Methods

Indicator

B5. Cotinine in nonsmoking children ages 3 to 17 years: Median and 95th percentile concentrations in blood serum, 1988-2020

B6. Cotinine in nonsmoking women ages 16 to 49 years: Median and 95th percentile concentrations in blood serum, 1988-2020

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.[i] Indicator B5 uses serum cotinine measurements in nonsmoking children ages 3 to 17 years (ages 4 to 17 for 1988-1994). Indicator B6 uses serum cotinine measurements in nonsmoking women ages 16 to 49 years. For these analyses, individuals with a serum cotinine level greater than 10 nanograms of cotinine per milliliter of serum (ng/mL) are considered active smokers, and so were excluded from the results. The NHANES 1988-1991 and 1991-1994 survey cycles included serum cotinine data for ages 4 years and over. The NHANES 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2020 survey cycles included serum cotinine data for ages 3 years and over. Improvements in laboratory methods made it possible to detect cotinine levels at lower concentrations starting with the 2001-2002 survey cycle.

Indicator B5 is the median and 95th percentile concentrations of the serum cotinine for nonsmoking children ages 3 to 17 (ages 4 to 17 for 1988-1994). The median is the estimated concentration such that 50% of all noninstitutionalized civilian nonsmoking children ages 3 to 17 have serum cotinine concentrations below this level. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian nonsmoking children ages 3 to 17 have serum cotinine concentrations below this level.

Indicator B6 is the median and 95th percentile concentrations of the serum cotinine for nonsmoking women ages 16 to 49. The median is the estimated concentration such that 50% of all noninstitutionalized civilian nonsmoking women ages 16 to 49 during the survey period have

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

serum cotinine concentrations below this level. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian nonsmoking women ages 16 to 49 during the survey period have serum cotinine concentrations below this level. These estimates for women of child-bearing age were adjusted by age-specific birth rates to estimate the median and 95th percentile prenatal exposure. Tables B5a and B5b present the median and 95th percentiles of serum cotinine for nonsmoking children ages 3 to 17 years for 2015-2020, stratified by race/ethnicity and family income. Table B5c presents the median and 95th percentiles of serum cotinine for nonsmoking children ages 3 to 17 years for 2015-2020, stratified by age group. Tables B6a and B6b present the median and 95th percentiles of serum cotinine for nonsmoking women ages 16 to 49 years for 2015-2020, stratified by race/ethnicity and family income. The survey data were weighted to account for over-sampling, non-response, and non-coverage.

In previous years, tables B5a, B5b, B5c, B6a, and B6b presented data from the two previous NHANES cycles, which consisted of four years of data. The present tables contain data from the NHANES 2015-2016 and 2017-March 2020 cycles. The data for 2020 only go through March 2020 because NHANES suspended field operations due to the COVID-19 pandemic and data collection for the 2019–2020 cycle was not completed. Data collected by NHANES from 2019-March 2020 were combined with data from the 2017-2018 cycle to create a nationally representative data file.

Data Summary

Indicator	B5. Cotinine in nonsmoking children ages 3 to 17 years: Median and 95th percentile concentrations in blood serum, 1988-2020[ii]									
Time Period	1988-2020									
Data	Serum cotinine in children ages 3 to 17									
Years 1988-2014	1988-1991***	1991-1994***	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014
Limits of Detection (ng/mL)*	0.05	0.05	0.05	0.05 or 0.015	0.015	0.015	0.015	0.015	0.015	0.015
Number of Values	4,082	3,834	3,521	3,786	3,379	3,547	2,819	2,936	2,951	3,117
Number of Non-missing Values Not Above	2,680 (66%)	3,250 (85%)	2,591 (74%)	2,955 (78%)	2,651 (78%)	2,635 (74%)	2,093 (74%)	2,191 (75%)	2,126 (72%)	2339 (75%)

[ii] The data for 2020 only go through March 2020 because NHANES suspended field operations due to the COVID-19 pandemic and data collection for the 2019–2020 cycle was not completed.

