

Reviewer's report

Title: Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study

Version: 1 **Date:** 11 June 2007

Reviewer: Jaime Wilger

Reviewer's report:

Major Compulsory Revisions

1. My main concern with this paper is whether or not NHANES was analyzed in accordance with the analytical guideline. NHANES data needs to be weighted and analyzed using a program (for example SUDAAN) that takes into account complex sample designs.

Here is the web tutorial that may be of help:

http://www.cdc.gov/nchs/tutorials/currentnhanes/SurveyDesign/Weighting/weighting_intro.htm

The following is taken from the analytical guidelines, which need to be read before any analysis, which are located at: http://www.cdc.gov/nchs/about/major/nhanes/nhanes2003-2004/analytical_guidelines.htm

NHANES is a complex sample survey. The overall sample design and weighting methodology has been similar over the history of the survey. The sample design and weighting methodology for NHANES 1999-2004 is very similar to past NHANES data releases. Primary Sampling Units are generally single counties, although small counties are sometimes combined to meet a minimum population size. In the years 1999-2001, NHANES was based on a design linked to the National Health Interview Survey (NHIS). The NHANES PSUs were a subset of the PSUs previously selected for the NHIS. An independent set of PSU's was selected for 2002-2006; the sampling frame for this design was all counties in the United States. The additional stages of selection in the probability design for NHANES 1999-2004 remain very similar to past NHANES designs. Clusters of households are selected, each person in a selected households is screened for demographic characteristics, and one or more persons per household are selected for the sample. For NHANES 1999-2000, there were 12,160 persons selected for the sample, 9,965 of those were interviewed (81.9 percent) and 9,282 (76.3 percent) were examined in the MEC. For NHANES 2001-2002, there were 13,156 persons selected for the sample, 11,039 of those were interviewed (83.9 percent), and 10,477 (79.6 percent) were examined in the MEC. For NHANES 2003-2004, there were 12,761 persons selected for the sample, 10,122 of those were interviewed (79.3 percent) and 9,643 (75.6 percent) were examined in the MEC.

As with any complex probability sample, the sample design information should be explicitly used when producing statistical estimates or undertaking statistical analysis of the NHANES data. In particular, sample weights and the first stage of the cluster design need to be considered. The sampling weights provided must be used to produce unbiased national estimates. The sample weights for NHANES 2003-2004 reflect the unequal probabilities of selection, non-response adjustments and adjustments to independent population controls. The proper sample weight must be used. If only data from the Interviewed sample is used, then the appropriate SAS variable is WTINT2YR. If data from the MEC examination is used, then the appropriate SAS variable is WTMEC2YR.

Because NHANES is a complex probability sample, analytic approaches based on data from simple random sample are usually not appropriate. Ignoring the complex design can lead to biased estimates and overstated significance levels. Sample weights and the stratification and clustering of the design must be incorporated into an analysis to get proper estimates and standard errors of estimates.

Data are sometimes collected on sub-samples of the full design for any NHANES survey. These data are available but public release of these files may lag behind the main data release for any two-year period due to extra time needed for processing and quality assurance review. In addition, each subsample involves another stage of selection and separate sample weights that account for that stage of selection and additional non-response. For analysis of subsample data, appropriate subsample weights must be used and they are included on any data file where relevant.

Minor Essential Revisions

2. Methods: This sentence in the paper needs to be slightly changed: "Dietary supplement intake was assessed in NHANES by asking participants about their dietary supplement usage patterns in the month prior to the examination, including use of any vitamins, minerals, or other dietary supplements." In NHANES participants are asked about their usage of dietary supplements in the past 30 days, during their home interview. Participants' home interview is before the examination at the Mobile Examination Center and depending on scheduling, an examination can be anywhere between a couple of days after the

home interview or weeks later. I would change that to read “in the past 30 days prior to the interview, or home interview”.

3. Methods: This sentence in the paper needs to be clarified or reworded: “We also identified 176 individuals who consumed a multivitamin/mineral and no other dietary supplements, and did so approximately every other day or more often.”

How are you identifying if an NHANES participant took the supplement approximately every other day or more often? NHANES only asks about the number of days the participant took the supplement in the past 30 days. I would change this to days, for example, “we only included participants who reported taking the supplement 20 days over the past 30 days.”

Discretionary Revisions

4. One limitation that should be touched upon in the write up is that diet was not included in this paper. NHANES does collect information on diet – 24 Hour Dietary Recall – on participants. Including diet would seem important, since it could be that people consuming an average of 17 dietary supplements in one month, may have healthier diets and healthier lifestyles in general, leading also to these optimal levels of biomarkers.

5. Minor change for Table 2. Characteristics of a convenience sample of long-term users of multiple dietary supplements (Multiple Supp) and multivitamin/mineral users (Single Supp) and nonusers (No Supp) from NHANES 2001-2002.

This should be made clearer, because it reads as if all samples are from NHANES.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.