National Health and Nutrition Examination Survey 2005–2006

Documentation, Codebook, and Frequencies

Vitamin D

Laboratory

Survey Years:
2005 to 2006

SAS Transport File:
VID_D.XPT

July 2008
Last Revised: May 2009

NHANES 2005–2006 Data Documentation

Laboratory Assessment: Vitamin D (VID_D)

First Published: June 2008 **Last Revised:** May 2009

Note: See Analytical Note on Vitamin D Analysis for NHANES 2000-2006 and NHANES III (1988-1994)

Component Description

Vitamin D

The objectives of this component are: 1) to provide data for monitoring secular trends in measures of nutritional status in the U.S. population; 2) to evaluate the effect of people's habits and behaviors such as physical activity and the use of alcohol, tobacco, and dietary supplements on people's nutritional status; and 3) to 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 subgroups, 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 for research to further define nutrient requirements as well as optimal levels for disease prevention and health promotion.

Eligible Sample

Participants aged 1 year and older who do not meet any of the exclusion criteria are eligible

Description of Laboratory Methodology

The Diasorin (formerly Incstar) 25-OH-Vitamin D assay consists of a two-step procedure. The first procedure involves an extraction of 25-OH-D and other hydroxylated metabolites from serum with acetonitrile. Following extraction, the treated sample is assayed by using an equilibrium RIA procedure. The RIA method is based on an antibody with specificity to 25-OH-D. The sample, antibody, and tracer are incubated for 90 min at 20-25 °C. Phase separation is accomplished after 20-minute incubation at 20-25 °C with a second antibody-precipitating complex. A NSB buffer is added after this incubation and prior to centrifugation to aid in reducing non-specific binding. More detailed information about the Diasorin RIA method can be found on the NHANES Web site in the Laboratory Procedures Manuals.

There was no change to the equipment, method, or laboratory site from

NHANES 2003-2004.

A detailed description of the laboratory method used can be found at NHANES web page in the Laboratory Procedures Manuals.

Laboratory Quality Control and Monitoring

The NHANES quality control and quality assurance protocols (QA/QC) meet the 1988 Clinical Laboratory Improvement Act mandates. Detailed quality control and quality assurance instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM). Read the LABDOC file for detailed QA/QC protocols.

A detailed description of the laboratory method used can be found at NHANES web page.

Data Processing and Editing

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

Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM). Vials are stored under appropriate frozen (–20°C) conditions until they are shipped to National Center for Environmental Health for testing.

Detailed instructions on specimen collection and processing can be found at the NHANES web page.

Analytic Notes

1. Analytical Note for NHANES 2000-2006 and NHANES III (1988-1994) 25-Hydroxyvitamin D Analysis

Data Advisory:

The purpose of this note is to inform users of serum 25-hydroxyvitamin D (25(OH)D) data from NHANES about two issues that should be addressed when analyzing these data. First, users are cautioned about making direct comparisons between serum 25-hydroxyvitamin D measurements from NHANES 2000-2006 (i.e., publicly released data for 2001-2006 and controlled-access data for 2000) and measurements obtained in NHANES III (1988-1994). NHANES III 25(OH)D data must be adjusted in order to make a valid comparison to the 2000-2006 NHANES survey years due to a reformulation of the DiaSorin radioimmunoassay (RIA) kit that resulted

in shifts in assay results between the two time periods. Second, data users should also be aware that the 25(OH)D data from the 2000-2006 NHANES were most likely affected by drifts in the assay performance (method bias and imprecision) over time. These assay drifts are likely due to reagent and calibration lot changes in the reformulated DiaSorin assay. These QC drifts may affect comparability, and therefore interpretability, of the data from any combination of NHANES data from 2000-2006, even when comparisons are not being made with NHANES III. Therefore, users of these various NHANES data sets are cautioned that changes in 25(OH)D results over the time period 1988-2006 are affected by the two methodological issues described above and both should be considered when evaluating whether, and how much, differences over time are due to true changes in the vitamin D status of the US population.

Background

Measurements of serum 25-hydroxyvitamin D were performed as part of the nutrition biomarker component of NHANES III (1988-1994) and in the years 2000-2006 of NHANES. These 25(OH)D data are available on public use data files on the NCHS/NHANES website for NHANES III and NHANES 2001-2002, 2003-2004 and 2005-2006. The 25(OH)D data collected in 2000 are available through the NCHS Research Data Center (not available in public data sets) because of a disclosure risk of confidential information for a single-year data release. Readers should be aware that all issues discussed below in regard to the publicly available data for 2001-2006 also apply to the controlled-access data from 2000.

