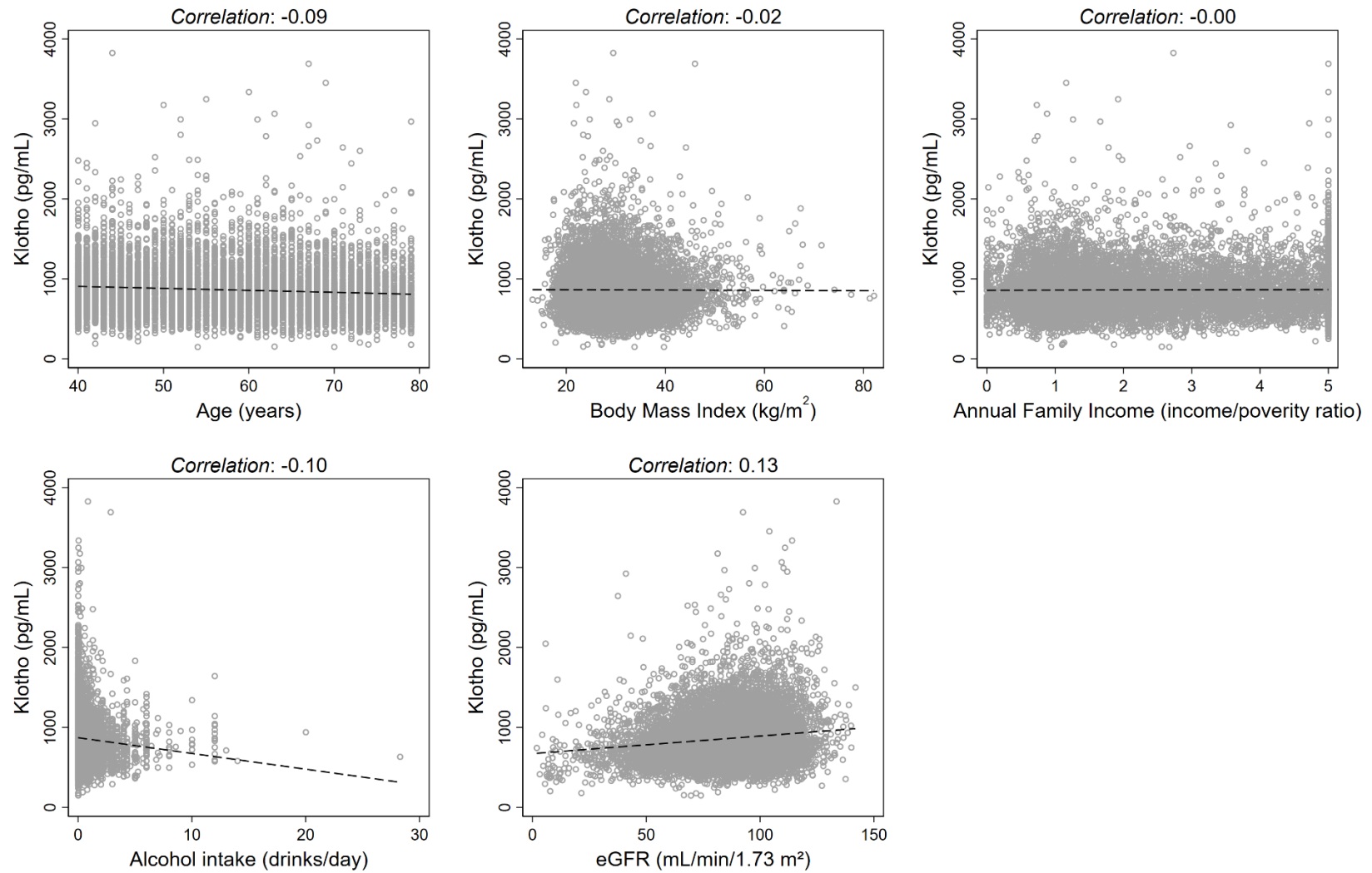
