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Association of Mitochondrial DNA levels with Frailty and All-Cause Mortality

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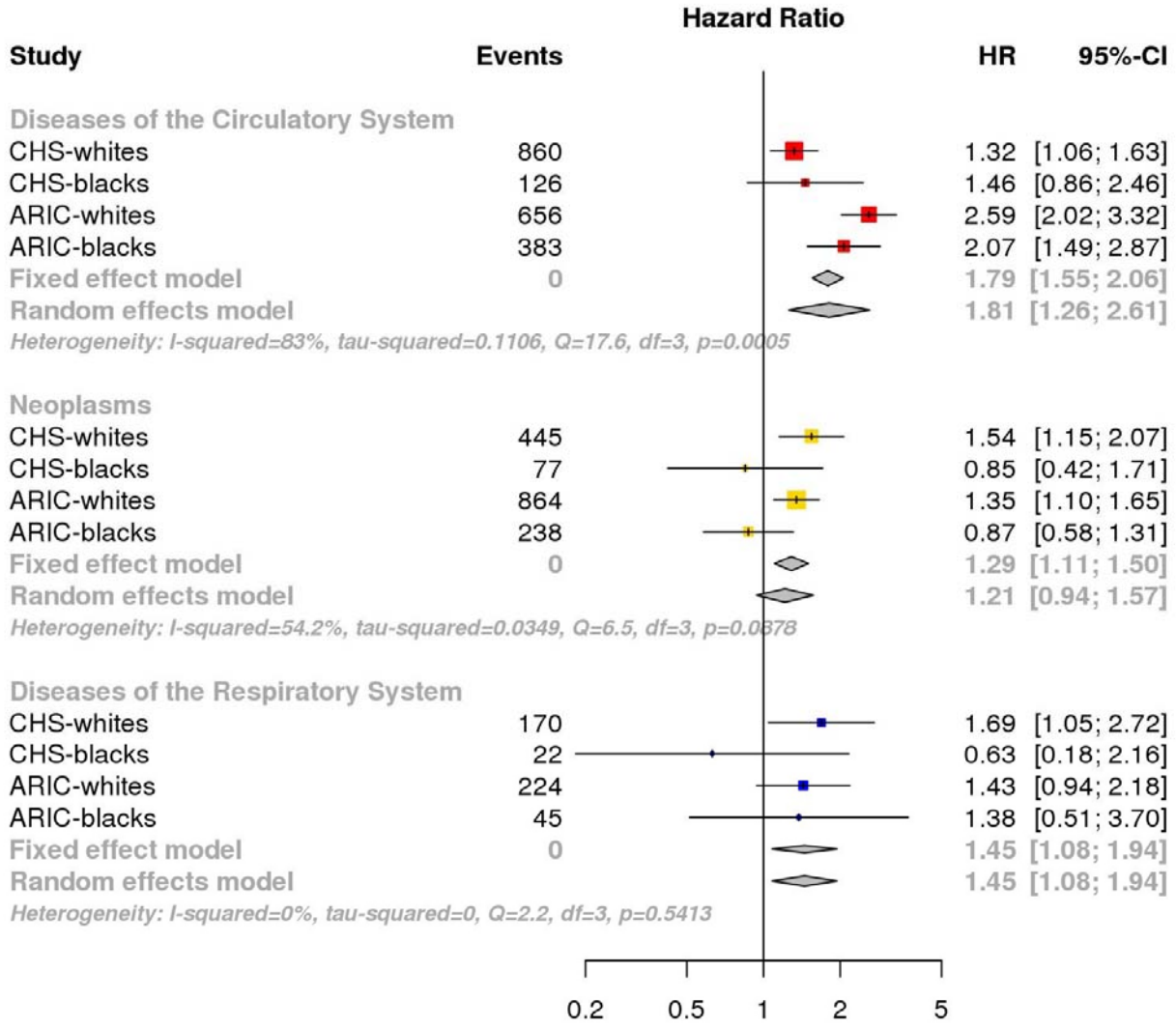
Supplementary Figure 1: Effects of mtDNA copy number on cause-specific mortality



Hazards ratio reflect effect of lowest quintile of mtDNA relative to highest quintile on survival. Baseline models were adjusted for age, sex, and collection site. Heterogeneity between estimates of HR for subgroups of cause of death was evaluated using a random effects model. Diseases of the circulatory system were defined by ICD9 codes 390-459, neoplasms by 140-239 and diseases of the respiratory system by 460-519.

Supplementary Table 1: Sample characteristics stratified by collection site-adjusted quintiles

CHS-Whites

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Pval
No. of samples	819	822	821	822	822	
Age (in yrs)	73.0 +/- 0.2	72.8 +/- 0.2	72.5 +/- 0.2	72.2 +/- 0.2	71.9 +/- 0.2	<0.001
Number of males--no (%)	407 (49.7)	409 (49.7)	368 (44.8)	328 (39.9)	302 (36.7)	<0.001
Follow up time (in yrs)	11.09 +/- 0.18	11.7 +/- 0.17	12.27 +/- 0.17	12.4 +/- 0.17	12.99 +/- 0.16	<0.001
No. of deaths--no (%)	580 (70.8)	539 (65.7)	494 (60.2)	487 (59.3)	430 (52.3)	<0.001
Mean age at death (in yrs)	83.15 +/- 0.27	83.4 +/- 0.26	83.7 +/- 0.28	83.26 +/- 0.27	83.49 +/- 0.3	0.42

