DOES CREATININE ADJUSTMENT METHOD AFFECT ESTIMATED BPA LEVELS?

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Outline

- What is BPA?
- Why do we need to adjust for creatinine?
- What are some possible approaches for adjustment?
- Do these approaches affect BPA comparisons among subgroups?

Bisphenol A (BPA)

- BPA has been found in over 90% of urine specimens collected from national samples of the United States population
  - BPA levels differ among subgroups, including by sex and race/ethnicity
- Human exposure to BPA usually occurs when foods and beverages stored in containers that contain BPA are ingested
  - Recent declines in exposure may be due to voluntary changes prompted, in part, by local regulations
- Research, primarily using animal models, has suggested that BPA may affect human development, reproduction, brain chemistry and structure, the immune system, and behavior.
- BPA may be associated with heart disease, obesity, and diabetes.

Creatinine

- Creatinine is used to correct for urine concentration
- For the NHANES data, urinary creatinine is used as a reference analyte against which other urine analytes, such as BPA, are analyzed.
- Without adjustment for urine concentration, BPA levels would be overestimated for respondents with highly concentrated urine samples and underestimated for respondents with dilute samples.
- Creatinine levels have been shown to vary by factors such as age, sex, and race/ethnicity.
- Comparisons among studies of BPA levels can be difficult when different methods are used to adjust for urine concentration.

Data: 2003-2012 NHANES

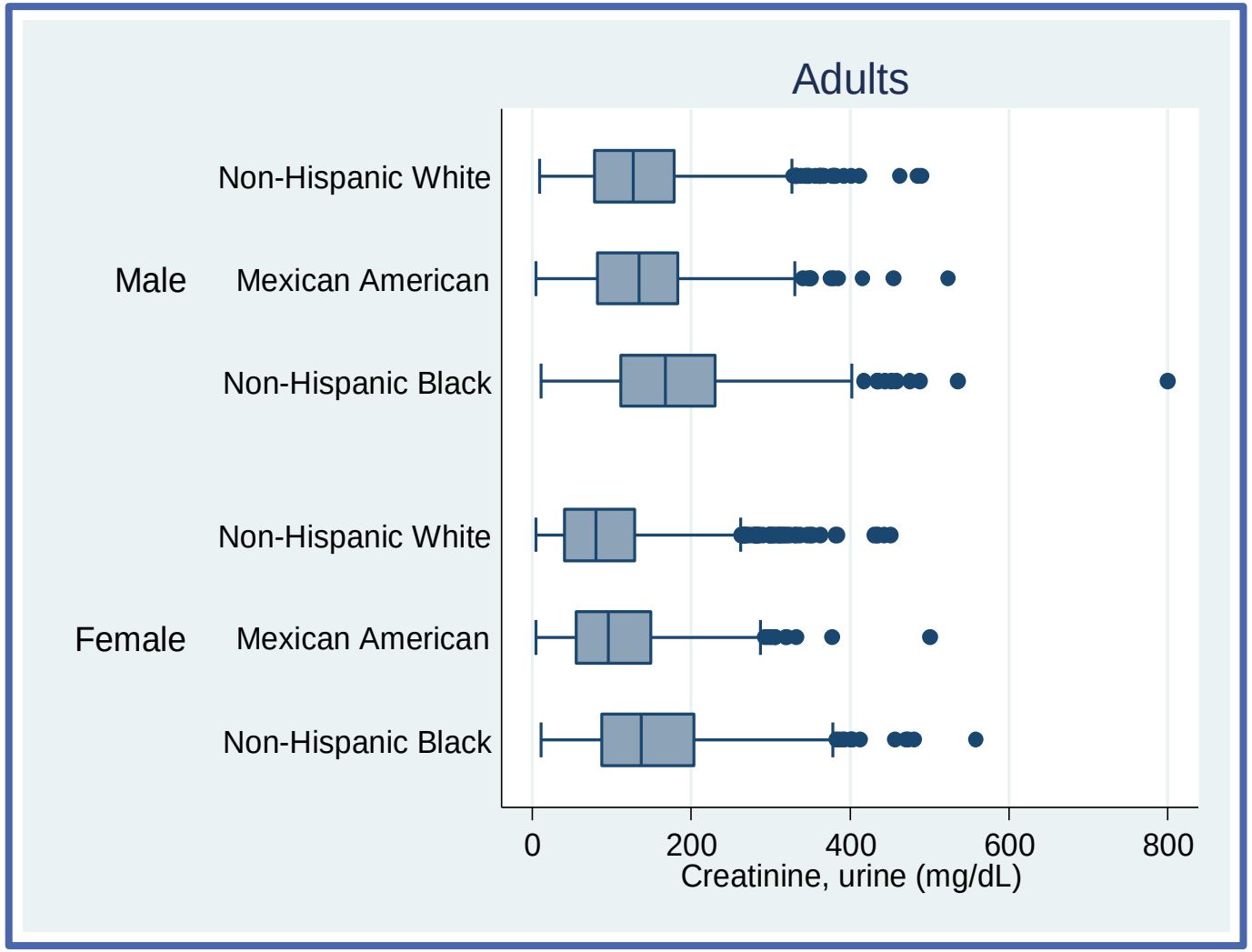
- Since 1999, NHANES has been conducted continuously with approximately 10,000 respondents from 30 locations in each two-year data cycle.
- BPA is measured on a 1/3 sample
- Analytic sample for this study limited to adults ages 20 and over with complete data on BPA, creatinine, race/ethnicity, sex, age, poverty status, urbanization, education and cigarette smoking (6,608)
- Analysis done using Stata, incorporating sample weights, clustering and stratification.

