# National Health and Nutrition Examination Survey

## 2017-March 2020 Data Documentation, Codebook, and Frequencies

## Cotinine and Hydroxycotinine - Serum (P_COT)

**Data File: P_COT.xpt**

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**Last Revised: NA**

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## Component Description

The NHANES program suspended field operations in March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic. As a result, data collection for the NHANES 2019-2020 cycle was not completed and the collected data are not nationally representative. Therefore, data collected from 2019 to March 2020 were combined with data from the NHANES 2017-2018 cycle to form a nationally representative sample of NHANES 2017-March 2020 pre-pandemic data. These data are available to the public. Please refer to the Analytic Notes section for more details on the use of the data.

The specific aims of the component are: 1) to measure the prevalence and extent of tobacco use; 2) to estimate the extent of exposure to environmental tobacco smoke (ETS), and determine trends in exposure to ETS; and 3) to describe the relationship between tobacco use (as well as exposure to ETS) and chronic health conditions, including respiratory and cardiovascular diseases.

Cotinine and trans-3'-hydroxycotinine (hydroxycotinine) are the primary metabolites of nicotine. The concentrations of cotinine and hydroxycotinine in body fluids can be used as markers for active smoking and as indices for secondhand smoke (SHS) exposure. Because their concentrations are greater and their elimination half-lives significantly longer, these metabolites are generally preferred over nicotine itself as biomarkers. Cotinine, the primary proximal metabolite of nicotine, is generally regarded as the marker of choice. The estimated elimination half-life of cotinine is about 15-20 hours; by contrast, the half-life of nicotine is only 0.5-3 hours. The half-life of hydroxycotinine is approximately 5-6 hours, but when hydroxycotinine is generated from cotinine, its elimination half-life becomes similar to that of cotinine.

Cotinine and hydroxycotinine can be measured in serum, urine, and saliva—the half-life of cotinine in all three fluids is essentially the same. Cotinine concentrations tend to be three to eight times higher in urine than in serum; however, plasma or serum is the fluid of choice for studies requiring a quantitative assessment of exposure. For that reason, serum was chosen as the matrix for the National Health and Nutrition Examination Survey (NHANES) cotinine analyses. In serum, hydroxycotinine concentrations tend to be two to four times lower than cotinine concentrations.

The tobacco component for NHANES also included questionnaire items on current and past use of cigarettes, pipes, cigars, and smokeless tobacco. Questions were asked regarding exposure to ETS at home, at work, and in utero among children. In addition, use of nicotine replacement products (e.g., gum and patch) was collected using questionnaires.

## Eligible Sample

Examined participants aged 3 years and older in the NHANES 2017-March 2020 pre-pandemic sample were eligible.

## Description of Laboratory Methodology

Serum cotinine and hydroxycotinine are measured by an isotope-dilution high-performance liquid

chromatography/atmospheric pressure chemical ionization tandem mass spectrometric (ID HPLC-APCI MS/MS) method. Briefly, the serum sample is spiked with methyl-D3-cotinine and methyl-D3-hydroxycotinine as internal standards. The sample is basified and then applied to a supported liquid extraction (SLE) plate. The analytes are extracted with an isopropanol/methylene chloride mixture, the organic extract is concentrated, and the residue is injected onto a C18 HPLC column. The eluent from these injections is monitored by APCI-MS/MS. The m/z 80 product ion from the m/z 177 quasi-molecular ion is measured for cotinine and the m/z 80 product ion from the m/z 193 quasi-molecular ion is measured for hydroxycotinine. Additional ions for the internal standards and for confirmation are also monitored for the respective compounds. Analyte concentrations are derived from the area ratios of native-to-labeled compounds in the sample by comparisons to a standard curve.

Refer to the Laboratory Method Files section for a detailed description of the laboratory methods used.

