ASSESSING TOTAL NUTRIENT EXPOSURES FROM ALL SOURCES IN U.S. ADULTS

by

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To my Mom, Dad, Amelia, beloved family, and friends, for their continued love and support.

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LIST OF ABBREVIATIONS

Abbreviation	**Term**
DS	Dietary Supplement
DSHEA	Dietary Supplement Health and Education Act
MVM	Multivitamin-mineral
DRI	Dietary Reference Intakes
FBQ	Frequency-based Questionnaire
24HR	24-hour Dietary Recall
FFQ	Food Frequency Questionnaire
NHANES	National Health and Nutrition Examination Survey
DSMQ	Dietary Supplements and Prescription Medicine Questionnaire
NHIS	National Health Interview Survey
NHANES-DSD	NHANES Dietary Supplement Database
DSLD	Dietary Supplement Label Database
UL	Tolerable Upper Intake Level
RDA	Recommended Dietary Allowances
EAR	Estimated Average Requirement
AI	Adequate Intake
NCI	National Cancer Institute
ISU	Iowa State University
NRC	National Research Council
MSM	Multiple Source Method
SPADE	Statistical Program to Assess Habitual Dietary Exposure
PIR	Family Income-to-Poverty Ratio
SNAP	Supplemental Nutrition Assistance Program
DGA	Dietary Guidelines for Americans
BMI	Body Mass Index
SE	Standard Error
MEC	Mobile Examination Center
DSQ	Dietary Supplement Questionnaire

ABSTRACT

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Dietary supplement (DS) use in the United States is pervasive, with approximately half of U.S. adults currently taking a DS. Although no consensus exists as to whether DS are beneficial to the prevention of chronic disease, strong scientific evidence supports sufficient nutrient intakes for optimal health. The Dietary Guidelines for Americans recommend that nutrient needs be met primarily through nutrient dense foods; however, it is recognized that in certain cases, dietary supplements and fortified foods may be necessary in order to meet nutrient needs. Currently, little is known regarding whether inclusion of DS can improve micronutrient intakes of some U.S. population subgroups, and how DS use patterns relate to income indicators among U.S. adults. Since DS contain nutrients in amounts as high as the National Academies for Science, Engineering, and Mathematics' Dietary Reference Intakes, failing to evaluate the contributions of DS to total nutrient intakes when assessing the nutritional adequacy of the U.S. population may lead to inaccurate findings. Therefore, the overarching aims of the research presented in this thesis were to 1) provide updated estimates of DS use, 2) to examine the relationship between DS use and demographic, socioeconomic, and health-related characteristics, and 3) to examine the contributions of DS to total usual micronutrient intakes relative to the DRIs for adequacy (i.e., the EAR or AI) and excess (i.e., the UL) among U.S. adults by sex, age, race/Hispanic origin, and income, using data from the NHANES, 2011-2014.

The thesis begins with a narrative review evaluating the body of evidence investigating the best practices for dietary supplement assessment and total nutrient exposures. Collectively, little is known about the measurement error structure of DS reporting, and currently no standardized methods are available to assess the prevalence of use and nutrient exposures from DS. Chapters 2 and 3 are comprised of two cross-sectional studies using data from the National Health and Nutrition Examination Survey (NHANES) with regard to DS usage patterns and previous related literature relative to the research aims, the contribution of dietary supplements to total

micronutrient intakes, and the prevalence of DS use by demographic, socioeconomic and health-related characteristics among U.S. adults.

The evaluation of the prevalence of dietary supplement use by socioeconomic and health-related characteristics indicates that one or more DS are used by over half of U.S. adults (52%), particularly multivitamin-mineral DS, and income is associated with DS use, type, and number of supplements taken. This study provided additional information on DS use in relationship to family income, food security, and SNAP participation status. To our knowledge, this study is the first to use NHANES data to provide information assessing the relationship between DS use and various indicators of participants' economic status among U.S. adults, including food security.

The study that evaluated the contribution of dietary supplements to total micronutrient intakes among U.S. adults by a number of demographic characteristics, and suggests that the use of micronutrient-containing DS substantially contributed to total nutrient intakes and reduced the risk of inadequacy for several micronutrients across all sex, age, race, and income groups in the U.S. population. However, many U.S. adults still have inadequate intakes of potassium, magnesium, calcium, vitamin D, vitamin A, and/or vitamin C and these population subgroups at risk for inadequacy differ by sex, age, and race/Hispanic origin, and income. Use of DS substantially reduced the prevalence of inadequate intakes for calcium and vitamins D and C, but not for the other 17 micronutrients assessed. DS use also increased the risk of potentially excessive intakes, especially among DS users.

Collectively, the findings from the studies presented in this thesis contribute additional, updated evidence on the use of DS and their contributions to total nutrient exposures in different subpopulations of U.S. adults. Our outcomes point to a need for further investigation into how DS contribute to nutrient exposures and nutrient disparities present in certain subgroups of the U.S. adult population, as well as a standardization of methods to assess the prevalence of use and nutrient exposures from DS.

