

WEB MATERIAL

Cadmium Exposure and Ovarian Reserve in Women Aged 35–49 Years: The Impact on Results of a Creatinine Adjustment Approach to Correct for Urinary Dilution

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Web Table 1. Association between Quartiles of Urinary Cadmium and Elevated Follicle Stimulating Hormone Among Women Aged 35–49 Years (unweighted $n = 1,681$), Not Adjusting for Urinary Creatinine Concentrations, Third National Health and Nutrition Examination Survey, 1988–1994.

Exposure	FSH Level (IU/L)		Age-Adjusted Model ^a		Multivariable-Adjusted Model ^b	
	≥10 (%) ^c	<10 (%) ^c	RR	95% CI	RR	95% CI
Cadmium (ng/ml)						
Quartile 1 (<0.16)	17	26	1.0	Referent	1.0	Referent
Quartile 2 (0.16-0.38)	24	28	1.3	0.8, 1.9	1.2	0.8, 1.9
Quartile 3 (0.39-0.77)	27	24	1.4	1.0, 2.0	1.2	0.9, 1.7
Quartile 4 (>0.77)	31	23	1.5	1.1, 2.2	1.3	0.9, 1.8
<i>P</i> for trend				0.02		0.23

Abbreviations: CI, confidence interval; FSH, follicle stimulating hormone; RR, relative risk.

^a Adjusted for exact age at sample collection (continuous).

^b Adjusted for exact age at sample collection, race/ethnicity, smoking status, history of unilateral oophorectomy, and history of hysterectomy.

^c Weighted percent incorporating complex survey sampling design.

Web Table 2. Associations between Quartiles of Urinary Cadmium and Elevated Follicle Stimulating Hormone Among Women Aged 35–49 Years, Considering Three Approaches to Creatinine Adjustment and Restricted to Participants Who had Not Smoked Cigarettes in the Prior Ten Years (unweighted $n = 1,105$), Third National Health and Nutrition Examination Survey, 1988–1994.

Exposure	FSH Level (IU/L)		Age-Adjusted Model ^a		Multivariable-Adjusted Model ^b	
	≥10 (%) ^c	<10 (%) ^c	RR	95% CI	RR	95% CI
Standardized (μg/g) ^d						
Quartile 1 (<0.24)	27	34	1.0	Referent	1.0	Referent
Quartile 2 (0.24-0.41)	23	32	0.8	0.6, 1.2	0.8	0.5, 1.1
Quartile 3 (0.41-0.72) ^e	31	21	1.2	0.8, 1.7	1.1	0.7, 1.6
Quartile 4 (>0.72)	19	13	1.0	0.7, 1.6	1.0	0.6, 1.6
<i>P</i> for trend				0.43		0.62
Covariate adjustment (ng/ml) ^f						
Quartile 1 (<0.16)	19	30	1.0	Referent	1.0	Referent
Quartile 2 (0.16-0.38)	34	30	1.8	1.0, 3.0	1.7	1.0, 2.8
Quartile 3 (0.39-0.77)	21	23	1.5	0.9, 2.6	1.5	0.9, 2.4
Quartile 4 (>0.77)	26	17	2.1	1.2, 3.8	2.0	1.1, 3.6
<i>P</i> for trend				0.04		0.06
Covariate-adjusted standardization (ng/ml) ^g						
Quartile 1 (<0.181)	27	34	1.0	Referent	1.0	Referent
Quartile 2 (0.181-0.333) ^h	20	30	0.8	0.5, 1.2	0.8	0.5, 1.2
Quartile 3 (0.333-0.608)	31	23	1.3	0.8, 1.9	1.2	0.7, 1.8
Quartile 4 (>0.608)	22	14	1.3	0.9, 1.9	1.2	0.7, 1.8
<i>P</i> for trend				0.05		0.22

Abbreviations: CI, confidence interval; FSH, follicle stimulating hormone; RR, relative risk.

^a Adjusted for exact age at sample collection (continuous).

^b Adjusted for exact age at sample collection, race/ethnicity, history of unilateral oophorectomy, and history of hysterectomy.

^c Weighted percent incorporating complex survey sampling design.

^d Standardized: Cadmium concentrations were divided by urinary creatinine concentrations and multiplied by 100.

