Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods

Additional information on cohort description, genotyping methods, ancestry evaluation, definitions of comorbidities, laboratory testing, and follow-up for cardiovascular outcomes is provided below. We included several larger cohorts beginning in middle-age with HF hospitalization data including ejection fraction and with available genotyping data. "Black" in this study refers to self-reported race based upon fixed categories obtained during study intake at baseline. These cohorts are based in the United States. The race descriptor does not imply ancestry.

Cohort Descriptions

Atherosclerosis Risk in Communities (ARIC) Study

ARIC is a prospective observational study designed to evaluate the natural history of atherosclerosis risk factors in 4 communities across the United States (Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD) comprised of 15,792 participants, aged 45–64 years, recruited between 1987 and 1989.[1] V142I genotyping was available for 3,856 of the 4,266 Black participants in the ARIC study.[2] We excluded 313 participants with prevalent or unknown HF status at visit 1, leaving 3,543 (including 112 carriers) participants.

Multi-Ethnic Study of Atherosclerosis (MESA)

MESA is a cohort study of 6 communities (Maryland, Illinois, North Carolina, California, New York, and Minnesota).[3] Between July 2000 and August 2002, 6,814 participants free of clinical cardiovascular disease between 45-84 years were recruited, while 1,891 were self-reported as Black individuals. Through MESA SHARe (SNP Health Association Resource), 1,595 had available V142I genotyping and principal components data available after quality

control processes. We further excluded 11 participants without follow-up, leaving 1,584 participants including 49 carriers.

REasons for Geographic and Racial Differences in Stroke (REGARDS)

REGARDS recruited 30,239 White and Black adults at least 45 years old living in the United States between January 2003 and October 2007.[4] Community-dwelling participants were randomly selected from a commercially available list to create a sample balance on race and sex across the stroke buckle (within the stroke belt along the coastal plains of Georgia, North Carolina, and South Carolina), the stroke belt (the remainder of Georgia, North Carolina, and South Carolina and Alabama, Arkansas, Louisiana, and Tennessee), and rest of the continental US. Of 12,514 self-reported Black participants, 8,916 participants underwent genotyping with 8,669 passing genotypic quality control. Of these, 139 participants with suspected HF at baseline or missing HF status, as well as 3 individuals without follow-up, were further excluded, leaving 8,527 self-identified Black participants (of whom 262 were carriers).[5]

Women's Health Initiative (WHI)

Women were eligible to participate in the WHI if they were 50 to 79 years of age, generally healthy, and postmenopausal at the time of enrollment.[6] A total of 161,808 participants were enrolled between 1993-1998 in the observational or clinical trial arms, including 14,618 self-reported Black participants. Among Black participants, we included those enrolled as part of the PAGE II (Population Architecture using Genomics and Epidemiology) and SHARe genetic studies.[7] After combining WHI PAGE II and SHARe genetic studies and removing overlap, 9,873 women had available genotyping. After removing 178 participants with HF at baseline and 11 participants without follow-up, a total of 9,684 Black women (including 331 carriers) were included.

Genotyping

ARIC

The V142I *transthyretin* variant (rs76992529) was determined by direct genotyping with the Illumina HumanExome BeadChip, version 1.0 with a 100% call rate. The methods of genotyping, allele calling, and quality control have been published previously.[8] Principal component analysis was performed using EIGENSTRAT.[9] The median African genetic ancestry percentage for ARIC (N=3059 with available data) was 84.8% (25^{th}-75^{th} percentile 77.6%-89.4%), using methods previously described.[10,11]

MESA

V142I was directly genotyped using the Illumina HumanExome BeadChip, version 1.0 with a 100% call rate. Methods for genotyping, allele calling, and quality control have been described previously.[8] Principal components of ancestry were obtained using data from the MESA SHARe genome wide association study genotyping effort (Affy 6.0 array) and analysis using EIGENSTRAT.[9] The median African genetic ancestry percentage for MESA (N=1584) was 81.0% (25^{th}-75^{th} percentile 69.2%-88.5%), using methods previously described.[12]

REGARDS

Direct genotyping was accomplished using Illumina Infinium Multi-Ethnic AMR/AFR BeadChip arrays (Illumina Inc) using quality control methods previously published.[5,13] The variant call rate was 100% in REGARDS. Principal component analysis was performed using SmartPCA version 7.2.1 software (EIGENSTRAT).[9] The median African genetic ancestry percentage for REGARDS (N=7514 with available data) was 84.2% (25^{th}-75^{th} percentile 75.4%-90.5%) using methods previously described.[5,14]

WHI

WHI samples were directly genotyped as part of the larger PAGE II study on the Multi-Ethnic Genotyping Array by the Center for Inherited Disease Research. Quality control was performed by the University of Washington Genetic Analysis center and included technical filters, removing variant with discordant calls in duplicates or Mendelian errors, and Hardy-Weinberg outliers.[15] The V142I call rate was 100% in PAGE II. The WHI SHARe samples were genotyped at Affymetrix Inc on the Genome-wide Human SNP Array 6.0 and the variant was imputed using the TOPMed reference panel using Michigan imputation server.[16,17] Quality control performed at the Fred Hutchinson Cancer Research Center and included removal of relatives, single nucleotide polymorphisms (SNPs) with low call rates or concordance rates, and Hardy-Weinberg outliers.[18] Specific quality control criteria for imputation included a minimum sample call rate of 95%, minimum SNP call rate of 90%, minor allele frequency of 1%, and Hardy-Weinberg p-value cutoff 1e-6. For the V142I variant, the imputation quality was high (r^2=0.999). Information on the calculation of PCs (performed using the SNPRelate package in R) has been previously published.[7] The median African genetic ancestry percentage for WHI (N=8210 with available data) was 79.3% (25^{th}-75^{th} percentile 68.7%-86.9%) using methods previously described.[19,20]

Definitions of comorbidities

Hypertension was defined in each study by a systolic blood pressure ≥140, diastolic blood pressure ≥90, or the use of anti-hypertensive medications. Diabetes mellitus definitions differed modestly by cohort. In ARIC and WHI, diabetes was defined by a self-report of diabetes, fasting serum glucose of ≥126 mg/dl, a non-fasting glucose ≥200 mg/dl, or pharmacologic treatment for diabetes. In MESA, diabetes mellitus was defined by fasting serum glucose of ≥126 mg/dl or treatment for diabetes mellitus. In REGARDS, fasting glucose levels

≥126 mg/dL or random level ≥200 mg/dL, use of diabetes medication, or both, were used to identify diabetes status. Prevalent coronary heart disease was defined by reported history of myocardial infarction or revascularization in WHI, while ARIC and REGARDS additionally included electrocardiographic evidence of myocardial infarction.

