

**SUPPLEMENTAL MATERIAL**

**Supplemental Table S1.** Hazard ratio (95%CI) of incident diabetes by urinary zinc levels (mg/g) comparing p75<sup>th</sup> to p25<sup>th</sup> in subgroups of participants in the SHS (N= 1,339) and SHFS (N=1,903).

	SHS				SHFS			
	Cases/ Non cases	HR (95%CI) of incident DM	P value	P value interaction	Cases/ Non cases	HR (95%CI) of incident DM	P value	P value interaction
<b>Sex</b>								
Female	239/514	1.21 (1.03, 1.42)	0.02	0.85	146/999	1.17 (0.94, 1.45)	0.16	0.07
Male	162/424	1.27 (1.05, 1.53)	0.01		112/646	1.08 (0.84, 1.38)	0.57	
<b>BMI</b>								
BMI<30	181/631	1.11 (0.92, 1.33)	0.27	0.22	64/909	1.37 (0.98, 1.81)	0.07	<0.01
BMI≥30	220/307	1.46 (1.20, 1.76)	<0.01		194/736	1.03 (0.87, 1.24)	0.71	
<b>Center site</b>								
Arizona	33/72	1.77 (0.98, 3.20)	0.06	0.16	52/147	1.25 (0.89, 1.75)	0.19	0.92
Oklahoma	176/420	1.11 (0.94, 1.31)	0.20		90/720	1.02 (0.77, 1.34)	0.91	
North Dakota and South Dakota	192/446	1.27 (1.05, 1.55)	0.01		116/778	1.06 (0.84, 1.34)	0.63	

Model was adjusted for sex (female, male), site, baseline education (<12 years completed, ≥12 years completed), smoking status (never, former, and current), BMI (kg/m<sup>2</sup>), eGFR (mL/min/1.73 m<sup>2</sup>) and HOMA-IR score.

**Supplemental Table S2.** Hazard ratio (95% CI) of incident diabetes by urinary zinc levels (mg/g) comparing p75<sup>th</sup> to p25<sup>th</sup> in participants in the Strong Heart Study (N=922) and in the Strong Heart Family Study (N=1,419), excluding participants with prediabetes at baseline.

SHS (N=922)	Q1(< 0.34)	Q2 (0.34 - 0.46)	Q3 (0.46 - 0.61)	Q4 (> 0.61)	HR (95% CI) 0.61 vs. 0.34	P value	HR (95% CI) non-linear*	P value
Cases / Non cases	43 / 187	56 / 175	59 / 171	61 / 170	219 / 703		219 / 703	
Model 1	1.00 (Ref)	1.31 (0.88, 1.95)	1.51 (1.01, 2.24)	1.45 (0.98, 2.16)	1.17 (0.99, 1.38)	0.06	1.27 (0.90, 1.80)	0.17
Model 2	1.00 (Ref)	1.30 (0.87, 1.95)	1.54 (1.02, 2.30)	1.51 (1.01, 2.27)	1.21 (1.02, 1.44)	0.03	1.30 (0.91, 1.85)	0.15
Model 3	1.00 (Ref)	1.29 (0.86, 1.93)	1.50 (1.00, 2.25)	1.48 (0.99, 2.23)	1.20 (1.01, 1.42)	0.041	1.28 (0.90, 1.82)	0.17
Model 2+ arsenic	1.00 (Ref)	1.31 (0.87, 1.95)	1.54 (1.03, 2.30)	1.51 (1.01, 2.27)	1.21 (1.02, 1.44)	0.031	1.30 (0.91, 1.85)	0.15
Model 2+ selenium	1.00 (Ref)	1.29 (0.87, 1.93)	1.52 (1.01, 2.27)	1.50 (1.00, 2.25)	1.21 (1.01, 1.43)	0.034	1.30 (0.91, 1.85)	0.15
SHFS (N=1,419)	Q1(< 0.40)	Q2 (0.40 - 0.58)	Q3 (0.58 - 0.84)	Q4 (> 0.84)	HR (95% CI) 0.84 vs. 0.40	P value	HR (95% CI) non-linear*	P value
Cases / Non cases	25 / 330	36 / 318	38 / 317	29 / 326	128 / 1291		128 / 1291	
Model 1	1.00 (Ref)	1.49 (0.88, 2.51)	1.71 (1.00, 2.90)	1.26 (0.71, 2.21)	1.09 (0.88, 1.35)	0.44	1.33 (0.96, 1.84)	0.09
Model 2	1.00 (Ref)	1.42 (0.84, 2.43)	1.57 (0.92, 2.70)	1.12 (0.63, 1.99)	1.04 (0.84, 1.30)	0.70	1.25 (0.90, 1.74)	0.18
Model 3	1.00 (Ref)	1.43 (0.84, 2.43)	1.56 (0.91, 2.67)	1.09 (0.61, 1.93)	1.03 (0.83, 1.28)	0.80	1.25 (0.90, 1.75)	0.18
Model 2+ arsenic	1.00 (Ref)	1.42 (0.83, 2.42)	1.56 (0.91, 2.67)	1.11 (0.62, 1.97)	1.04 (0.83, 1.29)	0.75	1.24 (0.89, 1.72)	0.20
Model 2+ selenium	1.00 (Ref)	1.43 (0.84, 2.43)	1.57 (0.92, 2.69)	1.09 (0.61, 1.95)	1.03 (0.82, 1.29)	0.80	1.24 (0.90, 1.72)	0.19

