America's Children and the Environment, Third Edition

DRAFT Indicators

Biomonitoring: Phthalates

EPA is preparing the third edition of *America's Children and the Environment* (ACE3), following the previous editions published in December 2000 and February 2003. ACE is EPA's compilation of children's environmental health indicators and related information, drawing on the best national data sources available for characterizing important aspects of the relationship between environmental contaminants and children's health. ACE includes four sections: Environments and Contaminants, Biomonitoring, Health, and Special Features.

EPA has prepared draft indicator documents for ACE3 representing 23 children's environmental health topics and presenting a total of 42 proposed children's environmental health indicators. This document presents the draft text, indicators, and documentation for the phthalates topic in the Biomonitoring section.

For more information on America's Children and the Environment, please visit www.epa.gov/ace. For instructions on how to submit comments on the draft ACE3 indicators, please visit www.epa.gov/ace/ace3drafts/.

Phthalates

Phthalates are a class of manufactured chemicals commonly used to increase the flexibility of plastics in a wide array of consumer products. Phthalates are also used as additives in many personal care products, such as cosmetics. More than 470 million pounds of phthalates are produced or imported in the United States each year.[1]

There are about 25 different manmade chemicals that make up the chemical class of phthalates. By far the most common use of phthalates is in the production of polyvinyl chloride (PVC) products.[2] PVC is the second most commonly used plastic in the world, and is present in pipes and tubing, construction materials, packaging, electrical wiring, and thousands of consumer goods.[3] Phthalates are also used in wall coverings, tablecloths, floor tiles, furniture upholstery, carpet backings, shower curtains, garden hoses, rainwear, pesticides, some toys, shoes, automobile upholstery, food packaging, medical tubing, and blood storage bags.[4-7] Phthalates are not strongly bound in these products and can therefore leach out.[8] Phthalates are also used frequently in cosmetics, nail polish, hair products, skin care products, and some medications.[5,6,9]

The Consumer Product Safety Improvement Act of 2008 (CPSIA) banned the use of six phthalates in toys and child care articles at concentrations greater than 0.1 percent: di-2-ethylhexyl phthalate (DEHP), dibutyl phthalate (DBP), butyl benzyl phthalate (BBzP), di-isononyl phthalate (DINP), di-isodecyl phthalate (DIDP), and di- n-octyl phthalate (DnOP). The Consumer Product Safety Commission has also appointed a Chronic Hazard Advisory Panel to examine the cumulative health risks of phthalates and phthalate substitutes, and to recommend whether to continue the ban of DINP, DIDP, and DnOP and whether any other phthalates or phthalate substitutes should be banned.[1]

For most phthalates, the major route of exposure is food ingestion, although personal care products and inhalation have been shown to dominate for certain phthalates.[10-12] Sometimes food stored in plastic food packaging can absorb the phthalates that may be present in the packaging. Fatty foods stored in these containers, such as dairy products, fish, seafood, and oils, are most likely to absorb phthalates.[7] Phthalates stored in a mother's body can enter her breast milk. Ingestion of that breast milk and infant formula containing phthalates may also contribute to infant phthalate exposure.[13] The phthalates that may be present in dust can be ingested by infants and children through hand-to-mouth activities.[8] Finally, infants and small children can be exposed to phthalates by sucking on toys and other objects made with phthalate-containing plastics.

Other routes of phthalate exposure include inhalation, drinking contaminated water, and absorption through the skin.[10] Phthalates can be released in small amounts to the air people breathe inside homes or schools from the many consumer products that contain them.[6,14] People living near phthalate-producing factories or hazardous waste sites may be exposed to phthalates released into the air or ground water where they live.[4,6,7] Individuals may be exposed to phthalates during the use of many personal care products containing phthalates, such as nail polish, hair products, cosmetics, and lotions.[9] Phthalates in these products may be absorbed

through contact with the skin or may be inhaled if some of the product is present in the air.[4] Certain medical devices, such as intravenous tubing or flexible bags containing blood, medications, or nutritional products, contain phthalates. These can be a source of phthalate exposure to children and women of childbearing age when the tubing or bags are used to administer medications, nutritional products, or blood to the individual. This can be a very significant route of exposure, especially for premature infants in intensive care units, whose small size and fragile physical condition may increase their risk of adverse health effects from phthalate exposure.[15-17]

Phthalate exposures, assessed from urinary concentrations of phthalate metabolites (i.e., breakdown products), appear to be higher for children compared with adolescents and adults. Studies of phthalate metabolites in children's urine are limited, but the few that have been published have found children's urinary phthalate metabolite levels to be higher than levels in adults and to decrease with age (i.e., younger children had more phthalate metabolites in their urine than older children did).[18-20] The exception is monoethyl phthalate (MEP), a metabolite of diethyl phthalate, which has been found to be present in higher levels in adult urine compared with children's urine.[18] Levels of MEP are most likely associated with use of consumer products that contain diethyl phthalate, such as detergents, soaps, cosmetics, shampoos, and perfumes.[18]

Phthalates are suspected endocrine disruptors.[21,22] Endocrine disruptors act by interfering with the biosynthesis, secretion, action, or metabolism of naturally occurring hormones.[23,24] Given the importance of hormones in human physiology, there is concern in the scientific community over the potential for endocrine disruptors to adversely affect children's health, particularly in reproduction, development, and behavior. Male laboratory animals exposed to phthalates have been known to display elements of "phthalate syndrome," which includes infertility, decreased sperm count, cryptorchidism (undescended testes), hypospadias (malformation of the penis in which the urethra does not open at the tip of the organ), and other reproductive tract malformations.[25] A number of animal studies have found associations between phthalate exposure and changes in male hormone production, altered sexual differentiation, and changes to reproductive organs, including hypospadias.[26-35] A recent study of female rats suggests that exposure to DEHP advances the onset of puberty.[36] These findings in animal studies, although typically occurring at exposure levels much higher than what the general population may be exposed to, suggest a concern for health effects in children as well.

There are only a limited number of human studies looking at the relationship between phthalate exposure and hormonal and reproductive health changes, although the literature in this area is growing. Some studies have suggested that exposure to phthalates may cause changes in the hormonal and reproductive systems of infants and children. Prenatal exposure to some phthalates at typical U.S. population levels has been associated with male reproductive effects, as indicated by physical measures of the distance between the anus and the genitals in male infants, where a shorter distance is a marker of feminization.[37,38] One study found that boys born to women exposed to phthalates at work were more likely to be born with hypospadias.[39] Another study observed an association between increased concentrations of phthalate metabolites concentrations in breast milk and altered reproductive hormone levels in newborn boys.[40] Childhood levels of certain phthalate metabolites have been weakly associated with pubic hair development in a group of 6-8 year old girls.[41] Exposure to phthalates has also been associated

with changes in thyroid hormones and function. A recent study found negative associations between urinary phthalate metabolite concentrations and thyroid hormone levels and growth in children.[42]

Childhood exposure to phthalates may increase the incidence of allergies and asthma in children. A review article of published studies concluded that there is an association between indicators of phthalate exposure in the home and risk of asthma and allergies in children.[43] Examples of the exposure indicators and outcomes considered in these studies include an association between some phthalates in surface dust and increased risk of runny nose, eczema, and asthma,[44] and increased risk of bronchial obstruction associated with the presence of PVC in the home.[45]

Some studies suggest that typical population-level prenatal exposure to DEHP is associated with shorter pregnancy duration as well as alterations of thyroid hormone levels in pregnant women.[46-49] The health risks associated with preterm birth and maternal thyroid hormone disruption during pregnancy make this a cause for concern. Babies born prematurely are at a greater risk of mortality and complications such as acute respiratory, gastrointestinal, immunologic, central nervous system, hearing, and vision problems, while moderate deficits in maternal thyroid hormone levels during early pregnancy have been associated with reduced childhood IQ scores and other neurodevelopmental effects, as well as unsuccessful or complicated pregnancies.[50,51]

Finally, there is a growing concern that exposure to phthalates may lead to neurodevelopmental problems in children. One study found an association between prenatal exposure to phthalates and decrements in an infant's overall quality of responsiveness, attention to visual and auditory stimuli, and quality of movement.[52] A follow-up study of the same group of children at ages 4 to 9 years found an association between prenatal phthalate exposure and behavioral deficits commonly found in children with clinically diagnosed attention-deficit/hyperactivity disorder (ADHD) and conduct disorder.[53] Another study found that children with higher levels of phthalate metabolites in their urine were more inattentive and hyperactive, and displayed more symptoms of ADHD compared with those who had lower levels.[54] The exposure levels in these studies are comparable to typical exposures in the U.S. population. Studies of laboratory animals have also found that rats exposed to phthalates display hyperactive behaviors.[55-57]

The following indicators present urinary metabolite levels of three important phthalates: dibutyl phthalate (DBP), butyl benzyl phthalate (BBzP), and di-2-ethylhexyl phthalate (DEHP) for women of childbearing age (ages 16 to 49 years) and children ages 6 to 17 years. These three phthalates were chosen because they are commonly detected in humans and their potential connection to adverse children's health outcomes is well supported by the scientific literature.

DBP is used primarily in latex adhesives, cellulose plastics, dyes, and cosmetics and other personal care products.[58] The largest use of BBzP is in the production of PVC flooring materials, but it is also used in the manufacture of automotive materials, artificial leather, and food conveyor belts.[22,59] DEHP is currently the only phthalate plasticizer used in PVC medical devices such as blood bags and plastic tubing. DEHP is also used in flooring, wallpaper auto upholstery, raincoats, toys, and food packaging.[60]

Human health studies have associated exposures to DBP with altered reproductive hormone levels in newborn boys, and shifts in thyroid hormone levels in pregnant women.[40,46] Signs of feminization in young boys (as measured by reduced anogenital distance), altered hormone levels in newborn boys, and increased risk of rhinitis and eczema are health effects that have been associated with BBzP exposure in some studies.[37,38,40,44] DEHP has been associated with increased risk of asthma and bronchial obstruction, increased risk of ADHD symptoms, and shortened pregnancy durations.[44,45,47,49,54,61] The exposure levels in these studies are comparable to typical exposures in the U.S. population.

Indicator PHTL1: Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine, 1999-2006

Indicator PHTL2: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, 1999-2006

Overview

Indicators PHTL1 and PHTL2 present concentrations of phthalate metabolites in the urine of U.S. women ages 16 to 49 years and children ages 6 to 17 years. The data are from a national survey that collects urine for a representative sample of the population, and then measures the concentration of phthalate metabolites in the urine. Indicator PHTL1 shows the change in women's phthalate metabolite levels over time and Indicator PHTL2 shows the change in children's phthalate metabolite levels over time. The focus is on both women of child-bearing age and children because urine levels of phthalate metabolites in both population groups have been associated with adverse children's health outcomes.

