Supplementary Online Content

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

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eMethods. Illumina Global Screening Array Genotyping and Quality Control

Bead studio files were converted to PLINK format by Genome Studio v2.0 (Illumina, Inc., San Diego, CA) and mapped to the GRCh37 reference genome. Both datasets were quality checked to retain high-quality samples and variants in the datasets. The QC steps were performed using PLINK v1.9. We applied quality control thresholds of 95 % for marker call rate and 90% for sample call rates. We also removed any samples with sex errors. Next, we merged these two datasets to identify any related samples. PLINK IBD check was performed on LD pruned merged data. We applied a graph-based algorithm on all pairs of samples with Pi-hat>0.1875 to generate a dataset of unrelated individuals. The most connected sample in the graph was removed in order to retain more samples.

Principal component analyses using smartpca module of Eigensoft package was performed on the merged dataset of unrelated individuals. PCA was performed by merging 1000 Genomes data with our data in order to project eigenvectors on 1000 Genomes dataset. Next, we performed quadratic discriminant analyses (QDA) to label samples by their genetically informed ancestry. For QDA, 1000 genomes super-population labels were used as training set to identify labels for PMBB dataset. PMBB GSA merged dataset consist of 45% AFR and 47% EUR samples. The table below shows the percent of samples for each label of genetically informed ancestry:

GIA	Percent
AFR	45.1
AMR	4.3
EAS	0.3
EUR	46.9
Other	3.0
SAS	0.3

eTable 1. List of CPT (Current Procedural Terminology), Diagnosis and Procedure Codes to Identify Evaluation for Hereditary Transthyretin (TTR) Amyloid Cardiomyopathy (hATTR-CM) and Diagnosis of Amyloid.

Diagnosis	*ICD*/CPT Code	Definition
Amyloidosis	E85; E85.0; E85.1, E85.2; E85.3; E85.4; E85.8; E85.81; E85.82; E85.89; E85.9	Amyloidosis; Non-neuropathic heredofamilial amyloidosis; Neuropathic heredofamilial amyloidosis; Heredofamilial amyloidosis, unspecified; Secondary systemic amyloidosis; Organ-limited amyloidosis; Other amyloidosis; Light chain (AL) amyloidosis; Wild-type transthyretin-related (ATTR) amyloidosis; Other amyloidosis; Amyloidosis, unspecified
Fat Pad Biopsy	10021; 11101	Fine needle aspiration surgical procedures; Biopsy procedures on the skin
Technetium 99m pyrophosphate cardiac imaging	78803; 78800	Technetium 99m pyrophosphate cardiac imaging

eTable 2. Carrier Rates of *TTR* V122I by Ancestry Group.

	PMBB	
Ancestry group	**Total participants**	***TTR* Val122Ile carriers**
African	5,737	190 (3.3%)
	Bio*Me*	
Ancestry group	**Total participants**	***TTR* Val122Ile carriers**
African	6,609	211 (3.2%)
Hispanic / Latino	9,006	114 (1.31%)
European	8,710	4 (0.05%)
Other	2,747	7 (0.25%)

eTable 3. Carrier Counts and Rates of *TTR* V122I by 154 Countries/Regions of Origin.

Continent	Country	Total Individuals	Rare Variant Carriers	Carrier Rate
Africa				
	Gambia	5	2	40%
	West Africa	10	1	10%
	Ghana	42	4	9.5%
	Nigeria	31	3	9.7%
	Ivory Coast	25	2	8.0%
	Africa	18	1	5.6%
	Guinea	20	1	5.0%
	Senegal	46	2	4.3%
	Liberia	11	0	0
	South Africa	18	0	0
	Mali	9	0	0
	Egypt	68	0	0
	Zimbabwe	5	0	0
	Sierra Leone	12	0	0
	Kenya	9	0	0
	Morocco	20	0	0
	Ethiopia	8	0	0
	Cameroon	6	0	0
	Botswana	1	0	0
	Sudan	3	0	0
	Mauritania	1	0	0
	Togo	3	0	0
	Angola	1	0	0
	Jordan	5	0	0
	Uganda	4	0	0
	Burkina Faso	1	0	0
	Zambia	1	0	0
	Algeria	1	0	0
	Libya	2	0	0
	Tunisia	2	0	0
Central America				
	St. Maarten	3	1	33%
	St. Croix	3	1	33%
	Bahamas	11	2	18%
	Belize	39	3	7.7%
	Honduras	128	9	7.0%
	St. Lucia	16	1	6.2%