CHAPTER 1. BEST PRACTICES FOR DIETARY SUPPPLEMENT ASSESSMENT AND ESTIMATION OF TOTAL USUAL NUTRIENT INTAKES IN POPULATION-LEVEL RESEARCH AND MONITORING: A REVIEW OF THE LITERATURE

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1.1 Abstract

The use of DS is pervasive and can provide substantial amounts of micronutrients to those who use them. Therefore when characterizing dietary intakes, describing the prevalence of inadequacy or excess, or assessing relationships between nutrients and health outcomes, it is critical to incorporate DS intakes to improve exposure estimates. Unfortunately, little is known about the best methods to assess DS, and the structure of measurement error in DS-reporting. Several characteristics of nutrients from DS are salient to understand when comparing to those in foods. First, DS can be consumed daily or episodically, in bolus form and can deliver discrete and often very high doses of nutrients that are not limited by energy intakes. These characteristics contribute to bimodal and distributions severely skewed to the right. Labels on DS often provide nutrient forms that differ from those found in conventional foods, and underestimate analytically-derived values. Finally, the bioavailability of many nutrient-containing DS is not known and it may not be the same as the nutrients in a food matrix. Current methods to estimate usual intakes are not designed specifically to handle DS. Two temporal procedures are described to refer to the order that nutrient intakes are combined relative to usual intake procedures, referred to as a

“shrinking” of the distribution to remove random error. The “shrink then add” is preferable to the “add then shrink” approach when users and non-users are combined for most research questions. Stratifying by DS use before usual intake methods is another defensible option. This review describes how to incorporate nutrient intakes from DS to usual intakes from foods, and describes the available methods and fit-for-purpose of different analytical strategies to address research questions where total usual intakes are of interest at the group level for use in nutrition research and to inform policy decisions.

1.2 Introduction

Accurate nutrient exposure assessment is critical for the two main functions in nutritional epidemiology: characterizing the intake distributions and relating dietary intakes to health outcomes. Traditionally studies investigating diet and health relationships have failed to include nutrient exposures from DS. However, more than half of US adults and one-third of children use DS and the majority of these products contain essential nutrients (1-5).

DS are defined in the U.S. under the 1994 DSHEA as any product, other than tobacco, intended to supplement the diet and is not a conventional food. DS ingredients include micronutrients, macronutrients, herbals, botanicals, phytochemicals, zoochemicals, and well as many other concentrates, metabolites, constituents, extracts, or combinations (e.g., probiotics, glucosamine, and melatonin). MVM DS are the product that is most commonly used; however, no legal or regulatory definition of the term “micronutrient supplement” or MVM exists (6). For example, different reports have characterized MVMs as products containing ≥ 3 vitamins, ≥ 3 vitamins plus ≥ 1 mineral, and ≥ 9 or ≥ 10 total micronutrients (1, 3, 5, 7, 8).

While the effects of DS on diet-related health promotion efforts, chronic disease prevention, and treatment remain unclear (9), it is evident that these products meaningfully contribute to nutrient exposures, providing nearly 100% of the Daily Value for some nutrients, such as vitamins C, D, E and many of the B vitamins.

Thus, characterizing nutrient intakes from diet alone provides an incomplete assessment of total nutrient intakes and provides biased estimates of population prevalence estimates and nutrient-disease associations in studies may be misleading. However, there are unique challenges involved when incorporating DS-nutrients in the estimation of total nutrient intakes, particularly when usual intakes are the primary objective.

Usual or habitual intakes (i.e., long-term average daily intakes) are, in general, the most relevant nutrition indicator for research and monitoring of a population (10). Dietary recommendations are intended to be met over time because nutrients can be stored in the body, making it unnecessary to achieve nutrient intake recommendations each day (11). Long-term nutrient intake, as opposed to intake on a given day, is the ideal measure to determine whether a group or population is meeting or exceeding the DRI (12) and to determine links with health outcomes that manifest over time. However, difficulties arise when attempting to use dietary assessment methods to inform decisions about long-term, usual intake because they are prone to measurement error. Furthermore, the challenges with DS are different than those with foods; unlike foods, DS usage patterns can substantially vary over time (13). It is therefore simplistic and incorrect to assume that what is good for measuring foods is equally as good for measuring DS. Research is needed to understand the measurement error structure of usual nutrient intakes from DS, especially at the group or population level (13).

This article reviews the methods to assess usage patterns of DS and the databases available to analyze their content, with an emphasis on the U.S. context. Also discussed are the challenges encountered and suggested best practices for measuring and estimating total usual nutrient intakes that include the contributions of DS at the group or population level when long-term or habitual intakes are of primary interest.

1.3 Measuring Dietary Supplement Use

Currently no standardized methods are available to assess the prevalence of use and nutrient exposures from DS. Supplement use has been measured by methods that focus solely on supplements, such as FBQ, supplement inventories, and short screening tools. Their use has also been measured in conjunction with food and beverage intake, using methods such as 24HR, FFQ, food diaries or records, and in some screening tools, all of which may query intake of foods, beverages, and supplements. Mobile applications and web-based platforms have also been used to measure DS.

Little is known about the accuracy, reliability, and measurement error structure of DS assessment methods. However, consideration of the rich literature that explores and quantifies the measurement error inherent in dietary assessment and specifying the similarities and differences between traditional dietary assessment and DS assessment can inform an understanding of the error that can be expected to be inherent in DS assessment. Dietary assessment methods are subject to different types of measurement error for quantifying energy and nutrients from the diet (see section on measurement error below). The 24HR is the least-biased method to assess energy intakes from foods (i.e., inclusive of beverages) when compared to other measures, but both recalls and frequency methods underestimate true dietary intakes as assessed by recovery biomarkers (14-16). Yet, the extent and distortion that dietary and DS measurement error contribute to estimates of total nutrient intake and its relationship with health outcomes have not been characterized. Most 24HR methods have the ability to collect data on DS use (17). Some modules facilitate collection and coding for any DS reported, but must be used in conjunction with the assessment of foods and beverages while others offer a stand-alone method to query only DS (17). The collection of DS data as part of the 24HR adds a time burden for both the participant and interviewer. The Automated-Self-Administered 24HR has recently been used with a DS module, and was validated against a traditional 24HR over the phone (18). The Automated-Self-Administered 24HR reduces interviewer burden, allows the participant to answer questions at his or her own pace, reduces data transcription errors, and is available to the research community without cost.