Laboratory testing

Laboratory testing is presented from the baseline visit from each cohort. Laboratory analyses for glucose, creatinine, and low-density lipoprotein cholesterol were more comprehensively assessed in study participants from ARIC, REGARDS, and MESA (missingness≤5.1%). In WHI, a majority of participants have available laboratory values that were performed in a subset of WHI participants that oversampled Black participants. Out of the 9,864 participants, a total of 7,938, 7,729, and 7,694 have available glucose, creatinine, and cholesterol levels, respectively.

Outcome Ascertainment

ARIC

Incident HF events post visit 1 were initially identified using International Classification of Diseases discharge codes, and HF events were later adjudicated (beginning in 2005). Ejection fraction abstracted from the first incident adjudicated HF hospitalization starting in 2005 was used to classify HF as HFpEF (EF≥50%) or HFrEF (EF <50%). When EF was unavailable from this hospitalization, the most recent abstracted ejection fraction from a prior hospitalization—if available—was used. If the prior LVEF was normal, it was only used if it was from within 6 months before the HF hospitalization and without an interval MI.[21] Among HF-free participants by 2005, there were subsequently 417 HF hospitalizations including 41 with

indeterminate EF. Deaths were ascertained through review of hospital discharge records and death certificates, supplemented by next-of-kin interviews or physician questionnaires for out-of-hospital deaths. Events were ascertained during follow-up visits for the ARIC study as well as through annual calls to participants (semi-annual since 2012), ongoing surveillance of health department certificate files, and review of local hospital-discharge lists (with outcomes determined on the basis of International Classification of Diseases codes). Follow-up is complete through December 31, 2020 for all outcomes. The methods utilized for quality control, detection, and adjudication of events have been previously presented.[22,23]

MESA

Medical records were reviewed and diagnoses of HF events while hospitalized were adjudicated by a panel of MESA physicians using standardized criteria. The present study included probable or definite HF events. Probable HF required HF symptoms, a physician diagnosis of HF, and treatment. Definite HF required at least one additional finding, including abnormalities on chest X-ray, echocardiography, or ventriculography. HFpEF hospitalization was defined by an ejection fraction EF≥50% (or qualitatively reported as normal) while HFrEF was defined by an ejection fraction EF<50% (or qualitatively reported as low). Among 114 HF hospitalizations, 16 were indeterminate for EF.

Identification of cardiovascular events was based on participant self-report via telephone follow-up visits, which were performed at 9–12-month intervals.[24] Further events were identified by personal participant notification, the National Death Index, public notices, and MESA clinic visits. Medical records and death certificates were requested for all cases. When relevant, interviewers contacted the next of kin in order to obtain copies of death certificates. Finally, two

blinded members of the MESA mortality and morbidity review committee performed an independent classification of cardiovascular events and assigned incidence dates. In case of disagreement, adjudication was performed by the full MESA mortality and morbidity review committee.[24] Event reporting is complete through December 31, 2018 for HF hospitalization subtypes (HFrEF and HFpEF) and December 31, 2019 for HF hospitalization and mortality.

REGARDS

Suspected hospitalizations for heart failure were identified based on the biannual follow-up call to the participants or their proxies. Two clinician investigators adjudicated medical records using standardized forms, and a committee resolved any disagreements. Hospitalizations for heart failure were identified based on (1) signs and symptoms; (2) biomarkers; and (3) imaging.[5] HFrEF was defined by documented EF <50% or qualitative report of reduced LVEF. HFpEF was defined by documented EF ≥50% or qualitatively normal EF.[25] Among 532 HF hospitalizations, 69 were unclassified for EF. Mortality was assessed using death certificates, autopsy reports, the National Death Index, and interviews with proxies. The latest all-cause mortality data available (up through December 31, 2020) were used for the analysis, while HF event reporting is complete through December 31, 2018.

WHI

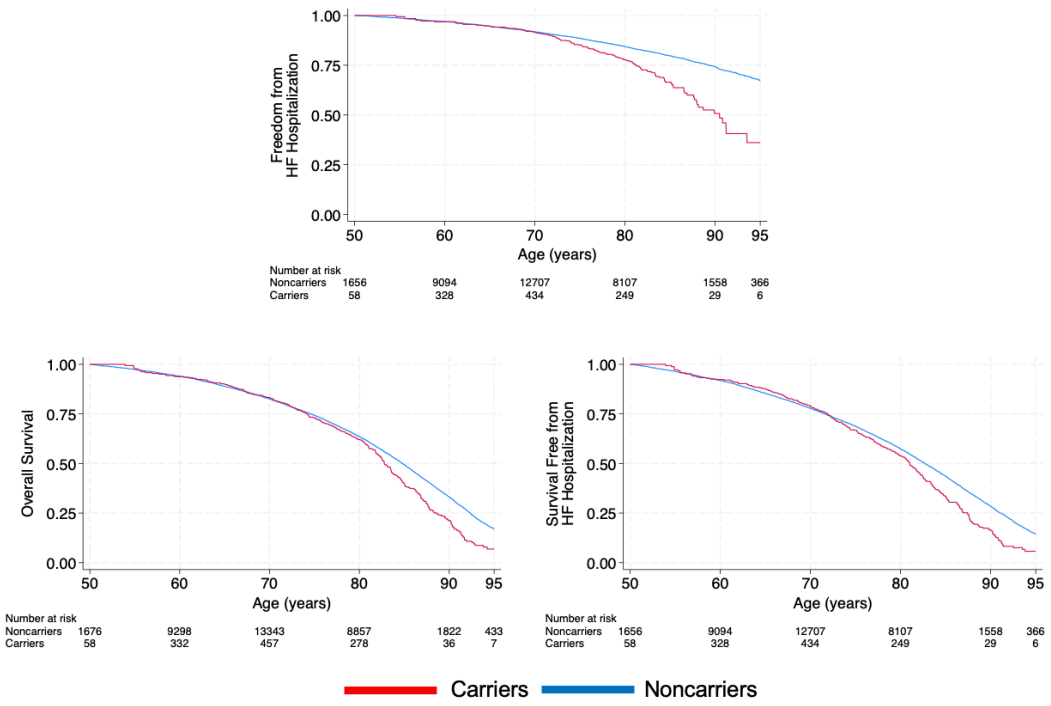
All HF events including confirmed cases of HF hospitalization and patient-reported hospitalization for HF were sent to University of North Carolina for adjudication by trained physicians. Available medical records for HF hospitalizations were reviewed, and HF hospitalizations were classified into 1 of 5 categories (definite acute decompensated HF, possible acute decompensated HF, chronic stable HF, unclassifiable, or HF unlikely) based on the

