prevalence at baseline was

high for obesity (41% among men, 60% among women) and diabetes (20% among men, 23% among women), but relatively low for current smoking (18% among men, 10% among women; Table 1). Compared with participants who did not develop AF during follow-up, among those who developed AF, the average at baseline was older, a larger proportion were current smokers, had hypertension and diabetes, the average forced expiratory volume in one second (FEV<sub>1</sub>) was lower, and the electrocardiographic PR interval was longer. History of MI, measured through baseline ECG or self-report, was much more common among participants who developed AF.

Using all three AF ascertainment sources (study ECGs, hospital surveillance, and Medicare claims; Method 2 in Table 2) over an average of 8.5 years of follow-up in the JHS sample, we identified 239 incident AF cases and 69 with an AF diagnosis that preceded baseline (“prevalent AF”). For incident AF, 15 of 239 cases (6%) were identified by the single study ECG during follow-up. There was substantial agreement on incident AF cases between the hospital surveillance and Medicare claims data; 90% of the incident AF cases identified by Medicare claims data were also identified by hospital surveillance. Compared with AF ascertainment from ECGs and hospital surveillance alone (Method 1 in Table 2), the inclusion of Medicare claims data (Method 2 in Table 2) identified an additional 26 prevalent and 15 incident AF cases not otherwise identified. Additionally, among AF cases identified by both Medicare claims data and hospital surveillance, the inclusion of Medicare claims data identified AF cases an average of 25 days earlier than the hospital surveillance data. All subsequent analyses used incident AF ascertained from study ECG, hospitalization surveillance, and Medicare claims (Method 2).

Of the 239 incident and 69 prevalent AF cases, 119 incident and 45 prevalent AF cases occurred among JHS participants who were also enrolled in the Atherosclerosis Risk in Communities (ARIC) study, from which JHS drew about one-fifth of its participants. Participants enrolled in both studies were considerably older at the JHS baseline visit than the JHS cohort as a whole (67 vs. 55 years).

Age- and sex-specific AF incidence rates in JHS were similar to those among AAs in CHS and MESA, as shown in Figure 1, with similar point estimates and overlapping confidence intervals. All three populations show a marked trend of increasing AF incidence with increasing age, and show similar age-specific incidence in men and women.

Table 3 summarizes hazard ratios for potential AF risk factors from individual age and sex-adjusted models in the left column, and from a single multivariable model in the right column. In the multivariable model, greater age and height, hypertension, smaller FEV<sub>1</sub>, and a history of myocardial infarction were all associated with incident AF. Higher BMI showed an association with incident AF, but only among obese individuals. Among participants with BMI <30, no such association was seen. We explored non-linear association with BMI further and found similar results among non-smokers. Sex did not show an association with incident AF.

Our secondary analysis including heart failure as a covariate showed similar magnitudes of association with AF for all variables (Supplementary Table). Heart failure was significantly associated with incident AF, with a hazard ratio of 2.93 in the multivariable model (95% CI: 1.52, 5.63).

## DISCUSSION

Our analysis of data from the Jackson Heart Study identified prevalent and incident AF in a large contemporary cohort of African-American participants, evaluated methods of AF ascertainment including study ECG, hospital surveillance, and Medicare claims data, calculated age and sex-specific AF incidence rates, and described associations of risk factors with incident AF.

Strengths of this study include the JHS cohort, which offers a large sample size and a contemporary population of particular interest in AF research. With access to Medicare claims data in addition to study ECGs and hospital surveillance, the ascertainment of AF in JHS is likely more complete than in cohort studies which do not have access to such data. Indeed, in this study we demonstrated the utility of adding the Medicare claims data for defining and dating the clinical recognition of AF.

However, several limitations should be recognized. Because AF can be transient and/or asymptomatic, it is possible that AF cases did not come to medical attention and were not identified using our ascertainment methods. In our ascertainment of incident AF for this study, we used data from fee-for-service Medicare. However, not all participants were over age 65 and eligible for coverage. Additionally, for those over 65, not all were enrolled in fee-for-service Medicare.

A previous study investigated the contribution of including Medicare claims data for AF ascertainment in the ARIC cohort, and found that inclusion of Medicare claims data offers a more complete picture of AF incidence (3). Our current study complements

these previous findings. Additionally, better dating of AF diagnosis through inclusion of Medicare claims data offers more precision when calculating person-time and AF incidence rates. Finally, in our study, inclusion of Medicare claims data yielded an additional 15 AF events, or 6% of total cases, a small but important increase over ascertainment limited to study ECG and ICD9 hospital surveillance data. Hospital discharge diagnosis codes for AF have been shown to have a positive predictive value of 89% (16), but the positive predictive value of Medicare outpatient, carrier, and home health claims for AF have not been determined. Additional study is needed of the validity of these types of Medicare claims data.