## Laboratory Method Files

Cotinine and Hydroxycotinine in Serum Laboratory Procedure Manual (March 2020)

Cotinine and Hydroxycotinine in Serum Laboratory Procedure Manual (July 2022)

## Laboratory Quality Assurance and Monitoring

Serum specimens are processed, stored, and shipped to the Division of Laboratory Sciences, National Center for Environmental Health, and Centers for Disease Control and Prevention, Atlanta, GA for analysis.

Detailed instructions on specimen collection and processing are discussed in the 2017-2018 and 2019-2020 Laboratory Procedures Manuals (LPMs). Vials are stored under appropriate frozen (–20°C) conditions until they are shipped to National Center for Environmental Health for testing.

The NHANES quality assurance and quality control (QA/QC) protocols meet the 1988 Clinical Laboratory Improvement Amendments mandates. Detailed QA/QC instructions are discussed in the NHANES LPM.

**Mobile Examination Centers (MECs)**

Laboratory team performance is monitored using several techniques. NCHS and contract consultants use a structured competency assessment evaluation during visits to evaluate both the quality of the laboratory work and the quality-control procedures. Each laboratory staff member is observed for equipment operation, specimen collection and preparation; testing procedures and constructive feedback are given to each staff member. Formal retraining sessions are conducted annually to ensure that required skill levels were maintained.

**Analytical Laboratories**

NHANES uses several methods to monitor the quality of the analyses performed by the contract laboratories. In the MEC, these methods include performing blind split samples collected on “dry run” sessions. In addition, contract laboratories randomly perform repeat testing on 2% of all specimens.

NCHS developed and distributed a quality control protocol for all CDC and contract laboratories, which outlined the use of Westgard rules (Westgard et al., 1981) when running NHANES specimens. Progress reports containing any problems encountered during shipping or receipt of specimens, summary statistics for each control pool, QC graphs, instrument calibration, reagents, and any special considerations are submitted to NCHS quarterly. The reports are reviewed for trends or shifts in the data. The laboratories are required to explain any identified areas of concern.

All QC procedures recommended by the manufacturers were followed. Reported results for all assays meet the Division of Laboratory Sciences’ quality control and quality assurance performance criteria for accuracy and precision, similar to the Westgard rules (Caudill, et al., 2008).

## Data Processing and Editing

The data were reviewed. Incomplete data or improbable values were sent to the performing laboratory for confirmation.

## Analytic Notes

The COVID-19 pandemic required suspension of NHANES 2019-2020 field operations in March 2020 after data were collected in 18 of the 30 survey locations in the 2019-2020 sample. Data collection was cancelled for the remaining 12 locations. Because the collected data from 18 locations were not nationally representative, these data were combined with data from the previous cycle (2017-2018) to create a 2017-March 2020 pre-pandemic data file. A special weighting process was applied to the 2017-March 2020 pre-pandemic data file. The resulting sample weights in the present file should be used to calculate estimates from the combined cycles. These sample weights are not appropriate for independent analyses of the 2019-2020 data and will not yield nationally representative results for either the 2017-2018 data alone or the 2019-March 2020 data alone. Please refer to the NHANES website for additional information for the NHANES 2017-March 2020 pre-pandemic data, and for the previous 2017-2018 public use data file with specific weights for that 2-year cycle.

Refer to the 2017-2018 and 2019-2020 Laboratory Data Overview for general information on NHANES laboratory data.

There are over 800 laboratory tests performed on NHANES participants. However, not all participants provided biospecimens or enough volume for all the tests to be performed. The specimen availability can also vary by age or other population characteristics. For example, in 2017-March 2020 approximately 76% of children aged 1-17 years who were examined in the MEC provided a blood specimen through phlebotomy, while 95% of examined adults aged 18 and older provided a blood specimen. Analysts should evaluate the extent of missing data in the dataset related to the outcome of interest as well as any predictor variables used in the analyses to determine whether additional re-weighting for item non-response is necessary.

Please refer to the NHANES Analytic Guidelines and the on-line NHANES Tutorial for further details on the use of sample weights and other analytic issues.

**Sample Weights**

Exam sample weights should be used for analyses.