Most large epidemiological studies use a FFQ to obtain information about dietary intake, and many include items on DS. However, the FFQs most commonly used in the U.S. differ markedly in how they query DS. They inquire about different DS or product categories and use differing methods for assigning the default values for nutrients and other bioactive constituents. The DS questions on various FFQs differ from one another in the number of products listed, frequency of use responses, duration of use categories, and the dosages, making comparisons of intakes across studies difficult, if not impossible (19). Rios-Avila et al. (19) performed a qualitative examination of the specific modalities employed by some of the most widely used FFQ in large epidemiological cohorts and found tremendous variation in the way FFQs assess DS use including the Diet History Questionnaire II (20), the Harvard (Willett) FFQ (21), the 2014 Block FFQ and physical activity screener (22), the Women's Health Initiative FFQ (23), the Vitamins and Lifestyle FFQ (24), and the Multiethnic Cohort Study FFQ and the additional supplement questionnaire used to validate the Multiethnic Cohort's FFQ supplement data (25-27). The FFQs differed on number of DS queried with a range of 3 to 49 supplements, and the questions varied considerably on the types of DS: one FFQ did not ask about multivitamins with minerals, four did not ask about herbal/botanicals, and two did not ask about non-vitamin/non-mineral supplements.

The "dosage" or amount of nutrients consumed were not uniformly queried, if queried at all. Considerable variation in the questions about product use duration were also noted. FFQs are particularly problematic for assessing herbals and botanical supplements since they rarely provide detail on the product and the bioactive constituents may be unknown. At present the best solution to these problems is to use a FFQ with DS questions that have been validated for the population under study.

1.3.1 Issues with Measuring Dietary Supplement Use

Many issues can arise when collecting DS data: it may be incomplete or missing; it may be impossible to collect detailed information; only product types may be queried (e.g., MVM on an FFQ); or participants may not recall desired details necessary to identify the product; and, errors may be introduced while recording information from the product label. All of these factors can prevent identifying the exact product used by a participant. In these cases, default formulations need to be assigned to reported products, and the manner in which the default is chosen may introduce error.

All self-reported nutrient intake assessment methods rely on databases for estimates of nutrient content. Maintaining the currency and accuracy of DS databases is challenging due to the sheer number of products on the market (at least 85,000 products on the market at a given time) and the reformulation and rapid turnover of DS products, estimated to be about a third of products annually. Brand specificity of formulations and changes even in the same brand over time is another challenge to accurate assignment of nutrient contents to reported DS. Similar issues may arise for dietary reporting if the database does not capture important differences among brands. However, the amount of error that may be introduced by matching a particular product to a more general product for DS as a default, compared with foods, has the potential to be magnified because of the vastly greater ranges in nutrient content in DS compared with foods. Thus, even if accurate information on the brand is collected through reporting, photographing of the product label, or scanning the UPC (although many UPCs are generalized and reused over time), erroneous information may still result if the product database does not include those brands or is not current.

1.4 Dietary Supplement Use in the United States

This section presents information on DS use obtained from nationally representative data sources and other indicators of DS use such as sales data.

1.4.1 The National Health and Nutrition Examination Survey

The NHANES is a nationally representative, cross-sectional Federal program of studies designed to describe the health and nutritional status of the non-institutionalized resident population of the United States (28). NHANES collects data via interviews in participants' homes; augmented by a dietary interview and physical examination with the collection of biospecimens, such as blood and urine, in a mobile examination center; and, a follow-up telephone interview.

DS use has been collected as part of NHANES since the early 1970s (4). The NHANES protocol for DS assessment includes an in-home inventory method in which participants show trained interviewers the containers/bottles of all DS that they used in the 30 days prior to the interview. The interviewer records information from the product label, including product name, manufacturer, strength for many single nutrient products and form (e.g., tablet, powder, or liquid). The inventory is collected in tandem with the DSMQ that assesses more details such as the amount typically taken, the frequency taken in the past 30 days, how long the product or a similar product was taken, and the motivation(s) for taking the product. This level of detail is quite unusual for recording supplement use, but it is critical to obtain the most accurate information, especially if the goal is to estimate an average daily exposure of nutrients from all dietary supplements taken. Since 2007, DS information has been collected as part of an additional module at the end of the interview consisting of two 24HRs, in addition to the inventory and DSMQ collected in the home. During the in-person and telephone 24HR, conducted approximately three to ten days apart, the interviewer asks the participants if they used the products reported in the home inventory and DSMQ or any new products in the previous 24 hours.

The NHANES DSMQ data indicate that estimated use of any DS has increased among adults from pre- to post-DSHEA, that is, from: NHANES III (1988-94) to the continuous NHANES (i.e., 1999 and beyond) (29, 30). It has remained generally stable since the early 2000s with about half of US adults reporting regular use of at least one DS (1, 2, 5). Use of DS is lower among US infants and children than among adults, with about one-third of children (2-18 y) routinely taking them (3, 4, 31). Across time in both adults and children, MVM supplements account for the vast majority of total DS use. Limited national estimates exist on the use of DS during pregnancy and lactation, but it has been estimated that 77% of US pregnant females take a prenatal vitamin, with use being highest in the third trimester (32). Older adults are the highest users of DS across all age groups, with about 70% taking at least one DS and almost 30% taking 4 or more products (33). Some subgroups of the population have very high use of dietary supplements. These include athletes, members of the armed forces and others with an interest in physical performance, those with chronic and other diseases, and users of other complementary and alternative medicines. But, NHANES is unlikely to capture these specific population subgroups in sufficient numbers to make meaningful estimates.