Continent	Country	Total Individuals	Rare Variant Carriers	Carrier Rate
	Virgin Islands (U.S. or British)	17	1	5.9%
	St. Thomas	24	1	4.2%
	Costa Rica	25	1	4.0%
	Panama	64	2	3.1%
	Jamaica	324	4	2.5%
	Dominican Republic	1,678	34	2.0%
	Trinidad & Tobago	183	4	2.2%
	El Salvador	60	1	1.7%
	Haiti	128	2	1.6%
	Puerto Rico	2,296	30	1.3%
	Cuba	142	2	1.4%
	Anguilla	1	0	0
	Guatemala	66	0	0
	St. Kitts & Nevis	14	0	0
	Antigua & Barbuda	32	0	0
	Dominica	6	0	0
	Grenada	28	0	0
	Nicaragua	24	0	0
	Aruba	2	0	0
	St. Vincent & the Grenadines	20	0	0
	West Indies	8	0	0
	Curacao	3	0	0
	Montserrat	5	0	0
	Barbados	72	0	0
North America				
	USA	17,099	212	1.2%
	African Ancestry (AA)	5,314	168	3.2%
	Hispanic/Latino Ancestry (HA)	3,313	33	1.0%
	European Ancestry (EA)	7,340	4	0.054%
	East & Southeast Asian Ancestry (ESA)	183	0	0
	Native American Ancestry (NA)	73	1	1.4%
	*Other Ancestry (OA)**	786	6	0.76%
	Mexico	287	1	0.35%
	Canada	91	0	0
	Bermuda	6	0	0
	Iceland	7	0	0

Continent	Country	Total Individuals	Rare Variant Carriers	Carrier Rate
South America				
	Venezuela	47	1	2.1%
	Guyana	244	1	0.41%
	Ecuador	378	1	0.26%
	Argentina	58	0	0
	Peru	109	0	0
	Brazil	102	0	0
	Colombia	224	0	0
	Chile	35	0	0
	South America	2	0	0
	Bolivia	14	0	0
	Paraguay	3	0	0
	Uruguay	9	0	0
Europe				
	Czech Republic	24	0	0
	Italy	142	0	0
	Spain	50	0	0
	Romania	41	0	0
	Hungary	28	0	0
	Ireland	58	0	0
	Kosovo	2	0	0
	France	54	0	0
	Scotland	12	0	0
	Estonia	4	0	0
	Greece	64	0	0
	Austria	13	0	0
	Sweden	12	0	0
	Belgium	12	0	0
	United Kingdom	111	0	0
	Moldova	14	0	0
	Portugal	18	0	0
	Germany	111	0	0
	Poland	97	0	0
	Ukraine	79	0	0
	Finland	3	0	0
	Croatia	15	0	0
	Netherlands	15	0	0
	Malta	5	0	0
	Latvia	9	0	0
	Montenegro	3	0	0
	Belarus	10	0	0
	Slovenia	6	0	0

Continent	Country	Total Individuals	Rare Variant Carriers	Carrier Rate
	Bulgaria	13	0	0
	Albania	16	0	0
	Bosnia & Herzegovina	4	0	0
	Macedonia	2	0	0
	Scandinavia	1	0	0
	Serbia	6	0	0
	Switzerland	13	0	0
	Armenia	3	0	0
	Denmark	4	0	0
	Norway	3	0	0
	Lithuania	1	0	0
	Yugoslavia	8	0	0
Middle East				
	Israel	89	0	0
	Saudi Arabia	5	0	0
	Yemen	18	0	0
	Iran	34	0	0
	Lebanon	17	0	0
	Syria	9	0	0
	Iraq	5	0	0
	United Arab Emirates	2	0	0
	Bahrain	1	0	0
Asia				
	Philippines	213	0	0
	Uzbekistan	13	0	0
	Taiwan	26	0	0
	Pakistan	76	0	0
	Russia	155	0	0
	China	173	0	0
	India	215	0	0
	Korea	66	0	0
	Sri Lanka	8	0	0
	Bangladesh	153	0	0
	Nepal	12	0	0
	Turkey	28	0	0
	Hong Kong	24	0	0
	Indonesia	5	0	0
	Cambodia	4	0	0
	Japan	82	0	0
	Cyprus	5	0	0
	Malaysia	8	0	0

Continent	Country	Total Individuals	Rare Variant Carriers	Carrier Rate
	Vietnam	12	0	0
	Thailand	12	0	0
	Georgia	3	0	0
	Laos	1	0	0
	Afghanistan	7	0	0
	Burma	1	0	0
	Singapore	4	0	0
	Tibet	2	0	0
Australia				
	Australia	23	0	0
	New Zealand	5	0	0
Unknown				
	Unknown	35	0	0

Participants with self-report country/region of origin from United States of America (USA) were categorized into six additional self-report ancestry groups of African Ancestry (AA), Hispanic/Latino Ancestry (HA), European Ancestry (EA), East & Southeast Asian Ancestry (ESA), Native American Ancestry (NA) and Other Ancestry (OA)*. The OA is miscellaneous ancestry.

eTable 4. Sex-Stratified Analysis of Prevalent Heart Failure or Cardiomyopathy in PMBB.

		Male				Female				Interaction		
Model	**Covariates**	**OR**	**95%CI**	**p-value**		**OR**	**95%CI**	**p-value**		**ROR**	**95%CI**	**p-value**
1	V122I variant carrier status + age + PC1-5	2.7	1.6, 4.5	<0.001		0.92	0.46, 1.9	0.81		2.9	1.2, 7.0	0.02
2	Model 1 + hypertension	2.5	1.4, 4.3	0.001		0.90	0.44, 1.8	0.76		2.8	1.1, 6.8	0.03
3	Model 2 + MI/coronary revascularization	2.5	1.4, 4.5	0.002		0.85	0.41, 1.8	0.66		3.0	1.2, 7.5	0.02

PC – principal component; MI – myocardial infarction; OR – odds ratio; CI – confidence interval; ROR – relative odds ratio

eTable 5. Age-Stratified Analysis of Prevalent Heart Failure or Cardiomyopathy Among Male Participants in PMBB.