NHANES

Data for these indicators are from the National Health and Nutrition Examination Survey (NHANES). NHANES is a nationally representative survey designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population, conducted by the Centers for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted with approximately 5,000 people each year. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants.[62] Concentrations of phthalate metabolites in urine have been measured in a representative subset of NHANES participants ages 6 and older beginning with the 1999–2000 survey cycle. NHANES data from 1999–2006 for women of child-bearing age and children are used for Indicators PHTL1 and PHTL2.

Indicators PHTL1 and PHTL2 use data from all cycles of NHANES for which data have been reported (the 1999–2000 cycle through the 2005–2006 cycle) to show the trend over time for women ages 16 to 49 years and children ages 6 to 17 years.

Phthalate Metabolites

Both indicators present urinary metabolite levels of three important phthalates: dibutyl phthalate (DBP), butyl benzyl phthalate (BBzP), and di-2-ethylhexyl phthalate (DEHP). The primary urinary metabolites of DBP are mono-n-butyl phthalate (MnBP) and mono-isobutyl phthalate (MiBP). The urinary levels of MnBP and MiBP were measured together for the NHANES 1999–2000 survey cycle, but for the following years were measured separately. Indicators PHTL1 and PHTL2 present the combined urinary levels of MnBP and MiBP for each survey cycle. The primary urinary metabolite of BBzP is mono-benzyl phthalate (MBzP). For DEHP, three

metabolites are included: mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP).[i] The urinary levels of MEHP, MEOHP, and MEHHP are summed together, as is common in phthalates research, to provide a more complete picture of an individual's total DEHP exposure than is given by any individual metabolite.[48,63-65]

In NHANES and many research studies, biomonitoring of phthalates is conducted by measuring phthalate metabolites in urine rather than the phthalates themselves. This is because phthalates may be present in the sampling and laboratory equipment used to study human exposure levels, and contamination of samples could occur. Also phthalate metabolism is so rapid that the parent phthalate may not appear in urine.[10] Furthermore, the phthalate metabolites, and not the parent phthalates, are generally considered to be the biologically active molecules.[10,66] Unlike other contaminants that have a tendency to accumulate in the human body, phthalates are metabolized and excreted quickly, with elimination half-lives on the order of hours.[67] Therefore, phthalate metabolites measured in humans are indicative of recent exposures. In 2003–2006, the DBP metabolites and BBzP metabolite were detected in 99% of children ages 6 to 17 years and women ages 16 to 49 years. All three metabolites of DEHP were detected in about 75% of both groups. The widespread detection of phthalate metabolites, combined with the fact that phthalates have short half-lives, indicates that phthalate exposure is widespread and relatively continuous.

Creatinine Adjustment

NHANES data for phthalates are based on a single urine sample for each person surveyed, and can be subject to substantial variability due to normal changes in an individual's urinary output. For example, a urine sample from an individual who is dehydrated would be smaller in volume, and have a higher chemical concentration than if he or she were well-hydrated. This variability is due only to the volume of the urine sample and may mask differences between individuals in levels of phthalates.

The indicators therefore report phthalate metabolite measurements in micrograms per gram of creatinine, rather than micrograms per liter of urine, to help account for normal fluctuations in urine output. Creatinine is a byproduct of muscle metabolism that is excreted in urine at a relatively constant rate, independent of the volume of urine. The constant excretion of creatinine in urine allows for an adjustment that accounts for the measurement variability due to changes in urinary output.

Creatinine correction is widely used in urinary biomonitoring,[62] but the adjustment does have important limitations. Urinary creatinine concentrations can vary due to age, sex, diet, health status (specifically renal function), body-mass index, race/ethnicity, and pregnancy status.[68,69] Thus the creatinine adjustment improves the comparability of chemical measurements across individuals, but the variability in creatinine concentrations may still affect comparisons between individuals or populations.

[i] A fourth DEHP metabolite, mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), is now measured in NHANES but was not measured prior to 2003–2004. At least one other DEHP metabolite has been measured in laboratory studies but is not measured in NHANES.

Birthrate Adjustment

Indicator PHTL1 uses measurements of phthalate metabolites in urine of women ages 16 to 49 years to represent the distribution of children's prenatal exposures to phthalates. However, women of different ages have a different likelihood of giving birth. For example, in 2003–2004, women aged 27 years had a 12% annual probability of giving birth, and women aged 37 years had a 4% annual probability of giving birth.[70] A birthrate-adjusted distribution of women's urine phthalate metabolite levels is used in calculating this indicator, meaning that the data are weighted using the age-specific probability of a woman giving birth.[71]

Data Presented in the Indicators

Indicators PHTL1 and PHTL2 present median phthalate metabolite levels over time for women ages 16 to 49 years and children ages 6 to 17 years. The median is the value in the middle of the distribution of urinary phthalate metabolite levels: half of the individuals have urine levels greater than the median, and half have urine levels below the median. The median can be thought of as representing a typical exposure.

Additional information on the 95th percentile levels of urinary phthalates for both women of childbearing age and children is presented in the supplemental data tables for this indicator, along with information showing how urine levels of phthalates vary by race/ethnicity and family income.

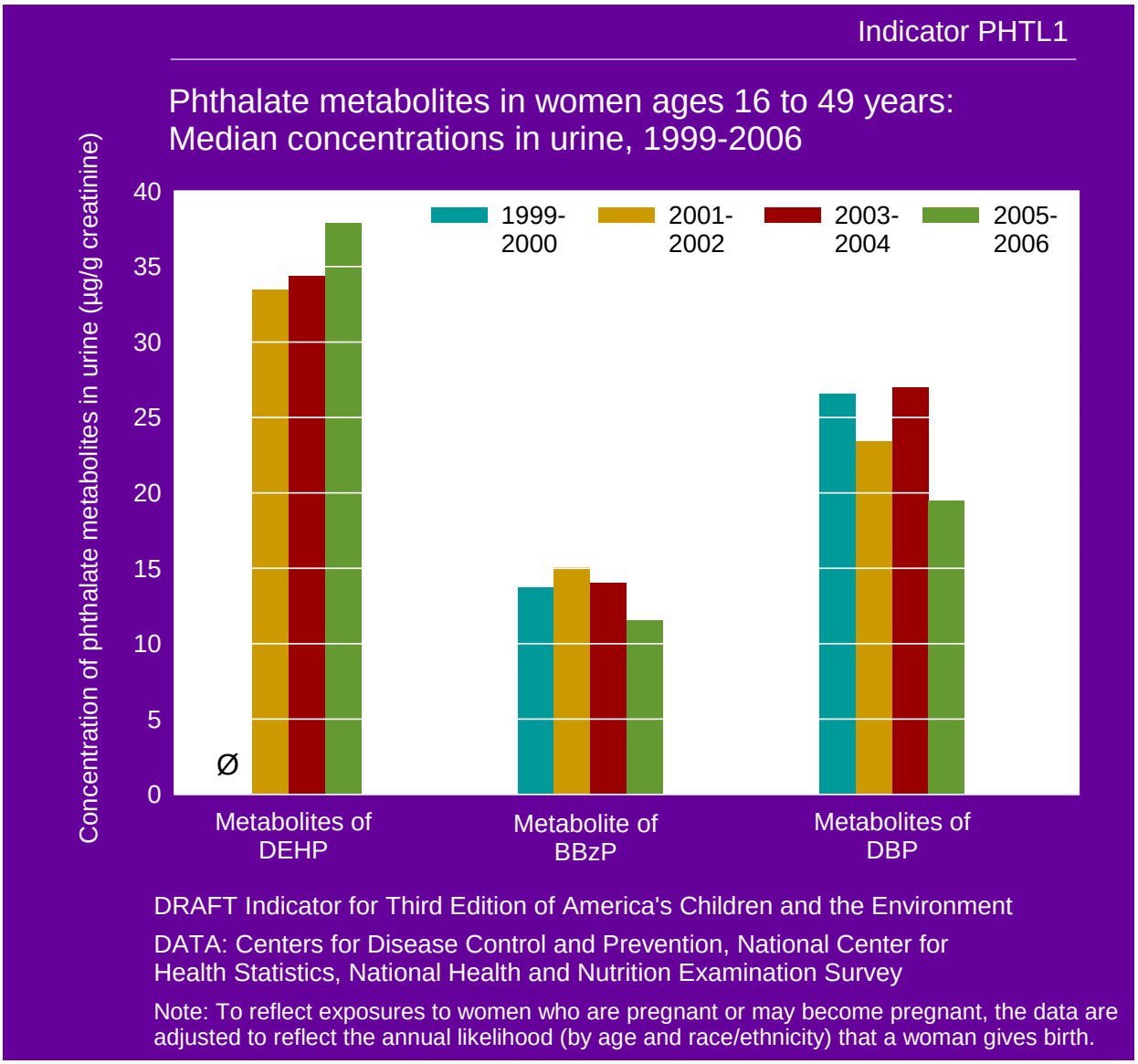
NHANES only provides phthalate metabolite data for children ages 6 years and older, which means that the indicator is not able to capture the exposure of premature infants, who may have high levels of phthalate exposure due to the use of medical equipment containing phthalates; or young children, whose play and mouthing behaviors may increase their exposure to phthalates in toys and house dust.

Statistical Testing

Statistical analysis has been applied to the biomonitoring indicators to determine whether any changes in chemical concentrations over time, or any differences in chemical concentrations between demographic groups, are statistically significant. These analyses use a 5% significance level ($p \leq 0.05$), meaning that a conclusion of statistical significance is made only when there is no more than a 5% chance that the observed change over time or difference between demographic groups occurred randomly. It should be noted that when statistical testing is conducted for differences among multiple demographic groups (e.g., considering both race/ethnicity and income level), the large number of comparisons involved increases the probability that some differences identified as statistically significant may actually have occurred randomly.

A finding of statistical significance for a biomonitoring indicator depends not only on the numerical difference in the value of a reported statistic between two groups, but also on the number of observations in the survey, the amount of variability among the observations, and various aspects of the survey design. For example, if two groups have different median levels of a chemical in blood or urine, the statistical test is more likely to detect a difference when samples

have been obtained from a larger number of people in those groups. Similarly, if there is low variability in levels of the chemical within each group, then a difference between groups is more likely to be detected. A finding that there is or is not a statistically significant difference in exposure levels between two groups or in exposure levels over time does not necessarily suggest any interpretation regarding the health implications of those differences.