Much less is known about DS use in NHANES from both the 24HR and the DSMQ. Using both short-term (i.e., the previous 24 hours) and long-term (i.e., the previous 30 days) may provide an ideal measurement tool to ensure capturing both habitual and episodic DS use. Nicastro et al. recommend using both methods to best assess MVM use because prevalence estimates are lower on the 24HR alone than the DSMQ in both men and women (34). The majority of those who used MVM use (63%) did so daily. The results for other users seem to reflect a potential digit-preference bias because the estimated numbers of days supplements were used were multiples of 5 (34). Interestingly, those who used DS less frequently, as estimated from the DSMQ (1--9 days during a 30-day period), were more likely to use MVM on any given day, as estimated from the 24HR; whereas more frequent MVM use was associated with a similar proportion of use on a given day. Most MVMs (67%) were used in a 30-day period and on a given day, but a higher percentage of default values were assigned for the estimates for a given day (26%) when compared to the estimates for a 30-day period (12%) or both time periods (9%) (34). While these findings provide some insights on methodological differences for the 24HR and the DSMQ, it should be noted that the 24HR interviewer specifically asks participants if he/she took a product reported in the home interview; thus, more research is needed to garner specific details of how DS reporting may differ based on method.

In NHANES, data are collected on DS of all types, but detailed quantitative estimates are made only for nutrient-containing DS. Quantitative information on intakes cannot be assessed for many other types of supplements for reasons mainly related to not having a comprehensive analytic composition database and having to rely on what is declared on the product label. These issues include: lack of knowledge of what the bioactive(s) ingredients actually are, lack of analytical data on known bioactive ingredients, lack of information on the label about the amounts of the presumed bioactive(s) listed in proprietary blends, and other issues (35-37).

1.4.2 The National Health Interview Survey

The NHIS, conducted by the National Center for Health Statistics, is a nationally representative, cross-sectional, household-based survey designed to describe the health of the non-institutionalized resident population (38). NHIS has been collecting data on the health of the U.S. population since 1957. While NHANES incorporates both examination and household interview components in a smaller nationally representative sample, the NHIS includes only a household interview with a larger nationally representative sample. This allows for an increase in the scope of the questions asked regarding DS. NHIS does not collect detailed data on DS from the product label or detailed information on the frequency of consumption or amount typically taken. Also, it does not collect dietary intake (foods and beverages). However, NHIS can be used to estimate the prevalence of use of selected types of DS. It has the advantage of a very large sample (i.e., 35,000 households containing about 87,500 persons per year), so estimates for less commonly used products are possible. As a result, the NHIS is commonly used to estimate prevalence of herbal and botanical supplements used in complementary health practices.

In 2002, 2007, and 2012, the Child and Adult Alternative Health supplement module was administered in NHIS to randomly selected participants to assess nutrient and non-nutrient DS use (39, 40). The DS module is included approximately once or twice a decade as funds permit. Estimates from NHIS indicate that non-vitamin and non-mineral supplements (e.g., herbal and botanical supplements) remain the most common form of complementary health practice in adults (18.9% in 2002, 17.7% in both 2007 and 2012) (39). While the prevalence of these general types of DS has remained unchanged overtime, the specific type of non-mineral, non-vitamin DS has changed over time (41).

1.4.3 Other Indicators of Dietary Supplement Use

DS sales data are available from the Nutrition Business Journal and other sources to monitor consumer expenditures on DS. They are not useful for estimating the prevalence of DS use directly since they provide estimates in dollar amounts; thus, products with a low prevalence of use but a very high price would appear to be similar in dollars expended to products used widely with very low prices. Moreover, data are presented by marketing category, such as performance supplement or memory supplements rather than by more objective criteria. However, the data can be of utility to forecast trends in product types and monitor patterns in the sales of products or categories. Also, some products, such as sports bars and energy drinks that may not actually be DS from the regulatory standpoint are included in the aggregate numbers. Therefore, care needs to be taken in disaggregating the true DS from other products that are also listed. Sales data are released annually and provide an up-to-date barometer of changes in the marketplace. According to Nutrition Business Journal, total supplement sales in 2016 were $41.2 billion, with the majority being comprised of micronutrient supplements (42).

1.5 Dietary Supplement Databases

High quality DS composition databases are essential in order to assign nutrient values to products reported in surveys and studies (43). However, this has been and continues to be a difficult task due to the ever-evolving marketplace (44). In addition, some existing products are reformulated and others drop out of the market, complicating the currency of DS databases.

1.5.1 The NHANES Dietary Supplement Database

The NHANES-DSD provides information on the nutrient values of DS reported by NHANES respondents since 1999. The NHANES-DSD was developed because no freely available and comprehensive DS database existed. The database contains label information from prescribed and over-the-counter DS, nonprescription antacids containing calcium and/or magnesium (although these are not DS based on the definition provided in DSHEA), and default and generic formulations of products. The current NHANES-DSD provides product information for products reported in NHANES from 1999-2014. It includes products that may no longer be on the market or have been reformulated, thus allowing researchers to use the database to retroactively assign nutrient values for studies that were conducted during periods of time in the past.

As previously discussed, many issues can arise when collecting DS data including assigning of default formulations to reported products. NHANES assigns defaults by using the most common product formulation and by using the most common strength/doses. These default formulations are also included in the NHANES-DSD for researchers to use when analyzing NHANES, and they can also be used in other studies. More information on the NHANES-DSD can be found elsewhere (45).

1.5.2 Dietary Supplement Label Database

In 2013, DSLD, a federal effort of the National Institutes of Health, sponsored by the Office of Dietary Supplements and National Library of Medicine, was released online. This database contains labels and product information of currently marketed DS, as well as labels since 2012 of products no longer available, with the goal to eventually contain all DS marketed in the United States. This important tool allows researchers to analyze data collected over various time points. More on the functions and potential of the DSLD is described elsewhere (46).