						Interaction*		
Age Category	**n**	**OR**	**95%CI**	**P-value**		**OR**	**95%CI**	**P-value**
50 to <60 years old	575	1.6	0.63, 3.9	0.33		*ref*	*ref*	*ref*
60 to < 70 years old	659	3.4	1.3, 9.5	0.02		2.2	0.57, 8.7	0.25
≥ 70 years old	521	3.1	1.2, 8.3	0.02		2.0	0.52, 7.6	0.31

*Compared to youngest age category.
n – sample size; OR – odds ratio; CI – confidence interval;
ref – reference category

eTable 6. Clinically Obtained Echocardiographic Characteristics of Participants by *TTR* V122I Carrier Status in PMBB.

Characteristic	Non-Carriers	Carriers	P-value	Adjusted β-coefficient *	Adjusted P-value*
Participants with echocardiogram– no.	1562	56	—	—	—
Number of Echocardiograms – median	2 (1, 4)	2 (1, 3)	0.55	—	—
LV ejection fraction					
No. patients with data	1562 (100%)	56 (100%)	1		
Median (IQR)	60 (45, 65)	55 (39, 65)	0.04	-0.04 (-0.16, 0.08)	0.5
Left atrial volume index — mL/m^2					
No. patients with data	838 (52%)	31 (55%)	0.89		
Median (IQR)	32 (24, 42)	28 (23, 45)	0.24	0.14 (-0.02, 0.29)	0.08
Interventricular septum diastolic thickness – mm					
No. patients with data	1490 (95.3%)	55 (98.2%)	0.51		
Median (IQR)	11 (10, 13)	12 (11, 14)	0.01	0.08 (0.03, 0.14)	0.02
LV posterior wall diastolic thickness – mm					
No. patients with data	1488 (95.2%)	55 (98.2%)	0.51		
Median (IQR)	11 (10, 12)	12 (11, 14)	0.002	0.1 (0.05, 0.14)	<0.001
LV end diastolic diameter – mm					
No. patients with data	1425 (92.2%)	51 (91.1%)	1		
Median (IQR)	46 (41, 52)	46 (41, 52)	0.70	-0.01 (-0.06, 0.04)	0.62
Relative wall thickness					
No. patients with data	1420 (90.9%)	51 (91.1%)	1		
Median (IQR)	0.48 (0.40, 0.56)	0.49 (0.43, 0.63)	0.09	0.04 (0.01, 0.06)	0.003
LV Mass – g					
No. patients with data	1419 (90.8%)	51 (91.1%)	1		
Median (IQR)	189 (147, 242)	206 (165, 292)	0.02	0.11 (0.01, 0.20)	0.03

LV – left ventricular; IQR: interquartile range

* Age, sex, and principal components (PC) 1-5 adjusted effect estimate (95% confidence interval), and p-value for the effect of *TTR* V122I carrier status on natural log transformed echo parameter

eTable 7. Association of *TTR* V122I Carrier Status With Clinically Obtained Transthoracic Echocardiographic Parameters in PMBB.

Characteristic	Adjusted β-coefficient	Std. Error	P-value
LVEF			
Model 0	-0.069	0.062	0.26
Model 1	-0.044	0.061	0.46
Model 2	-0.046	0.061	0.45
Model 3	-0.032	0.061	0.60
Left atrial volume index			
Model 0	0.129	0.078	0.10
Model 1	0.135	0.077	0.08
Model 2	0.129	0.076	0.09
Model 3	0.119	0.077	0.12
Interventricular septum diastolic thickness			
Model 0	0.092	0.027	<0.001
Model 1	0.084	0.027	0.002
Model 2	0.078	0.027	0.003
Model 3	0.077	0.027	0.004
LV posterior wall diastolic thickness			
Model 0	0.103	0.024	<0.001
Model 1	0.095	0.024	<0.001
Model 2	0.089	0.024	<0.001
Model 3	0.088	0.024	<0.001
LV end diastolic diameter			
Model 0	0.005	0.026	0.86
Model 1	-0.012	0.024	0.62
Model 2	-0.014	0.024	0.57
Model 3	-0.017	0.024	0.48
Log Relative wall thickness			
Model 0	0.036	0.013	0.006
Model 1	0.038	0.013	0.003
Model 2	0.037	0.013	0.004
Model 3	0.038	0.013	0.003
LV mass			
Model 0	0.143	0.053	0.007
Model 1	0.106	0.049	0.03
Model 2	0.094	0.048	0.05
Model 3	0.089	0.048	0.06

Model 0: *TTR* V122I carrier status
Model 1: *TTR* V122I carrier status + principal component (PC) 1-5 + age + sex
Model 2: Model 1 + hypertension
Model 3: Model 2 + myocardial infarction or revascularization
Effect estimates and standard errors are presented on the *ln(x+1)* scale. LV – left ventricular; LVEF – left ventricular (LV) ejection fraction

eTable 8. Clinically Obtained Echocardiographic Characteristics of Participants With Heart Failure or Cardiomyopathy by *TTR* V122I Carrier Status in PMBB.