Ø The estimate is not reported because the metabolites MEOHP and MEHHP were not measured in 1999–2000.

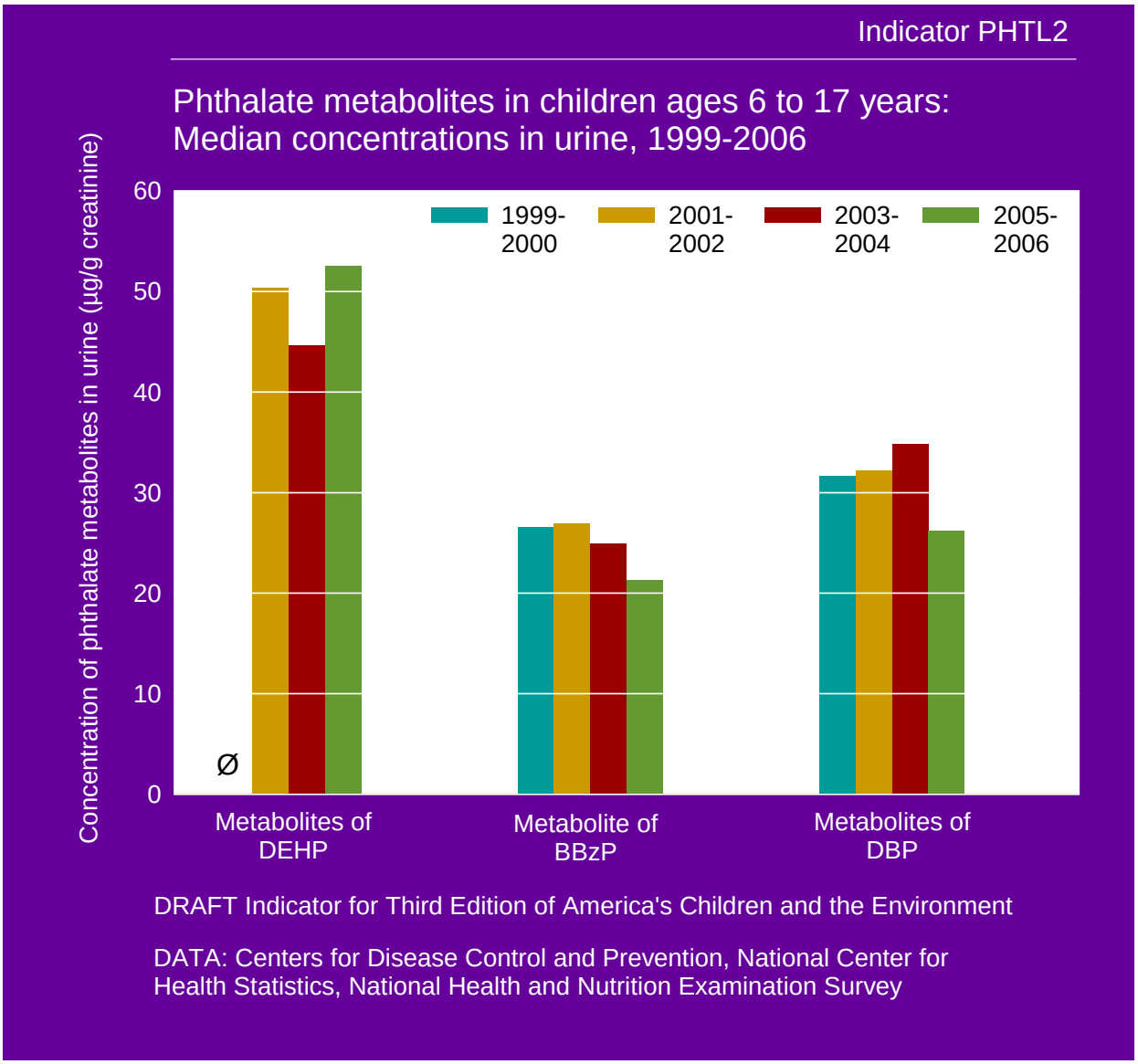
- Between 2001–2002 and 2005–2006, the median level of the DEHP metabolites (MEHP, MEOHP, and MEHHP) in women ages 16 to 49 years increased from 33.5 to 37.9 µg/g creatinine, although this increase was not statistically significant.

- In 1999–2000, the median levels of BBzP metabolite and DBP metabolites in women ages 16 to 49 years were 13.7 µg/g creatinine and 26.6 µg/g creatinine, respectively. In 2005–2006, the median levels of BBzP metabolite and DBP metabolites for women ages 16 to 49 years were 11.5 µg/g creatinine and 19.4 µg/g creatinine, respectively. The decline for BBzP metabolite was statistically significant but the decline for DBP metabolites was not.

- The combined concentrations of the DEHP metabolites (MEHP, MEOHP, and MEHHP) in the 95th percentile (5% of women have concentrations at this level or higher) range from 10 to 12 times higher than the median levels presented in this graph. The concentrations of BBzP and DBP metabolites in urine at the 95th percentile range from 3 to 6 times higher than the median levels presented in this graph. (See Table PHTL1a.)

- Median levels of these urinary phthalate metabolites generally do not vary significantly by race and ethnicity. (See Table PHTL1b.)

- Median levels of urinary phthalate metabolites vary by family income. Women living below the poverty level had higher concentrations of metabolites of DBP and BBzP in their urine compared with women living at or above the poverty level. Women living at or above the poverty level had higher levels of the DEHP metabolites (MEHP, MEOHP, and MEHHP) compared with women living below the poverty level. (See Table PHTL1b.)
    - Statistical note: The difference between income groups was only statistically significant for the DEHP metabolites after adjustment for demographic characteristics (differences in race/ethnicity or age profile above and below poverty) and for the BBzP metabolites without adjustment for demographic characteristics.



- In 1999–2000, the median levels of BBzP metabolite and DBP metabolites in children ages 6 to 17 years were 26.6 µg/g creatinine and 31.6 µg/g creatinine, respectively. In 2005–2006, the median levels of BBzP metabolite and DBP metabolites for children ages 6 to 17 years were 21.3 µg/g creatinine and 26.2 µg/g creatinine, respectively. Both declines were statistically significant. There has been no statistically significant change in the median levels of DEHP metabolites.

- Among children ages 6 to 17 years, the concentrations of metabolites of DBP and BBzP in urine at the 95th percentile (5% of children have concentrations at this level or higher) range from 4 to more than 6 times higher than the median levels. The combined concentrations of the DEHP metabolites (MEHP, MEOHP, and MEHHP) in the 95th percentile range from 6 to 8 times higher than the median levels presented in this graph.

(See Table PHTL2a.)

- For all the phthalate metabolites shown here, children living below the poverty level had higher median concentrations detected in their urine compared with children living at or above the poverty level, but these differences were not statistically significant. (See Table PHTL2b.)

- Median levels of urinary phthalate metabolites generally did not vary significantly by race and ethnicity among children ages 6 to 17 years. (See Table PHTL2b.)

- Children ages 6 to 10 years had the highest median levels of phthalate metabolites in their urine. In most cases, children ages 6 to 10 years had more than two times as much phthalate metabolite detected as adolescents ages 16 to 17 years. The age group differences were statistically significant. (See Table PHTL2c.)

Data Tables

Table PHTL1: Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine, 1999-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	1999-2000	2001-2002	2003-2004	2005-2006
DEHP metabolites	Ø	33.5	34.4	37.9
BBzP metabolite	13.7	15.1	14.0	11.5
DBP metabolites[ii]	26.6	23.4	27.0	19.4

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.
- The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.

Ø The estimate is not reported because the metabolites MEOHP and MEHHP were not measured in 1999-2000.

[ii] The primary urinary metabolites of DBP are mono-n-butyl phthalate (MnBP) and mono-isobutyl phthalate (MiBP). The urinary levels of MnBP and MiBP were measured together for the NHANES 1999–2000 survey cycle, but for the following years were measured separately. Indicators PHTL1 and PHTL2 present the combined urinary levels of MnBP and MiBP for each survey cycle.

Table PHTL1a: Phthalate metabolites in women ages 16 to 49 years: 95th percentile concentrations in urine, 1999-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	1999-2000	2001-2002	2003-2004	2005-2006
DEHP metabolites	Ø	355.3	408.6*	NA**
BBzP metabolite	NA**	85.9	62.3	58.4
DBP metabolites	114.5*	79.8	99.2	77.8

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.
- The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.
- Phthalates do not accumulate in bodily tissues; thus, the distribution of NHANES urinary phthalate metabolite levels may overestimate high-end exposures as a result of collecting one-time urine samples rather than collecting urine for a longer time period.[72]

* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

** The estimate is not reported because it has large uncertainty: the relative standard error, RSE, is at least 40% (RSE = standard error divided by the estimate).

Ø The estimate is not reported because the metabolites MEOHP and MEHHP were not measured in 1999-2000.

Table PHTL1b. Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine by race/ethnicity and family income, 2003-2006

		Concentration of phthalate metabolites in urine (µg/g creatinine)					
					≥Poverty (Detail)		
	Race / Ethnicity	All Incomes	< Poverty Level	≥ Poverty Level	100-200% of Poverty Level	> 200% of Poverty Level	Unknown Income
DEHP metabolites	All Races/ Ethnicities	35.2	32.2	36.5	34.6	39.8	NA**
	White non-Hispanic	36.6	31.0	39.8	37.8	39.8	NA**
	Black non-Hispanic	35.9	33.3	45.7	33.5	58.0	NA**
	Mexican-American	29.6	33.9	27.1	26.5	30.8	NA**
	Other†	38.0	26.8*	37.1	NA**	42.9	NA**
BBzP metabolite	All Races/ Ethnicities	12.8	16.9	11.9	15.8	11.0	11.5
	White non-Hispanic	13.3	15.3	12.8	17.9	12.3	13.5
	Black non-Hispanic	14.1	19.1	12.5	18.8	10.0	NA**
	Mexican-American	12.7	13.5	12.4	15.1	10.8	NA**
	Other†	10.3	17.8*	8.2	NA**	7.7	NA**
DBP metabolites	All Races/ Ethnicities	24.5	26.2	24.1	25.7	22.9	27.7
	White non-Hispanic	21.6	25.2	21.0	21.4	20.8	20.2*
	Black non-Hispanic	24.9	24.9	24.9	28.3	22.3	NA**
	Mexican-American	26.3	26.4	25.8	27.6	25.7	27.7*
	Other†	30.3	43.8*	30.3	29.4*	30.3	NA**

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.