Consistent with previously published findings from CHS, ARIC and MESA, our results show lower estimates for AF incidence in African American men and women compared with white men and women (1, 2, 10). Regarding differences in AF incidence between men and women, published findings from large cohort studies of mostly white participants have generally found significantly higher rates of AF among men than women in each age group, with particularly great differences at older ages (10, 11). Among African American participants in JHS, MESA, and CHS, there was no suggestion of higher AF incidence rates in men than in women in any age stratum. However, confidence intervals in all three cohorts were wide, and estimated AF incidence, particularly in the older age strata, is imprecise.

In the multivariable Cox proportional hazards model, hypertension, higher BMI in the obese range, and history of myocardial infarction were significantly associated with AF risk, consistent with previously published results from analyses of predominantly white cohorts (Framingham Heart Study, CHS, ARIC, and the Age, Gene, Environment

Susceptibility Study) (10, 11). Existing analyses of AF incidence in AA have reported an association of greater BMI, modeled as a linear or categorical term, with incident AF (10, 17, 18). However, in the present analysis, our investigation of non-linear associations between BMI and incident AF revealed that the association of greater BMI with AF was limited to individuals with a BMI in the obese range (BMI > 30). In the Danish Diet, Cancer and Health Study (19), and in a prior combined analysis of MESA and JHS data, we have previously shown nonlinear associations between BMI and AF have been analyzed, similarly suggesting increased risk of incident AF with increasing BMI only among obese individuals (20). In CHS, measures including BMI were assessed for nonlinearity using cubic splines and were found to have a U shape curve (21). Impaired fasting glucose and diabetes were not significantly associated with AF risk in our multivariable model, which included adjustment for BMI. This finding is consistent with previously published results, which have implicated diabetes as an independent AF risk factor in whites but have either failed to find significant associations or have found smaller associations in African Americans (10, 11). In our secondary analysis that included heart failure as a risk factor, power to detect associations was lower because fewer participants were included in the analysis starting at exam 2 and because follow-up time was shorter. However, our results support previously published results implicating heart failure in risk of incident AF (11, 12).

In summary, findings from the JHS indicate that Medicare claims data are useful for AF ascertainment in cohort studies, and should be considered as an important ascertainment tool going forward. In this contemporary African American cohort, with a high prevalence of obesity and diabetes and a relatively low prevalence of current



smoking, AF incidence is similar to that reported in African Americans from cohorts recruited one to two decades earlier. Associations with established AF risk factors are similar, except that in JHS, the association of greater BMI with incident AF was observed only among those with BMI in the obese range. The results reported here underscore the importance of efforts to control blood pressure and body weight for the prevention of AF.

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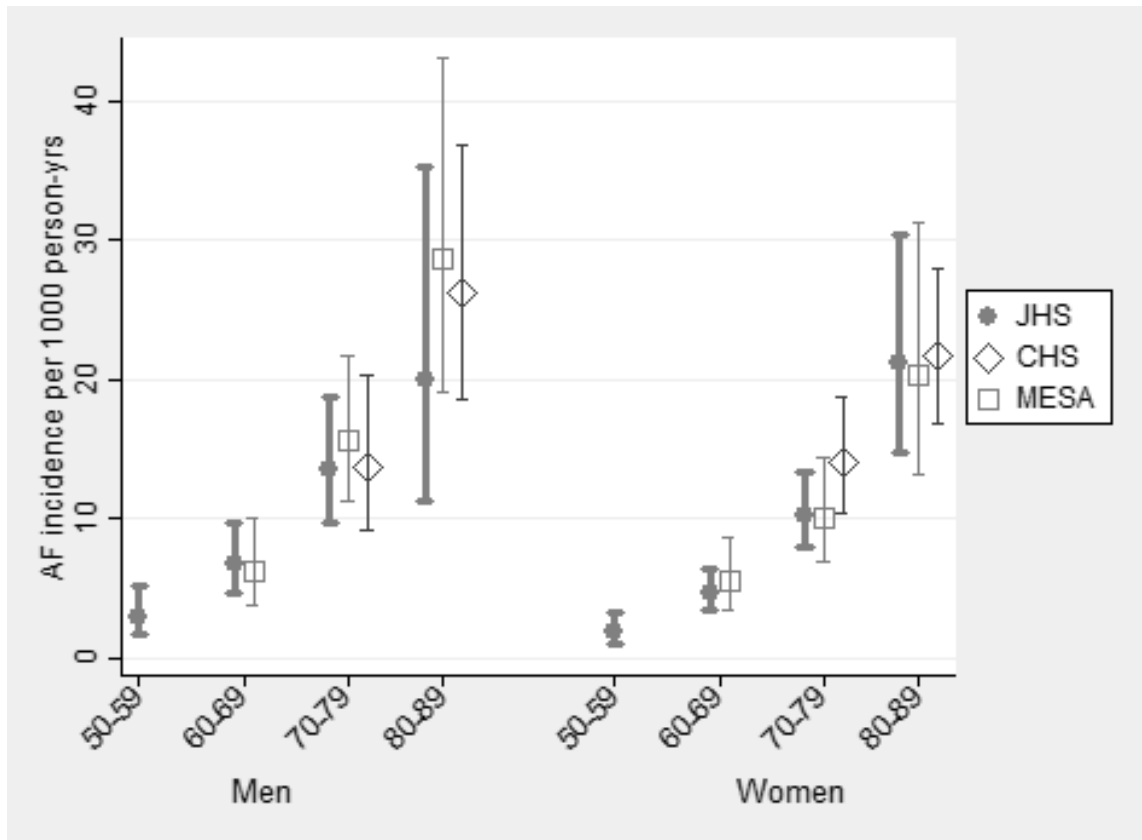
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Figure legend