Characteristic	Non-Carriers	Carriers	P-value
Participants with echocardiogram– no.	785	39	
Number of Echocardiograms – median	3 (2,6)	2 (1,4)	0.01
LV ejection fraction			
No. patients with data	785 (100%)	39 (100%)	1
Median — percent	50 (35, 35)	50 (35, 53)	0.89
Left atrial volume index			
No. patients with data	482 (61%)	21 (54%)	0.40
Median — mL/m^2	36 (28, 48)	38 (28, 55)	0.86
Interventricular septum diastolic thickness			
No. patients with data	759 (96.7%)	38 (97.4%)	1
Median — mm	11 (10, 13)	12 (11, 15)	0.009
LV posterior wall diastolic thickness			
No. patients with data	758 (96.7%)	38 (97.4%)	1
Median — mm	11 (10, 13)	12 (11, 14)	0.003
LV end diastolic diameter – mm			
No. patients with data	728 (92.7%)	35 (89%)	0.52
Median — mm	49 (43, 56)	48 (43, 54)	0.33
Relative wall thickness			
No. patients with data	725 (92.3%)	35 (90%)	1
Median — mm	0.45 (0.37, 0.55)	0.51 (0.39, 0.65)	0.03
LV Mass			
No. patients with data	725 (92.3%)	35 (90%)	1
Median — g	213 (169, 273)	231 (179, 302)	0.09

LV – left ventricular

eTable 9. Association of *TTR* V122I Carrier Status With Clinically Obtained Transthoracic Echocardiographic Parameters in Participants With Heart Failure or Cardiomyopathy in PMBB.

Characteristic	Adjusted β-coefficient	Std. Error	P-value
LVEF			
Model 0	0.015	0.084	0.86
Model 1	0.074	0.082	0.37
Model 2	0.068	0.082	0.40
Model 3	0.072	0.082	0.38
Left atrial volume index			
Model 0	0.063	0.090	0.48
Model 1	0.060	0.091	0.51
Model 2	0.069	0.091	0.45
Model 3	0.058	0.091	0.52
Interventricular septum diastolic thickness			
Model 0	0.115	0.034	0.001
Model 1	0.105	0.034	0.002
Model 2	0.101	0.034	0.003
Model 3	0.102	0.034	0.003
LV posterior wall diastolic thickness			
Model 0	0.122	0.029	<0.001
Model 1	0.114	0.030	<0.001
Model 2	0.111	0.029	<0.001
Model 3	0.110	0.029	<0.001
LV end diastolic diameter			
Model 0	-0.035	0.033	0.30
Model 1	-0.071	0.031	0.02
Model 2	-0.071	0.031	0.02
Model 3	-0.072	0.031	0.02
Log Relative wall thickness			
Model 0	0.058	0.016	<0.001
Model 1	0.067	0.016	<0.001
Model 2	0.066	0.016	<0.001
Model 3	0.067	0.016	<0.001
LV mass			
Model 0	0.117	0.063	0.06
Model 1	0.040	0.058	0.49
Model 2	0.038	0.057	0.51
Model 3	0.037	0.058	0.52

Model 0: *TTR* V122I carrier status
Model 1: *TTR* V122I carrier status + principal component (PC) 1-5 + age + sex
Model 2: Model 1 + hypertension
Model 3: Model 2 + myocardial infarction or revascularization
Effect estimates and standard errors are presented on the *ln(x+1)* scale. LV – left ventricular; LVEF – left ventricular (LV) ejection fraction

eTable 10. Number and Percentage of Participants With Left Ventricular Hypertrophy Among Bio*Me* Participants (Self-Reported African and Hispanic/Latino Ancestries) Without Heart Failure (total N=4,094).

Echo	Type	N (%)
Left ventricular hypertrophy	concentric hypertrophy	809 (20)
	localized hypertrophy	236 (5.8)
	not assessed	2,768 (68)
	not present	281 (6.9)

eTable 11. Genetic Association of *TTR* V122I on Left Ventricular (LV) Hypertrophy Among Individuals Without Heart Failure in Bio*Me*.

Age Group	Cohort	Beta	SE	*P*-value	OR	95% Upper CI	95% Lower CI	Non-Carrier No LVH	Carrier No LVH	Non-Carrier LVH	Carrier LVH
>65											
	AA	0.2	0.43	0.64	1.2	0.52	2.8	430	13	266	11
	HA	-0.32	0.67	0.64	0.73	0.16	2.4	806	10	317	3
	Meta	0.049	0.36	0.89	1.1	0.52	2.1	1,236	23	583	14
>45 & ≤65											
	AA	0.19	0.5	0.7	1.2	0.43	3.1	574	13	222	7
	HA	-0.28	1.1	0.8	0.76	0.039	4.6	762	7	174	1
	Meta	0.11	0.45	0.8	1.1	0.46	2.7	1,336	20	396	8
≤45											
	AA	2.7	0.85	1.4×10^{-3}	15	3	93	189	3	18	5
	HA*	0.18	2	1	1.2	0.0033	28	240	2	21	0
	Meta	2.3	0.78	2.9×10^{-3}	10	2.2	47	429	5	39	5

*Firth Logistic Regression; LVH – left ventricular hypertrophy; SE – standard error; OR – odds ratio; CI – confidence interval; AA – African Ancestry; HA – Hispanic/Latino Ancestry; Meta – meta-analysis

eTable 12. Genetic Association of *TTR* V122I With Diastolic Intraventricular Septal Thickness Among Individuals Without Heart Failure in Bio*Me*.