Methods

- Log-linear regression models to assess different creatinine adjustment approaches
  - Dependent variable ln(BPA/creatinine)
  - Dependent variable ln(BPA) with functions of creatinine as an independent variable in different models
    - ln(creatinine)
    - sqrt(creatinine)
    - z-score overall
    - z-score by race (non-Hispanic black versus others)
    - z-score by sex
    - z-score by sex and race
  - Independent variables: race/ethnicity, sex, age, poverty status, urbanization, education and cigarette smoking
  - Results expressed as relative percent change (100% * (e^b-1))

Creatinine

Distribution of creatinine among adults, by race/ethnicity and sex



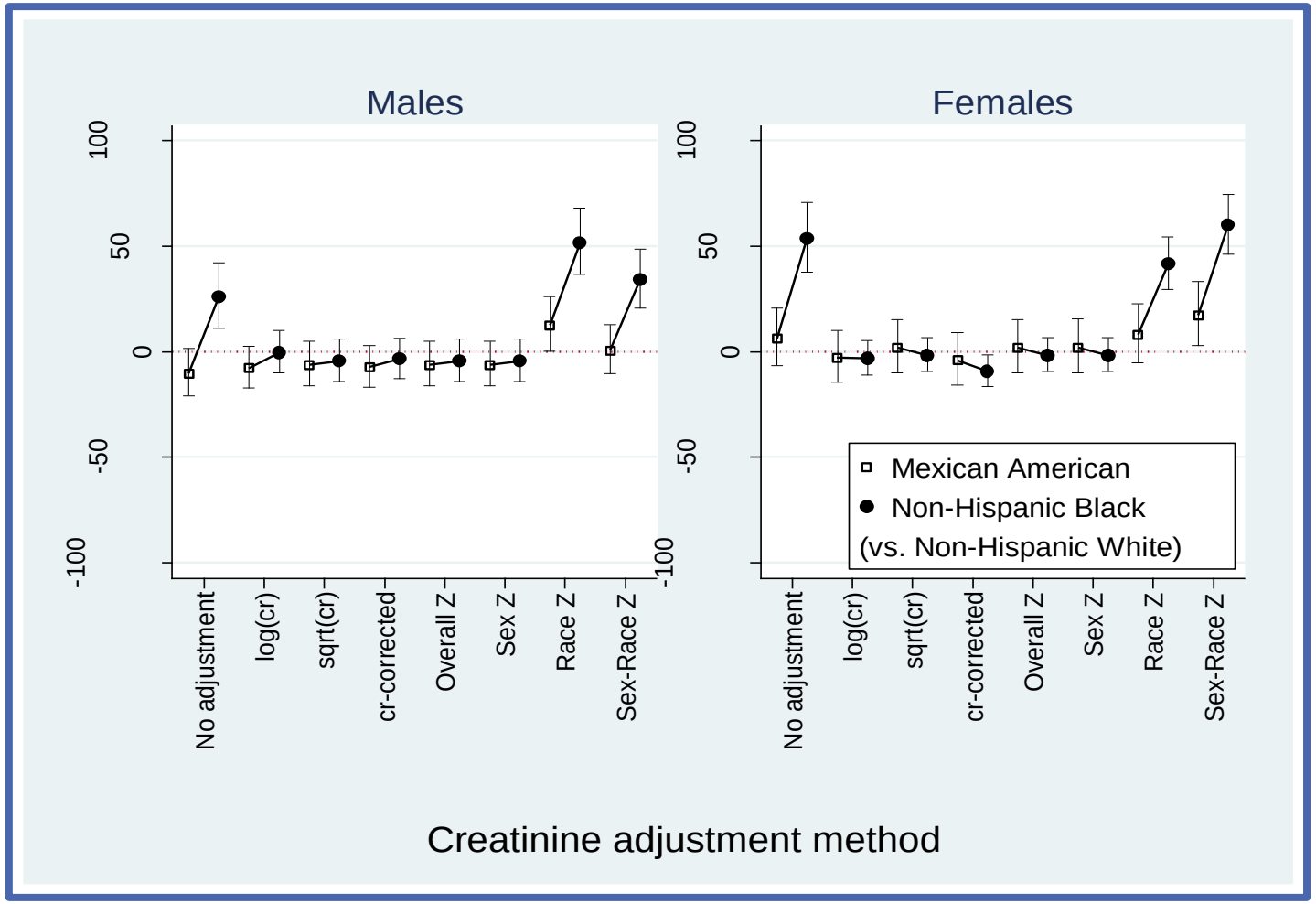
Estimated median and percentiles of BPA (µg/L) by sex and race/Hispanic origin, for adults