Abbreviations: Q, quartile; OR, odds ratio; CI, confidence interval.

Model 1 was adjusted for sex (female, male), and stratified by site. Model 2 was further adjusted for education (<12 years completed, ≥12 years completed), smoking status (never, former, and current), BMI (kg/m<sup>2</sup>) and eGFR (mL/min/1.73 m<sup>2</sup>). Model 3 was model 2 and further adjusted for HOMA-IR score. In sensitivity analyses, we also adjusted for urinary arsenic (µg/g) and urinary selenium (µg/g) levels, in separate models.

\*Association obtained from zinc modelled as restricted quadratic splines for hazard regression models (SHS) and cubic splines for mixed effects hazard regression models (SHFS) with knots at the 10th, 50th and 90th percentiles. The p-value of non-linearity was obtained from a Wald-test of the spline terms

**Supplemental Table S3.** Odds ratio (95%CI) of prevalent prediabetes by urinary zinc levels (mg/g) comparing p75<sup>th</sup> to p25<sup>th</sup> in participants in the Strong Heart Study (N=1,339) and in the Strong Heart Family Study (N=1,903).

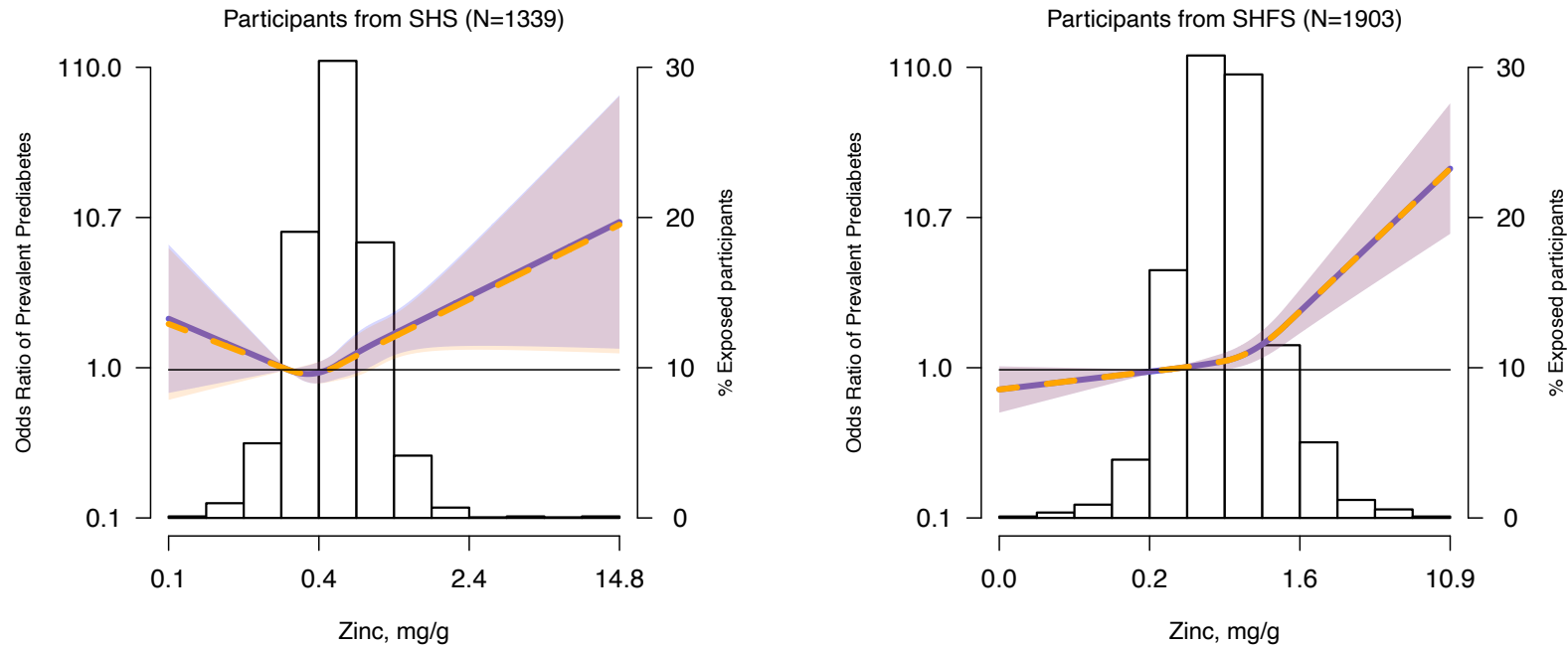
SHS (N=1,339)	Q1 (<0.34)	Q2 (0.34 – 0.47)	Q3 (0.47 – 0.63)	Q4 (>0.63)	OR(95%CI) 0.63 vs. 0.34	P value	OR (95%CI) non-linear*	P value
Cases / Non cases	96/239	87/245	103/234	131/204	417/922		417/922	
Model 1	1.00 (Ref)	0.89 (0.63, 1.25)	1.11 (0.79, 1.55)	1.58 (1.13, 2.19)	1.25 (1.08, 1.46)	0.003	1.52 (1.13, 2.06)	0.01
Model 2	1.00 (Ref)	0.87 (0.61, 1.24)	1.07 (0.76, 1.52)	1.55 (1.10, 2.19)	1.26 (1.08, 1.47)	0.004	1.44 (1.05, 1.97)	0.02
Model 2 + insulin	1.00 (Ref)	0.89 (0.62, 1.28)	1.01 (0.70, 1.44)	1.52 (1.07, 2.16)	1.24 (1.05, 1.45)	0.01	1.37 (1.00, 1.89)	0.05
SHFS (N=1,903)	Q1 (<0.41)	Q2 (0.41 – 0.60)	Q3 (0.60 – 0.86)	Q4 (> 0.86)	OR(95%CI) 0.86 vs. 0.41	P value	OR (95%CI) non-linear*	P value
Cases/ Non cases	91/385	123/352	130/346	140/336	484/1419		484/1419	
Model 1	1.00 (Ref)	1.25 (1.03, 1.52)	1.39 (1.08, 1.78)	1.34 (1.09, 1.64)	1.12 (1.00, 1.26)	0.04	1.36 (1.16, 1.60)	0.003