Age Group	Cohort	Beta	SE	*P*-value	95% Lower CI	95% Upper CI	N
>65							
	AA	-0.0036	0.039	0.9	-0.08	0.072	715
	HA	-0.033	0.046	0.5	-0.12	0.057	1,120
	Meta	-0.016	0.03	0.6	-0.074	0.042	1,835
45< & ≤65							
	AA	0.0087	0.039	0.8	-0.068	0.086	814
	HA	-0.0021	0.058	1.0	-0.12	0.11	927
	Meta	0.0053	0.033	0.9	-0.058	0.069	1,741
≤45							
	AA	0.17	0.063	0.008	0.044	0.29	214
	HA	-0.022	0.12	0.9	-0.25	0.21	262
	Meta	0.12	0.056	0.02	0.016	0.23	476

SE – standard error; CI – Confidence Interval; N – sample size; AA –African Ancestry, HA – Hispanic/Latino Ancestry; Meta – meta-analysis

eTable 13. Genetic Association of *TTR* V122I With Additional Echocardiographic Parameters Among Individuals Without Heart Failure in Bio*Me*.

Characteristic		Non-Carriers	Carriers	P-value	Adjusted β-coefficient*	Adjusted P*
LV ejection fraction						
>65	No. patients with data	1770 (97%)	37 (100%)	0.63		
	Median (IQR)	62 (58 , 66)	60 (57 , 65)	0.53	1.8×10^{-5} (-0.066, 0.066)	1
>45 & <=65	No. patients with data	1707 (98%)	29 (100%)	1		
	Median (IQR)	62 (57, 65)	61 (55 , 64)	0.39	3.6×10^{-3} (-0.060, 0.068)	0.9
<=45	No. patients with data	459 (97%)	10 (100%)	0.94		
	Median (IQR)	61 (57, 65)	66 (64 , 69)	0.0023	0.11 (0.002, 0.210)	0.05
Left atrial volume index — mL/m²						
>65	No. patients with data	797 (44%)	18 (49%)	0.65		
	Median (IQR)	25 (17, 32)	23 (17, 32)	0.55	-0.083 (-0.30, 0.14)	0.5
>45 & <=65	No. patients with data	832 (48%)	16 (55%)	0.53		
	Median (IQR)	24 (18, 31)	22 (15, 28)	0.18	-0.11 (-0.34, 0.11)	0.3
<=45	No. patients with data	218 (46%)	4 (40%)	1		
	Median (IQR)	24 (19, 30)	26 (25, 26)	0.8	0.0081 (-0.005, 0.02)	0.2
Interventricular septum diastolic thickness – mm						
>65	No. patients with data	1799 (98%)	36 (97%)	0.47		
	Median (IQR)	11 (10, 12)	11 (9.5, 12)	0.95	-0.016 (-0.074, 0.042)	0.6
>45 & <=65	No. patients with data	1713 (98%)	28 (97%)	0.45		
	Median (IQR)	10 (9, 12)	11 (9.8, 12)	0.42	0.0053 (-0.058, 0.069)	0.9
<=45	No. patients with data	466 (99%)	10 (100%)	0.98		
	Median (IQR)	9 (8, 10)	11 (10, 12)	0.002	0.12 (0.016, 0.23)	0.02
Characteristic		**Non-Carriers**	**Carriers**	**P-value**	**Adjusted β-coefficient***	**P***
LV posterior wall diastolic thickness – mm						
>65	No. patients with data	1796 (98%)	36 (97%)	0.5		
	Median (IQR)	10 (9, 11)	10 (9, 12)	0.67	-9.8×10^{-4} (-0.0580, 0.056)	1
>45 & <=65	No. patients with data	1710 (98%)	28 (97%)	0.48		
	Median (IQR)	10 (9, 11)	10 (9, 11)	0.29	8.6×10^{-5} (-0.06, 0.06)	1
<=45	No. patients with data	466 (99%)	10 (100%)	0.98		
	Median (IQR)	9 (8, 10)	11 (10, 11)	0.002	0.12 (0.008, 0.2)	0.04

LV end diastolic diameter – mm						
>65	No. patients with data	1804 (99%)	36 (97%)	0.41		
	Median (IQR)	43 (40, 47)	43 (40, 46)	0.94	0.003 (-0.042, 0.048)	0.9
>45 & <=65	No. patients with data	1721 (98%)	29 (100%)	1		
	Median (IQR)	44 (41, 48)	44 (42, 46)	0.44	-0.022 (-0.066, 0.023)	0.3
<=45	No. patients with data	466 (99%)	10 (100%)	0.98		
	Median (IQR)	45 (42, 49)	44 (41, 46)	0.87	-0.0011 (-0.069, 0.067)	1
LV Mass – g						
>65	No. patients with data	1663 (91%)	32 (86%)	0.38		
	Median (IQR)	150 (110, 180)	150 (120, 180)	0.74	0.022 (-0.11, 0.15)	0.7
>45 & <=65	No. patients with data	1650 (94%)	26 (90%)	0.23		
	Median (IQR)	150 (120, 180)	150 (130, 170)	0.73	-0.035 (-0.16, 0.091)	0.6
<=45	No. patients with data	462 (98%)	8 (80%)	0.75		
	Median (IQR)	140 (110, 170)	170 (150, 210)	0.033	0.20 (-0.016, 0.42)	0.07