CHS-Blacks

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Pval
No. of samples	156	157	156	157	157	
Age (in yrs)	74.0 +/- 0.5	73.1 +/- 0.5	72.8 +/- 0.5	72.5 +/- 0.4	72.2 +/- 0.4	0.002
Number of males--no (%)	74 (47.44)	53 (33.76)	52 (33.33)	62 (39.49)	61 (38.85)	0.18
Follow up time (in yrs)	9.86 +/- 0.34	10.19 +/- 0.36	10.15 +/- 0.35	10.98 +/- 0.34	10.67 +/- 0.35	0.03
No. of deaths--no (%)	94 (0.6026)	87 (0.5541)	92 (0.5897)	73 (0.465)	83 (0.5287)	0.07
Mean age at death (in yrs)	82.77 +/- 0.73	82.18 +/- 0.71	81.72 +/- 0.74	81.86 +/- 0.77	81.2 +/- 0.67	0.09

ARIC-Whites

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Pval
No. of samples	1804	1805	1805	1805	1805	NA
Age (in yrs)	58.85 +/- 0.14	58.23 +/- 0.14	58.13 +/- 0.14	57.84 +/- 0.14	57.56 +/- 0.14	<0.001
Number of males--no (%)	896 (49.7)	853 (47.3)	845 (46.8)	814 (45.1)	835 (46.3)	0.002
Follow up time (in yrs)	15.77+/-0.13	16.66+/-0.12	16.58+/-0.11	17.14+/-0.1	17.03+/-0.11	<0.001
No. of deaths--no (%)	638 (35.4)	497 (27.5)	501 (27.8)	399 (22.1)	400 (22.2)	<0.001
Mean age at death (in yrs)	72.05 +/- 0.31	72.7 +/- 0.34	72.97 +/- 0.32	71.91 +/- 0.38	72.26 +/- 0.38	0.68

ARIC-Blacks

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Pval
No. of samples	496	497	496	497	497	NA
Age (in yrs)	57.99 +/- 0.28	57.28 +/- 0.27	57.3 +/- 0.27	57.18 +/- 0.27	56.64 +/- 0.26	0.002
Number of males--no (%)	188 (37.9)	178 (35.8)	193 (38.9)	185 (37.2)	177 (35.6)	0.68
Follow up time (in yrs)	14.5+/-0.28	15.44+/-0.25	15.77+/-0.24	15.87+/-0.23	16.32+/-0.23	<0.001
No. of deaths--no (%)	225 (45.4)	195 (39.2)	185 (37.3)	172 (34.6)	150 (30.2)	<0.001
Mean age at death (in yrs)	69.43 +/- 0.53	69.99 +/- 0.54	70.21 +/- 0.52	70.09 +/- 0.61	69.89 +/- 0.63	0.8

Data are presented as Mean±SD. Quintiles were calculated from collection site- (and PCs for ARIC) adjusted mtDNA copy number (details in Methods). 'Pval for trend' is the pvalue for effect of trait on standardized mtDNA copy number as a continuous variable.

Supplementary Table 2: Sample characteristics stratified by whether participants were included in the study.

CHS

	Included	Excluded
No. of samples	4,892	995
Age at visit1 (in yrs)	72.6 +/- 5.5	74.3 +/- 6.0
Number of males--no (%)	2,118 (43.3)	377 (37.9)
Follow up time from visit1 (in yrs)	11.8 +/- 4.9	10.8 +/- 4.9
No. of deaths--no (%)	2,960 (60.5)	726 (72.9)
Prevalent CHD at visit1--no (%)	917 (18.7)	237 (23.8)
Prevalent diabetes at visit1--no (%)	763 (15.6)	190 (19.1)
Prevalent hypertension at visit1--no (%)	2,858 (58.4)	599 (60.2)

ARIC

	Included	Excluded
No. of samples	11,509	4,283
Age at baseline (in yrs)	54.0 +/- 5.7	54.4 +/- 5.9
Number of males--no (%)	5,166 (44.9)	1,916 (44.7)
Follow up time from baseline (in yrs)	19.7 +/- 5.1	18.1 +/- 6.6
No. of deaths--no (%)	3,362 (29.2)	1,548 (36.1)
Prevalent CHD at baseline--no (%)	566 (5.0)	200 (4.8)
Prevalent diabetes at baseline--no (%)	1,267 (11.1)	603 (14.3)
Prevalent hypertension at baseline--no (%)	3,832 (33.5)	1,672 (39.3)

Data are presented as Mean +/- standard deviation.

Supplementary Table 3: Detailed breakdown of time of DNA collection by cohort

CHS

Whites	**BL**	**BL + 3**
	4,104	4
Blacks	**BL**	**BL + 3**
	194	578

ARIC

Whites	**visit1**	**visit2**	**visit3**	**visit4**
	367	7,201	1,395	32
Blacks	**visit1**	**visit2**	**visit3**	**visit4**
	117	1,922	398	35

CHS DNA was isolated at baseline (BL) for majority of the white participants, and at a subsequent visit 3 years following baseline for majority of the black participants.
ARIC visits were carried out 2-3 years apart—visit1 (1987-89), visit2 (1990-92), visit3 (1993-95), and visit4 (1996-98).