Indicator	B5. Cotinine in nonsmoking children ages 3 to 17 years: Median and 95th percentile concentrations in blood serum, 1988-2020[ii]									
10 ng/mL**										
Number of Missing Values**	1,270 (31%)	466 (12%)	771 (22%)	689 (18%)	580 (17%)	782 (22%)	662 (23%)	673 (23%)	778 (26%)	730 (23%)
Number of Values Above 10 ng/mL	132 (3%)	118 (3%)	159 (5%)	142 (4%)	148 (4%)	130 (4%)	64 (2%)	72 (2%)	47 (2%)	48 (2%)
Percentage Below Limit of Detection***	13	18	37	26	18	22	20	29	35	40
Years 2015-2020*****	2015-2016	2017-2018	2017-2020							
Limits of Detection (ng/mL)*	0.015	0.015	0.015							
Number of Values	2,999	2,565	4,456							
Number of Non-missing Values Not Above 10 ng/mL**	2,229 (74%)	1,862 (73%)	2,982 (67%)							
Number of Missing Values**	737 (25%)	662 (26%)	1,389 (31%)							
Number of Values Above 10 ng/mL	33 (1%)	41 (2%)	85 (2%)							
Percentage Below Limit of	36	38	39							

Indicator	B5. Cotinine in nonsmoking children ages 3 to 17 years: Median and 95th percentile concentrations in blood serum, 1988-2020[ii]									
Detection***										

*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 not above 10 ng/mL include those below the analytical LOD, which are reported as LOD/√2, and exclude values above 10 ng/mL. Missing values are the number of sampled children ages 3 to 17 years in the Mobile Examination Center (MEC) sample that have no value reported for the particular variable used in calculating the indicator.
***This percentage is survey-weighted using the NHANES MEC survey weights for the given period and is for the percentage among children of ages 3 to 17 years with cotinine at or below 10 ng/mL.
****For NHANES III, in 1988-1994, serum cotinine data were not measured in children age 3 years, so these data are for children ages 4 to 17 years.
***** Data collected by NHANES from 2019-March 2020 were combined with data from the 2017-2018 cycle to create a nationally representative data file.

Indicator	B6. Cotinine in nonsmoking women ages 16 to 49 years: Median and 95th percentile concentrations in blood serum, 1988-2020[iii]									
Time Period	1988-2020									
Data	Serum cotinine in women ages 16 to 49									
Years 1988-2014	1988-1991	1991-1994	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014
Limits of Detection (ng/mL)*	0.05	0.05	0.05	0.05 or 0.015	0.015	0.015	0.015	0.015	0.015	0.015
Number of Values	2,685	3,226	1,944	2,140	1,900	2,085	1,749	1,996	1,742	1,921
Number of Non-missing Values Not Above 10 ng/mL**	1,779 (66%)	2,284 (71%)	1,324 (68%)	1,490 (70%)	1,315 (69%)	1,489 (71%)	1,206 (69%)	1,395 (70%)	1,277 (73%)	1391 (72%)
Number of Missing Values**	236 (9%)	169 (5%)	290 (15%)	231 (11%)	204 (11%)	220 (11%)	175 (10%)	140 (7%)	169 (10%)	156 (8%)
Number of Values Above 10 ng/mL	670 (25%)	773 (24%)	330 (17%)	419 (20%)	381 (20%)	376 (18%)	368 (21%)	461 (23%)	296 (17%)	374 (19%)
Percentage Below Limit	11	18	49	32	24	28	27	34	39	41

[iii] The data for 2020 only go through March 2020 because NHANES suspended field operations due to the COVID-19 pandemic and data collection for the 2019–2020 cycle was not completed.

Indicator	B6. Cotinine in nonsmoking women ages 16 to 49 years: Median and 95th percentile concentrations in blood serum, 1988-2020[iii]									
of Detection***										
Years 2015-2020*****	2015-2016	2017-2018	2017-2020							
Limits of Detection (ng/mL)*	0.015	0.015	0.015							
Number of Values	1,851	1,620	2,833							
Number of Non-missing Values Not Above 10 ng/mL**	1,377 (74%)	1,162 (72%)	1,377 (49%)							
Number of Missing Values**	191 (10%)	175 (11%)	191 (7%)							
Number of Values Above 10 ng/mL	283 (15%)	283 (17%)	1265 (44%)							
Percentage Below Limit of Detection***	44	40	44							

*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 not above 10 ng/mL include those below the analytical LOD, which are reported as LOD/√2, and exclude values above 10 ng/mL. Missing values are the number of sampled women ages 16 to 49 years in the Mobile Examination Center (MEC) sample that have no value reported for the particular variable used in calculating the indicator.
***This percentage is survey-weighted using the NHANES survey weights and age-specific birth rates for the given period and is for the percentage among women of ages 16 to 49 years with cotinine at or below 10 ng/mL.
****Data collected by NHANES from 2019-March 2020 were combined with data from the 2017-2018 cycle to create a nationally representative data file.