Model 2	1.00 (Ref)	1.24 (1.02, 1.50)	1.37 (1.07, 1.77)	1.30 (1.05, 1.60)	1.11 (0.99, 1.25)	0.08	1.32 (1.12, 1.57)	0.008
Model 2 + insulin	1.00 (Ref)	1.25 (1.04, 1.51)	1.36 (1.06, 1.76)	1.28 (1.03, 1.60)	1.11 (0.98, 1.27)	0.09	1.33 (1.10, 1.59)	0.03

Abbreviations: Q, quartile; OR, odds ratio; CI, confidence interval.

Model 1 was adjusted for age (years) sex (female, male) and stratified by site. Model 2 was further adjusted for education (<12 years completed, ≥12 years completed), smoking status (never, former, and current), BMI (kg/m<sup>2</sup>) and eGFR (mL/min/1.73 m<sup>2</sup>). We further adjusted an additional model including insulin concentrations at baseline (mIU/L).

\*Association obtained from zinc modelled as restricted quadratic splines for logistic regression models (SHS) and cubic splines for GEE models (SHFS) with knots at the 10th, 50th and 90th percentiles. The p-value of non-linearity was obtained from a wald-test of the spline terms.

## Supplemental Figure S1.



Odds ratios of prevalent prediabetes by urinary zinc levels (mg/g) in the SHS (N=1339) and in the SHFS (N=1903). Lines (shaded areas) represent the odds ratio (95% confidence interval) of prevalent diabetes based on restricted quadratic splines for log-transformed zinc distribution with knots at the 10th, 50th and 90th percentiles (0.26, 0.47, 0.82 mg/g creatinine) for SHS, and cubic splines for log-transformed zinc distribution with knots at the 10th, 50th and 90th percentiles (0.29, 0.60, 1.32 mg/g) for SHFS. The reference value was set at the 10th of zinc distribution. Blue lines (blue shaded areas) represent the estimated odds ratios in models adjusted for age, sex, baseline education (<12 y, ≥12 y), smoking status (never, former, and current), BMI (kg/m<sup>2</sup>) and eGFR (mL/min/1.73 m<sup>2</sup>). Orange lines (orange shaded areas) represent the estimated odds ratios (95% confidence interval) in models further adjusted for insulin concentrations at baseline (mIU/L). The histogram represents the frequency distribution of zinc in the study sample.