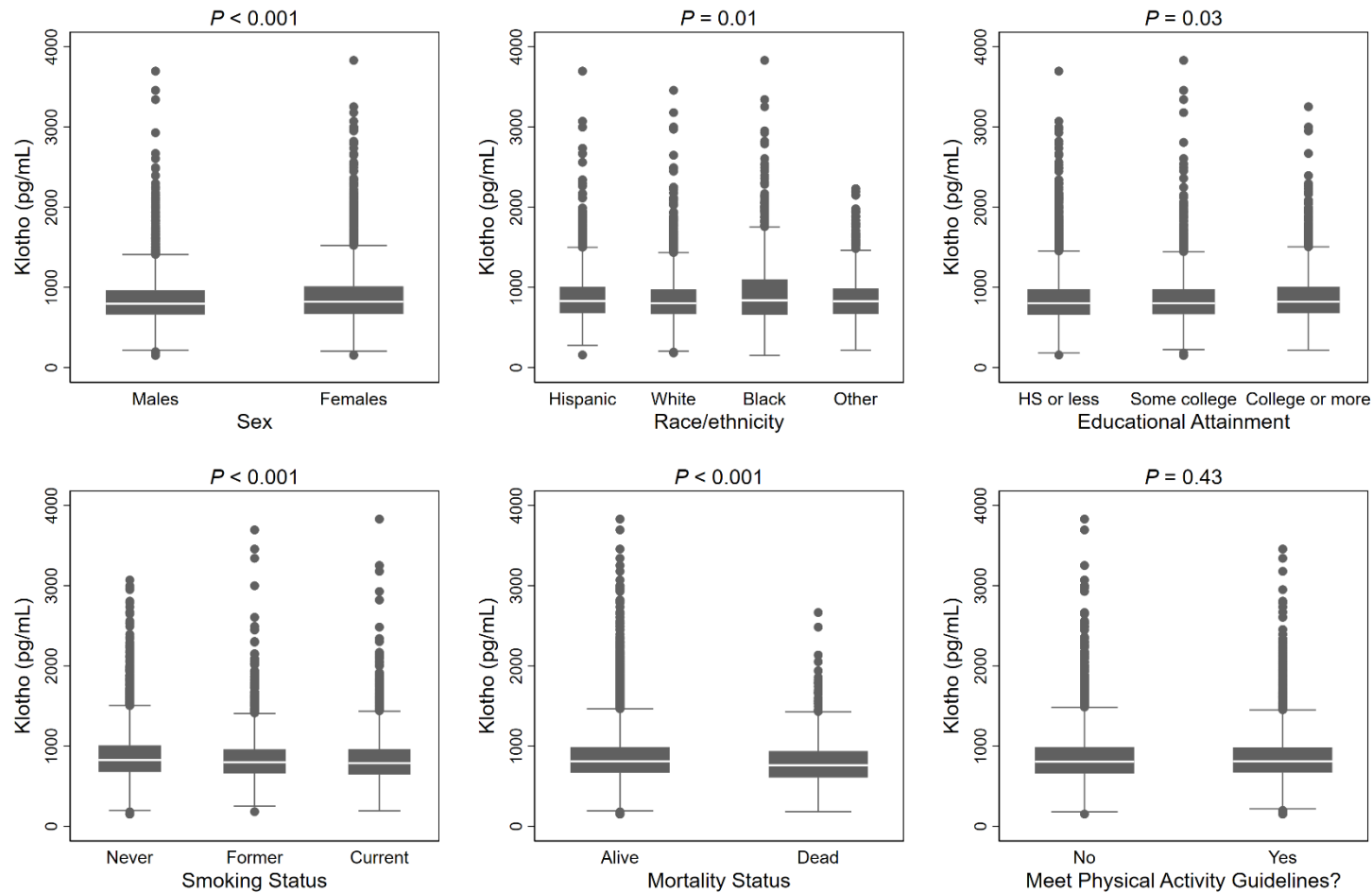