**Figure 1:** Incidence rates of atrial fibrillation among African Americans in the Jackson Heart Study (JHS), Cardiovascular Health Study (CHS) and Multi-Ethnic Study of Atherosclerosis (MESA), by age group and sex.



**Table 1:** Characteristics of 5,235 Jackson Heart Study participants free of prevalent atrial fibrillation at baseline (2000-2004): women and men without and with a subsequent diagnosis of incident atrial fibrillation

	All Participants	Men			Women		
		All	Without Incident AF	With Incident AF	All	Without Incident AF	With Incident AF
N	5,235	1,908	1,813	95	3,327	3,183	144
Age, yrs, mean (SD)	55.1 (12.8)	54.4 (13.0)	53.9 (12.8)	63.5 (11.2)	55.6 (12.7)	55.1 (12.6)	67.0 (9.6)
Height, cm, mean (SD)	168.9 (9.3)	177.5 (7.0)	177.5 (7.0)	177.1 (7.3)	164.0 (6.4)	164.0 (6.4)	164.3 (6.0)
Current Smoker (%)	13.2	18.2	18.1	20.1	10.3	10.2	14.1
Glucose Status							
Normal (%)	44.3	43.3	43.8	35.2	44.8	45.6	27.6
Elevated (%)	34.0	36.5	36.3	40.4	32.5	32.6	31.2
Diabetes (%)	21.7	20.2	19.9	24.4	22.6	21.8	41.3
Hypertension (%)	56.1	52.0	50.6	77.9	58.4	57.2	84.7
BMI, kg/m <sup>2</sup> , mean (SD)							
<25	14.5	18.5	18.4	20.0	12.2	12.3	11.9
25 – 30	32.1	40.4	40.6	35.8	27.4	27.3	27.9
30+	53.4	41.2	41.0	44.2	60.4	60.4	60.3
FEV <sub>1</sub> , L, mean (SD)	2.39 (0.71)	2.91 (0.71)	2.90 (0.70)	2.45 (0.69)	2.09 (0.51)	2.10 (0.50)	1.71 (0.41)
History of MI	7.3	9.4	8.4	27.4	6.1	5.7	16.0
Insured (%)	86.3	86.0	85.7	92.6	86.5	86.2	94.3
Years of Education	14.6 (3.9)	14.5 (4.1)	14.5 (4.0)	13.1 (4.5)	14.7 (3.8)	14.8 (3.8)	12.4 (4.7)
ECG PR Interval (ms)	165.9 (27.0)	170.0 (27.8)	169.5 (27.7)	179.6 (27.8)	163.5 (26.1)	163.2 (25.8)	168.9 (31.6)

BMI = Body Mass Index, FEV<sub>1</sub> = Forced Expiratory Volume, One Second, MI = Myocardial Infarction, ECG = Electrocardiogram

**Table 2:** Incident and prevalent atrial fibrillation among 5,306 Jackson Heart Study participants, by method of ascertainment

		Method 2 **			Total
		No AF	Prevalent AF	Incident AF	
Method 1 *	No AF	4,998	26	15	5,039
	Prevalent AF	0	43	0	43
	Incident AF	0	0	224	224
	Total	4,998	69	239	5,306

AF = Atrial Fibrillation

\* Method 1: Study ECGs and Hospital Surveillance were used to ascertain prevalent and incident AF

\*\* Method 2: Study ECGs, Hospital Surveillance, and Medicare Claims data were used to ascertain prevalent and incident AF

**Table 3:** Age and sex adjusted and multivariable adjusted hazard ratios of incident atrial fibrillation in Jackson Heart Study participants (N = 5,235) according to baseline characteristics, 2000-2004.

