

National Health and Nutrition Examination Survey

2017-March 2020 Data Documentation, Codebook, and Frequencies

Folate Forms - Total & Individual - Serum (P_FOLFMS)

Data File: P_FOLFMS.xpt

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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 objectives of this component are to: 1) provide data for monitoring secular trends in measures of nutritional status in the U.S. population; 2) evaluate the effect of people's habits and behaviors, such as physical activity and the use of alcohol, tobacco, and dietary supplements on nutritional status; and 3) evaluate the effect of changes in nutrition and public health policies, including welfare reform legislation, food fortification policy, and child nutrition programs on the nutritional status of the U.S. population.

These data will be used to estimate deficiencies and toxicities of specific nutrients in the population and subgroup, to provide population reference data, and to estimate the contribution of diet, supplements, and other factors to serum levels of nutrients. Data will be used in research to further define nutrient requirements as well as optimal levels for disease prevention and health promotion.

Eligible Sample

All examined female participants aged 12-49 years, and other examined participants (all males as well as females 1-11 years and 50+ years) one year and older from a one-half subsample in the NHANES 2017-March 2020 pre-pandemic sample were eligible.

Description of Laboratory Methodology

Five folate forms, 5-methyltetrahydrofolate, folic acid, tetrahydrofolate, 5-formyltetrahydrofolate, 5,10-methenyltetrahydrofolate, and an oxidation product of 5-methyltetrahydrofolate called MeFox (pyrazino-s-triazine derivative of 4- α -hydroxy-5-methyltetrahydrofolate) are measured by isotope-dilution high performance liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) (Fazili, et al. 2013). The assay is performed by combining specimen (150 μ L serum) with an ammonium formate buffer and an internal standard mixture. Sample extraction and clean-up is performed by automated 96-probe solid phase extraction (SPE) using 96-well phenyl SPE plates and takes ~1 h for a 96-well plate. Folate forms are separated within 6 min using isocratic mobile phase conditions and measured by LC-MS/MS. Quantitation is based on peak area ratios interpolated against a five-point aqueous linear calibration curve using $1/x^2$ weighting.

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

Laboratory Method Files

[Folate Forms](#) (July 2020)

[Folate Forms](#) (December 2021)

Laboratory Quality Assurance and Monitoring

Serum specimens are processed, stored, and shipped to the Division of Laboratory Sciences, National Center for Environmental Health, 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 NHANES Laboratory Procedures Manuals \(LPMs\)](#). Vials are stored under appropriate frozen (-30°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 LPMs.

Mobile Examination Centers (MECs)

Laboratory team performance is monitored using several techniques. NCHS and contract consultants use a structured QA evaluation during unscheduled visits to evaluate both the quality of the laboratory work and the QC 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 during “dry run” sessions. In addition, contract laboratories randomly perform repeat testing on 2% of all specimens.

NCHS developed and distributed a QC protocol for all the 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' QA/QC 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.

One variable was created in this data file. The variable (LBDFOT) was created using the following formula:

LBDFOT: The serum folate value in nmol/L (LBDFOTSI) was converted to ng/mL (LBDFOT) by dividing LBDFOTSI by 2.265 (rounded to 3 significant figures).

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 demographic data 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 documents](#) 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 age 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.

Serum Folate Forms for NHANES 2017– March 2020

In NHANES 2017–March 2020, a comprehensive list of serum folate forms was measured by isotope-dilution high performance liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) (Table 1). Serum total folate (LBDFOTSI) was calculated by adding LBXSF1SI-LBXSF5SI. LBXSF6SI was not included in the total folate calculation, due to evidence that it may already be present in vivo (Pfeiffer, et al. 2015). An imputed value of LOD divided by the square root of 2 was used for individual folate forms with results that were < LOD.

Please refer to the Analytic Notes for the 2011-2012 Folate Forms – Serum ([FOLFMS_G](#)) file for additional details on the comparability in serum total folate and folate forms measured between NHANES 2011– March 2020 and the previous survey cycles.

Table 1. Folate forms measured by LC-MS/MS

Analyte	Abbreviation	Variable Name
5-Methyltetrahydrofolate	5-methylTHF	LBXSF1SI
Pteroylglutamic acid (Folic Acid)	Folic acid	LBXSF2SI
5-Formyltetrahydrofolate	5-formylTHF	LBXSF3SI
Tetrahydrofolate	THF	LBXSF4SI
5,10-Methenyltetrahydrofolate	5,10-methenylTHF	LBXSF5SI
Pyrazino-s-triazine derivative of 4- α -hydroxy-5-methyltetrahydrofolate	MeFox	LBXSF6SI
Serum total folate (sum of folate forms)	tFOL	LBDFOTSI

Subsample Weights

The analytes included in this dataset were measured in all examined female participants aged 12-49 years, and in a one-half subsample of other examined participants one year and older. Special sample weights are required to analyze these data properly. Variable (WTFOLPRP) encoding of the specific sample weights for this subsample is included in this data file and should be used when analyzing these data. These special sample weights were created to account for the subsample selection probability, as well as the additional nonresponse to these lab tests. Therefore, if participants were eligible for the subsample, but did not provide a blood specimen, they would have the sample weight value assigned as "0" in their records.

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 design 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 time of venipuncture, and the conditions precluding venipuncture.

This 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., LBDSF1LC) 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. The other variable prefixed LBX (ex., LBXSF1SI) provides the analytic result for that analyte. For analytes with analytic results below the lower limit of detection (ex., LBDSF1LC=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 lower limit of detection (LLOD, in nmol/L) for the 6 folate forms are shown below. Because total folate is calculated from the sum of folate forms, a lower limit of detection does not apply.