	Median	25th percentile	75th percentile
Male, non-Hispanic White	2.00	1.00	3.80
Male, Mexican American	2.00	1.10	3.70
Male, non-Hispanic Black	2.70	1.50	5.00
Female, non-Hispanic While	1.60	0.70	3.40
Female, Mexican American	1.90	0.90	4.00
Female, non-Hispanic Black	2.80	1.40	5.30

Results

Adjusted relative percent change in BPA among adults:

Mexican American and non-Hispanic Black compared to non-Hispanic White, by sex

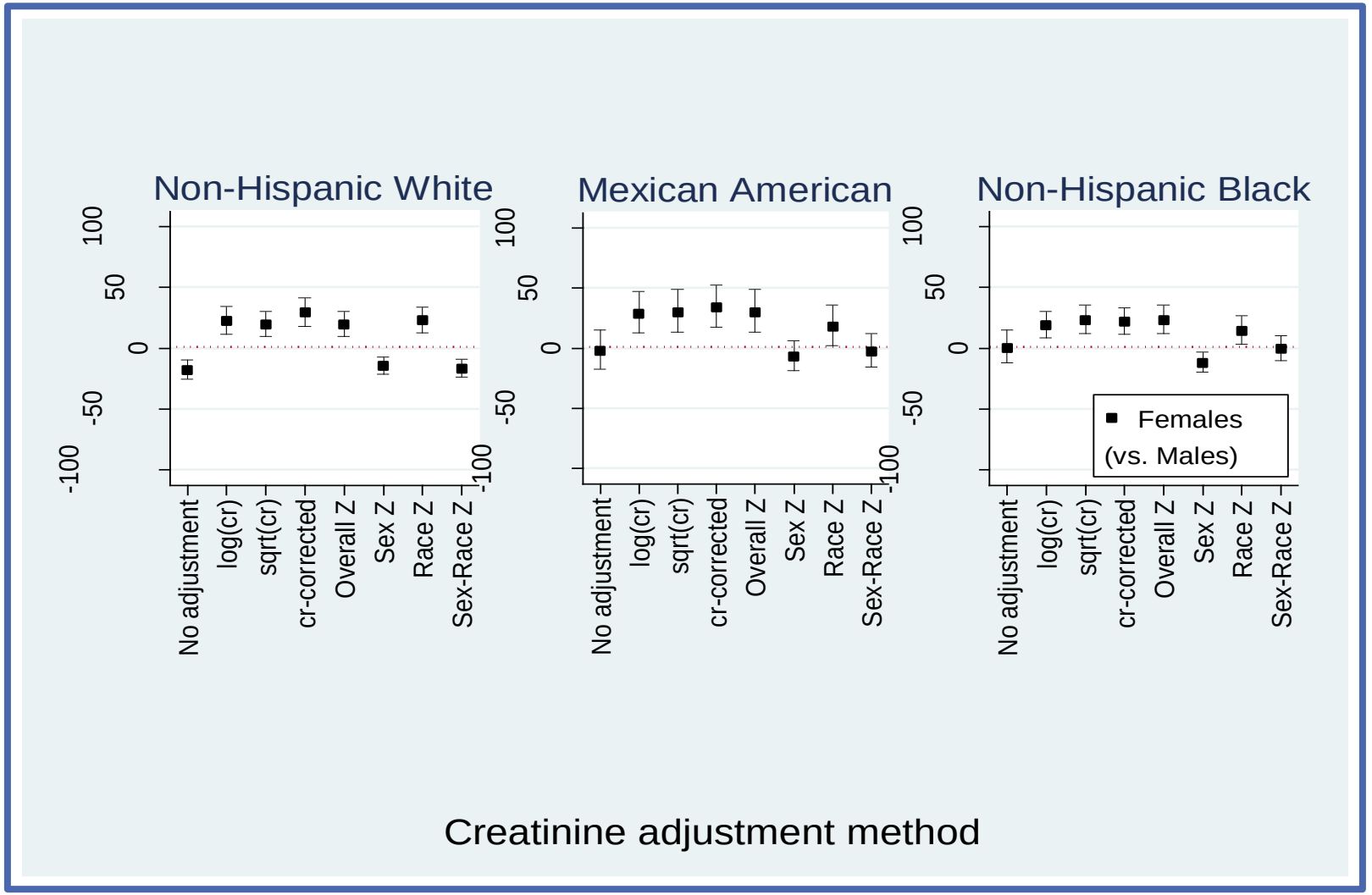


Race/ethnicity difference in BPA level is largely absent except when creatinine adjustment done using race/ethnicity-specific or sex-race/ethnicity-specific z-score methods.

Results

Adjusted relative percent change in BPA among adults:

Females versus Males, by race/ethnicity



Female adults consistently have higher BPA levels than males when creatinine adjustments are not sex-specific, regardless of race/ethnicity.

Adjusted relative percent change in BPA among adults, by income and education

	No creat-inine	ln(creat)	Sqrt (creat)	(BPA/ creat)	Z-Overall	Z-Sex	Z-Race	Z-Race*sex
Income								
>= 400%	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
200-399%	16.3*	9.9*	9.8*	9.0*	9.8*	9.8*	10.2*	10.2*
100-299%	18.7*	12.7*	13.1*	11.9*	13.1*	13.1*	13.0*	13.1*
Below Poverty	33.3*	25.6*	24.7*	24.5*	24.7*	24.7*	24.1*	24.0*
Education								
More than HS	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Completed HS	5.3	-0.9	-0.5	-1.8	-0.5	-0.5	-0.7	-0.7
Less than HS	-3.1	-8.6*	-9.0*	-9.3*	-9.0*	-9.0*	-9.3*	-9.3*

Relative percent change in BPA among adults, by urbanization and smoking status