- The distribution of the data for women ages 16 to 49 years is adjusted for the likelihood that a woman of a particular age and race/ethnicity gives birth in a particular year. The intent of this adjustment is to approximate the distribution of exposure to pregnant women. Results will therefore differ from a characterization of exposure to adult women without consideration of birthrates.

† "Other" includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

* The estimate should be interpreted with caution because the standard error of the estimate is relatively large: the relative standard error, RSE, is at least 30% but is less than 40% (RSE = standard error divided by the estimate).

** The estimate is not reported because it has large uncertainty: the relative standard error, RSE, is at least 40% (RSE = standard error divided by the estimate).

Table PHTL2: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, 1999-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	1999-2000	2001-2002	2003-2004	2005-2006
DEHP metabolites	Ø	50.4	44.7	52.5
BBzP metabolite	26.6	26.9	24.9	21.3
DBP metabolites	31.6	32.2	34.9	26.2

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTE: Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.

Ø The estimate is not reported because the metabolites MEOHP and MEHHP were not measured in 1999-2000.

Table PHTL2a: Phthalate metabolites in children ages 6 to 17 years: 95th percentile concentrations in urine, 1999-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	1999-2000	2001-2002	2003-2004	2005-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	1999-2000	2001-2002	2003-2004	2005-2006
DEHP metabolites	Ø	282.3	329.7	406.9
BBzP metabolite	114.3	163.2	160.5	109.3
DBP metabolites	117.0	131.4	139.2	103.9

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTES:

- Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.
- Phthalates do not accumulate in bodily tissues; thus, the distribution of NHANES urinary phthalate metabolite levels may overestimate high-end exposures as a result of collecting one-time urine samples rather than collecting urine for a longer time period.[72]

Ø The estimate is not reported because the metabolites MEOHP and MEHHP were not measured in 1999-2000.

Table PHTL2b. Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, by race/ethnicity and family income, 2003-2006

		Concentration of phthalate metabolites in urine (µg/g creatinine)					
	Race / Ethnicity	All Incomes	< Poverty Level	≥ Poverty Level	≥Poverty (Detail)		Unknown Income
					100-200% of Poverty Level	> 200% of Poverty Level	
DEHP metabolites	All Races/ Ethnicities	48.1	55.5	46.4	48.2	45.7	58.2
	White non-Hispanic	46.9	59.4	45.6	55.5	45.1	NA**
	Black non-Hispanic	48.6	53.7	46.5	47.6	46.5	40.4
	Mexican-American	43.8	45.2	42.0	44.3	38.3	NA**
	Other†	55.6	63.3	52.1	51.1	55.6	NA**
DEHP metabo:	All Races/ Ethnicities	23.0	25.1	22.6	28.5	21.6	20.8

		Concentration of phthalate metabolites in urine (µg/g creatinine)					
	Race / Ethnicity	All Incomes	< Poverty Level	≥ Poverty Level	≥Poverty (Detail)		Unknown Income
					100-200% of Poverty Level	> 200% of Poverty Level	
	White non-Hispanic	23.5	25.3	23.2	33.1	21.6	20.8
	Black non-Hispanic	21.2	25.5	19.4	19.5	19.0	16.8
	Mexican-American	21.0	20.2	22.0	18.7	23.9	14.8
	Other†	28.4	33.0	27.7	29.0	20.4	NA**
DBP metabolites	All Races/ Ethnicities	29.8	33.2	28.6	33.9	27.2	32.5
	White non-Hispanic	29.0	29.7	28.4	35.0	27.0	NA**
	Black non-Hispanic	30.5	37.4	27.6	29.5	27.1	32.5
	Mexican-American	31.6	33.2	30.8	28.6	31.6	NA**
	Other†	33.3	36.3	31.4	40.8	24.8	NA**

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTE: Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.

† "Other" includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

** The estimate is not reported because it has large uncertainty: the relative standard error, RSE, exceeds 40% (RSE = standard error divided by the estimate).

Table PHTL2c: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine by age group, 2003-2006

	Concentration of phthalate metabolites in urine (µg/g creatinine)			
	All Ages	6-10 Years	11-15 Years	16-17 Years
DEHP metabolites	48.1	68.8	41.3	33.2

BBzP metabolite	23.0	35.4	19.3	14.5
DBP metabolites	29.8	42.0	25.9	20.9

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health and Nutrition Examination Survey

NOTE: Values below the limit of detection are assumed equal to the limit of detection divided by the square root of 2.

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Metadata

Metadata for	National Health and Nutrition Examination Survey (NHANES)
Brief description of the data set	The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States, using a combination of interviews, physical examinations, and laboratory analysis of biological specimens.
Who provides the data set?	Centers for Disease Control and Prevention, National Center for Health Statistics.
How are the data gathered?	Laboratory data are obtained by analysis of blood and urine samples collected from survey participants at NHANES Mobile Examination Centers. Health status is assessed by physical examination. Demographic and other survey data regarding health status, nutrition and health-related behaviors are collected by personal interview, either by self-reporting or, for children under 16 and some others, as reported by an informant.
What documentation is available describing data collection procedures?	See http://www.cdc.gov/nchs/nhanes.htm for detailed survey and laboratory documentation by survey period.
What types of data relevant for children's environmental health indicators are available from this database?	Concentrations of environmental chemicals in urine, blood, and serum. Body measurements. Health status, as assessed by physical examination, laboratory measurements and interview responses. Demographic information.
What is the spatial representation of the database (national or other)?	NHANES sampling procedures provide nationally-representative data. Analysis of data for any other geographic area (region, state, etc.) is possible only by special arrangement with the NCHS Research Data Center, and such analyses may not be representative of the specified area.
Are raw data (individual measurements or survey responses) available?	Individual laboratory measurements and survey responses are generally available. Individual survey responses for some questions are not publicly released.
How are database files obtained?	http://www.cdc.gov/nchs/nhanes.htm
Are there any known data quality or data analysis concerns?	Some environmental chemicals have large percentages of values below the detection limit. Data gathered by interview, including demographic information, and responses regarding health status, nutrition and health-related behaviors are self-reported, or (for individuals age 16 years and younger) reported by an adult informant.

Metadata for	**National Health and Nutrition Examination Survey (NHANES)**
What documentation is available describing QA procedures?	http://www.cdc.gov/nchs/nhanes.htm includes detailed documentation on laboratory and other QA procedures. Data quality information is available at http://www.cdc.gov/nchs/about/policy/quality.htm.
For what years are data available?	Some data elements were collected in predecessors to NHANES beginning in 1959; collection of data on environmental chemicals began with measurement of blood lead in NHANES II, 1976-1980. The range of years for measurement of environmental chemicals varies; apart from lead and cotinine (initiated in NHANES III), measurement of environmental chemicals began with 1999-2000 or later NHANES.
What is the frequency of data collection?	Data are collected on continuous basis, but are grouped into NHANES cycles: NHANES II (1976-1980); NHANES III phase 1 (1988-1991); NHANES III phase 2 (1991-1994); and continuous two-year cycles beginning with 1999-2000 and continuing to the present.
What is the frequency of data release?	Data are released in two-year cycles (e.g. 1999-2000); particular data sets from a two-year NHANES cycle are released as available.
Are the data comparable across time and space?	Detection limits can vary across time, affecting some comparisons. Some contaminants are not measured in every NHANES cycle. Within any NHANES two-year cycle, data are generally collected and analyzed in the same manner for all sampling locations.
Can the data be stratified by race/ethnicity, income, and location (region, state, county or other geographic unit)?	Data are collected to be representative of the U.S. population based on age, sex, and race/ethnicity. The public release files allow stratification by these and other demographic variables, including family income range and poverty income ratio. Data cannot be stratified geographically except by special arrangement with the NCHS Research Data Center.

1

Methods

Indicator

Indicator PHTL1: Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine, 1999-2006

Indicator PHTL2: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, 1999-2006

Summary

Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention, has conducted the National Health and Nutrition Examination Surveys (NHANES), a series of U.S. national surveys of the health and nutrition status of the noninstitutionalized civilian population. The National Center for Environmental Health at CDC measures environmental chemicals in blood and urine samples collected from NHANES participants.[iii] This indicator uses creatinine-adjusted urine measurements of three phthalate metabolites in women ages 16 to 49 years and children ages 6 to 17 years. The three phthalate metabolites analyzed are mono-n-butyl phthalate (MBP), mono-benzyl phthalate (MBzP), and the sum of the three metabolites mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP). The NHANES 1999-2000, 2001-2002, 2003-2004, and 2005-2006 surveys included urine phthalate metabolite data for these three metabolites for children and adults ages 6 years and over, except that MEOHP and MEHHP were not measured in 1999-2000. Indicator PHTL1 gives the trend in the median creatinine-adjusted concentrations of the phthalate metabolites for women ages 16 to 49 years for 1999-2006. The median is the estimated concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have a phthalate metabolite concentration below this level; the population distribution was adjusted by age-specific birthrates to estimate the median pre-natal exposure to phthalate metabolites. Table PHTL1a gives the 95th percentile creatinine-adjusted concentrations of phthalate metabolites for women ages 16 to 49 years for 1999-2006. The 95th percentile for women is the estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have a phthalate metabolite concentration below this level. Table PHTL1b gives the median concentration of phthalate metabolites for women ages 16 to 49 in 2003-2006, stratified both by race/ethnicity and family income. Indicator PHTL2 presents the trend in the median creatinine-adjusted concentrations of the phthalate metabolites for children ages 6 to 17 years for 1999-2006. Table PHTL2a presents the trend in the 95th percentile concentration of phthalate metabolites for children ages 6 to 17 in 1999-2006. Table PHTL2b displays the median concentration of phthalate metabolites for children ages 6 to 17 years in 2003-2006, stratified both by race/ethnicity and family income. Table PHTL2c displays the

[iii] Centers for Disease Control and Prevention. 2009. Fourth National Report on Human Exposure to Environmental Chemicals. Atlanta, GA. Available at: www.cdc.gov/exposurereport.

median concentration of phthalate metabolites for children ages 6 to 17 in 2003-2006, stratified by age. The survey data were weighted to account for the complex multi-stage, stratified, clustered sampling design.