1.5.3 Dietary Supplement Ingredient Database

Both the NHANES-DSD and DSLD provide DS composition data from labeled values. However, nutrient levels from labels can differ from analytically derived values, especially for certain nutrients (47-49). The United States Department of Agriculture, Nutrient Data Laboratory, in collaboration with Office of Dietary Supplements, has been working to compare the labelled levels of nutrients to the actual amounts in products (50). This effort has included studies on products such as adult MVMs, children's MVMs, non-prescription prenatal MVMs, omega-3 fatty acids, and green tea DS. The results and reports of these studies are available online together with interactive calculators that provide national estimates on nutrients available in selected products (51).

1.6 The Concept of Usual and Total Nutrient Intakes

As previously stated, usual intakes represent the long-term average intake patterns of a group, and are generally more salient when evaluating nutrient adequacy and excess or when examining diet and disease relationships. However, it should be noted that there are certain research questions for which short-term intakes are of interest. For example, in NHANES, sodium and potassium intake from the first 24HR and blood pressure are both measured on the same day at the medical examination – thus, to assess the relationship of intakes with blood pressure, where a short temporal association is assumed, usual intakes would not be of interest, rather relating recent intakes may be of more utility (52). Similarly, the timing of a dietary supplement consumed may be of interest. For example, NHANES participants who consumed folic acid during the time period when they were instructed to refrain from eating foods had much higher concentrations of the biomarker unmetabolized folic acid than those who did not take the supplement (53).

1.6.1 Total Nutrient Intakes

The phrase "total nutrient intake" refers to the concept of capturing nutrients obtained from all sources, including diet and DS. Exposure to nutrients comes from well recognized sources like foods, beverages, and DS, and can come from other sources that are often over-looked like prescription drugs (e.g., niacin or omega-3 fatty acids) and over-the-counter medications (e.g., antacids), and minerals found in tap and bottled water (e.g., sodium or other minerals), all of which are captured in NHANES. It is important to capture intakes from all of these sources since they may be quite large (54-57).

Total nutrient intake estimation methods are an important research goal. Without inclusion of nutrients derived from DS, the prevalence of inadequacy may be overestimated and the prevalence of intakes above the UL may be underestimated when assessing the intakes of population groups (57-62). Furthermore, characterizing total usual nutrient intake will aid understanding of how cumulative nutrition exposures can influence health and clarify the relationship between nutrient exposure and health.

1.7 Challenges to Estimation of Usual and Total Nutrient Intakes

In this section we describe the types of challenges encountered in estimating total usual nutrient intakes, including those shared with diet (e.g., measurement error, skewness, various consumption patterns), as well as those unique to combining the two components of intake (e.g., "spikes" in the distribution due to uniform dosages of DS).

1.7.1 Measurement Error

All dietary assessment methods have measurement error that complicates estimation of usual or habitual intakes. Any deviation between measurement and "truth" (e.g. the true intake) is referred to as measurement error. This error may be either random or systematic. Validation studies evaluating self-report dietary assessment methods (e.g., FFQs, records, and 24HR) against recovery biomarkers have consistently found that diet assessment methods are subject to both random and systematic error (14, 63, 64). Both types of errors, whether associated with the estimation of the intake distribution (**Figure 1.1**), or of the relationships between diet and some health parameter, can bias the obtained distribution and therefore research results. However, the random error component for the 24HR contributes a larger share relative to the total error than for FFQ that displays considerably more systematic error. FFQs, while intended to capture longer-term intakes that the 24HR or records, are subject to systematic error for which no statistical methods have been developed to mitigate. The 24HR has less systematic error and more random error than FFQs. Nevertheless, even if a 24HR provides a good, relatively unbiased measure of intake on a single day, due to a great deal of random error due to variability in what people eat, it cannot provide a reliable estimate of an individual's usual nutrient intakes or exposures unless a large number of 24HRs on random days are averaged across days of the week and season of the year, which is generally impractical (13, 65, 66). Statistical methods to model certain characteristics of usual nutrient intakes using small numbers of replicated short-term assessments to mitigate random error, are described in detail in the section on methods for estimating usual intakes from food sources below.

Biomarkers to estimate measurement error

Recovery biomarkers exhibit a direct relationship with consumed foods and beverages, but are limited to energy, potassium, sodium, and protein. Thus, our knowledge of the structure of measurement error in dietary assessment methods comes from studies utilizing recovery biomarkers. While less is known about how well self-report instruments measure other dietary components beyond that for recovery biomarkers (67), these findings provide additional justification for the use of 24HR rather than FFQ as the instrument of choice for population surveys to measure foods and beverages, with the caveat that more complicated methods to adjust for random error may need to be used in analysis. However, because so little is known about measurement error associated specifically with DS at present (68, 69), it is recommended that multiple types of information be combined when possible (34, 70).

Concentration biomarkers are thought to reflect dietary intakes and can be used to compare nutrient "status" to an end point of interest, but they are not necessarily useful for assessing measurement error (71-73). For example, in U.S. adults, usual total folate intakes followed the same patterns of distribution as serum and red blood cell folate indicating rank order comparability; but, less agreement was garnered when cut-points were applied to classify risk of inadequacy (74). In contrast, unlike folic acid that is almost ubiquitously consumed in the U.S. because of fortification, much less agreement has been observed between the biomarker (serum 25-OH-vitamin D) and dietary intakes for vitamin D, especially in terms of the prevalence of risk of inadequacy, potentially because vitamin D is highly concentrated in DS, is not uniformly found in the food supply, and can be synthesized from UV exposure (56, 75, 76). Many issues exist with the use of cut-points for nutritional biomarkers and should be considered in interpreting findings such as these, as reviewed elsewhere (77).

No methods exist to estimate the bioavailability and bioaccessibility of nutrients specifically from DS (78). Issues to consider regarding bioavailability from foods, compared with DS, differ from nutrient to nutrient, and by other factors, as reviewed elsewhere (78). Briefly, bioavailability is impacted by the dissolvability and dissolution of the actual supplement, the form of the nutrients and their matrix, timing and coadministration with foods, and many other factors. Metabolomics may be useful in the future to understanding bioavailability of nutrients from supplements (79).