Overview of Data Files

The following files are needed to calculate these indicators. 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 III: Second Laboratory file LAB2.DAT. This text file contains the measured serum cotinine (COP), age in years at screening (HSAGEIR), sex (HSSEX), race/ethnicity (DMARETHN), poverty income ratio (DMPPIR), NHANES III Phase (SDPPHASE), the Final Examination (Mobile Examination Center (MEC) only) weights (WTPFEX1 for Phase I, WTPFEX2 for Phase 2, WTPFEX6 for Total sample), the pseudo-stratum codes (SDPSTRA1 for Phase 1, SDPSTRA2 for Phase 2, and SDPSTRA6 for Total sample), and the pseudo-PSU codes (SDPPSU1 for Phase 1, SDPPSU2 for Phase 2, and SDPPSU6 for Total sample).

- NHANES 1999-2000: Demographic file demo.xpt. Laboratory file lab06.xpt. The demographic file demo.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file lab06.xpt contains SEQN and the serum cotinine (LBXCOT). The two files are merged using the common variable SEQN.

- NHANES 2001-2002: Demographic file demo_b.xpt. Laboratory file l06_b.xpt. The demographic file demo_b.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file l06_b.xpt contains SEQN, the serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). The two files are merged using the common variable SEQN.

- NHANES 2003-2004: Demographic file demo_c.xpt. Laboratory file l06cot_c.xpt. The demographic file demo_c.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file l06cot_c.xpt contains SEQN and the serum cotinine (LBXCOT). The two files are merged using the common variable SEQN.

- NHANES 2005-2006: Demographic file demo_d.xpt. Laboratory file cot_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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cot_d.xpt contains SEQN and the serum cotinine (LBXCOT). The two files are merged using the common variable SEQN.

- NHANES 2007-2008: Demographic file demo_e.xpt. Laboratory file cotnal_e.xpt. The demographic file demo_e.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cotnal_e.xpt contains SEQN and the serum cotinine (LBXCOT). The two files are merged using the common variable SEQN.

- NHANES 2009-2010: Demographic file demo_f.xpt. Laboratory file cotnal_f.xpt. The demographic file demo_f.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cotnal_f.xpt contains SEQN and the serum cotinine (LBXCOT). The two files are merged using the common variable SEQN.

- NHANES 2011-2012: Demographic file demo_g.xpt. Laboratory file cotnal_g.xpt. The demographic file demo_g.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cotnal_g.xpt contains SEQN, serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). The two files are merged using the common variable SEQN.

- NHANES 2013-2014: Demographic file demo_h.xpt. Laboratory file cot_h.xpt. The demographic file demo_h.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cot_h.xpt contains SEQN, serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). The two files are merged using the common variable SEQN.

- NHANES 2015-2016: Demographic file demo_i.xpt. Laboratory file cot_i.xpt. The demographic file demo_i.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cot_i.xpt contains SEQN, serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). The two files are merged using the common variable SEQN.

- NHANES 2017-2018: Demographic file demo_j.xpt. Laboratory file cot_j.xpt. The demographic file demo_j.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cot_j.xpt contains SEQN, serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). The two files are merged using the common variable SEQN.