	Age & Sex Adjusted			Multivariable Model		
	HR	95% CI	p-value	HR	95% CI	p-value
Male	1.35	1.04, 1.75	0.025	1.32	0.89, 1.94	0.168
Age (per 5 years)	1.48	1.39, 1.57	<0.001	1.06	1.04, 1.07	<0.001
Height (per 10 cm)	1.12	1.01, 1.23	0.025	1.04	1.02, 1.06	<0.001
BMI						
<30 (per 5 units)	0.85	0.66, 1.08	0.187	0.87	0.68, 1.13	0.300
30+ (per 5 units)	1.32	1.19, 1.47	<0.001	1.27	1.14, 1.42	<0.001
Fasting Glucose						
Normal (<100 mg/dL)	Ref.	N/A	N/A	Ref.	N/A	N/A
Impaired (100 ≤ x < 126 mg/dL)	1.02	0.74, 1.40	0.918	0.90	0.65, 1.24	0.517
Diabetic (≥126 mg/dL)	1.44	1.05, 1.98	0.025	1.04	0.74, 1.47	0.824
Hypertension	2.06	1.47, 2.90	<0.001	1.73	1.22, 2.46	0.002
History of MI	3.33	1.70, 3.20	<0.001	1.91	1.38, 2.64	<0.001
FEV <sub>1</sub> (per 0.5L)	0.72	0.63, 0.82	<0.001	0.53	0.38, 0.73	<0.001
ECG PR Interval, ms						
120 – 199	Ref.	N/A	N/A	Ref.	N/A	N/A
< 120	1.39	0.57, 3.41	0.468	1.60	0.65, 3.93	0.309
≥ 200	1.09	0.75, 1.58	0.646	1.01	0.70, 1.46	0.971
Current Smoker	1.77	1.25, 2.52	0.001	1.57	1.08, 2.28	0.019
Insured	1.36	0.80, 2.31	0.261	1.48	0.87, 2.54	0.150
Years of Education	0.96	0.94, 0.99	0.018	0.98	0.95, 1.01	0.162

\* P≤0.003; In the multivariable model, a P value significance threshold of <0.003 was used to account for multiple comparisons

BMI = body mass index, FEV<sub>1</sub> = forced expiratory volume in 1 second, Hx = history,

ECG = electrocardiographic, MI = Myocardial Infarction



**Supplementary Table:** Age and sex-adjusted and multivariable-adjusted hazard ratios of incident atrial fibrillation in Jackson Heart Study participants (N = 4,205), according to baseline and Exam 2 characteristics, including a history of heart failure

	Age & Sex Adjusted			Multivariable Model		
	HR	95% CI	p-value	HR	95% CI	p-value
Male	1.33	0.91, 1.94	0.142	1.43	0.78, 2.65	0.245
Age (per 5 years)	1.48	1.36, 1.62	<0.001	1.38	1.21, 1.57	<0.001
Height (per 10 cm)	1.16	0.87, 1.56	0.317	1.47	1.07, 2.01	0.017
BMI						
<30 (per 5 units)	1.00	0.67, 1.49	0.991	1.06	0.13, 8.71	0.958
30+ (per 5 units)	1.35	1.15, 1.59	<0.001	3.39	1.30, 8.80	0.013
Fasting Glucose						
Normal (<100 mg/dL)	Ref.	N/A	N/A	Ref.	N/A	N/A
Impaired (100 ≤ x < 126 mg/dL)	1.37	0.78, 2.39	0.270	1.35	0.63, 2.86	0.428
Diabetic (≥126 mg/dL)	1.34	0.72, 2.49	0.354	0.91	0.39, 2.09	0.811
Hypertension	2.42	1.28, 4.56	0.006	2.13	1.09, 4.17	0.028
History of MI	1.60	0.78, 3.30	0.198	1.14	0.54, 2.42	0.728
Heart Failure	4.25	2.32, 7.76	<0.001	3.07	1.59, 5.90	0.001
FEV <sub>1</sub> (per 0.5L)	0.68	0.55, 0.84	<0.001	0.69	0.55, 0.86	0.001
ECG PR Interval, ms						
120 – 199	Ref.	N/A	N/A	Ref.	N/A	N/A
< 120	1.93	0.60, 6.21	0.272	1.93	0.60, 6.21	0.272
≥ 200	0.82	0.46, 1.46	0.500	0.82	0.56, 1.46	0.499
Current Smoker	1.94	1.14, 3.29	0.015	1.74	1.00, 3.04	0.052
Insured	1.24	0.57, 2.69	0.587	1.32	0.60, 2.92	0.488
Years of Education	0.90	0.75, 1.07	0.238	0.98	0.94, 1.03	0.423

\* P≤0.003; In the multivariable model, a P value significance threshold of <0.003 was used to account for multiple comparisons

BMI = body mass index, FEV<sub>1</sub> = forced expiratory volume in 1 second, Hx = history,

ECG = electrocardiographic, MI = Myocardial Infarction