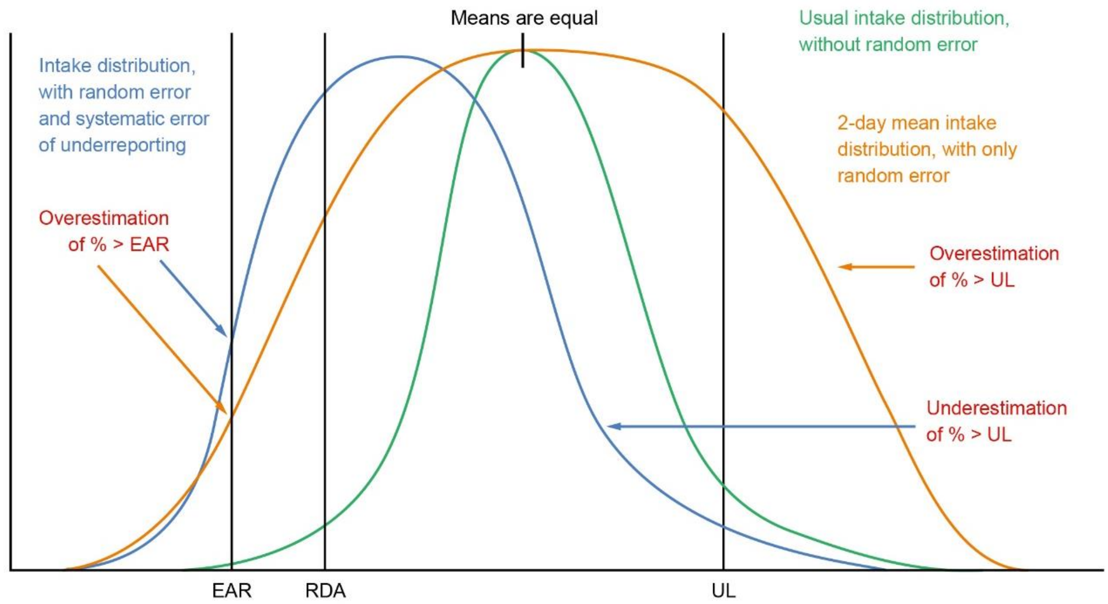


Figure 1.1 Hypothetical nutrient distributions with different types of measurement error and the impact on estimation of population prevalence (%) of meeting or exceeding the DRI guidelines.

Random error

Due to day-to-day variation in intakes, a single day's intake, even if captured perfectly, is unlikely to be a reliable reflection of habitual or usual intake. This error in within person variability is generally thought of as "random" or "classical" measurement error because the average of many single day intakes for an individual is, by definition, usual intake for that individual. If assessments are subject only to random error and this error is ignored, the estimate of the variance of the distribution is inflated; this leads to estimates of inadequate or excess intake that are too high (66). Furthermore, when assessing diet-disease relationships, the presence of random error leads to attenuation or other aberrations from the true relationship.

Dietary intakes vary from day to day due to variation in the types of foods that are consumed as well as the amounts consumed. Additional random error can be introduced by, for example, estimation errors in amounts consumed or food-to-nutrient conversion errors. In contrast, DS intakes are expected to have much less random error than food intakes, if consumed almost every day. Still, random variation in DS assessment can arise from taking partial doses, changing DS formulations, or not consuming the DS on a given day.

Systematic error

As opposed to random error, if a measure has "systematic" error, or bias, the average of many repeated measures does not yield an estimate of true usual intake. If usual intake is assessed using a measure that systematically under- or over-reports intake of a nutrient by a fixed amount, the estimated usual intake distribution will have the correct shape but will be shifted to the left (under) or right (over) (16).

Systematic error may reflect i) general additive bias (i.e., a constant source of over- or under-reporting), ii) intake-related bias, which is related to the individual's true intake, or iii) person-specific bias, which is associated with an individual's personal characteristics such as age or social desirability. Systematic errors at the group level are generally in the direction of under-reporting (16), especially for energy intake, but systematic errors at the individual level can go in either direction. Other forms of systematic error, such as underreporting by a fixed fraction of true intake, will cause other distortions. It is important to note that additive bias that does not vary from person-to-person does not impact diet-outcome relationships. For example, in a group of people who were all taking 2000 IU of vitamin D per day, the relationship with vitamin D and the outcome would not be impacted by assuming they were all taking 1000 IU of vitamin D per day, as the ranking of individuals would not change. Of course, if the goal was to make an inference on the dose of vitamin D that should be consumed for health benefit, this information on actual dose would be relevant.

The impact of intake-related bias on estimating a distribution is dependent on the direction of the bias. It can be shifted left and have a narrower distribution than true intake when intakes are consistently reported as a proportion of true intakes (e.g., 10% less). In contrast it may be shifted right and have a wider distribution, when reported intakes are consistently over-reported by some proportion (e.g., 10% more). Sometimes, intake-related bias and general additive bias occur together, resulting in the "flattened slope" phenomenon, where individuals with low true intake tend to over-report while individuals with high intakes tend to under-report. In such cases, the shift could be either right or left, but the effects on variance are still determined by the intake-related bias. With regard to diet-outcome relationships, if intakes are proportionally under-reported, then the relationship between diet and the outcome will be exaggerated in various ways; if they are proportionally over-reported, the relationship will be attenuated. Assuming that doses are not missed (which, of course, they sometimes are), it seems unlikely that DS users would exhibit much more intake-related bias, as DS doses tend to be constant over time.