algorithm used in the ARIC study.[23] A designation of definite acute decompensated HF or possible acute decompensated HF was considered incident HF. HF with an EF <50% was defined as HFrEF, and HF with an ejection fraction ≥50% was classified as HFpEF. If no left ventricular EF was available or if the HF case was designated as recovered left ventricular EF, it was designated as unclassified.[26] Among 758 HF hospitalizations, 144 were unclassified for EF. All-cause mortality was ascertained by extracting health information from hospital records or the National Death Index. Data are complete through February 19, 2022.

eFigure 1

Title: Kaplan-Meier Curves for Heart Failure and Mortality Events by V142I Carrier Status

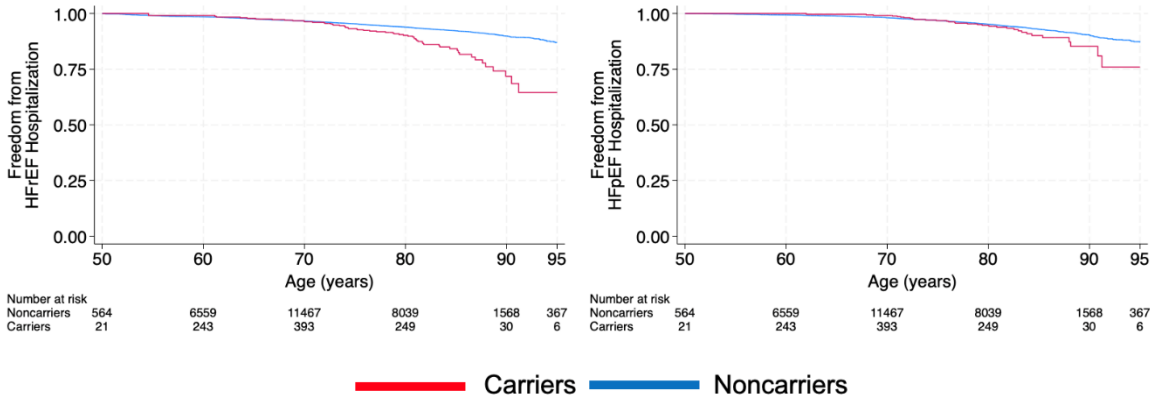
Caption: Kaplan-Meier estimated curves for HF hospitalization, overall survival, and survival free from HF hospitalization shown by genotype status between ages 50-95. The median (interquartile range) years for noncarriers and carriers for each outcome was 13.5 (8.3-21.7) and 13.2 (7.8-20.9) for HF hospitalization, 14.6 (9.0-22.7) and 14.4 (8.4-22.5) for overall survival, and 13.5 (8.3-21.7) and 13.2 (7.8-20.9) for survival free from HF. HF, heart failure.



eFigure 2

Title: Kaplan-Meier Curves for Heart Failure Events by V142I Carrier Status

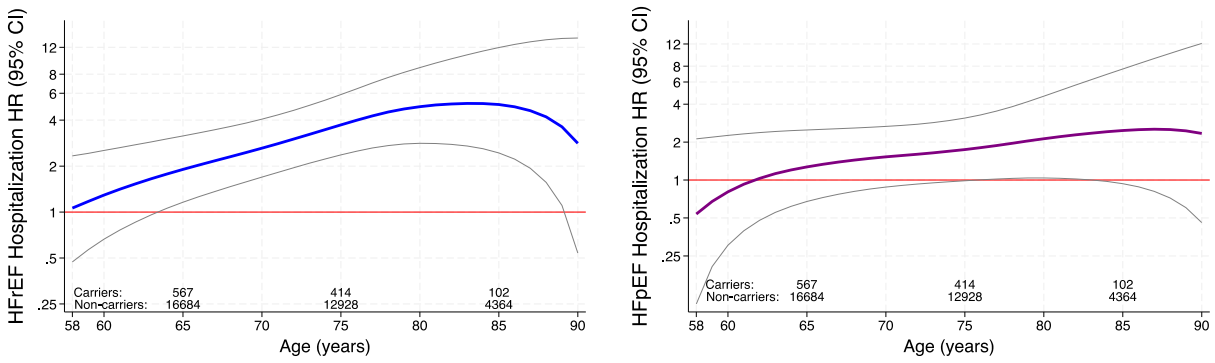
Caption: Kaplan-Meier estimated curves for HF subtypes by genotype status between ages 50-95. The median (interquartile range) years for noncarriers and carriers for each outcome were 12.9 (7.8-17.3) and 12.5 (7.2-16.0). HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.