Measurements of serum 25(OH)D were performed in NHANES III (1988-1994) and NHANES 2000-2006, at the National Center for Environmental Health, CDC, Atlanta, GA using the DiaSorin RIA kit (Stillwater MN). The DiaSorin assay kit had been reformulated by the manufacturer between 1994 and 2000 by introducing an antibody that provided improved binding. On average, 25(OH)D values from the reformulated RIA assay used in NHANES 2000-2004 were 12% lower than the original RIA assay values from NHANES III. In addition, drifts in the serum 25(OH)D assay performance (as reflected in QC pool shifts in the mean, up or down, by up to 10%) due to changes in reagent and calibrator lots over the period of 2000-2006 have been observed in the CDC laboratory.

Preliminary steps have been taken to address the changes in assay

method between NHANES III and NHANES 2000-2004. A method comparison study between NHANES III and NHANES 2000-2004 was conducted, which is described in detail in Appendix 1 that accompanied a paper published in the American Journal of Clinical Nutrition.[1] This appendix is available on the AJCN website but not in the printed version of the paper, so it is briefly summarized here. To assess the magnitude of assay changes that might have an impact on any observed trends in serum 25(OH)D in the population, the CDC laboratory reanalyzed a subset of 150 banked serum samples from NHANES III using the reformulated version of the RIA assay. The serum samples were selected to represent the entire distribution of serum 25(OH)D values in NHANES III. The NHANES III results as measured with the reformulated assay were regressed on the NHANES III values obtained with the original assay for these 150 specimens. The average difference between the reformulated and original RIA was -12% and is described by the following equation:

$$\textbf{NHANES III } 25(OH)D_{\text{2000-2004 RIA assay}} = (0.8429 * \textbf{NHANES III } 25(OH)D_{\text{1988-1994 RIA assay}}) + 2.5762 \text{ nmol/L } (r = 0.8966).$$

This adjustment equation was generated after first accounting for the assay drifts during 2000-2004 with the reformulated DiaSorin assay.

Impact of assay variation on serum 25(OH)D measurements from the NHANES 2000-2006

The weighted mean of 25(OH)D for NHANES 2001-2006 was 59.0 nmol/L, with a range of single-year means of 52.5-66.8 nmol/L. As indicated above, the variation between single years appeared to be due to method variation (arising from method bias and imprecision) over time that results from reagent and calibration lot-to-lot variation.

An approach to address the observed methods variations of 25(OH)D over time in NHANES is currently being developed. However, because this approach will likely take many months to complete, an interim approach was used to assess the potential impact of including data from time periods with greater assay variability on means and prevalences. This approach repeats analyses published in AJCN (Looker et al), which included the data with greater variability, by excluding the data of concern.

Results from these analyses indicated that the impact of including the data from the time period of concern was minimal on results calculated

for NHANES 2000-2004. In specific, excluding the time period of concern produced means for NHANES 2000-2004 that were lower on average by -1.3 to -1.9 nmol/L (range -3.1 to +1.1 nmol/L) than means presented in the AJCN article. Percentile data from NHANES 2000-2004 were also minimally affected when excluding the time period of concern: 5^{th} percentile values were higher on average by 0.6 nmol/L (range -1.8 to +4 nmol/L), 50^{th} percentile values did not differ (range -2.5 to +2.4 nmol/L) and 95^{th} percentile values were lower by -1.5 nmol/L (range -6.2 to +5.7 nmol/L). Finally, when the time period of concern was excluded, prevalence estimates for values below cut-points from NHANES 2000-2004 were slightly higher on average than the prevalences presented in the AJCN article. For example, estimates of the prevalence < 25 nmol/L were higher, on average, by 0.25 percentage points (range -0.1 to +0.6). Estimates of the prevalence < 37.5 nmol/L to < 75 nmol/L were higher, on average, by 1.5 to 2.2 percentage points (range -3.3 to +6.4).

In summary, excluding the data from the time period of concern resulted in means and percentiles for NHANES 2000-2004 that were slightly lower and prevalence estimates that were slightly higher than those originally obtained when the entire 2000-2004 dataset was used.

