

National Health and Nutrition Examination Survey

2015-2016 Data Documentation, Codebook, and Frequencies

Cotinine and Hydroxycotinine - Serum (COT_I)

Data File: COT_I.xpt

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Last Revised: NA

Component Description

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 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.

There were no changes to the lab method, lab equipment, or lab site for this component in the NHANES 2015-2016 cycle.

Laboratory Method Files

[Cotinine and Hydroxycotinine in Serum Laboratory Procedure Manual](#) (April 2019)

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 [NHANES Laboratory Procedures Manual \(LPM\)](#). 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 Act 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

Refer to the [2015-2016 Laboratory Data Overview](#) for general information on NHANES laboratory data.

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 2015-2016 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).

Starting in the 2015-2016 NHANES cycle, the variable URXUCR (urine creatinine) will not be reported in this file. URXUCR can be found in the data file titled "Albumin & Creatinine – Urine".

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 LBD (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
LBXHCT	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 1370	Range of Values	7666	7666	
.	Missing	942	8608	

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	5115	5115	
1	Below lower detection limit	2551	7666	
2	Detectable result and exceeds the calibrated range of assay	0	7666	
.	Missing	942	8608	

LBXHCT - Hydroxycotinine, Serum (ng/mL)

Variable Name: LBXHCT**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 781	Range of Values	7666	7666	
.	Missing	942	8608	

LBDHCTL - Hydroxycotinine, Serum Comment Code

Variable Name: LBDHCTL
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	3480	3480	
1	Below lower detection limit	4186	7666	
2	Detectable result and exceeds the calibrated range of assay	0	7666	
.	Missing	942	8608	