^e The lower value for quartile 3 was 0.4103 before rounding.

^f Covariate adjustment: Creatinine was included in the regression model as a covariate.

^g Covariate-adjusted standardization: Cadmium concentrations were divided by the ratio of observed creatinine concentrations and predicted creatinine concentrations. Predicted creatinine concentrations were determined by fitting a model for ln-transformed creatinine as a function of exact age at sample collection, fat-free mass, body mass index, race/ethnicity, smoking, alcohol consumption, frequency of exercise in past month, and history of non-gestational diabetes.

^h The upper value for quartile 2 was 0.3326 before rounding.

Web Table 3. Associations between Quartiles of Urinary Cadmium and Elevated Follicle Stimulating Hormone Among Women Aged 35–49 Years, Considering Three Approaches to Creatinine Adjustment and Restricted to Premenopausal Women (unweighted $n = 1,615$), Third National Health and Nutrition Examination Survey, 1988–1994.

Exposure	FSH (IU/L)		Age-Adjusted Model ^a		Multivariable-Adjusted Model ^b	
	≥10 (%) ^c	<10 (%) ^c	RR	95% CI	RR	95% CI
Standardized (μg/g) ^d						
Quartile 1 (<0.24)	18	28	1.0	Referent	1.0	Referent
Quartile 2 (0.24-0.41)	17	28	0.9	0.6, 1.5	0.9	0.5, 1.5
Quartile 3 (0.41-0.72) ^e	29	24	1.4	0.9, 2.3	1.2	0.8, 2.0
Quartile 4 (>0.72)	36	21	1.6	1.1, 2.4	1.3	0.8, 2.0
<i>P</i> for trend				<0.001		0.05
Covariate adjustment (ng/ml) ^f						
Quartile 1 (<0.16)	18	26	1.0	Referent	1.0	Referent
Quartile 2 (0.16-0.38)	23	27	1.4	0.9, 2.4	1.4	0.8, 2.3
Quartile 3 (0.39-0.77)	27	24	1.9	1.2, 2.9	1.6	1.0, 2.6
Quartile 4 (>0.77)	32	23	2.5	1.5, 4.0	2.0	1.2, 3.3
<i>P</i> for trend				<0.001		0.01
Covariate-adjusted standardization (ng/ml) ^g						
Quartile 1 (<0.181)	19	27	1.0	Referent	1.0	Referent
Quartile 2 (0.181-0.333) ^h	17	28	0.9	0.6, 1.6	0.9	0.6, 1.6
Quartile 3 (0.333-0.608)	30	24	1.5	0.9, 2.3	1.3	0.8, 2.0
Quartile 4 (>0.608)	34	21	1.7	1.1, 2.5	1.3	0.9, 2.0
<i>P</i> for trend				<0.001		0.06

Abbreviations: CI, confidence interval; FSH, follicle-stimulating hormone; RR, relative risk.

^a Adjusted for exact age at sample collection (continuous).

^b Adjusted for exact age at sample collection, race/ethnicity, smoking status, history of unilateral oophorectomy, and history of hysterectomy.

^c Weighted percent incorporating complex survey sampling design.

^d Standardized: Cadmium concentrations were divided by urinary creatinine concentrations and multiplied by 100.

^e The lower value for quartile 3 was 0.4103 before rounding.

^f Covariate adjustment: Creatinine was included in the regression model as a covariate.

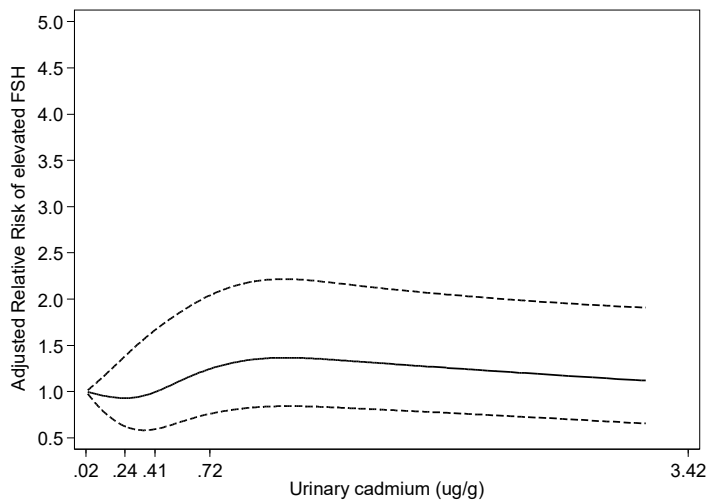
^g Covariate-adjusted standardization: Cadmium concentrations were divided by the ratio of observed creatinine concentrations and predicted creatinine concentrations. Predicted creatinine concentrations were determined by fitting a model for ln-transformed creatinine as a function of exact age at sample collection, fat-free mass, body mass index, race/ethnicity, smoking, alcohol consumption, frequency of exercise in past month, and history of non-gestational diabetes.