Data Summary

Women ages 16 to 49 years

Indicator		Indicator PHTL1: Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine, 1999-2006			
Time Period		1999-2006			
Data		Urine phthalate metabolites (creatinine adjusted) in women ages 16 to 49			
MBP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	0.9	1.1	0.4	0.6
	Number of Non-missing Values**	618	659	606	616
	Number of Missing Values	24	29	20	18
	Percentage Below Limit of Detection***	2	23	2	1
MBzP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	0.8	0.3	0.1	0.3
	Number of Non-missing Values**	618	659	606	616
	Number of Missing Values	24	29	20	18
	Percentage Below Limit of Detection***	1	1	0	2
MEHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	1.2	1.0	0.9	1.2
	Number of Non-missing Values**	618	659	606	616
	Number of Missing Values	24	29	20	18
	Percentage Below Limit of Detection***	21	19	23	27
MEOHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	No data	1.1	0.4	0.7

Indicator		Indicator PHTL1: Phthalate metabolites in women ages 16 to 49 years: Median concentrations in urine, 1999-2006			
Time Period		1999-2006			
Data		Urine phthalate metabolites (creatinine adjusted) in women ages 16 to 49			
	Number of Non-missing Values**	0	659	606	616
	Number of Missing Values	0	29	20	18
	Percentage Below Limit of Detection***	No data	6	0	1
MEHHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	No data	1.0	0.3	0.7
	Number of Non-missing Values**	0	659	606	616
	Number of Missing Values	0	29	20	18
	Percentage Below Limit of Detection***	No data	3	0	0

* The Limit of Detection (LOD) is defined as the level at which the measurement has a 95% probability of being greater than zero.
**Non-missing values include those below the analytical LOD, which are reported as LOD/√2.
***This percentage is survey-weighted using the NHANES survey weights for the given period and is weighted by age-specific birthrates.

Children ages 6 to 17 years

Indicator		Indicator PHTL2: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, 1999-2006			
Time Period		1999-2006			
Data		Urine phthalate metabolites (creatinine adjusted) in children ages 6 to 17			
MBP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	0.9	1.1	0.4	0.6
	Number of Non-missing Values**	900	960	895	896
	Number of Missing Values	40	45	36	31
	Percentage Below Limit of Detection***	0	17	1	0
MBZ	Years	1999-2000	2001-2002	2003-2004	2005-2006

Indicator		Indicator PHTL2: Phthalate metabolites in children ages 6 to 17 years: Median concentrations in urine, 1999-2006			
Time Period		1999-2006			
Data		Urine phthalate metabolites (creatinine adjusted) in children ages 6 to 17			
	Limits of Detection (ng/mL)*	0.8	0.3	0.11	0.3
	Number of Non-missing Values**	900	960	895	896
	Number of Missing Values	40	45	36	31
	Percentage Below Limit of Detection***	1	0	0	1
MEHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	1.2	1.0	0.9	1.2
	Number of Non-missing Values**	900	960	895	896
	Number of Missing Values	40	45	36	31
	Percentage Below Limit of Detection***	15	16	26	26
MEOHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	No data	1.1	0.4	0.7
	Number of Non-missing Values**	0	960	895	896
	Number of Missing Values	0	45	36	31
	Percentage Below Limit of Detection***	No data	1	0	0
MEHHP	Years	1999-2000	2001-2002	2003-2004	2005-2006
	Limits of Detection (ng/mL)*	No data	1.0	0.3	0.7
	Number of Non-missing Values**	0	960	895	896
	Number of Missing Values	0	45	36	31
	Percentage Below Limit of Detection***	No data	1	0	0

* The Limit of Detection (LOD) is defined as the level at which the measurement has a 95% probability of being greater than zero.
**Non-missing values include those below the analytical LOD, which are reported as LOD/√2.
***This percentage is survey-weighted using the NHANES survey weights for the given period and is weighted by age-specific birthrates.

Overview of Data Files

The following files are needed to calculate this indicator. The files together with the survey documentation and SAS programs for reading in the data are available at the NHANES website: http://www.cdc.gov/nchs/nhanes.htm.

- NHANES 1999-2000: Demographic file demo.xpt. Urinary Phthalates, Urinary PAHs, and Urinary Phytoestrogens Laboratory file phpypa.xpt. The demographic file demo.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The Urinary Phthalates, Urinary PAHs, and Urinary Phytoestrogens laboratory file phpypa.xpt contains SEQN, the three phthalate metabolite concentrations (URXMBP, URXMZP, URXMHP), urine creatinine (URXUCR) and the sub-sample survey weight (WTSPH2YR). The two files are merged using the common variable SEQN.

- NHANES 2001-2002: Demographic file demo_b.xpt. Urinary Phthalates, Urinary PAHs, and Urinary Phytoestrogens Laboratory file phpypa_b.xpt. The demographic file demo_b.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The Urinary Phthalates, Urinary PAHs, and Urinary Phytoestrogens laboratory file phpypa_b.xpt contains SEQN, the five phthalate metabolite concentrations (URXMBP, URXMZP, URXMHP, URXMOH, URXMHH), urine creatinine (URXUCR) and the sub-sample survey weight (WTSPH2YR). The two files are merged using the common variable SEQN.

- NHANES 2003-2004: Demographic file demo_c.xpt. Urinary Phthalates Laboratory file l24ph_c.xpt. The demographic file demo_c.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The Urinary Phthalates laboratory file l24ph_c.xpt contains SEQN, the five phthalate metabolite concentrations (URXMBP, URXMZP, URXMHP, URXMOH, URXMHH), the five phthalate metabolite non-detect comment codes (URDMBPLC, URDMZPLC, URDMHPLC, URDMOHLC, URDMHHLC), urine creatinine (URXUCR) and the sub-sample B survey weight (WTSB2YR). The two files are merged using the common variable SEQN.

- NHANES 2005-2006: Demographic file demo_d.xpt. Urinary Phthalates Laboratory file phthte_d.xpt. The demographic file demo_d.xpt is a SAS transport file that contains the subject identifier (SEQN), age (RIDAGEYR), sex (RIAGENDR), race/ethnicity (RIDRETH1), poverty income ratio (INDFMPIR), pseudo-stratum (SDMVSTRA) and the pseudo-PSU (SDMVPSU). The Urinary Phthalates laboratory file phthte_d.xpt

contains SEQN, the five phthalate metabolite concentrations (URXMBP, URXMZP, URXMHP, URXMOH, URXMHH), the five phthalate metabolite non-detect comment codes (URDMBPLC, URDMZPLC, URDMHPLC, URDMOHLC, URDMHHLC), urine creatinine (URXUCR) and the sub-sample B survey weight (WTSB2YR). The two files are merged using the common variable SEQN.

National Health and Nutrition Examination Surveys (NHANES)

Since the 1970s, the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention, has conducted the National Health and Nutrition Examination Surveys (NHANES), a series of U.S. national surveys of the health and nutrition status of the noninstitutionalized civilian population. The National Center for Environmental Health at CDC measures environmental chemicals in blood and urine samples collected from NHANES participants. This indicator uses urine phthalate metabolite concentration measurements for the five metabolites listed in the following table from NHANES 1999-2000, 2001-2002, 2003-2004, and 2005-2006 in women ages 16 to 49 and children ages 6 to 17. The NHANES data were obtained from the NHANES website: http://www.cdc.gov/nchs/nhanes.htm. Following the CDC recommended approach, values below the analytical limit of detection (LOD) were replaced by LOD/√2.[iv]

Phthalate metabolite	Full name	SAS name	SAS name for non-detect comment code*
MBP	mono-n-butyl phthalate	URXMBP	URDMBPLC
MBzP	mono-benzyl phthalate	URXMZP	URDMZPLC
MEHP	mono-2-ethylhexyl phthalate	URXMHP	URDMHPLC
MEOHP	mono-(2-ethyl-5-oxohexyl) phthalate	URXMOH	URDMOHLC
MEHHP	mono-(2-ethyl-5-hydroxyhexyl) phthalate	URXMHH	URDMHHLC

*The non-detect comment code equals 1 if the measurement is below the analytical limit of detection, and equals 0 if the measurement is at or above the analytical limit of detection. The non-detect comment code variables were not included in NHANES 1999-2000 and 2001-2002.

This analysis uses the creatinine-adjusted urine phthalate metabolite concentrations (µg/g creatinine). The unadjusted phthalate metabolite concentration is reported as ng/mL, which is the same as µg/L. The creatinine concentration is reported as mg/dL. The creatinine-adjusted phthalate metabolite concentration was calculated from the raw data as the ratio Unadjusted phthalate metabolite/(0.01× Creatinine) µg/g creatinine. The analytes studied are MBP, MBzP,

[iv] See Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of nondetectable values. *Applied Occupational and Environmental Hygiene* 5:46–51.

and the sum of MEHP, MEOHP, and MEHHP. In NHANES 1999-2000, MEOHP and MEHHP were not measured and the sum of MEHP, MEOHP, and MEHHP is missing. In NHANES 2001-2002, 2003-2004, and 2005-2006, every sample measurement either had all three of MEHP, MEOHP, and MEHHP, or none of these phthalate metabolites.

The NHANES use a complex multi-stage, stratified, clustered sampling design. Certain demographic groups were deliberately over-sampled, including Mexican-Americans and Blacks. Oversampling is performed to increase the reliability and precision of estimates of health status indicators for these population subgroups. The publicly released data includes survey weights to adjust for the over-sampling, non-response, and non-coverage. The statistical analyses used the sub-sample laboratory survey weights (WTSPH2YR for 1999-2000 and 2001-2002 and WTSB2YR for 2003-2004 and 2005-2006) to re-adjust the urine phthalate metabolite data to represent the national population.

Age-Specific Birthrates

In addition to the NHANES survey weights, the data for women of child-bearing age (ages 16 to 49) were also weighted by the birthrate for women of the given age and race/ethnicity to estimate pre-natal exposures. Thus the overall weight in each two year period is the product of the NHANES survey weight and the total number of births in the two calendar years for the given age and race/ethnicity, divided by twice the corresponding population of women at the midpoint of the two year period.[v]

Race/Ethnicity and Family Income

For this indicator, the percentiles were calculated for demographic strata defined by the combination of race/ethnicity and family income.

The family income was characterized based on the INDFMPIR variable, which is the ratio of the family income to the poverty level. The National Center for Health Statistics used the U.S. Census Bureau Current Population Survey to define the family units, and the family income for the respondent was obtained during the interview. The U.S. Census Bureau defines annual poverty level money thresholds varying by family size and composition. The poverty income ratio (PIR) is the family income divided by the poverty level for that family. Family income was stratified into the following groups:

- Below Poverty Level: PIR < 1
- Between 100% and 200% of Poverty Level: 1 ≤ PIR ≤ 2
- Above 200% of Poverty level: PIR > 2
- Above Poverty Level: PIR ≥ 1 (combines the previous two groups)
- Unknown Income: PIR is missing

[v]Axelrad, D.A., Cohen, J. 2010. Calculating summary statistics for population chemical biomonitoring in women of childbearing age with adjustment for age-specific natality. *Environmental Research* 111 (1): 149-155.