- NHANES 2017-2020: Demographic file demo_j.xpt. Laboratory file cot_j.xpt. The demographic file demo_j.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), pseudo-PSU (SDMVPSU), and the two year MEC weight (WTMEC2YR). The laboratory file cot_j.xpt contains SEQN, serum cotinine (LBXCOT), and the cotinine non-detect comment code (LBDCOTLC). 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. Indicator B5 uses serum cotinine measurements in children ages 4 to 17 from NHANES 1988-1991 and 1991-1994, and uses serum cotinine measurements in children ages 3 to 17 from NHANES 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2020. Indicator B6 uses serum cotinine measurements in women ages 16 to 49 from NHANES 1988-1991, 1991-1994, 1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2020. As a result of the suspension of NHANES data collection efforts due to the COVID-19 pandemic, data from the 2019-March 2020 cycle were not nationally representative. These data were thus combined with data from the 2017-2018 NHANES cycle to create a nationally representative dataset for 2017-2020.

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]

The NHANES use a complex multi-stage, stratified, clustered sampling design. Certain demographic groups were deliberately over-sampled, including Mexican-Americans, Blacks, and, from 2007 onwards, All Hispanics, then, from 2011 onwards, Asians, 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-

[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.

response, and non-coverage. The statistical analyses used the applicable Mobile Examination Center (MEC) survey weights (WTPFEX1 for 1988-1991, WTPFEX2 for 1991-1994, and WTMEC2YR for 1999 and later) to re-adjust the serum cotinine data to represent the national population.

Age-Specific Birth Rates

In addition to the NHANES MEC survey weights, for Indicator B6, the data for women of child-bearing age (ages 16 to 49) were also weighted by the birth rate for women of the given age and race/ethnicity to estimate prenatal 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]

Adjusted Survey Weight =
MEC survey weight × U.S. Births (NHANES cycle, age, race/ethnicity) /
{Number of years in NHANES cycle × U.S. Women (NHANES cycle midpoint, age, race/ethnicity)}.

Race/Ethnicity and Family Income

For Tables B5a, B5b, B6a, and B6b, 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 definition of a "family" as "a group of two people or more (one of whom is the householder) related by birth, marriage, or adoption and residing together" to group household members into family units, and the corresponding 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
- Above Poverty Level: PIR ≥ 1
- Unknown Income: PIR is missing

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

For 2015-2020, the weighted percentage of non-smoking women ages 16 to 49 years with unknown income was 7% and the weighted percentage of non-smoking children ages 3 to 17 years with unknown income was 8%.

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 these indicators, the RIDRETH1 categories 2, 5, and missing were combined into a single "All Other Races/Ethnicities" category. This produced the following categories:

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

The "All Other Races/Ethnicities" category includes multiracial persons and individuals whose racial or ethnic identity is not White non-Hispanic, Black non-Hispanic, or Mexican-American. Except for non-Mexican American Hispanics in 2007-2020 and Asian non-Hispanics in 2011-2020, persons of "All Other Races/Ethnicities" are selected into the survey with a probability that is very much lower than White non-Hispanic, Black non-Hispanic and Mexican-American individuals, and as a group they are not representative of all other race and ethnicities in the United States.

Calculation of Indicator

Indicator B5 is the median and 95th percentile for serum cotinine in children of ages 3 to 17 years (ages 4 to 17 years for 1988-1994). The median is the estimated concentration such that 50% of all noninstitutionalized civilian nonsmoking children ages 3 to 17 years have serum cotinine concentrations below this level. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian nonsmoking children ages 3 to 17 years have serum cotinine concentrations below this level. Indicator B6 is the median and 95th percentile for serum cotinine in women of ages 16 to 49 years. The median is the estimated concentration such that 50% of all noninstitutionalized civilian nonsmoking women ages 16 to 49 years during the survey period

have serum cotinine concentrations below this level. The 95th percentile is the estimated concentration such that 95% of all noninstitutionalized civilian nonsmoking women ages 16 to 49 years during the survey period have serum cotinine concentrations below this level. Tables B5a and B5b present the median and 95th percentiles of serum cotinine for nonsmoking children ages 3 to 17 years for 2015-2020, stratified by race/ethnicity and family income. Table B5c presents the median and 95th percentiles of serum cotinine for nonsmoking children ages 3 to 17 years for 2015-2020, stratified by age group. Tables B6a and B6b present the median and 95th percentiles of serum cotinine for nonsmoking women ages 16 to 49 years for 2015-2020, stratified by race/ethnicity and family income. To adjust the NHANES data to represent prenatal exposures, the data for each woman surveyed was multiplied by the estimated number of births per woman of the given age and race/ethnicity.