LV – left ventricular; IQR – interquartile range

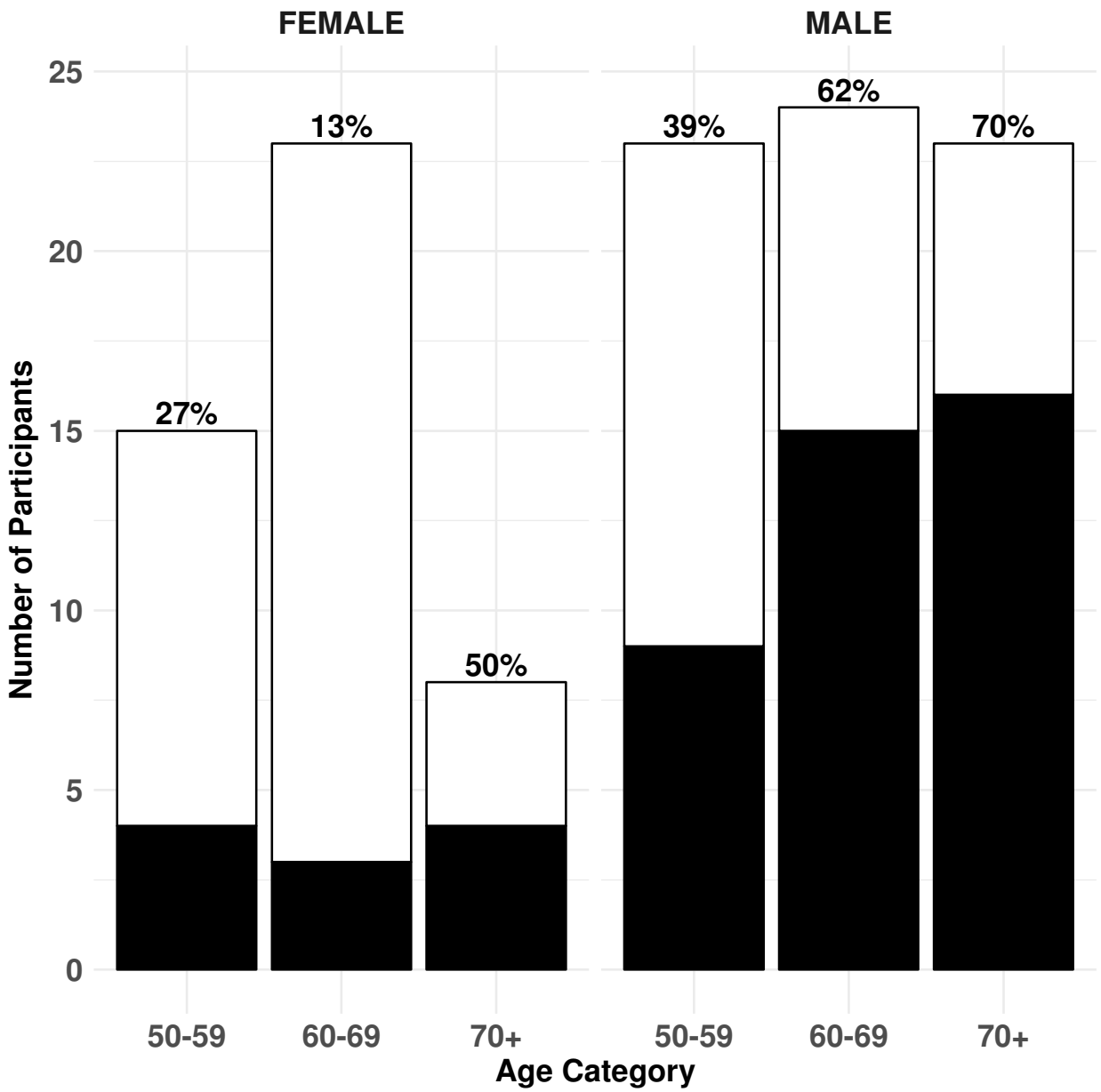
* Age, sex, and principal components (PC) 1-10 adjusted effect estimate (95% confidence interval), and p-value for the effect of *TTR* V122I carrier status on natural log transformed echo parameter

eTable 14. Characteristics of *TTR* V122I Carriers With Heart Failure That Underwent Detailed Chart Review.