eFigure 3

Title: V142I Hazard Ratio for Heart Failure Events by Age

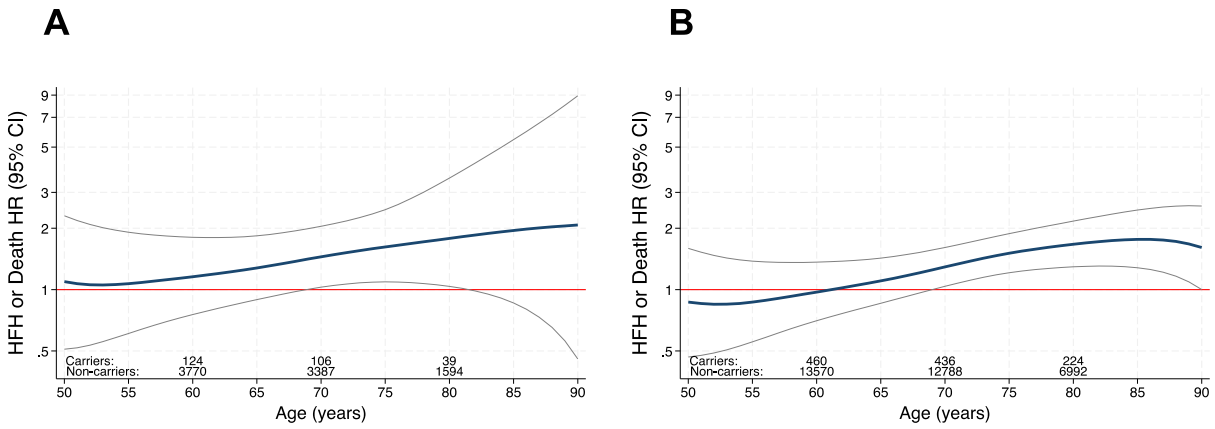
Caption: 10-year HRs and 95% CIs are estimated at each age for carriers versus noncarriers. HRs are shown between ages 58-90 for the HF subtypes of HFrEF and HFpEF hospitalization (age range is restricted at the lower end compared with other reported study outcomes due to fewer events). Analyses are adjusted for interactions between study genotyping platform and the first 10 principal components, while stratified by sex and study genotyping platform. CI, confidence interval; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio.



eFigure 4

Title: V142I Hazard Ratio for Heart Failure Hospitalization or Death by Age and Sex

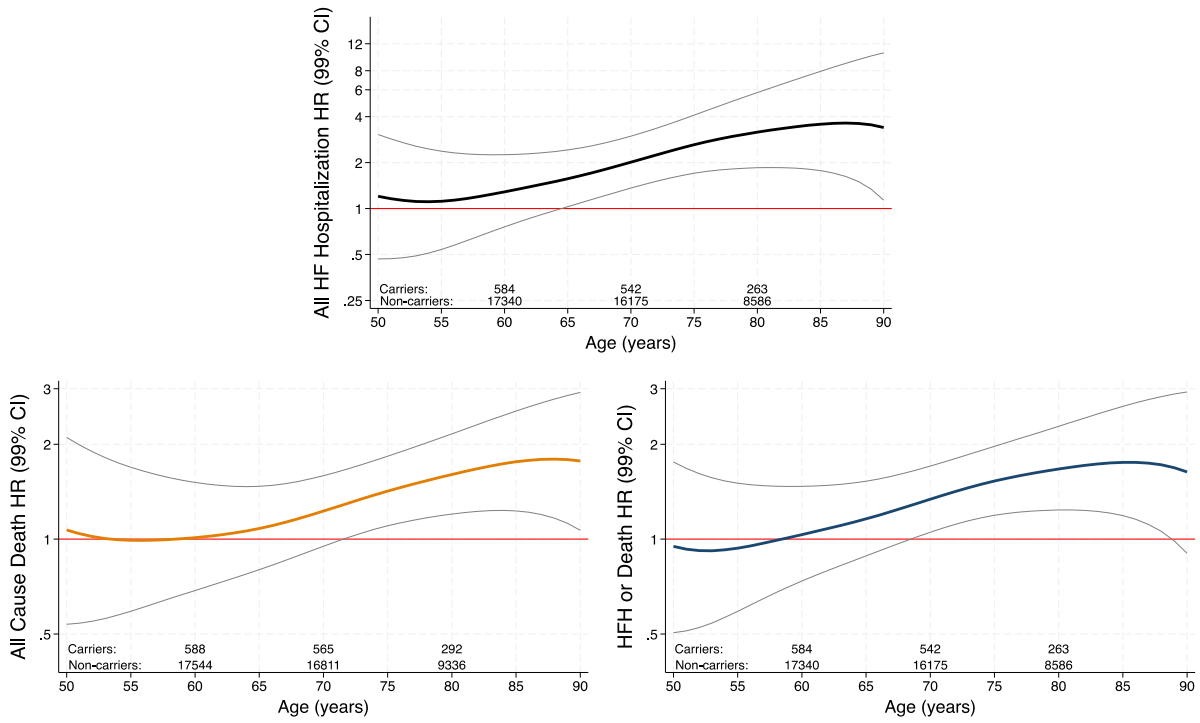
Caption: 10-year HRs and 95% CIs are estimated at each age for carriers versus noncarriers for the combined outcome of HFH or death in men (A) and women (B). Analyses are adjusted for interactions between study genotyping platform and the first 10 principal components, while stratified by study genotyping platform. HR, hazard ratio; HFH, heart failure hospitalization; CI, confidence interval.



eFigure 5.

Title: V142I Hazard Ratio for Adverse Cardiovascular Events by Age using 99% Confidence Intervals

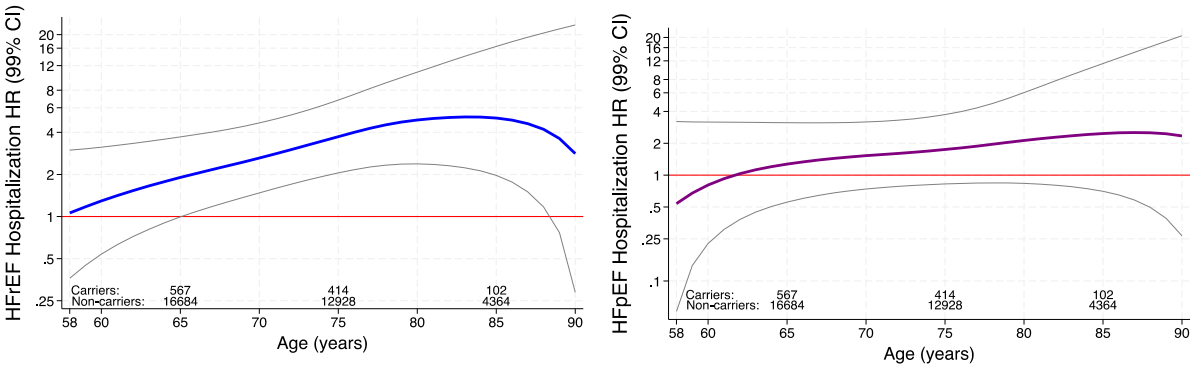
Caption: 10-year HRs and 99% CIs are estimated at each age between 50-90 for carriers versus noncarriers. Analyses are adjusted for interactions between study genotyping platform and the first 10 principal components, while stratified by sex and study genotyping platform. Nominal statistical significance was first achieved at ages 65, (HFH), 73 (death), and 68 (HFH or death). CI, confidence interval; HFH, heart failure hospitalization; HR, hazard ratio.



eFigure 6.