To simply demonstrate the calculations, we will use the NHANES 2009-2010 serum cotinine values for women ages 16 to 49 years of all race/ethnicities and all incomes as an example for Indicator B6. The calculations for Indicator B5 use the same calculations applied to the serum cotinine data for children ages 3 to 17, except that the birth rate adjustment is not applied.

We begin with all the non-missing NHANES 2009-2010 serum cotinine values for women ages 16 to 49 years. First, we exclude all serum cotinine values above 10 ng/mL to give the cotinine values for nonsmoking women. Each sampled woman has an associated annual survey weight that estimates the annual number of U.S. women represented by that sampled woman. The annual survey weight for each woman is WTMEC2YR. Each sampled woman also has an associated birth rate giving the numbers of annual births per woman of the given age, race, and ethnicity. The product of the annual survey weight and the birth rate 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 serum cotinine measurement for a nonsmoking woman between 16 and 49 years of age is 0.011 ng/mL with an annual survey weight of 19,000, a birth rate of 0.061, and thus an adjusted survey weight of 1,200 and so represents 1,200 births. The total of the adjusted survey weights for the sampled nonsmoking women equals 3.1 million, the total number of annual U.S. births to nonsmoking women ages 16 to 49 years. The second lowest measurement is also 0.011 ng/mL with an adjusted survey weight of 4,600, and so represents another 4,600 U.S. births. The highest measurement for nonsmoking women was 9.59 ng/mL, with an adjusted survey weight of 4,600, and so represents another 4,600 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 1,200 values of 0.011 ng/mL from the lowest measurement, 4,600 values of 0.011 ng/mL from the second lowest measurement, and so on, up to 4,600 values of 9.59 ng/mL from the highest measurement. Arranging these 3.1 million values in increasing order, the 1.55 millionth value is 0.03 ng/mL. Since half of the values are below 0.03 and half of the values are above 0.03, the median equals 0.03 ng/mL. To calculate the 95th percentile, note that 95% of 3.1 million equals 2.95 million. The 2.95 millionth value is 1.4 ng/mL. Since 95% of the values are below 1.4, the 95th percentile equals 1.4 ng/mL.

For 2009-2010, there were a total of 1,996 women participants of ages 16 to 49 in the NHANES survey. Of these 1,996 women, 461 had cotinine values above 10 ng/mL and 140 had missing cotinine measurements. These calculations assume that the remaining 1,395 (1,996 minus 461 and minus 140) sampled women with valid serum cotinine data at or below 10 ng/mL are representative of nonsmoking women giving birth without valid serum cotinine data. The calculations also assume that the sampled women are representative of women that actually gave birth in 2009-2010, 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 serum cotinine values and all serum cotinine values above 10 ng/mL. Suppose there are n women of ages 16 to 49 years with valid serum cotinine values at or below 10 ng/mL. Arrange the serum cotinine 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:

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

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.

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

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

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

or

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

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

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

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

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

(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.

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

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

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

or

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

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

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

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

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

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 birth rate adjusted calculations for women ages 16 to 49, the sample weight is adjusted by multiplying by the age-specific birth rate.

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

[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.

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:

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

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. If the relative standard error is too high, then the estimated percentile will not be accurately estimated. Furthermore, if the degrees of freedom (from Step 2) is too low, then the relative standard error will be less accurately estimated and thus may be underestimated. For these reasons, percentiles with high relative standard errors or with low degrees of freedom are unstable or unreliable.

For NHANES III, the corresponding pseudo-stratum and pseudo-primary sampling unit variables are SDPSTRAn and SDPPSUn, where n = 1 for Phase 1, n = 2 for Phase 2, and n = 6 for Total (the entire period 1988-1994). To correctly account for the statistical independence between the different NHANES cycles, the original stratum numbers for NHANES 1999-2000 and later were all increased by 49 (the number of pseudo-strata in NHANES III).