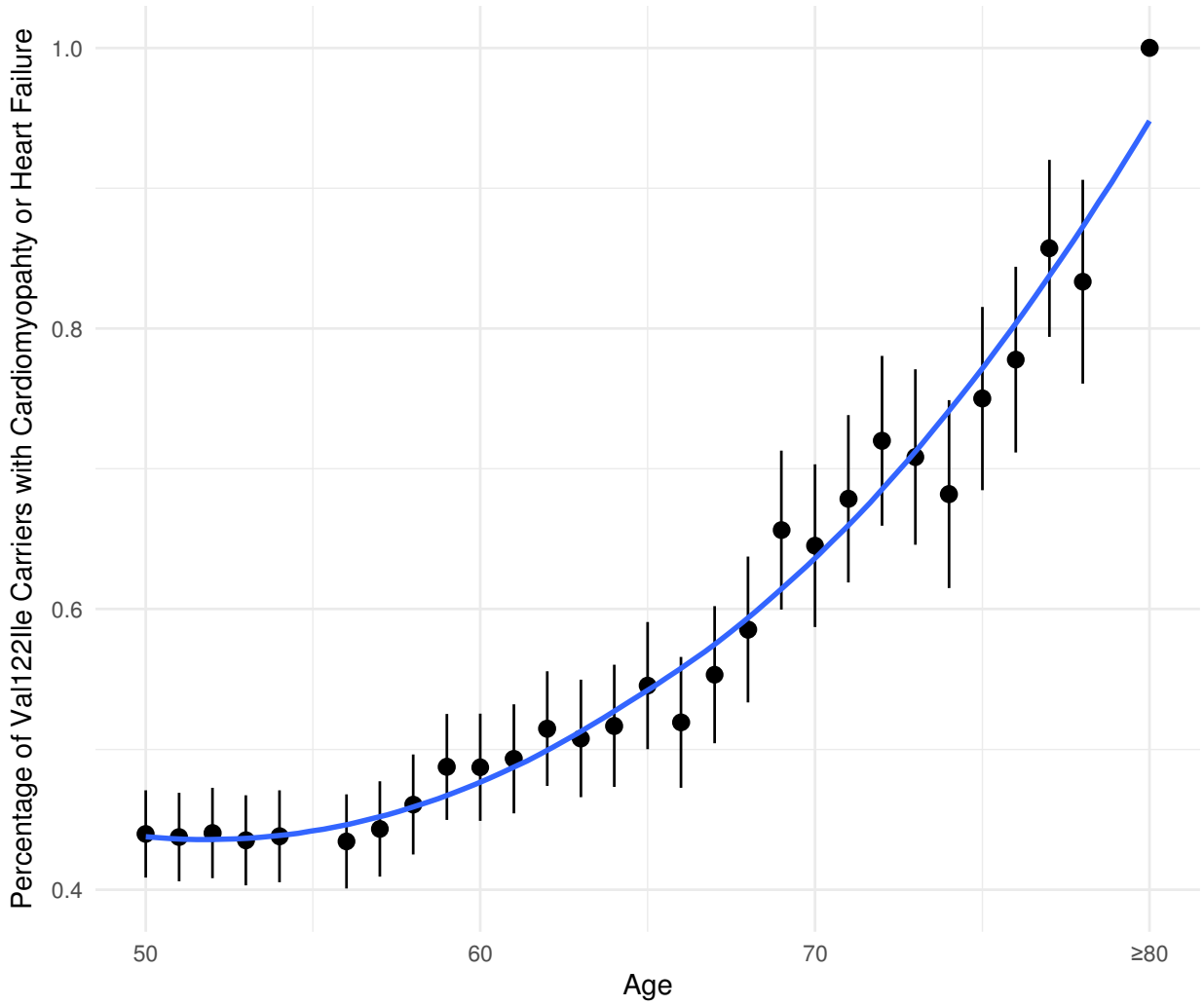
	***TTR* V122I Carriers with Heart Failure**	
	PMBB	**Bio*Me***
Total — no.	53	39
Male — no. (%)	40 (75%)	16 (41)
Age — yrs; median (IQR)	67 (59, 76)	71 (62, 81)
BMI — kg/m^2; median (IQR)	27 (24, 32)	30 (25.2, 34)
Hypertension — no. (%)	46 (86%)	33 (85%)
Diabetes — no. (%)	26 (49%)	29 (74%)
Arrhythmias — no. (%)		
Atrial fibrillation	22 (42%)	12 (31%)
Ventricular tachycardia	7 (13%)	6 (15%)
EKG abnormalities — no. (%)		
Low voltage	7 (13%)	9 (23%)
Conduction delays/block*	9 (17%)	10 (26%)
Pacemaker or ICD — no. (%)	19 (36%)	11 (28%)
LV ejection fraction — %; median (IQR)	40 (30, 60)	60 (44, 62)
RV systolic dysfunction		
Mild	10 (18%)	8 (21%)
Moderate	7 (13%)	6 (15%)
Severe	5 (9.4%)	2 (5%)
Diastolic dysfunction — no. (%)		
Mild	16 (30%)	4 (10%)
Moderate	5 (9.4%)	10 (26%)
Severe	5 (9.5%)	2 (5%)
IVSd — mm; median (IQR)	12 (10, 16)	12 (10, 12)
LVPWd – mm; median (IQR)	11 (10, 14)	11 (10, 12)
Ischemic cardiomyopathy — no. (%)	19 (36%)	6 (15%)
Carpal tunnel syndrome — no. (%)	7 (13%)	6 (15%)
Neuropathy — no. (%)	16 (31%)	8 (21%)
Diagnosed Amyloid — no. (%)	9 (17%)	1 (2.6%)