^h The upper value for quartile 2 was 0.3326 before rounding.

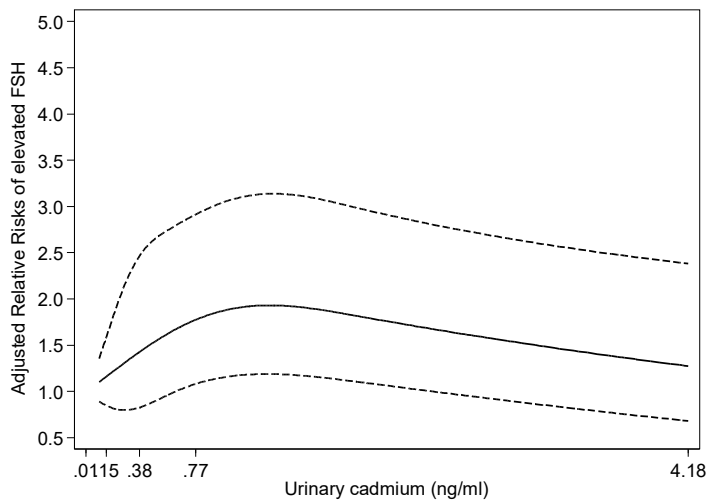
Web Figure 1. Adjusted relative risks (solid line) and 95% confidence intervals (dashed lines) for urinary cadmium and elevated follicle stimulating hormone using restricted cubic splines to characterize urinary cadmium concentrations, with knots at the 5th, 35th, 65th, and 95th percentiles of weighted sample distributions, Third National Health and Nutrition Examination Survey, 1988–1994.

The 1st percentile served as the reference urinary cadmium concentration. Results were obtained using Poisson regression, adjusting for age at sample collection, race/ethnicity, smoking status, history of unilateral oophorectomy, and history of hysterectomy. Each figure displays the association using an approach to adjust for urinary creatinine: A) standardization, B) covariate adjustment, and C) covariate-adjusted standardization. In the graphs, the *x*-axis was truncated to the 99th percentile; the *x*-axis ticks and labels are at the 1st, 25th, 50th, 75th, and 99th percentiles.

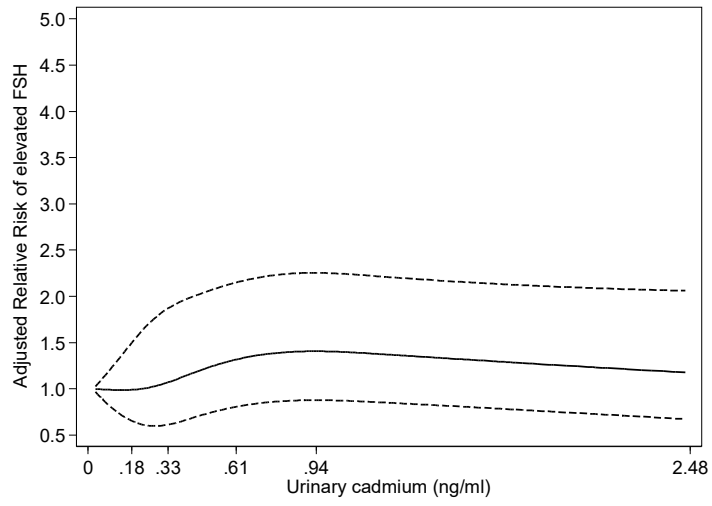
A)



B)



C)



Abbreviation: FSH, follicle-stimulating hormone.