Race/ethnicity was characterized using the RIDRETH1 variable. The possible values of this variable are:

- 1. Mexican American
- 2. Other Hispanic
- 3. Non-Hispanic White
- 4. Non-Hispanic Black
- 5. Other Race – Including Multi-racial
- "." Missing

Category 5 includes: all Non-Hispanic single race responses other than White or Black; and multi-racial responses.

For this indicator, the RIDRETH1 categories 2, 5, and missing were combined into a single "Other" category. This produced the following categories:

- White non-Hispanic: RIDRETH1 = 3
- Black non-Hispanic: RIDRETH1 = 4
- Mexican-American: RIDRETH1 = 1
- Other: RIDRETH1 = 2 or 5 or missing

The "Other" category includes Asian non-Hispanic; Native American non-Hispanic; Hispanic other than Mexican-American; those reporting multi-racial; and those with a missing value for race/ethnicity.

Calculation of Indicator

Indicator PHTL1 is the median for urine phthalate metabolites in women of ages 16 to 49 years, stratified by NHANES survey cycle. The median for women ages 16 to 49 is the estimated concentration such that 50% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have urine phthalate metabolites concentrations below this level. To adjust the NHANES data to represent pre-natal exposures, the data for each woman surveyed was multiplied by the estimated number of births per woman of the given age and race/ethnicity. Indicator PHTL2 is the median for urine phthalate metabolites in children of ages 6 to 17 years, stratified by NHANES survey cycle. The birthrate adjustment was not applied to children ages 6 to 17. Table PHTL1a is the 95th percentile for urine phthalate metabolites in women of ages 16 to 49 years, stratified by NHANES survey cycle. The 95th percentile for women ages 16 to 49 is the estimated concentration such that 95% of all noninstitutionalized civilian women ages 16 to 49 years during the survey period have urine phthalate metabolites concentrations below this level. Table PHTL1b is the median for urine phthalate metabolites in women of ages 16 to 49 years in 2003-2006, stratified by race/ethnicity and family income. Table PHTL2a is the 95th percentile for urine phthalate metabolites in children of ages 6 to 17, stratified by NHANES survey cycle. Table PHTL2b is the median for urine phthalate metabolites in children of ages 6 to 17 years in 2003-2006, stratified by race/ethnicity and family income. Table PHTL2c is the median concentration of phthalate metabolites for children ages 6 to 17 in 2003-2006, stratified by age.

To simply demonstrate the calculations, we will use the NHANES 2005-2006 creatinine-adjusted urine MBP values for women ages 16 to 49 years of all race/ethnicities and all incomes as an example. We have rounded all the numbers to make the calculations easier:

We begin with all the non-missing NHANES 2005-2006 urine MBP values for women ages 16 to 49 years. Assume for the sake of simplicity that valid MBP data were available for every sampled woman. Each sampled woman has an associated annual survey weight that estimates the annual number of U.S. women represented by that sampled woman. For 2005-2006, the associated annual survey weight for each woman is defined as WTSPH2YR. Each sampled woman also has an associated birthrate giving the numbers of annual births per woman of the given age, race, and ethnicity. The product of the annual survey weight and the birthrate estimates the annual number of U.S. births represented by that sampled woman, which we will refer to as the adjusted survey weight. For example, the lowest urine MBP measurement for a woman between 16 and 49 years of age is 1.5 μg/g creatinine with an annual survey weight of 100,000, a birthrate of 0.03, and thus an adjusted survey weight of 3,000, and so represents 3,000 births. The total of the adjusted survey weights for the sampled women equals 4 million, the total number of annual U.S. births to women ages 16 to 49 years. The second lowest measurement is 2.2 μg/g creatinine with an adjusted survey weight of 23,000, and so represents another 23,000 U.S. births. The highest measurement is 402.9 μg/g creatinine with an adjusted survey weight of 1,000, and so represents another 1,000 U.S. births.

To calculate the median, we can use the adjusted survey weights to expand the data to the entire U.S. population of births to women ages 16 to 49. We have 3,000 values of 1.5 μg/g creatinine from the lowest measurement, 23,000 values of 2.2 μg/g creatinine from the second lowest measurement, and so on, up to 1,000 values of 402.9 μg/g creatinine from the highest measurement. Arranging these 4 million values in increasing order, the 2 millionth value is 19.4 μg/g creatinine. Since half of the values are below 19.4 and half of the values are above 19.4, the median equals 19.4 μg/g creatinine. To calculate the 95th percentile, note that 95% of 4 million equals 3.8 million. The 3.8 millionth value is 77.8 μg/g creatinine. Since 95% of the values are below 77.8, the 95th percentile equals 77.8 μg/g creatinine.

In reality, the calculations need to take into account that urine MBP measurements were not available for every respondent, and to use exact rather than rounded numbers. There were urine MBP measurements for only 616 of the 634 sampled women ages 16 to 49 years. The adjusted survey weights for all 634 sampled women add up to 4.2 million, the U.S. population of births to women ages 16 to 49. The adjusted survey weights for the 616 sampled women with urine MBP data add up to 4.1 million. Thus the available data represent 4.1 million values and so represent only 97% of the U.S. population of births. The median and 95th percentiles are given by the 2.05 millionth (50% of 4.1 million) and 3.90 millionth (95% of 4.1 million) U.S. birth's value. These calculations assume that the sampled women with valid urine MBP data are representative of women giving birth without valid urine MBP data. The calculations also assume that the sampled women are representative of women that actually gave birth in 2005-2006, since NHANES information on pregnancy and births was not incorporated into the analysis.

Equations

These percentile calculations can also be given as the following mathematical equations, which are based on the default percentile calculation formulas from Statistical Analysis System (SAS) software. Exclude all missing urine MBP values. Suppose there are n women of ages 16 to 49 years with valid urine MBP values. Arrange the urine MBP concentrations in increasing order (including tied values) so that the lowest concentration is x(1) with an adjusted survey weight of w(1), the second lowest concentration is x(2) with an adjusted survey weight of w(2), …, and the highest concentration is x(n) with an adjusted survey weight of w(n).

1. Sum all the adjusted survey weights to get the total weight W:

$$W = \Sigma[1 \le i \le n]\ w(i)$$

2. Find the largest number i so that the total of the weights for the i lowest values is less than or equal to W/2.

$$\Sigma[j \le i]\ w(j) \le W/2 < \Sigma[j \le i + 1]\ w(j)$$

3. Calculate the median using the results of the second step. We either have

$$\Sigma[j \le i]\ w(j) = W/2 < \Sigma[j \le i + 1]\ w(j)$$

or

$$\Sigma[j \le i]\ w(j) < W/2 < \Sigma[j \le i + 1]\ w(j)$$

In the first case we define the median as the average of the i'th and i + 1'th values:

$$\text{Median} = [x(i) + x(i + 1)]/2 \text{ if } \Sigma[j \le i]\ w(j) = W/2$$

In the second case we define the median as the i + 1'th value:

$$\text{Median} = x(i + 1) \text{ if } \Sigma[j \le i]\ w(j) < W/2$$

(The estimated median does not depend upon how the tied values of x(j) are ordered).

A similar calculation applies to the 95th percentile. The first step to calculate the sum of the weights, W, is the same. In the second step, find the largest number i so that the total of the weights for the i lowest values is less than or equal to 0.95W.

$$\Sigma[j \le i]\ w(j) \le 0.95W < \Sigma[j \le i + 1]\ w(j)$$

In the third step we calculate the 95th percentile using the results of the second step. We either have

$$\Sigma[j \le i]\ w(j) = 0.95W < \Sigma[j \le i + 1]\ w(j)$$

or

$$\Sigma[j \le i]\ w(j) < 0.95W < \Sigma[j \le i + 1]\ w(j)$$

In the first case we define the 95th percentile as the average of the i'th and i + 1'th values:

$$95^{th}\ \text{Percentile} = [x(i) + x(i + 1)]/2 \text{ if } \Sigma[j \le i]\ w(j) = 0.95W$$

In the second case we define the 95th percentile as the i + 1'th value:

$$95^{th}\ \text{Percentile} = x(i + 1) \text{ if } \Sigma[j \le i]\ w(j) < 0.95W$$

Relative Standard Error

The uncertainties of the median and 95th percentile values were calculated using a revised version of the CDC method given in CDC 2005,[vi] Appendix C, and the SAS® program provided by CDC. The method uses the Clopper-Pearson binomial confidence intervals adapted for complex surveys by Korn and Graubard (see Korn and Graubard, 1999,[vii] p. 65). The following text is a revised version of the Appendix C. For the birthrate adjusted calculations for women ages 16 to 49, the sample weight is adjusted by multiplying by the age-specific birthrate.

Step 1: Use SAS® Proc Univariate to obtain a point estimate P_{SAS} of the percentile value. Use the Weight option to assign the exact correct sample weight for each chemical result.

Step 2: Use SUDAAN® Proc Descript with Taylor Linearization DESIGN = WR (i.e., sampling with replacement) and the proper sampling weight to estimate the proportion (p) of subjects with results less than and not equal to the percentile estimate P_{SAS} obtained in Step 1 and to obtain the standard error (se_p) associated with this proportion estimate. Compute the degrees-of-freedom adjusted effective sample size

$$n_{df} = (t_{num}/t_{denom})^2\ p(1 - p)/(se_p{}^2)$$

where t_{num} and t_{denom} are 0.975 critical values of the Student's t distribution with degrees of freedom equal to the sample size minus 1 and the number of PSUs minus the number of strata, respectively. Note: the degrees of freedom for t_{denom} can vary with the demographic sub-group of interest.

Step 3: After obtaining an estimate of p (i.e., the proportion obtained in Step 2), compute the Clopper-Pearson 95% confidence interval ($P_L(x,n_{df})$, $P_U(x,n_{df})$) as follows:

$$P_L(x,n_{df}) = v_1F_{v1,v2}\,(0.025)/(v_2 + v_1F_{v1,v2}(0.025))$$
$$P_U(x,n_{df}) = v_3F_{v3,v4}\,(0.975)/(v_4 + v_3F_{v3,v4}(0.975))$$

[vi] CDC Third National Report on Human Exposure to Environmental Chemicals. 2005
[vii] Korn E. L., Graubard B. I. 1999. *Analysis of Health Surveys.* Wiley.

where x is equal to p times n_{df}, $v_1 = 2x$, $v_2 = 2(n_{df} - x + 1)$, $v_3 = 2(x + 1)$, $v_4 = 2(n_{df} - x)$, and $F_{d1,d2}(\beta)$ is the β quantile of an F distribution with d1 and d2 degrees of freedom. (Note: If n_{df} is greater than the actual sample size or if p is equal to zero, then the actual sample size should be used.) This step will produce a lower and an upper limit for the estimated proportion obtained in Step 2.