Percentiles with a relative standard error less than 30% and with 12 or more degrees of freedom were treated as being reliable and were tabulated. Percentiles with a relative standard error that is 30% or greater but less than 40% and with 12 or more degrees of freedom were treated as being unstable; these values were tabulated but were flagged to be interpreted with caution. Percentiles with a relative standard error less than 40% and with between 7 and 11 degrees of freedom were also treated as being unstable; these values were tabulated but were flagged to be interpreted with caution. Percentiles with a relative standard error that is 40% or greater, or without an estimated relative standard error, or with 6 or less degrees of freedom, 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 (in the cases of children), 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 birth rate. For these statistical comparisons, the calculations with data from NHANES III (1988-1994) used survey weights, pseudo-strata, and pseudo-primary sampling unit values for the total sample (i.e., 1988-1994) and not for the individual phases (i.e., 1988-1991 and 1991-1994).

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. In this model, the weight is the inverse of the variance, so that percentiles with larger standard errors are given less of a statistical weight in the fitted regression model. 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 serum cotinine level depends strongly 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 Table 1 for nonsmoking children ages 3 to 17 years and in Table 4 for nonsmoking women ages 16 to 49 years. Comparisons between income groups are shown in Table 2 for nonsmoking children ages 3 to 17 years and in Table 5 for nonsmoking women ages 16 to 49 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 (for children), 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 (for children), and income distributions between the race/ethnicity groups. The adjustment for sex is applicable only for children, and thus appears only in Tables 1 and 2.

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 race/ethnicity group at or above the poverty level. The corresponding adjusted analyses include extra explanatory variables for age and sex (for children), so that race/ethnicity/income groups are compared after accounting for any differences due to age or sex. Although these comparisons only involve the two income groups with known incomes, these statistical models were fitted to all three income groups (including those with unknown income) to make a more general, better fitting model; this approach has no impact on the unadjusted p-values but has a small impact on the adjusted p-values. Also in Tables 2 and 5, the unadjusted p-value for the population "All" compares the percentiles for nonsmoking children ages 3 to 17 years or nonsmoking women ages 16 to 49 years below poverty level with those at or above poverty level, using the explanatory variables for the two income groups (below poverty, at or above poverty), excluding those with unknown income. The adjusted p-value includes adjustment terms for age, sex (for children), and race/ethnicity in the model.

Additional comparisons are shown in Table 3 for nonsmoking children ages 3 to 17 years and in Table 6 for nonsmoking women ages 16 to 49 years. Comparisons are shown for differences between children in different age groups, those below poverty and those at or above poverty, and for changes over time (trends). The Against = "age" unadjusted p-value compares the percentiles for those below poverty level with those at or above poverty level, using the explanatory variables for the different age groups. The adjusted p-value includes adjustment terms for sex (for children), race/ethnicity and income in the model. The Against = "income" unadjusted p-value compares the percentiles for those below poverty level with those at or above poverty level, using the explanatory variables for the two income groups (below poverty, at or above poverty). The adjusted p-value includes adjustment terms for age, sex (for children), and race/ethnicity in the model. The Against = "yearnum" p-value examines whether the linear trend in the percentile 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 (for

children), income, and race/ethnicity. The adjustment for sex is applicable only for children, and thus appears only in Table 3.

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 3-5, 6-10, 11-15, and 16-17. For more details on these statistical analyses, see the memorandum by Cohen (2010).[viii]

Table 7 shows the results of post-hoc analyses comparing percentiles between nonsmoking children ages 3-17 and nonsmoking women ages 16-49. Two-sided Welch's t-test was performed using P_{CDC}, standard errors, and effective sample sizes for the two age groups, derived using the approach described in the "Relative Standard Error" section. Welch's t-test assumes groups are independent; overlapping groups can impact estimates of variability and should be considered when interpreting results. In this case, the groups overlap for ages 16-17. Table B5c presents the median and 95th percentile concentrations for the 16-17 age group.

Table 1. Statistical significance tests comparing the percentiles of cotinine in nonsmoking children ages 3 to 17 years, between pairs of race/ethnicity groups, for 2015-2020.