Analysis Recommendations:

Based on the above information and analyses, NCHS strongly urges data users to follow the following recommendation before comparing serum 25(OH)D data from NHANES IIII with serum 25(OH)D data from NHANES 2000-2006:

Serum 25(OH)D data from NHANES III should be adjusted using the following equation if comparisons with 25(OH)D data from the full combined 2000-2006 NHANES are being made:

$$\textbf{NHANES III 25(OH)D}_{\textbf{2000-2004 RIA assay}} = (0.8429 * \textbf{NHANES III 25(OH)D}_{\textbf{1988-1994 RIA assay}}) + 2.5762 \text{ nmol/L}$$

Readers should be aware that this equation allows an approximation of NHANES III results to the level of the reformulated assay used in NHANES 2000-2004. However, it is imperfect in that it cannot simultaneously adjust for drifts in assay performance that may have occurred after 2004. As a result, it should be employed with caution when making comparisons between NHANES III and the publicly available NHANES 2001-2006 25(OH)D data.

Based on the above information and analyses, NCHS strongly urges data users to follow the recommendations below when comparing serum 25(OH)D data for the 2000-2006 NHANES survey period:

1. NCHS strongly discourages analysis of, or comparisons between, any of the two-year NHANES 2001-2006 25(OH)D data due to method variability and sample design limitations. Users are discouraged from using a four-year dataset based on 2001-2004 due to a higher possibility that results may be affected significantly by assay variability.
2. NCHS recommends the use of a data set which combines all years of data (2001-2006 or 2000-2006) to provide more stable estimates of means, percentiles, and prevalence estimates for 25(OH)D. Users should note the possibility of assay variability in their results from the combined dataset as a study limitation.
3. Given the observed QC data variability, users should exercise caution when analyzing and interpreting inter-relationships between 25(OH)D and other NHANES variables using the 2000-2006 NHANES dataset. At a minimum, users should note the possibility of variability due to laboratory methods issues in their results as a study limitation. This variability may be more of an issue for population subgroup analyses.
4. Some variables of interest relative to 25(OH)D were only collected in NHANES 2003-2006 (i.e. parathyroid hormone and sun exposure variables). Interpretation of any analyses conducted on this four-year data set may not be affected in any significant way by the observed variation in 25(OH)D data during this time period, but users should be aware of, and, at a minimum, list this issue as a potential limitation of analyses and findings conducted using this four-year data set.
5. Additional variables of interest relative to 25(OH)D, geography and seasonality, are only accessible through the NCHS Research Data Center (due to increased disclosure risk) and are subject to the analytic limitations of data used in that setting.

Future Plans

At present, there is no gold standard method for measuring serum 25(OH)D, so that no 25(OH)D data are accuracy-based regardless of

the assay used. The National Institute of Standards and Technology (NIST) will soon provide standard reference materials for 25(OH)D assays with certified values assigned by use of isotope dilution tandem mass spectrometry (LC-MS/MS) candidate reference measurement procedures.[2] CDC intends to generate regression equations that will permit the adjustment of the 25(OH)D data from various NHANES survey years to the NIST accuracy-based standard by reanalyzing subsets of specimens from NHANES 1988-1994 and 2000-2006 using a candidate LC-MS/MS method. This will improve the ability to analyze the 25(OH)D data from NHANES 2000 and beyond for all types of analyses, including comparisons between NHANES 2000-2006 and NHANES III. When these equations become available, this analytical note will be updated with a revised analytical note.

References

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2. General Analytical Note:

The analysis of NHANES 2005–2006 laboratory data must be conducted with the key survey design and basic demographic variables. The NHANES 2005–2006 Household Questionnaire Data Files contain demographic data, health indicators, and other related information collected during household interviews. The Household Questionnaire Data Files also contain all survey design variables and sample weights required to analyze these data. The Phlebotomy Examination file includes auxiliary information on duration of fasting, the time of day of the venipuncture, and the conditions precluding venipuncture. The Household Questionnaire and Phlebotomy Exam files may be linked to the laboratory data file using the unique survey participant identifier SEQN.

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Locator Fields

Title: Vitamin D

Contact Number: 1-866-441-NCHS

Years of Content: 2005–2006

First Published: June 2008

Revised: May 2009

Access Constraints: None

Use Constraints: None

Geographic Coverage: National

Subject: Vitamin D

Record Source: NHANES 2005–2006

Survey Methodology: NHANES 2005–2006 is a stratified multistage probability sample of the civilian non-institutionalized population of the U.S.

Medium: NHANES Web site; SAS transport files

National Health and Nutrition Examination Survey
Codebook for Data Production (2005-2006)

Vitamin D (VID_D)
Person Level Data

July 2008

SEQN	Target
	B(1 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Respondent sequence number
English Text: Respondent sequence number.	
English Instructions:	

LBXVID	Target
	B(1 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Vitamin D (ng/mL)
English Text: Vitamin D (ng/mL)	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
2 to 77	Range of Values	8306	8306	
.	Missing	1134	9440	