Title: V142I Hazard Ratio for Heart Failure Events by Age using 99% Confidence Intervals

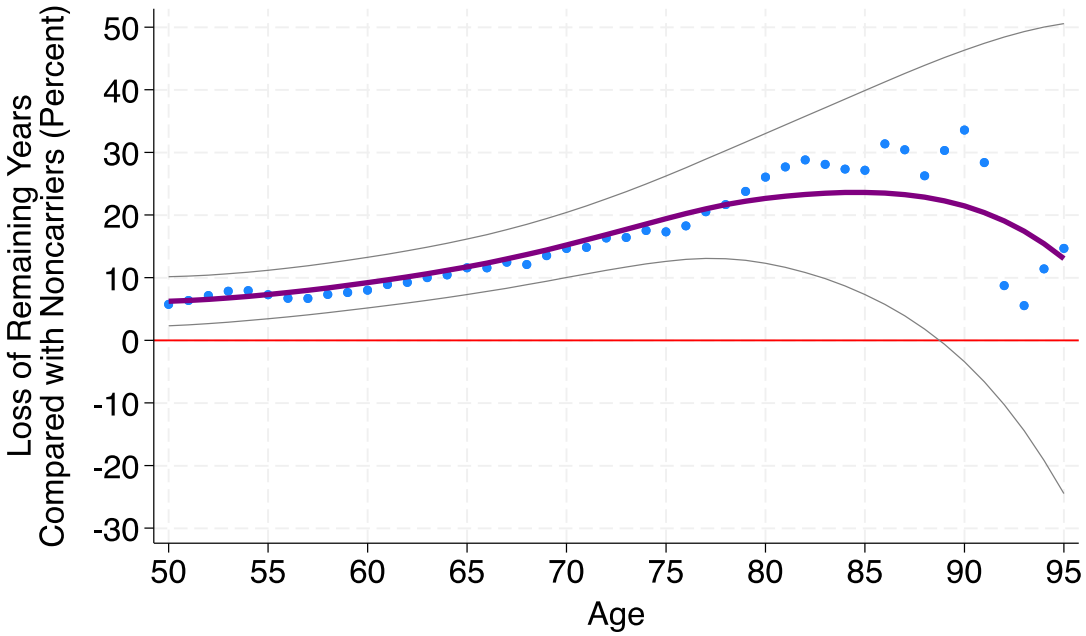
Caption: 10-year hazard ratios and 99% CIs are estimated at each age for carriers versus noncarriers. Hazard ratios are shown between ages 58-90 for the HF subtypes of HFrEF and HFpEF hospitalization (age range is restricted at the lower end compared with other reported study outcomes due to fewer events). Analyses are adjusted for interactions between study genotyping platform and the first 10 principal components, while stratified by sex and study genotyping platform. Nominal statistical significance was first achieved at age 65 for HFrEF hospitalization, whereas HFpEF hospitalization only momentarily achieved statistical significance at age 82 but not thereafter. CI, confidence interval; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio.



eFigure 7

Title: Relative Effect of V142I on Remaining Years of Life Compared with Noncarriers

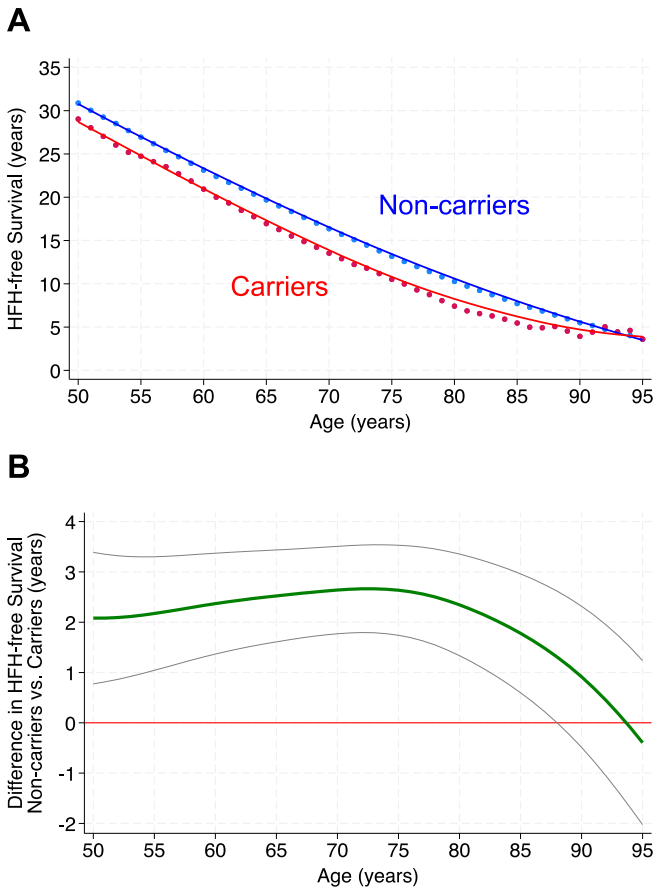
Caption: Estimated percent of remaining years lost among carriers compared with noncarriers for every year between 50 years and 95 years. The smoothed estimate is shown in the purple line, and 95% confidence intervals of the smoothed estimate is shown in gray lines after application of a locally weighted scatterplot smoothing procedure.