				P-VALUES					
Variable	Percentile	First race/ethnicity group	Second race/ethnicity group*	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)
cotinine	50	White non-Hispanic	Black non-Hispanic	0.010	0.064	0.045	0.043	0.285	0.196
cotinine	50	White non-Hispanic	Mexican-American	0.304	0.305	0.435	<0.001	0.412	0.977
cotinine	50	White non-Hispanic	Other	0.342	0.345	0.498	<0.001	0.616	0.866
cotinine	50	Black non-Hispanic	Mexican-American	0.005	0.024	0001	<0.001	0.202	0.274
cotinine	50	Black non-Hispanic	Other	0.006	0.0029	0.002	<0.001	0.973	0.241
cotinine	50	Mexican-American	Other	0.001	0.273	0.183	0.855	0.309	0.989
cotinine	95	White non-Hispanic	Black non-Hispanic	0.011	< 0.001	0.858	< 0.001	0.230	<0.001
cotinine	95	White non-Hispanic	Mexican-American	0.228	< 0.001	0.013	< 0.001	0.619	<0.001
cotinine	95	White non-Hispanic	Other	0.353	< 0.001	0.343	< 0.001	0.595	< 0.001
cotinine	95	Black non-Hispanic	Mexican-American	< 0.001	< 0.001	<0.001	< 0.001	0.168	< 0.001
cotinine	95	Black non-Hispanic	Other	< 0.001	< 0.001	0.189	< 0.001	0.129	< 0.001
cotinine	95	Mexican-American	Other	0.603	<0.001	0.269	< 0.001	0.873	0.791

[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.

* "Other" represents the "All Other Races/Ethnicities" category, which includes all other races and ethnicities not specified, together with those individuals who report more than one race.

Table 2. Statistical significance tests comparing the percentiles of cotinine in nonsmoking children ages 3 to 17 years, between those below poverty level and those at or above poverty level, for 2015-2020.

			P-Values for difference between income levels	
Variable	**Percentile**	**Population***	**Unadjusted**	**Adjusted (for age, sex)****
cotinine	50	All	0.038	0.185
cotinine	50	White non-Hispanic	0.441	<0.001
cotinine	50	Black non-Hispanic	0.003	< 0.001
cotinine	50	Mexican-American	0.406	0.800
cotinine	50	Other	0.754	0.889
cotinine	95	All	0.002	0.298
cotinine	95	White non-Hispanic	0.027	0.007
cotinine	95	Black non-Hispanic	0.039	< 0.001
cotinine	95	Mexican-American	0.839	0.031
cotinine	95	Other	0.333	<0.001

* "Other" represents the "All Other Races/Ethnicities" category, which includes all other races and ethnicities not specified, together with those individuals who report more than one race.
** Comparison for "All" is adjusted for age, sex, and race/ethnicity; comparisons for race/ethnicity categories are adjusted for age and sex.

Table 3. Other statistical significance tests comparing the percentiles of cotinine in nonsmoking children ages 3 to 17 years, for 2015-2020 (trends for 1988-2020).

					P-VALUES	
Variable	**Percentile**	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
cotinine	50	2015	2020	age	0.076	0.040
cotinine	50	2015	2020	income	0.038	0.185
cotinine	50	1998	2020	year	< 0.001	< 0.001
cotinine	95	2015	2020	age	0.033	< 0.001
cotinine	95	2015	2020	income	0.002	0.298
cotinine	95	1998	2020	year	< 0.001	< 0.001

*For Against = "age" the comparison is between the age groups 3-5, 6-10, 11-15, and 16-17 years, and the p-values are adjusted for sex, race/ethnicity, and income.
For Against = "income," the comparison is between those below the poverty level and those at or above the poverty level, and the p-values are adjusted for age, sex, and race/ethnicity.
For Against = "year" the comparison is the trend over different years, and the p-values are adjusted for age, sex, race/ethnicity, and income.

Table 4. Statistical significance tests comparing the percentiles of cotinine in nonsmoking women ages 16 to 49 years, between pairs of race/ethnicity groups, for 2015-2020.