Step 4: Use SAS Proc Univariate (again using the Weight option to assign weights) to determine the chemical percentile values P_{CDC}, L_{CDC} and U_{CDC} that correspond to the proportion p obtained in Step 2 and its lower and upper limits obtained in Step 3. Do not round the values of p and the lower and upper limits. For example, if p = 0.4832, then P_{CDC} is the 48.32'th percentile value of the chemical. The alternative percentile estimates P_{CDC} and P_{SAS} are not necessarily equal.

Step 5: Use the confidence interval from Step 4 to estimate the standard error of the estimated percentile P_{CDC}:

$$\text{Standard Error } (P_{CDC}) = (U_{CDC} - L_{CDC}) / (2t_{denom})$$

Step 6: Use the estimated percentile P_{CDC} and the standard error from Step 4 to estimate the relative standard error of the estimated percentile P_{CDC}:

$$\text{Relative Standard Error (\%)} = [\text{Standard Error } (P_{CDC}) / P_{CDC}] \times 100\%$$

The tabulated estimated percentile is the value of P_{SAS} given in Step 1. The relative standard error is given in Step 6, using P_{CDC} and its standard error.

The relative standard error depends upon the survey design. For this purpose, the public release version of NHANES includes the variables SDMVSTRA and SDMVPSU, which are the Masked Variance Unit pseudo-stratum and pseudo-primary sampling unit (pseudo-PSU). For approximate variance estimation, the survey design can be approximated as being a stratified random sample with replacement of the pseudo-PSUs from each pseudo-stratum; the true stratum and PSU variables are not provided in the public release version to protect confidentiality.

Percentiles with a relative standard error less than 30% were treated as being reliable and were tabulated. Percentiles with a relative standard error greater than or equal to 30% but less than 40% were treated as being unstable; these values were tabulated but were flagged to be interpreted with caution. Percentiles with a relative standard error greater than or equal to 40%, or without an estimated relative standard error, were treated as being unreliable; these values were not tabulated and were flagged as having a large uncertainty.

Questions and Comments

Questions regarding these methods, and suggestions to improve the description of the methods, are welcome. Please use the "Contact Us" link at the bottom of any page in the America's Children and the Environment website.

Statistical Comparisons

Statistical analyses of the percentiles were used to determine whether the differences between percentiles for different demographic groups were statistically significant. For these analyses, the percentiles and their standard errors were calculated for each combination of age group, sex, income group (below poverty, at or above poverty, unknown income), and race/ethnicity group using the method described in the "Relative Standard Error" section. In the notation of that section, the percentile and standard error are the values of P_{CDC} and Standard Error (P_{CDC}), respectively. These calculated standard errors account for the survey weighting and design and, for women, for the age-specific birthrate.

Using a weighted linear regression model, the percentile was assumed to be the sum of explanatory terms for age, sex, income and/or race/ethnicity and a random error term; the error terms were assumed to be approximately independent and normally distributed with a mean of zero and a variance equal to the square of the standard error. Using this model, the difference in the value of a percentile between different demographic groups is statistically significant if the difference between the corresponding sums of explanatory terms is statistically significantly different from zero. A p-value at or below 0.05 implies that the difference is statistically significant at the 5% significance level. No adjustment is made for multiple comparisons.

For each type of comparison, we present unadjusted and adjusted analyses. The unadjusted analyses directly compare a percentile between different demographic groups. The adjusted analyses add other demographic explanatory variables to the statistical model and use the statistical model to account for the possible confounding effects of these other demographic variables. For example, the unadjusted race/ethnicity comparisons use and compare the percentiles between different race/ethnicity pairs. The adjusted race/ethnicity comparisons use the percentiles for each age/sex/income/race/ethnicity combination. The adjusted analyses add age, sex, and income terms to the statistical model and compare the percentiles between different race/ethnicity pairs after accounting for the effects of the other demographic variables. For example, if White non-Hispanics tend to have higher family incomes than Black non-Hispanics, and if the level of a chemical strongly depends on family income only, then the unadjusted differences between these two race/ethnicity groups would be significant but the adjusted difference (taking into account income) would not be significant.

Comparisons between pairs of race/ethnicity groups are shown in Tables 1 and 2 for women ages 16 to 49 years and in Tables 4 and 5 for children ages 6 to 17 years. In Tables 1 and 4, for the unadjusted "All incomes" comparisons, the only explanatory variables are terms for each race/ethnicity group. For these unadjusted comparisons, the statistical tests compare the percentiles for each pair of race/ethnicity groups. For the adjusted "All incomes (adjusted for age, sex, income)" comparisons, the explanatory variables are terms for each race/ethnicity group together with terms for each age, sex, and income group. For these adjusted comparisons, the statistical test compares the pair of race/ethnicity groups after accounting for any differences in the age, sex and income distributions between the race/ethnicity groups. The adjustment for sex is applicable only to the analyses for children, and thus appears only in Tables 4, 5, and 6.

In Tables 1 and 4, for the unadjusted "Below Poverty Level" and "At or Above Poverty Level" comparisons, the only explanatory variables are terms for each of the twelve race/ethnicity/income combinations (combinations of four race/ethnicity groups and three income groups). For example, in row 1, the p-value for "Below Poverty Level" compares White non-Hispanics below the poverty level with Black non-Hispanics below the poverty level.

The same set of explanatory variables are used in Tables 2 and 5 for the unadjusted comparisons between one race/ethnicity group below the poverty level and the same or another race/ethnicity group at or above the poverty level. The corresponding adjusted analyses include extra explanatory variables for age and (in the case of children) sex, so that race/ethnicity/income groups are compared after accounting for any differences due to age or sex.

Additional comparisons are shown in Table 3 for women ages 16 to 49 years and in Table 6 for children ages 1 to 5 years. The AGAINST = "income" unadjusted p-value compares the chemical levels for those below poverty level with those at or above poverty level, using the explanatory variables for the three income groups (below poverty, at or above poverty, unknown income). The adjusted p-value includes adjustment terms for age, sex, and race/ethnicity in the model. The AGAINST = "age" p-value compares the given age groups to see if the chemical levels are significantly different among age groups; the adjusted p-value includes adjustment terms for sex (for children), income, and race/ethnicity. The AGAINST = "yearnum" p-value examines whether the linear trend is statistically significant (using the percentiles for each NHANES period regressed against the midpoint of that period); the adjusted model for trend adjusts for demographic changes in the populations from year to year by including terms for age, sex, income, and race/ethnicity.

For women, the age groups used were 16-19, 20-24, 25-29, 30-39, and 40-49. For children, the age groups used were 6-10, 11-15, and 16-17.

For more details on these statistical analyses, see the memorandum by Cohen (2010).[viii]

Table 1. Statistical significance tests comparing the percentiles of phthalate metabolites in women ages 16 to 49 years, between pairs of race/ethnicity groups, for 2003-2006.

				P-VALUES					
Variable	**Percentile**	**RACE1**	**RACE2**	**All incomes**	**All incomes (adjusted for age, income)**	**Below Poverty Level**	**Below Poverty Level (adjusted for age)**	**At or Above Poverty Level**	**At or Above Poverty Level (adjusted for age)**
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic	Black non-Hispanic	0.967	0.467	0.816	0.882	0.510	0.918
Sum of MEHP,	50	White non-Hispanic	Mexican-American	0.116	0.003	0.778	0.851	0.010	0.037

[viii] Cohen, J. 2010. *Selected statistical methods for testing for trends and comparing years or demographic groups in ACE NHIS and NHANES indicators.* Memorandum submitted to Dan Axelrad, EPA, 21 March, 2010.

				P-VALUES					
Variable	**Percentile**	**RACE1**	**RACE2**	**All incomes**	**All incomes (adjusted for age, income)**	**Below Poverty Level**	**Below Poverty Level (adjusted for age)**	**At or Above Poverty Level**	**At or Above Poverty Level (adjusted for age)**
MEOHP, and MEHHP									
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic	Other	0.753	0.010	0.684	0.702	0.608	0.001
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic	Mexican-American	0.317	0.138	0.916	0.969	0.023	0.185
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic	Other	0.781	0.204	0.429	0.413	0.360	0.026
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American	Other	0.150	0.852	0.423	0.184	0.251	0.315
MBzP	50	White non-Hispanic	Black non-Hispanic	0.742	0.904	0.289	0.475	0.851	0.371
MBzP	50	White non-Hispanic	Mexican-American	0.412	0.209	0.604	0.262	0.803	0.358
MBzP	50	White non-Hispanic	Other	0.148	0.028	0.706	0.059	0.018	0.875
MBzP	50	Black non-Hispanic	Mexican-American	0.388	0.242	0.136	0.020	0.952	0.876
MBzP	50	Black non-Hispanic	Other	0.140	0.022	0.904	0.002	0.030	0.762
MBzP	50	Mexican-American	Other	0.257	0.188	0.526	0.327	0.034	0.820
MBP	50	White non-Hispanic	Black non-Hispanic	0.120	0.656	0.919	0.591	0.096	0.652
MBP	50	White non-Hispanic	Mexican-American	0.027	0.823	0.519	0.350	0.065	0.941
MBP	50	White non-Hispanic	Other	0.002	0.893	0.224	0.184	0.007	0.241
MBP	50	Black non-Hispanic	Mexican-American	0.410	0.533	0.461	0.585	0.674	0.637
MBP	50	Black non-Hispanic	Other	0.034	0.644	0.217	0.325	0.072	0.366
MBP	50	Mexican-American	Other	0.112	0.983	0.264	0.751	0.148	0.249

Table 2. Statistical significance tests comparing the percentiles of phthalate metabolites in women ages 16 to 49 years, between pairs of race/ethnicity/income groups at different income levels, for 2003-2006.