* Right bundle branch block, 1st degree atrioventricular block, hemiblock, non-specific interventricular block

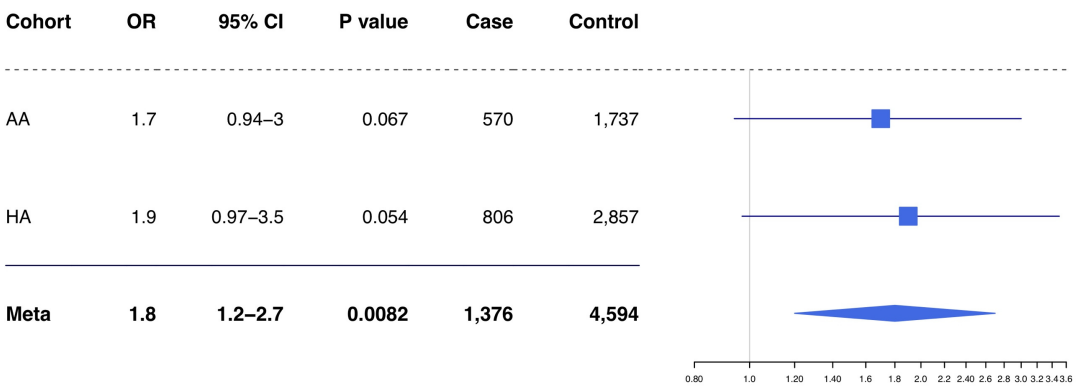
IQR – interquartile range; BMI – body mass index; EKG – Electrocardiogram; LV – Left Ventricular; RV – Right Ventricular; IVSd – Interventricular septum diastolic thickness; LVPWd – LV posterior wall diastolic thickness



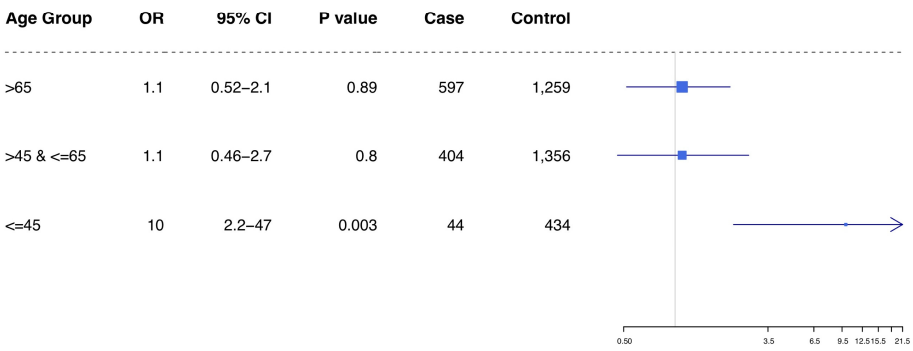
eFigure 1. Prevalence of Clinically Diagnosed Heart Failure or Cardiomyopathy by Age and Sex in *TTR* V122I Carriers in PMBB.



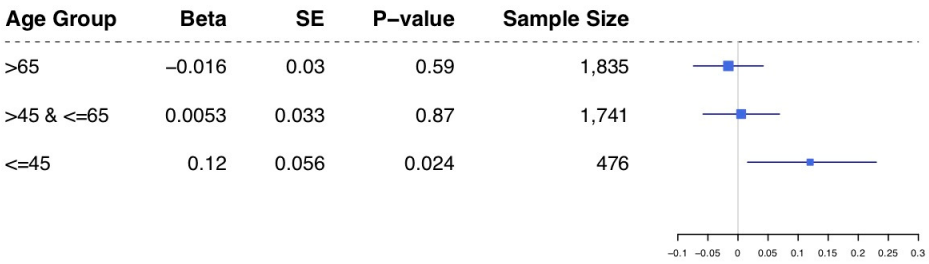
eFigure 2. Cumulative Prevalence of Clinically Diagnosed Heart Failure or Cardiomyopathy by Age in *TTR* V122I Carriers in PMBB. Each point represents the crude cumulative prevalence of cardiomyopathy or heart failure among *TTR* Val122Ile variant carriers of that age or older in the PMBB cohort. Error bars represent 95% confidence intervals for the crude cumulative prevalence. The blue line represents the loess regression line with associated 95% confidence interval of the regression in grey.



eFigure 3. Ancestry-Specific Association of *TTR* V122I Carrier Status With Prevalent Heart Failure in Bio*Me.* Age-, sex- and genetic principal component-adjusted OR were calculated using logistic regression separately in African ancestry (AA) and Hispanic/Latino ancestry (HA) and combined using inverse variance weighted meta-analysis. The range in the panel on the right represents the 95% confidence intervals around the point estimates; OR – odds ratio; CI – confidence interval.



eFigure 4. Genetic Association Results of Transthyretin (*TTR)* V122I on Left Ventricular Hypertrophy Among Bio*Me* Participants Without Heart Failure. OR – odds ratio; CI – confidence interval.



eFigure 5. Genetic Association Results of Transthyretin (*TTR)* V122I on Diastolic Intraventricular Septal Thickness Among Bio*Me* Participants Without Heart Failure. SE – standard error; CI – confidence interval.