**Demographic and Other Related Variables**

The analysis of NHANES laboratory data must be conducted using the appropriate survey design and demographic variables. The NHANES 2017-March 2020 Demographics File contains demographic data, health indicators, and other related information collected during household interviews as well as the sample weight variables. The recommended procedure for variance estimation requires use of stratum and PSU variables (SDMVSTRA and SDMVPSU, respectively) in the demographic data file.

The Fasting Questionnaire File includes auxiliary information such as fasting status, the length of fast, and the time of venipuncture.

The laboratory data file can be linked to the other NHANES data files using the unique survey participant identifier (i.e., SEQN).

**Detection Limits**

The detection limits were constant for all of the analytes in the data set. Two variables are provided for each of these analytes. The variable name ending in “LC” (ex., LBDCOTLC) indicates whether the result was below the limit of detection: the value “0” means that the result was at or above the limit of detection, “1” indicates that the result was below the limit of detection. For analytes with analytic results below the lower

limit of detection (ex. LBDCOTLC =1), an imputed fill value was placed in the analyte results field. This value is the lower limit of detection divided by the square root of 2 (LLOD/sqrt[2]). The other variable prefixed LBX (ex., LBXCOT) provides the analytic result for the analyte.

The lower limit of detection (LLOD in ng/mL) for Cotinine and Hydroxycotinine in serum:

| VARIABLE | SAS LABEL | LLOD |
|---|---|---|
| LBXCOT | Cotinine, serum | 0.015 |
| LBXHCOT | Hydroxycotinine, serum | 0.015 |

## References


- Caudill, S.P., Schleicher, R.L., Pirkle, J.L. Multi-rule quality control for the age-related eye disease study. Statist. Med. (2008) 27(20):4094-40106.
- Westgard J.O., Barry P.L., Hunt M.R., Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem (1981) 27:493-501.

## Codebook and Frequencies

### SEQN - Respondent Sequence Number

| | |
|---|---|
| **Variable Name:** | SEQN |
| **SAS Label:** | Respondent Sequence Number |
| **English Text:** | Respondent sequence number |
| **Target:** | Both males and females 3 YEARS - 150 YEARS |

# LBXCOT - Cotinine, Serum (ng/mL)

**Variable Name:** LBXCOT

**SAS Label:** Cotinine, Serum (ng/mL)

**English Text:** Cotinine, Serum (ng/mL)

**Target:** Both males and females 3 YEARS - 150 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---|---|---|---|---|
| 0.011 to 1620 | Range of Values | 11395 | 11395 | |
| . | Missing | 1632 | 13027 | |

# LBDCOTLC - Cotinine, Serum Comment Code

**Variable Name:** LBDCOTLC

**SAS Label:** Cotinine, Serum Comment Code

**English Text:** Cotinine, Serum Comment Code

**Target:** Both males and females 3 YEARS - 150 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---|---|---|---|---|
| 0 | At or above the detection limit | 7651 | 7651 | |
| 1 | Below lower detection limit | 3744 | 11395 | |
| . | Missing | 1632 | 13027 | |

# LBXHCOT - Hydroxycotinine, Serum (ng/mL)

**Variable Name:** LBXHCOT

**SAS Label:** Hydroxycotinine, Serum (ng/mL)

**English Text:** Hydroxycotinine, Serum (ng/mL)

**Target:** Both males and females 3 YEARS - 150 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---|---|---|---|---|
| 0.011 to 1520 | Range of Values | 11395 | 11395 | |
| . | Missing | 1632 | 13027 | |

# LBDHCOLC - Hydroxycotinine, Serum Comment Code

**Variable Name:** LBDHCOLC

**SAS Label:** Hydroxycotinine, Serum Comment Code

**English Text:** Hydroxycotinine, Serum Comment Code

**Target:** Both males and females 3 YEARS - 150 YEARS

| Code or Value | Value Description | Count | Cumulative | Skip to Item |
|---|---|---|---|---|
| 0 | At or above detection limit | 5401 | 5401 | |
| 1 | Below lower detection limit | 5994 | 11395 | |
| . | Missing | 1632 | 13027 | |