Supplemental Figure 1. Box plots for serum klotho concentrations (pg/mL) by survey cycle. Mean and standard deviations for the klotho concentrations were: 847.1 (292) for 2007-2008; 844.6 (296) for 2009-2010; 886.1 (307) for 2011-2012; and 841.4 (258) for 2013-2014. Median serum klotho concentration was 810 pg/mL (IQR= 318), but varied by survey cycle, with medians of 806 pg/mL (IQR= 327) in 2007-2008, 792 pg/mL (IQR= 326) in 2009-2010, 834 pg/mL (IQR= 326) in 2011-2012, and 808 pg/mL (IQR= 297) in 2013-2014. The middle line of the box represents the median value, with the edges of the box representing the 25<sup>th</sup> and 75<sup>th</sup> percentiles; the whiskers extend to 1.5×(interquartile range) and the dots represent values falling outside that range. P-value for differences determined by adjusted Wald F-test.



Supplemental Figure 2. Serum klotho concentrations by select participant characteristics. Scatter plots and linear fit lines for serum klotho concentrations by age, body mass index, eGFR, household income and alcohol consumption. Note: 20.5% of participants missing information on alcohol intake.



Supplemental Figure 3. Serum klotho concentrations by categorical participant characteristics. Box plots for serum klotho concentrations for sex, race/ethnicity, educational attainment, and smoking status. The middle line of the box represents the median value, with the edges of the box representing the 25<sup>th</sup> and 75<sup>th</sup> percentiles; the whiskers extend to 1.5×(interquartile range) and the dots represent values falling outside that range. *P-value* determined by Wald test using linear regression models that treat log-transformed klotho as the dependent variable and the participant characteristic as the independent variable.

Supplemental Table 1. Serum klotho concentrations by categorical participant characteristics.

	Mean (SD)	Median (IQR)
Sex		
Male	835 (259)	797 (299)
Female	872 (291)	822 (342)
Race		
Non-Hispanic White	846 (207)	804 (308)
Hispanic	869 (420)	830 (320)
Non-Hispanic Black	918 (588)	843 (444)
Other	860 (338)	827 (319)
Educational attainment		
High school degree/equivalency or less	847 (311)	805 (320)
Some college	849 (269)	803 (309)
College degree or more	869 (234)	822 (333)
Physical Activity		
Does not meet guidelines	854 (304)	808 (331)
Meets guidelines	855 (258)	811 (311)
Smoking Status		
Never	874 (277)	828 (331)
Former	836 (264)	800 (307)
Current	831 (293)	788 (316)
Mortality Status		
Alive	856 (273)	811 (318)
Dead	808 (348)	759 (335)

Abbreviations: interquartile range, IQR; standard deviation, SD

Supplemental Table 2. Hazard ratios and 95% confidence intervals for the association between serum klotho concentrations and all-cause mortality, before and after adjusting for alcohol consumption (n= 8,001)

	Age, Sex, survey cycle adjusted			Additional adjustment for alcohol		
	HR	95% CI	P-value	HR	95% CI	P-value
Klotho concentration						
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent
809-985 pg/mL	1.17	0.82, 1.66	0.38	1.16	0.82, 1.64	0.39
666 – 808 pg/mL	1.15	0.81, 1.63	0.43	1.14	0.79, 1.63	0.48
< 666 pg/mL	1.47	1.12, 1.93	0.01	1.45	1.09, 1.93	0.01
P-trend			0.04			0.06
Continuous, per 1-SD decrease	1.12	1.00, 1.27	0.03	1.12	0.99, 1.27	0.06

Alcohol consumption missing from 20.5% of full study sample.

Differences in association estimates between this Table and Table 3 of the manuscript are potentially due to selection bias based on those with missing data. We find little change in association estimates across the two models presented in this table, suggesting that alcohol consumption does not confound the association between klotho and mortality.

