

## **Supplemental Web Material**

Associations of cadmium and lead exposure with leukocyte telomere length: Findings from NHANES 1999-2002

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Web Table 1. Percent Difference (95% CI) in LTL (T/S ratio) by Blood Lead and Cadmium, NHANES 1999-2002 (N=6,796).<sup>a</sup>

	Blood lead (µg/dL)			Blood cadmium (µg/L)	
	Model 1	Model 2	Model 3	Model 4	Model 5
Per doubling of exposure	--	-0.07 (-1.38, 1.26)		-2.46 (-3.74, -1.17)*	
Quartile (Quartile 1 = ref)					
Quartile 2	--	--	1.41 (-0.40, 3.25)	--	-4.59 (-7.13, -1.98)*
Quartile 3	--	--	0.70 (-1.09, 2.53)	--	-5.35 (-8.33, -2.37)*
Quartile 4	--	--	0.20 (-2.37, 2.74)	--	-5.54 (-8.70, -2.37)*
<i>P for Trend</i>			0.90		0.001
Age	-0.60 (-0.60, -0.50)*	-0.60 (-0.70, -0.50)*	-0.60 (-0.70, -0.50)*	-0.60 (-0.60, -0.50)*	-0.50 (-0.60, -0.50)*
Age squared	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Female	1.61 (-0.10, 3.46)	1.61 (-0.60, 3.87)	1.61 (-0.50, 3.77)	2.53 (0.60, 4.50)*	2.43 (0.50, 4.39)*
Race/ethnicity (non-Hispanic white = ref)					
Non-Hispanic black	5.55 (1.92, 9.20)*	5.55 (1.92, 9.20)*	5.55 (2.02, 9.20)*	5.34 (1.92, 8.87)*	5.44 (2.02, 8.87)*
Mexican American	-3.92 (-7.87, 0.30)	-3.92 (-7.87, 0.30)	-3.82 (-7.87, 0.30)	-3.54 (-7.32, 0.40)	-3.34 (-7.13, 0.60)
Other Hispanic	5.13 (-3.44, 14.57)	5.13 (-3.34, 14.45)	5.13 (-3.44, 14.45)	5.13 (-3.34, 14.34)	5.34 (-3.05, 14.57)
Other	-0.10 (-4.88, 4.92)	0.10 (-4.88, 4.92)	-0.10 (-4.88, 4.92)	0.80 (-3.82, 5.76)	0.90 (-3.73, 5.87)
Education (< high school diploma = ref)					
High school	-3.25 (-5.73, -0.70)*	-3.15 (-5.73, -0.60)*	-3.15 (-5.73, -0.60)*	-2.96 (-5.45, -0.50)*	-2.96 (-5.45, -0.50)*
Some college	-1.98 (-4.59, 0.70)	-1.98 (-4.59, 0.70)	-1.98 (-4.59, 0.70)	-1.98 (-4.50, 0.70)	-1.88 (-4.40, 0.70)
College degree	-1.59 (-4.21, 1.11)	-1.59 (-4.21, 1.11)	-1.59 (-4.11, 1.11)	-1.49 (-4.02, 1.01)	-1.49 (-3.92, 1.11)
Smoking, pack years (0 =ref)					
<30	0.30 (-1.29, 1.82)	0.30 (-1.39, 1.92)	0.20 (-1.39, 1.82)	1.21 (-0.40, 2.84)	1.21 (-0.40, 2.84)
30-59	-2.27 (-4.97, 0.50)	-2.27 (-4.97, 0.50)	-2.18 (-4.88, 0.50)	-0.70 (-3.63, 2.43)	-1.29 (-4.21, 1.82)
≥60	-2.86 (-6.57, 1.11)	-2.76 (-6.57, 1.11)	-2.66 (-6.39, 1.21)	-1.39 (-5.35, 2.84)	-1.88 (-6.01, 2.43)
BMI (mg/kg <sup>2</sup> )	-0.20 (-0.30, -0.10)*	-0.20 (-0.30, -0.10)*	-0.20 (-0.30, -0.10)*	-0.20 (-0.40, -0.10)*	-0.20 (-0.40, -0.10)*
cotinine (ng/mL)	-0.30 (-0.50, -0.03)*	-0.30 (-0.50, 0.00)*	-0.3 (-0.50, 0.00)*	0.10 (-0.20, 0.40)	-0.10 (-0.30, 0.20)
Model R <sup>2</sup>	0.18	0.18	0.18	0.19	0.19

Abbreviation: BMI, body mass index; LTL, leukocyte telomere length

\*P < 0.05

<sup>a</sup> Regression coefficients rounded to three significant digits.