				P-VALUES					
Variable	Percentile	First race/ethnicity group	Second race/ethnicity group*	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)
cotinine	50	White non-Hispanic	Black non-Hispanic	0.302	0.031	0.800	0.863	0.158	0.090
cotinine	50	White non-Hispanic	Mexican-American	0.354	0.143	0.383	0.732	0.147	0.173
	50	White non-Hispanic	Other	NA	0.140	0.455	0.805	0.876	0.125
cotinine	50	Black non-Hispanic	Mexican-American	0.193	0.164	0.585	0.480	0.849	0.457
cotinine	50	Black non-Hispanic	Other	NA	0.114	0.613	0.577	0.855	0.434
cotinine	50	Mexican-American	Other	NA	0.861	0.314	0.174	0.849	0.918
cotinine	95	White non-Hispanic	Black non-Hispanic	0.006	< 0.001	0.122	< 0.001	0.038	< 0.001
cotinine	95	White non-Hispanic	Mexican-American	0.894	< 0.001	0.151	< 0.001	0.204	0.689
cotinine	95	White non-Hispanic	Other	0.975	< 0.001	0.130	< 0.001	0.496	0.003
cotinine	95	Black non-Hispanic	Mexican-American	0.017	< 0.001	0.009	< 0.001	< 0.001	< 0.001
cotinine	95	Black non-Hispanic	Other	0.007	< 0.001	0.010	< 0.001	0.135	< 0.001
cotinine	95	Mexican-American	Other	0.914	< 0.001	0.851	0.928	0.438	0.405

* "Other" represents the "All Other Races/Ethnicities" category, which includes all other races and ethnicities not specified, together with those individuals who report more than one race.

Table 5. Statistical significance tests comparing the percentiles of cotinine in nonsmoking women ages 16 to 49 years, between those below poverty level and those at or above poverty level, for 2015-2020.

			P-Values for difference between income levels	
Variable	Percentile	Population*	Unadjusted	Adjusted (for age)**
cotinine	50	All	0.015	0.907
cotinine	50	White non-Hispanic	0.989	0.659
cotinine	50	Black non-Hispanic	0.610	0.597
cotinine	50	Mexican-American	0.362	0.392
cotinine	50	Other	0.861	0.655
cotinine	95	All	0.054	< 0.001
cotinine	95	White non-Hispanic	0.003	< 0.001
cotinine	95	Black non-Hispanic	0.020	< 0.001
cotinine	95	Mexican-American	0.636	0.649
cotinine	95	Other	0.799	0.266

* "Other" represents the "All Other Races/Ethnicities" category, which includes all other races and ethnicities not specified, together with those individuals who report more than one race.
** Comparison for "All" is adjusted for age and race/ethnicity; comparisons for race/ethnicity categories are adjusted for age.

Table 6. Other statistical significance tests comparing the percentiles of cotinine in nonsmoking women ages 16 to 49 years, for 2015-2020 (trends for 1988-2020).

					P-VALUES	
Variable	**Percentile**	**From**	**To**	**Against**	**Unadjusted**	**Adjusted***
cotinine	50	2015	2020	income	0.006	0.924
cotinine	50	1998	2020	year	< 0.001	< 0.001
cotinine	95	2015	2020	income	0.030	< 0.001
cotinine	95	1998	2020	year	0.246	< 0.001

For Against = "income," the comparison is between those below the poverty level and those at or above the poverty level, and the p-values are adjusted for age and race/ethnicity.
For Against = "year" the comparison is the trend over different years, and the p-values are adjusted for age, race/ethnicity, and income.

Table 7. Statistical significance tests comparing the percentiles of cotinine between nonsmoking children ages 3 to 17 years and nonsmoking women ages 16 to 49 years, for 2015-2020.

					Comparison of Age Groups*			
Age Group	**Percentile**	**P_{CDC}****	**Standard Error(P_{CDC})****	**Effective Sample Size****	**Mean Difference (95% CI)**	**T Statistic**	**Degrees of Freedom**	**P-Values**
Children, 3-17	50	0.024	0.002	4091				
Women, 16-49	50	0.017	0.001	2539	0.007 (0.003, 0.012)	3.031	6348.36	0.002
Children, 3-17	95	1.83	0.242	4091				
Women, 16-49	95	1.19	0.225	2539	0.64 (-0.009, 1.289)	1.934	6451.17	0.053

* Statistical tests assume independence for dependent age groups.
** Statistical tests were performed using chemical percentile estimates (P_{CDC}), standard error of P_{CDC}, and degrees-of-freedom adjusted effective sample sizes from the revised CDC method for relative standard errors.