eFigure 8

Title: Effect of V142I on HFH-free Survival Compared with Noncarriers

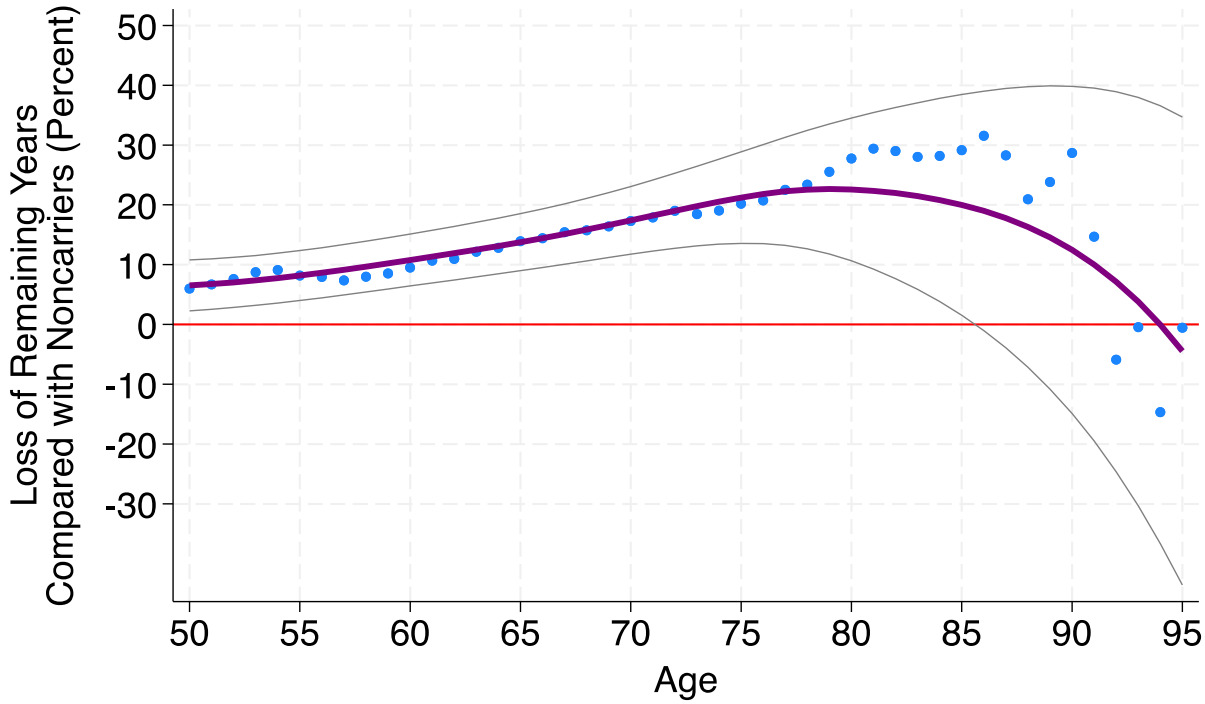
Caption: Estimated mean HFH-free survival in carriers and noncarriers for every year between 50 years and 95 years (panel A). The difference in mean years lost among carriers compared with noncarriers shown with the smoothed estimate (green line), and 95% CI of the smoothed estimate (gray lines) after application of a locally weighted scatterplot smoothing procedure (panel B). HFH, heart failure hospitalization.



eFigure 9:

Title: Relative Effect of V142I on Remaining Years of Life Free from HFH Compared with Noncarriers

Caption: Estimated percent of remaining years lost free from HFH among carriers compared with noncarriers for every year between 50 years and 95 years. The smoothed estimate is shown in the purple line, and 95% CI of the smoothed estimate is shown in gray lines after application of a locally weighted scatterplot smoothing procedure. HFH, heart failure hospitalization.



eTABLE 1. Hazard Ratios for Heart Failure Hospitalization and Death by Carrier Status and Cardiovascular Risk Factors

Outcomes	Hazard ratio HR (95% CI) N=22,499	P-value
Heart failure hospitalization		
▪ V142I carrier status	1.96 (1.64, 2.36)	<0.001
▪ Hypertension	1.73 (1.57, 1.91)	<0.001
▪ Diabetes mellitus	2.51 (2.30, 2.75)	<0.001
▪ Obesity	1.36 (1.25, 1.49)	<0.001
▪ Coronary heart disease	2.93 (2.57, 3.35)	<0.001
All-cause mortality		
▪ V142I carrier status	1.28 (1.14, 1.44)	<0.001
▪ Hypertension	1.30 (1.23, 1.36)	<0.001
▪ Diabetes mellitus	1.79 (1.70, 1.88)	<0.001
▪ Obesity	0.98 (0.94, 1.03)	0.45
▪ Coronary heart disease	1.42 (1.33, 1.54)	<0.001

Time scale for analyses was time from the baseline visit.
Models adjusted for interactions between study genotyping platform and the first 10 principal components and stratified by age, sex, and the genotyping platform.
CI, confidence interval.

eTable 2. Events and Hazard Ratios for Adverse Cardiovascular Outcomes by Number of Alleles

Outcomes	Number of Events	Hazard ratio HR (95% CI)
HFH		
▪ **0 alleles**	2373/22584 (10.5%)	0.55 (0.46, 0.66)
▪ **1 allele**	132/750 (17.6%)	Ref
▪ **2 alleles**	2/4 (50.0%)	20.14 (3.57, 113.59)
All-cause death		
▪ **0 alleles**	8744/22584 (38.7%)	0.79 (0.71, 0.89)
▪ **1 allele**	327/750 (43.6%)	Ref
▪ **2 alleles**	2/4 (50.0%)	2.79 (0.65, 12.02)
HFH or all-cause death		
▪ **0 alleles**	9290/22584 (41.1%)	0.77 (0.69, 0.86)
▪ **1 allele**	352/750 (46.9%)	Ref
▪ **2 alleles**	3/4 (75.0%)	7.75 (2.24, 26.79)

Models adjusted for interactions between study genotyping platform and the first 10 principal components and stratified by age, sex, and the genotyping platform.
The one homozygous participant who did not experience a HF or death event was lost to follow-up after approximately 3.5 years.
CI, confidence interval; HFH, heart failure hospitalization; ref, reference.

eTable 3. Interaction Analysis of the Variant with Select Variables for Study Outcomes