Person-specific bias has similar effects as that of random error, i.e., greater variability that can lead to excess estimates of the proportion of individuals in the tails of a distribution and attenuation of diet-outcome relationships. It is anticipated that the types of person-specific biases for DS might be similar to that seen for foods and nutrients, but at present the magnitude and direction of reporting errors for dietary supplements is unknown.

Challenges with DS are different than those with foods; unlike foods, DS usage patterns can substantially vary over time (13). It is therefore simplistic and incorrect to assume that what is good for measuring foods is equally as good for measuring DS. Research is needed to understand the measurement error structure of usual nutrient intakes from DS, especially at the group or population level (13).

1.7.2 Skewness in the Distribution

Distributions of nutrient intakes from foods and beverages, while generally continuous, rarely conform to a normal or Gaussian distribution and are typically right skewed, with some people consuming large amounts. However, because the normal distribution is described by its mean and variance, and it has other desirable statistical properties, dietary data is often transformed to approximate normality for analysis. When data are right skewed, distributions that pull in the tail are used, such as power transformations. The Box-Cox transformation is commonly used due to its equivalence with the natural log distribution for a parameter of 0. For many nutrients, simple normality transformations are effective and useful analysis tools.

The additive nature of nutrient intakes from DS can only compound the skewness phenomenon, by allowing even larger total intake amounts than would be seen from foods and beverages alone. Because nutrient intakes from DS are not constrained by energy intakes in the same way as those from foods and beverages, their contribution to skewness can be extreme. Even with the power transformation, it is typically not a normal distribution.

1.7.3 Spikes in the Distribution

The distributions from nutrients from foods are not as dramatically spiked because most nutrients are consumed, typically from multiple food sources, with certain exceptions like vitamin A. When considering the distributions of nutrient intakes solely from DS, individuals who do not use DS provide a “spike” at zero. Also, because the nutrient dosages in the most commonly used DS often cluster around specific amounts, such as multiples of the RDA, 100% of the Daily Value, or round numbers (e.g., 1000 mg), distributions of intakes from DS tend to be “spiky” or discrete, rather than continuous. Depending on the number, placement, and magnitude of the spikes in the DS distribution, the distribution of total intakes can be multimodal. Box-Cox or similar transformations retain these multiple modes; therefore, the transformed data will not approximate a (unimodal) normal distribution.

As illustrated in **Figure 1.2**, the raw distribution of calcium intakes from foods alone (Panel A) is easily transformed to approximate normality (Panel B). Almost all individuals in a population consume calcium from a variety of foods, but not every person uses a calcium supplement. Furthermore, unlike many nutrients that are aggregated across a large number of foods and beverages, nutrients from supplements usually come from one or two products for an individual, most manufacturers offer similar labeled doses across products (e.g., Vitamin D is typically available in 400, 1000, or 2000 IU, but not 1100 IU), and individuals usually consume the same amount of them on days when they take them. These factors therefore lead to spikes in the intake distributions from supplements.

When supplements are taken at much higher doses than typically are consumed in the diet, a multimodal distribution can arise. Typical power transformations, like the Box-Cox, can handle right skewed data rather easily; however, a transformation cannot smooth a spike or multimodal distribution. This is illustrated in **Figure 1.2**. The calcium found in MVMs is generally around 150-200 mgs, whereas a calcium supplement tends to be around 600 mgs (Panel C). Therefore, the application of traditional power transformations will not result in a normal unimodal distribution (Panel D). Rather, adding calcium supplements to the food-based intakes alters the distribution, especially when they are consumed at these constant, fixed doses. In addition, when modeling supplements separately, a large spike at zero occurs when many persons in the sample do not use supplements, and this must be modeled appropriately.

1.7.4 Consumption Patterns

DS consumption patterns differ from those of foods. Energy and most nutrients are consumed daily by nearly all people, but some foods, nutrients, or other bioactives are consumed episodically by some or many people. Nutrients found in more restricted sets of foods might be consumed episodically (i.e., not every day) by most people and never consumed by some people. Similarly, some people never use DS, and those who use DS consume them daily while others do so only episodically. For example, people may use vitamin C episodically (e.g., when they feel ill); these two different supplements may be used at different times and often along with a daily MVM. In addition, just as certain foods may be consumed only when in season, some people may use DS seasonally, or perhaps only when they are ill. For example, people may use vitamin D only in the winter months.

According to NHANES data, about 70% of MVM users use them regularly (i.e., 21-30 times during a given 30-day period) (80). Among older adults (≥60 y) in NHANES 2011-2014, 84% of MVM users reported daily consumption (33). Nationally representative estimates for Canadians (ages 1 year and older) suggest that supplemental nutrients are generally consumed daily 80-86% of the time (81). Another study among a racially-diverse group of older adults reported that regular use of DS over a 30-day period was more common in individuals who consumed fewer DS per day (82). Additionally, some people consume multiple DS daily, which is called "stacking". This phenomenon occurs frequently in older adults (33) and military and tactical populations (83) and can also present additional challenges based on frequency and the large combinations of nutrients that can result from different products being used, especially when MVMs are combined with other single nutrient DS.

1.7.5 Issues Unique to Combining Dietary and Supplement Data

Measurement error, as described earlier, is a problem not only for estimating dietary intake but also for estimating intakes from DS. The combination of two quantities measured with different error structures presents additional challenges for estimating total usual intake distributions. Furthermore, supplement information is typically collected via a questionnaire, and the average daily exposure estimated from this assessment is added to the nutrient estimates from food. Therefore, a constant is added to each recall day. While within-person variation is not affected by this calculation, between-person variation increases. From a biological perspective, this variation may be accurate. However, because a constant value is assumed for the supplement (e.g., 400 IU of vitamin D for all supplement users), the estimate of variation may not be random enough. In statistics, this is referred to as Berkson error, where the true intake is more variable than the measured intake. In addition, adding large supplement amounts to intakes can result in "spikes" in the data. Both of these lead to difficulties in statistical modeling. When supplement intake is measured with a 24HR, the reported amount is added to each day. While this also leads to spikes in intake amounts, Berkson error is less likely due to more specific information on supplement formulations (e.g., some supplements have 400 IU of vitamin D, whereas others have 2000 IU), and information that is specific to a given day as opposed to an average across days.