				P-VALUES	
Variable	**Percentile**	**RACEINC1**	**RACEINC2**	**Unadjusted**	**Adjusted (for age)**
Sum of MEHP, MEOHP, and	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.356	0.752

				P-VALUES	
Variable	**Percentile**	**RACEINC1**	**RACEINC2**	**Unadjusted**	**Adjusted (for age)**
MEHHP					
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.222	0.803
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.687	0.638
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Other, ≥ PL	0.659	0.359
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.170	0.438
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.135	0.536
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.233	0.642
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Other, ≥ PL	0.722	0.245
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.330	0.154
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.204	0.366
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.283	0.509
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Other, ≥ PL	0.809	0.064
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	White non-Hispanic, ≥ PL	0.127	0.838
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.085	0.814
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Mexican-American, ≥ PL	0.904	0.036
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Other, ≥ PL	0.357	0.003
MBzP	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.316	0.364
MBzP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.266	0.168
MBzP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.248	0.186
MBzP	50	White non-Hispanic, < PL	Other, ≥ PL	0.010	0.449
MBzP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.017	0.016
MBzP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.013	0.009
MBzP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.012	0.005
MBzP	50	Black non-Hispanic, < PL	Other, ≥ PL	< 0.0005	0.134
MBzP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.805	0.625
MBzP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.727	0.760
MBzP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.701	0.827
MBzP	50	Mexican-American, < PL	Other, ≥ PL	0.088	0.915

				P-VALUES	
Variable	**Percentile**	**RACEINC1**	**RACEINC2**	**Unadjusted**	**Adjusted (for age)**
MBzP	50	Other, < PL	White non-Hispanic, ≥ PL	0.430	0.076
MBzP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.404	0.458
MBzP	50	Other, < PL	Mexican-American, ≥ PL	0.395	0.336
MBzP	50	Other, < PL	Other, ≥ PL	0.139	0.473
MBP	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.229	0.048
MBP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.892	0.129
MBP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.666	0.069
MBP	50	White non-Hispanic, < PL	Other, ≥ PL	0.103	0.825
MBP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.289	0.106
MBP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.800	0.239
MBP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.596	0.123
MBP	50	Black non-Hispanic, < PL	Other, ≥ PL	0.092	0.852
MBP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.034	0.534
MBP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.465	0.751
MBP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.807	0.524
MBP	50	Mexican-American, < PL	Other, ≥ PL	0.187	0.575
MBP	50	Other, < PL	White non-Hispanic, ≥ PL	0.148	0.792
MBP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.229	0.953
MBP	50	Other, < PL	Mexican-American, ≥ PL	0.251	0.756
MBP	50	Other, < PL	Other, ≥ PL	0.396	0.394

Table 3. Other statistical significance tests comparing the percentiles of phthalate metabolites in women ages 16 to 49 years, for 2003-2006 (trends for 1999-2006).

					P-VALUES	
Variable	**Percentile**	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
Sum of MEHP, MEOHP, and MEHHP	50	2003	2006	income	0.184	0.027
Sum of MEHP, MEOHP, and MEHHP	50	2001	2006	yearnum	0.323	0.097
MBzP	50	2003	2006	income	0.011	0.096
MBzP	50	1999	2006	yearnum	0.013	< 0.0005
MBP	50	2003	2006	income	0.256	0.078
MBP	50	1999	2006	yearnum	0.121	< 0.0005

*For AGAINST = "income," the p-values are adjusted for age and race/ethnicity.
For AGAINST = "yearnum," the p-values are adjusted for age, race/ethnicity, and income.

Table 4. Statistical significance tests comparing the percentiles of phthalate metabolites in children ages 6 to 17 years, between pairs of race/ethnicity groups, for 2003-2006.

				P-VALUES					
Variable	**Percentile**	**RACE1**	**RACE2**	**All incomes**	**All incomes (adjusted for age, sex, income)**	**Below Poverty Level**	**Below Poverty Level (adjusted for age, sex)**	**At or Above Poverty Level**	**At or Above Poverty Level (adjusted for age, sex)**

				P-VALUES					
Variable	**Percentile**	**RACE1**	**RACE2**	**All incomes**	**All incomes (adjusted for age, sex, income)**	**Below Poverty Level**	**Below Poverty Level (adjusted for age, sex)**	**At or Above Poverty Level**	**At or Above Poverty Level (adjusted for age, sex)**
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic	Black non-Hispanic	0.741	0.389	0.745	0.321	0.843	0.391
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic	Mexican-American	0.503	0.017	0.394	0.436	0.322	0.017
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic	Other	0.404	0.002	0.845	0.003	0.620	0.221
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic	Mexican-American	0.192	0.141	0.313	0.506	0.215	0.183
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic	Other	0.495	< 0.0005	0.486	< 0.0005	0.670	0.097
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American	Other	0.198	< 0.0005	0.144	< 0.0005	0.406	0.018
MBzP	50	White non-Hispanic	Black non-Hispanic	0.298	0.949	0.946	0.006	0.153	0.235
MBzP	50	White non-Hispanic	Mexican-American	0.291	0.151	0.357	0.027	0.687	0.068
MBzP	50	White non-Hispanic	Other	0.230	0.221	0.665	0.360	0.407	0.082
MBzP	50	Black non-Hispanic	Mexican-American	0.938	0.046	0.147	0.137	0.210	0.368
MBzP	50	Black non-Hispanic	Other	0.071	0.164	0.671	0.295	0.108	0.388
MBzP	50	Mexican-American	Other	0.070	0.957	0.305	0.633	0.280	0.925
MBP	50	White non-Hispanic	Black non-Hispanic	0.422	0.388	0.232	0.001	0.655	0.984
MBP	50	White non-Hispanic	Mexican-American	0.212	0.685	0.578	0.005	0.419	0.629
MBP	50	White non-Hispanic	Other	0.287	0.901	0.568	0.034	0.603	0.473
MBP	50	Black non-Hispanic	Mexican-American	0.639	0.698	0.407	0.262	0.240	0.643
MBP	50	Black non-Hispanic	Other	0.509	0.552	0.918	0.817	0.444	0.480
MBP	50	Mexican-American	Other	0.702	0.723	0.772	0.643	0.970	0.689

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Table 5. Statistical significance tests comparing the percentiles of phthalate metabolites in children ages 6 to 17 years, between pairs of race/ethnicity/income groups at different income levels, for 2003-2006.

				P-VALUES	
Variable	**Percentile**	**RACEINC1**	**RACEINC2**	**Unadjusted**	**Adjusted (for age, sex)**
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.406	0.288
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.438	0.388
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.274	0.560
Sum of MEHP, MEOHP, and MEHHP	50	White non-Hispanic, < PL	Other, ≥ PL	0.723	0.131
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.329	0.903
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.387	0.639
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.121	0.165
Sum of MEHP, MEOHP, and MEHHP	50	Black non-Hispanic, < PL	Other, ≥ PL	0.920	0.251
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.936	0.272
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.787	0.764
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.399	0.403
Sum of MEHP, MEOHP, and MEHHP	50	Mexican-American, < PL	Other, ≥ PL	0.600	0.082
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	White non-Hispanic, ≥ PL	0.150	< 0.0005
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.172	< 0.0005
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Mexican-American, ≥ PL	0.070	< 0.0005
Sum of MEHP, MEOHP, and MEHHP	50	Other, < PL	Other, ≥ PL	0.517	0.011
MBzP	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.726	< 0.0005
MBzP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.268	0.003
MBzP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.559	0.010
MBzP	50	White non-Hispanic, < PL	Other, ≥ PL	0.708	0.012
MBzP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.551	0.320
MBzP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.074	0.928

				P-VALUES	
Variable	Percentile	RACEINC1	RACEINC2	Unadjusted	Adjusted (for age, sex)
MBzP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.329	0.575
MBzP	50	Black non-Hispanic, < PL	Other, ≥ PL	0.704	0.568
MBzP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.314	0.002
MBzP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.724	0.018
MBzP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.458	0.217
MBzP	50	Mexican-American, < PL	Other, ≥ PL	0.159	0.311
MBzP	50	Other, < PL	White non-Hispanic, ≥ PL	0.490	0.131
MBzP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.260	0.262
MBzP	50	Other, < PL	Mexican-American, ≥ PL	0.409	0.394
MBzP	50	Other, < PL	Other, ≥ PL	0.864	0.424
MBP	50	White non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.800	0.006
MBP	50	White non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.662	0.007
MBP	50	White non-Hispanic, < PL	Mexican-American, ≥ PL	0.866	0.017
MBP	50	White non-Hispanic, < PL	Other, ≥ PL	0.902	0.088
MBP	50	Black non-Hispanic, < PL	White non-Hispanic, ≥ PL	0.030	0.106
MBP	50	Black non-Hispanic, < PL	Black non-Hispanic, ≥ PL	0.015	0.104
MBP	50	Black non-Hispanic, < PL	Mexican-American, ≥ PL	0.138	0.071
MBP	50	Black non-Hispanic, < PL	Other, ≥ PL	0.203	0.074
MBP	50	Mexican-American, < PL	White non-Hispanic, ≥ PL	0.200	0.598
MBP	50	Mexican-American, < PL	Black non-Hispanic, ≥ PL	0.118	0.590
MBP	50	Mexican-American, < PL	Mexican-American, ≥ PL	0.551	0.394
MBP	50	Mexican-American, < PL	Other, ≥ PL	0.605	0.332
MBP	50	Other, < PL	White non-Hispanic, ≥ PL	0.445	0.484
MBP	50	Other, < PL	Black non-Hispanic, ≥ PL	0.390	0.479
MBP	50	Other, < PL	Mexican-American, ≥ PL	0.595	0.400
MBP	50	Other, < PL	Other, ≥ PL	0.598	0.324

Table 6. Other statistical significance tests comparing the percentiles of phthalate metabolites in children ages 6 to 17 years, for 2003-2006 (trends for 1999-2006).

					P-VALUES	
Variable	Percentile	From	To	Against	Unadjusted	Adjusted*
Sum of MEHP, MEOHP, and MEHHP	50	2003	2006	age	< 0.0005	< 0.0005
Sum of MEHP, MEOHP, and MEHHP	50	2003	2006	income	0.153	0.184
Sum of MEHP, MEOHP, and MEHHP	50	2001	2006	yearnum	0.797	0.010
MBzP	50	2003	2006	age	< 0.0005	< 0.0005
MBzP	50	2003	2006	income	0.359	0.047
MBzP	50	1999	2006	yearnum	0.010	< 0.0005
MBP	50	2003	2006	age	< 0.0005	< 0.0005
MBP	50	2003	2006	income	0.153	0.666
MBP	50	1999	2006	yearnum	0.004	0.238

*For AGAINST = "age," the p-values are adjusted for sex, race/ethnicity, and income.
For AGAINST = "income," the p-values are adjusted for age, sex, and race/ethnicity.
For AGAINST = "yearnum," the p-values are adjusted for age, sex, race/ethnicity, and income.