Covariate	Outcome = HFH: Subgroup hazard ratio (95% CI)	Outcome = HFH: Covariate* V142I interaction p-value	Outcome = Death: Subgroup hazard ratio (95% CI)	Outcome = Death: Covariate* V142I interaction p-value	Outcome = HFH or death: Subgroup hazard ratio (95% CI)	Outcome = HFH or death: Covariate*V 142I interaction p-value
Cohort		0.80		0.39		0.86
• MESA	1.86 (0.81, 4.24)		1.49 (0.96, 2.31)		1.39 (0.91, 2.14)	
• ARIC	1.53 (1.15, 2.03)		1.04 (0.82, 1.31)		1.14 (0.92, 1.42)	
• WHI	1.92 (1.42, 2.59)		1.21 (1.01, 1.45)		1.21 (1.02, 1.44)	
• REGARDS	1.96 (1.36, 2.82)		1.20 (0.99, 1.45)		1.22 (1.01, 1.46)	
Age at baseline		0.002*		0.002*		0.004*
• Age tertile 1 (<57.5 years)	1.41 (1.04, 1.91)		0.96 (0.76, 1.22)		1.06 (0.85, 1.31)	
• Age tertile 2 (57.5≤age<64.5 years)	1.87 (1.34, 2.60)		1.26 (1.03, 1.55)		1.26 (1.03, 1.54)	
• Age tertile 3 (≥64.5 years)	2.61 (1.96, 3.46)		1.49 (1.27, 1.75)		1.55 (1.33, 1.81)	
Sex		0.50		0.82		0.82
• Men	1.93 (1.41, 2.65)		1.16 (0.94, 1.43)		1.24 (1.01, 1.51)	

Covariate	Outcome = HFH: Subgroup hazard ratio (95% CI)	Outcome = HFH: Covariate* V142I interaction p-value	Outcome = Death: Subgroup hazard ratio (95% CI)	Outcome = Death: Covariate* V142I interaction p-value	Outcome = HFH or death: Subgroup hazard ratio (95% CI)	Outcome = HFH or death: Covariate*V 142I interaction p-value
• Women	1.70 (1.38, 2.10)		1.19 (1.05, 1.36)		1.20 (1.06, 1.37)	
Hypertension		0.67		0.054		0.047
• No hypertension	1.87 (1.35, 2.59)		1.00 (0.81, 1.24)		1.04 (0.84, 1.27)	
• Hypertension	1.77 (1.44, 2.18)		1.27 (1.12, 1.45)		1.31 (1.16, 1.49)	
Diabetes mellitus		0.08		0.61		0.60
• No diabetes mellitus	2.03 (1.65, 2.49)		1.17 (1.03, 1.34)		1.21 (1.07, 1.37)	
• Diabetes mellitus	1.35 (0.96, 1.89)		1.22 (0.99, 1.50)		1.24 (1.02, 1.52)	
Systolic blood pressure		0.96		0.15		0.21
• Systolic blood pressure below median (<130 mmHg)	1.65 (1.23, 2.21)		1.02 (0.85, 1.23)		1.08 (0.91, 1.28)	
• Systolic blood pressure above median (≥130 mmHg)	1.77 (1.42, 2.20)		1.28 (1.12, 1.47)		1.29 (1.13, 1.47)	

Covariate	Outcome = HFH: Subgroup hazard ratio (95% CI)	Outcome = HFH: Covariate* V142I interaction p-value	Outcome = Death: Subgroup hazard ratio (95% CI)	Outcome = Death: Covariate* V142I interaction p-value	Outcome = HFH or death: Subgroup hazard ratio (95% CI)	Outcome = HFH or death: Covariate*V 142I interaction p-value
Heart rate		0.99		0.82		0.31
• Heart rate below median (<68 beats per minute)	1.85 (1.43, 2.39)		1.20 (1.02, 1.41)		1.21 (1.03, 1.41)	
• Heart rate above median (≥68 beats per minute)	1.65 (1.29, 2.11)		1.15 (0.98, 1.34)		1.21 (1.04, 1.40)	
Body-mass index		0.32		0.98		0.99
• Body-mass index below median (<29.7 kg/m^2)	1.90 (1.47, 2.45)		1.18 (1.02, 1.37)		1.20 (1.04, 1.39)	
• Body-mass index above median (≥29.7 kg/m^2)	1.72 (1.35, 2.19)		1.16 (0.99, 1.37)		1.23 (1.05, 1.44)	
African ancestry		0.33		0.70		0.79
• African ancestry below	1.68 (1.25, 2.28)		1.18 (0.99, 1.40)		1.22 (1.03, 1.44)	

Covariate	Outcome = HFH: Subgroup hazard ratio (95% CI)	Outcome = HFH: Covariate* V142I interaction p-value	Outcome = Death: Subgroup hazard ratio (95% CI)	Outcome = Death: Covariate* V142I interaction p-value	Outcome = HFH or death: Subgroup hazard ratio (95% CI)	Outcome = HFH or death: Covariate*V 142I interaction p-value
median (<82.3%)						
• African ancestry above median (≥82.3%)	1.98 (1.57, 2.49)		1.22 (1.04, 1.42)		1.25 (1.07, 1.44)	

*p<0.05 with Bonferroni correction for multiple hypothesis testing.
Models adjusted for interactions between study genotyping platform and the first 10 principal components.
ARIC, Atherosclerosis Risk in Communities; HFH, heart failure hospitalization; MESA, Multi-Ethnic Study of Atherosclerosis; REGARDS, Reasons for Geographic and Racial Differences in Stroke; WHI, Women's Health Initiative.
Time scale for analyses was time from the baseline visit.
For continuous variables, interaction p-values shown for the interaction of the continuous variable*variant, and subgroups are then displayed by quantiles of the continuous variable for descriptive purposes.

eTable 4. Estimated Survival Time Comparing Carriers and Noncarriers by Age for All-Cause Mortality with Extrapolation to the United State Population