Variable Name	Analyte Description	LLOD
LBXSF1SI	5-Methyltetrahydrofolate	0.13
LBXSF2SI	Folic acid	0.14
LBXSF3SI	5-Formyltetrahydrofolate	0.20
LBXSF4SI	Tetrahydrofolate	0.25
LBXSF5SI	5,10-Methenyltetrahydrofolate	0.20
LBXSF6SI	MeFox	0.10
LBDFOTSI	Total folate, serum	n/a

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.
- Fazili Z, Whitehead RD Jr, Paladugula N, Pfeiffer CM. A high-throughput LC-MS/MS method suitable for population biomonitoring measures five serum folate vitamers and one oxidation product. *Anal Bioanal Chem.* 2013;405:4549–60.
- Pfeiffer C, Sternberg M, Fazili M, Lacher D, Zhang M, Johnson C, Hammer H, Baily R, Rader J, Yamini S, Berry RJ, Yetley E. *British Journal of Nutrition* (2015) 113:1965:1977.
- 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 1 YEARS - 150 YEARS

WTFOLPRP - Folate & Folate Form Weight Pre-Pandemic

Variable Name: WTFOLPRP
SAS Label: Folate & Folate Form Weight Pre-Pandemic
English Text: Folate & Folate Form Weight Pre-Pandemic
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
2613.502065 to 856106.12264	Range of Values	7472	7472	
0	No Lab Result	914	8386	
.	Missing	0	8386	

LBDFOTSI - Serum total folate (nmol/L)

Variable Name: LBDFOTSI
SAS Label: Serum total folate (nmol/L)
English Text: Serum total folate (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
3.27 to 573	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDFOT - Serum total folate (ng/mL)

Variable Name: LBDFOT
SAS Label: Serum total folate (ng/mL)
English Text: Serum total folate (ng/mL)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
1.44 to 253	Range of Values	7334	7334	
.	Missing	1052	8386	

LBXSF1SI - 5-Methyl-tetrahydrofolate (nmol/L)

Variable Name: LBXSF1SI
SAS Label: 5-Methyl-tetrahydrofolate (nmol/L)
English Text: 5-Methyl-tetrahydrofolate (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
2.28 to 331	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF1LC - 5-Methyl-tetrahydrofolate cmt

Variable Name: LBDSF1LC
SAS Label: 5-Methyl-tetrahydrofolate cmt
English Text: 5-Methyl-tetrahydrofolic comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	7334	7334	
1	Below lower detection limit	0	7334	
.	Missing	1052	8386	

LBXSF2SI - Folic acid (nmol/L)

Variable Name: LBXSF2SI
SAS Label: Folic acid (nmol/L)
English Text: Folic acid (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.099 to 368	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF2LC - Folic acid cmt

Variable Name: LBDSF2LC
SAS Label: Folic acid cmt
English Text: Folic acid comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	7317	7317	
1	Below lower detection limit	17	7334	
.	Missing	1052	8386	

LBXSF3SI - 5-Formyl-tetrahydrofolate (nmol/L)

Variable Name: LBXSF3SI
SAS Label: 5-Formyl-tetrahydrofolate (nmol/L)
English Text: 5-Formyl-tetrahydrofolate (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.141 to 345	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF3LC - 5-Formyl-tetrahydrofolate cmt

Variable Name: LBDSF3LC
SAS Label: 5-Formyl-tetrahydrofolate cmt
English Text: 5-Formyl-tetrahydrofolate comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	86	86	
1	Below lower detection limit	7248	7334	
.	Missing	1052	8386	

LBXSF4SI - Tetrahydrofolate (nmol/L)

Variable Name: LBXSF4SI
SAS Label: Tetrahydrofolate (nmol/L)
English Text: Tetrahydrofolate (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.177 to 19.8	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF4LC - Tetrahydrofolate cmt

Variable Name: LBDSF4LC
SAS Label: Tetrahydrofolate cmt
English Text: Tetrahydrofolate comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	6781	6781	
1	Below lower detection limit	553	7334	
.	Missing	1052	8386	

LBXSF5SI - 5,10-Methenyl-tetrahydrofolate (nmol/L)

Variable Name: LBXSF5SI
SAS Label: 5,10-Methenyl-tetrahydrofolate (nmol/L)
English Text: 5,10-Methenyl-tetrahydrofolate (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.141 to 43.7	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF5LC - 5,10-Methenyl-tetrahydrofolate cmt

Variable Name: LBDSF5LC
SAS Label: 5,10-Methenyl-tetrahydrofolate cmt
English Text: 5,10-Methenyl-tetrahydrofolate comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	698	698	
1	Below lower detection limit	6636	7334	
.	Missing	1052	8386	

LBXSF6SI - Mefox oxidation product (nmol/L)

Variable Name: LBXSF6SI
SAS Label: Mefox oxidation product (nmol/L)
English Text: Mefox oxidation product (nmol/L)
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0.113 to 48.5	Range of Values	7334	7334	
.	Missing	1052	8386	

LBDSF6LC - Mefox oxidation product cmt

Variable Name: LBDSF6LC
SAS Label: Mefox oxidation product cmt
English Text: Mefox oxidation product comment code
Target: Both males and females 1 YEARS - 150 YEARS

Code or Value	Value Description	Count	Cumulative	Skip to Item
0	At or above the detection limit	7334	7334	
1	Below lower detection limit	0	7334	
.	Missing	1052	8386	