Supplemental Table 3. Hazard ratios and 95% confidence intervals for the association between serum klotho concentrations and cause-specific mortality. (N= 10,069)

	Heart disease mortality			Cancer mortality		
	HR	95% CI	P-value	HR	95% CI	P-value
Klotho concentration						
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent
809-985 pg/mL	1.11	0.53, 2.32	0.77	0.91	0.48, 1.72	0.76
666 – 808 pg/mL	1.00	0.42, 2.37	0.99	1.09	0.61, 1.95	0.77
< 666 pg/mL	1.29	0.62, 2.71	0.49	1.31	0.77, 2.24	0.32
P-trend			0.57			0.24
Continuous, per 1-SD decrease	1.03	0.69, 1.56	0.86	1.08	0.79, 1.47	0.62

Models adjusted for age, sex and survey cycle.

By the end of study follow-up, 104 (1.0%) participants died from heart disease and 177 (1.8%) died from cancer.

Supplemental Table 4. Hazard ratios (and 95% confidence intervals) for the association between klotho concentrations and all-cause mortality, stratified by participant characteristics.

	HR	95% CI	P-value	HR	95% CI	P-value	P-interaction
Klotho concentration	Does not meet PA guidelines			Meets PA guidelines			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.03
809-985 pg/mL	1.46	1.03, 2.05	0.03	0.67	0.41, 1.08	0.10	
666 – 808 pg/mL	1.41	0.98, 2.04	0.06	0.76	0.45, 1.29	0.31	
< 666 pg/mL	1.67	1.23, 2.25	0.001	0.97	0.61, 1.55	0.90	
P-trend			0.02			0.88	
	eGFR ≥ 60			eGFR < 60			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.98
809-985 pg/mL	0.92	0.43, 2.00	0.84	1.01	0.70, 1.47	0.94	
666 – 808 pg/mL	1.02	0.46, 2.26	0.96	1.02	0.70, 1.48	0.93	
< 666 pg/mL	1.32	0.62, 2.80	0.46	1.21	0.87, 1.68	0.25	
P-trend			0.33			0.29	
	Males			Females			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.50
809-985 pg/mL	0.99	0.67, 1.46	0.95	1.01	0.64, 1.59	0.98	
666 – 808 pg/mL	0.95	0.60, 1.51	0.83	1.17	0.71, 1.95	0.53	
< 666 pg/mL	1.16	0.78, 1.71	0.46	1.59	1.12, 2.24	0.01	
P-trend			0.50			0.02	
	< 65 years old			≥ 65 years old			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.95
809-985 pg/mL	0.92	0.53, 1.58	0.75	1.08	0.78, 1.51	0.63	
666 – 808 pg/mL	1.03	0.63, 1.67	0.92	1.08	0.68, 1.73	0.73	
< 666 pg/mL	1.23	0.77, 1.96	0.38	1.42	0.96, 2.10	0.08	
P-trend			0.36			0.09	
	< 30 kg/m <sup>2</sup>			≥ 30 kg/m <sup>2</sup>			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.33
809-985 pg/mL	0.97	0.68, 1.39	0.87	1.07	0.71, 1.60	0.75	
666 – 808 pg/mL	0.82	0.54, 1.25	0.35	1.43	0.86, 2.38	0.17	
< 666 pg/mL	1.10	0.79, 1.55	0.57	1.68	1.06, 2.64	0.03	
P-trend			0.71			0.03	

	Non-current smokers			Current smokers			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.10
809-985 pg/mL	0.84	0.61, 1.15	0.28	2.00	1.03, 3.67	0.03	
666 – 808 pg/mL	1.01	0.71, 1.43	0.97	1.34	0.65, 2.76	0.43	
< 666 pg/mL	1.23	0.91, 1.66	0.18	1.68	0.86, 3.27	0.13	
P-trend			0.12			0.35	
	Non-White			White			
> 985 pg/mL	1.00	Referent	Referent	1.00	Referent	Referent	0.46
809-985 pg/mL	0.78	0.51, 1.18	0.23	1.11	0.78, 1.56	0.56	
666 – 808 pg/mL	0.92	0.62, 1.38	0.68	1.11	0.73, 1.68	0.63	
< 666 pg/mL	1.11	0.80, 1.53	0.53	1.40	1.01, 1.94	0.05	
P-trend			0.40			0.10	

Models adjusted for age, sex and survey cycle.

Abbreviations: physical activity, PA.