Age	Estimated Number of US Black Individuals Alive at this Age*	Estimated Carrier Percentage**	Estimated Number of US Black Carriers	Expected Carrier Years of Life Lost	Expected Carrier Years Lost (95% CI)	Total Number of Carrier Years Lost	Total Number of Carrier Years Lost (95% CI)
50	580173	3.34	19378	1.88	.64, 3.12	36430	12321, 60540
51	528030	3.46	18270	2.03	.79, 3.27	37088	14428, 59747
52	537207	3.33	17889	2.22	.98, 3.46	39714	17578, 61849
53	537831	3.47	18663	2.37	1.13, 3.61	44231	21174, 67287
54	548848	3.53	19374	2.33	1.13, 3.53	45142	21937, 68348
55	537323	3.42	18376	2.08	.97, 3.19	38223	17872, 58574
56	537461	3.34	17951	1.86	.84, 2.88	33389	15010, 51768
57	537976	3.34	17968	1.80	.82, 2.78	32343	14725, 49961
58	537529	3.40	18276	1.91	.94, 2.88	34907	17213, 52601
59	535193	3.38	18090	1.93	.99, 2.87	34913	17841, 51985
60	552619	3.45	19065	1.96	1.04, 2.88	37368	19745, 54991
61	522514	3.40	17765	2.11	1.19, 3.03	37485	21173, 53797
62	514206	3.36	17277	2.12	1.22, 3.02	36628	21109, 52147
63	490646	3.34	16388	2.22	1.33, 3.11	36380	21863, 50898
64	481196	3.40	16361	2.24	1.37, 3.11	36648	22412, 50884
65	446094	3.38	15078	2.40	1.54, 3.26	36187	23160, 49214
66	414634	3.34	13849	2.31	1.46, 3.16	31991	20243, 43738
67	389828	3.31	12903	2.40	1.56, 3.24	30968	20152, 41784
68	374097	3.22	12046	2.24	1.42, 3.06	26983	17092, 36873
69	353244	3.24	11445	2.41	1.59, 3.23	27583	18234, 36931
70	341567	3.31	11306	2.51	1.70, 3.32	28378	19213, 37543
71	309155	3.27	10109	2.44	1.64, 3.24	24667	16568, 32765
72	276004	3.35	9246	2.58	1.78, 3.38	23855	16483, 31227
73	244443	3.23	7896	2.48	1.69, 3.27	19581	13316, 25846

Age	Estimated Number of US Black Individuals Alive at this Age*	Estimated Carrier Percentage**	Estimated Number of US Black Carriers	Expected Carrier Years of Life Lost	Expected Carrier Years Lost (95% CI)	Total Number of Carrier Years Lost	Total Number of Carrier Years Lost (95% CI)
74	224601	3.21	7210	2.53	1.74, 3.32	18241	12547, 23934
75	206468	3.14	6483	2.38	1.59, 3.17	15430	10323, 20537
76	188913	3.11	5875	2.39	1.60, 3.18	14042	9425, 18659
77	169655	3.19	5412	2.56	1.77, 3.35	13855	9589, 18120
78	162007	3.14	5087	2.57	1.78, 3.36	13074	9045, 17103
79	141921	3.19	4527	2.67	1.87, 3.47	12088	8474, 15701
80	131531	3.04	3999	2.77	1.96, 3.58	11076	7852, 14300
81	118382	3.11	3682	2.78	1.96, 3.60	10235	7216, 13254
82	109414	2.97	3250	2.74	1.90, 3.58	8904	6162, 11646
83	96804	2.84	2749	2.52	1.64, 3.40	6928	4511, 9345
84	88080	2.64	2325	2.31	1.39, 3.23	5371	3241, 7502
85	81191	2.48	2014	2.15	1.19, 3.11	4329	2405, 6253
86	72280	2.37	1713	2.34	1.36, 3.32	4009	2327, 5690
87	61961	2.26	1400	2.13	1.09, 3.17	2983	1520, 4445
88	56278	2.02	1137	1.71	.58, 2.84	1944	661, 3226
89	42401	1.95	827	1.84	.67, 3.01	1521	552, 2491
90	28787	1.94	558	1.88	.64, 3.12	1050	356, 1744
91	11899	1.65	196	1.49	.09, 2.89	293	18, 567
92	33221	1.41	468	0.42	-1.12, 1.96	197	-524, 918
93	32763	1.47	482	0.25	-1.30, 1.80	120	-626, 866
94	65137	1.47	958	0.47	-1.05, 1.99	450	-1008, 1908
95	33307	1.59	530	0.54	-.86, 1.94	286	-456, 1028
Total	**13284819**		**435851**			**957505**	**534475, 1380535**

*Obtained from the United States Census Bureau's 2022 American Community Survey (5-year)
**Obtained from the current analysis

eTable 5. Estimated Survival Time Comparing Carriers and Noncarriers by Age for Heart Failure Hospitalization or Death

Age	Expected Carrier Years of Life Lost	Expected Carrier Years Lost (95% CI)
50	1.85	.58, 3.12
51	2.01	.74, 3.28
52	2.22	.96, 3.48
53	2.49	1.23, 3.75
54	2.52	1.29, 3.75
55	2.20	1.07, 3.33
56	2.08	1.02, 3.14
57	1.87	.88, 2.86
58	1.97	1.00, 2.94
59	2.04	1.09, 2.99
60	2.20	1.26, 3.14
61	2.39	1.46, 3.32
62	2.38	1.47, 3.29
63	2.56	1.66, 3.46
64	2.61	1.73, 3.49
65	2.74	1.86, 3.62
66	2.74	1.88, 3.60
67	2.83	1.97, 3.69
68	2.78	1.94, 3.62
69	2.79	1.95, 3.63
70	2.83	2.00, 3.66
71	2.81	1.98, 3.64
72	2.87	2.04, 3.70
73	2.67	1.85, 3.49
74	2.63	1.81, 3.45
75	2.66	1.84, 3.48
76	2.61	1.78, 3.44
77	2.70	1.87, 3.53
78	2.67	1.83, 3.51
79	2.76	1.91, 3.61
80	2.85	1.98, 3.72
81	2.86	1.97, 3.75
82	2.68	1.75, 3.61
83	2.45	1.47, 3.43
84	2.32	1.29, 3.35
85	2.25	1.17, 3.33
86	2.30	1.17, 3.43
87	1.94	.70, 3.18
88	1.34	-.04, 2.72
89	1.42	-.02, 2.86

Age	Expected Carrier Years of Life Lost	Expected Carrier Years Lost (95% CI)
90	1.58	.06, 3.10
91	0.76	-1.00, 2.52
92	-0.28	-2.05, 1.49
93	-0.02	-1.76, 1.72
94	-0.59	-1.86, .68
95	-0.02	-1.30, 1.26

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