	No creat-inine	ln(creat)	Sqrt (creat)	(BPA/ creat)	Z-Overall	Z-Sex	Z-Race	Z-Race* sex
Urbanization								
Large Central Metro	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Large Fringe Metro	4.5	1.5	3.5	1.1	3.5	3.5	3.6	3.6
Medium & Small metro	5.5	5.3	7.4	5.3	7.4	7.4	7.4	7.4
Micro & Noncore	6.3	4.0	6.0	3.6	6.0	6.0	6.4	6.4
Smoking								
Never Smoker	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Former Smoker	2.3	2.2	2.3	2.2	2.3	2.3	2.3	2.3
Current Smoker	-0.5	7.8*	6.5*	9.0*	6.5*	6.6*	6.6*	6.5*

Results - Summary

- Four creatinine adjustments (natural log, square root, overall z-score, and BPA/creatinine) produced similar relative percent differences in BPA for sex and for race/ethnicity subgroups
- Adjustments using race/ethnicity -specific z-score or sex- race/ethnicity-specific z-score resulted in dissimilar relative percent differences for race/ethnicity subgroups.
- Adjustments using sex-specific z-score or sex- race/ethnicity-specific z-score resulted in dissimilar relative percent differences for sex subgroups.
- All creatinine adjustments led to similar results by poverty status, education, urbanization and smoking status.

Conclusions

- The similarity of results obtained using common creatinine adjustment methods facilitates comparisons across studies that used those methods.

- However, using sex-specific z-score creatinine adjustment methods will affect comparisons between males and females, and using race/ethnicity-specific z-score adjustment will affect comparisons across race groups.

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