Web Table 2. Percent Difference (95% CI) in LTL (T/S ratio) by Urine Cadmium, NHANES 1999-2002 (N=2,093).<sup>a</sup>

	Urine cadmium (µg/L)		
	Model 1	Model 2	Model 3
Per doubling of exposure	--	-1.10 (-2.26, 0.07)	--
Quartile (Quartile 1 = ref)			
Quartile 2	--	--	-1.09 (-4.97, 2.94)
Quartile 3	--	--	-4.59 (-8.97, 0.20)
Quartile 4	--	--	-4.50 (-8.79, -0.20)*
<i>P for Trend</i>			0.02
Age	-0.50 (-0.70, -0.40)*	-0.50 (-0.60, -0.40)*	-0.50 (-0.60, -0.30)*
Age squared	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)
Female	1.51 (-0.80, 3.87)	2.22 (-0.30, 4.81)	2.43 (0.10, 4.92)*
Race/ethnicity (Non-Hispanic white = ref)			
Non-Hispanic black	7.57 (3.67, 11.63)*	7.68 (3.77, 11.63)*	7.68 (3.87, 11.63)*
Mexican American	-2.76 (-6.57, 1.21)	-2.47 (-6.39, 1.51)	-2.37 (-6.20, 1.71)
Other Hispanic	11.29 (2.02, 21.41)*	11.63 (2.22, 22.02)*	11.63 (2.33, 21.77)*
Other	-1.00 (-7.69, 6.29)	-0.4 (-7.13, 6.82)	-0.20 (-7.13, 7.25)
Education (college degree= ref)			
< High school	-5.16 (-8.06, -2.18)*	-4.97 (-7.78, -2.08)*	-4.97 (-7.87, -1.98)*
High school	-0.70 (-4.40, 3.15)	-0.50 (-4.21, 3.36)	-0.60 (-4.40, 3.36)
Some college	-3.05 (-6.48, 0.60)	-2.86 (-6.29, 0.70)	-2.86 (-6.29, 0.70)
Smoking, pack years (0 =ref)			
<30	-3.63 (-6.11, -1.00)*	-3.25 (-5.73, -0.60)*	-3.05 (-5.64, -0.39)*
30-59	-5.64 (-9.61, -1.49)*	-4.78 (-8.97, -0.30)*	-4.69 (-8.88, -0.34)*
≥60	-7.69 (-14.62, -0.20)*	-6.57 (-13.93, 1.21)	-6.29 (-13.93, 1.61)
BMI (mg/kg <sup>2</sup> )	-0.20 (-0.40, 0.01)	-0.20 (-0.40, -0.01)*	-0.20 (-0.50, -0.00)*
cotinine (ng/mL)	-0.10 (-0.50, 0.20)	-0.10 (-0.40, 0.30)	-0.04 (-0.40, 0.30)
creatinine (mg/dl)	-1.29 (-2.96, 0.40)	0.10 (-2.27, 2.43)	0.30 (-2.27, 3.05)
Model R <sup>2</sup>	0.19	0.19	0.20

Abbreviation: BMI, body mass index; LTL, leukocyte telomere length

\*P < 0.05

<sup>a</sup>Regression coefficients rounded to three significant digits.

Web Table 3. Estimation of natural direct association, natural indirect association, and total association of smoking on LTL (T/S Ratio) (N = 6,796).<sup>a</sup>

	Estimate (95% CI)	P value
Natural direct association	-0.016 (-0.034, 0.001)	0.07
Natural indirect association	-0.015 (-0.021, -0.010)	<0.0001
Total association	-0.032 (-0.049, -0.015)	0.0002

Abbreviation: LTL, leukocyte telomere length

<sup>a</sup>Exposure = smoking history (< 30 pack years versus  $\geq$  30 pack years of smoking), Mediator = blood cadmium levels (natural log transformed), Outcome = LTL (natural log transformed). Models adjusted for age, age squared, sex, race/ethnicity, educational attainment, and body mass index.

Web Table 4. Percent Difference (95% CI) in LTL (T/S ratio) by Cumulative Smoking History and Serum Cotinine (N=6,796)<sup>a</sup>

	Model	Model 2	Model 3
Smoking, pack years (0 = ref)			
<30	-0.60 (-1.88, 0.60)		0.30 (-1.29, 1.82)
30-59	-3.44 (-6.20, -0.60)*		-2.27 (-4.97, 0.50)
≥ 60	-3.82 (-7.69, 0.20)		-2.86 (-6.57, 1.11)
<i>P for Trend</i>	0.009		0.09
cotinine (ng/mL)			
		-0.30 (-0.50, -0.10)*	-0.30 (-0.50, -0.03)*

\*P < 0.05

<sup>a</sup>Models adjusted for age, age squared, sex, race/ethnicity, educational attainment, and body mass index.