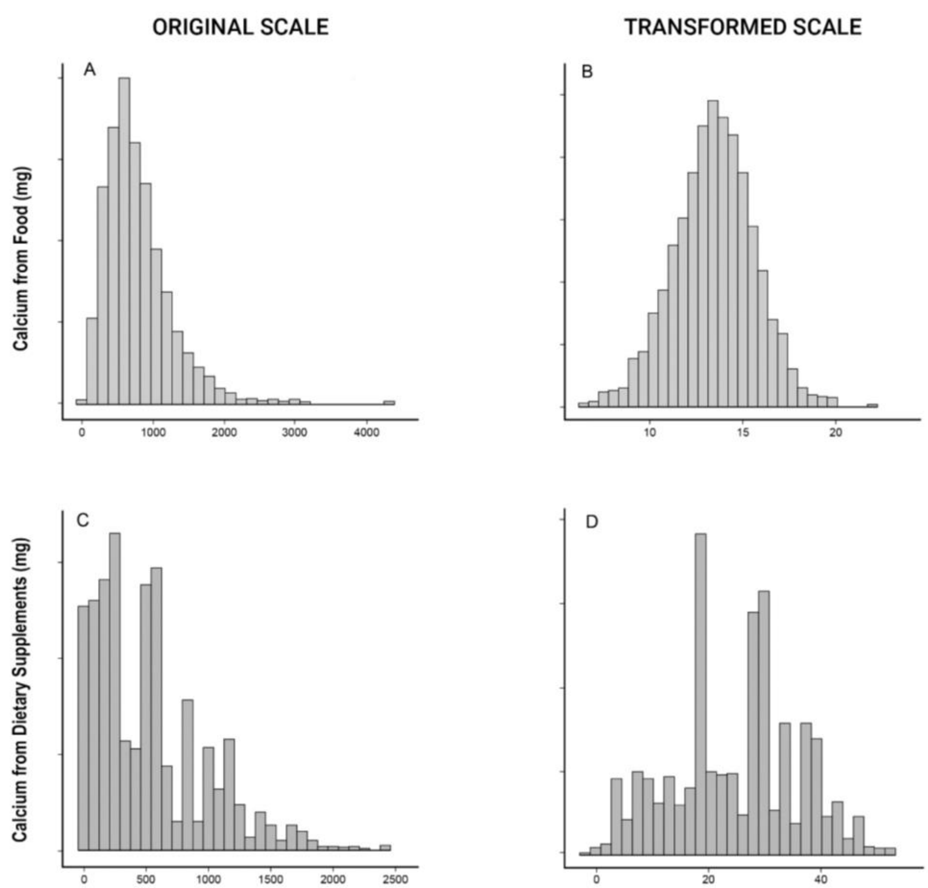


Figure 1.2 Calcium intake distributions from foods (A and B) and from dietary supplements (C and D) in the original (A and C) and transformed scale (B and D).

Correlation between dietary supplement use and dietary intake

DS contribute considerably to the intakes of individuals who use these products. Interestingly, adult DS users tend to have higher nutrient intakes from the diet alone across a range of nutrients (58, 59, 84, 85); however, this phenomenon is not seen in children and adolescents . Additionally, the use of nutrient-containing DS is associated with private health insurance, higher self-assessed health, higher educational attainment and income, more frequent exercise, and lower likelihood of smoking. This has been described previously as the “healthy user” effect, and may introduce a potential source of differential measurement error leading to confounding of associations between total nutrient intakes and health outcomes. Conversely, DS use can also be very high in certain population groups, like cancer survivors or those newly diagnosed with cancer (86-88).

Database considerations

As previously described, accurate estimates of nutrients from DS rely on up-to-date products and formulas in databases. Furthermore, default values in databases are used when not enough information is collected on the products reported and may introduce an additive source of measurement error. In some cases, the number of defaults can be very large. Any deviation in nutrient estimates consumed from DS and the default value represents another source of measurement error, the type (random, intake-related, or person-specific bias) and degree of which are largely unknown.

1.7.6 Application of Dietary Reference Intakes

Nutrient adequacy at the group level is typically assessed using the EAR. Several nutrients have insufficient scientific evidence to determine an EAR, particularly among infants; and for these cases, an AI has been established, defined as the amount consumed by apparently healthy individuals (89). The RDA is set at two standard deviations above the EAR, and is typically used for individual level purposes. The UL, is the DRI value that is typically used to define intakes that are potentially excessive (i.e., the highest level of intake not associated with adverse effects).
Assessment of nutrient intakes from both diet and DS is essential for determining prevalence of nutrient inadequacies or excesses in a group or population. Without inclusion of DS, the population prevalence of inadequacy (i.e., <EAR) may be overestimated, and the population prevalence of

intakes >UL for nutrients may be underestimated. While DS help users to achieve the EAR for, children and adults who use DS are much more likely to have exposures that exceed the UL than those who do not (54, 55, 57, 84, 90). Indeed, for some nutrients, the proportion of total intake from DS may be quite large. For example, very few foods provide vitamin D, with the exceptions of fortified milk and fatty fish; but very large amounts of vitamin D may be obtained from DS. Alternatively, for other nutrients, some individuals may get both large amounts from their diet and large amounts from DS.

The comparison of population intakes to the DRIs may present challenges, some of which are specific to the inclusion of DS, as illustrated by three examples (**Table 1.1**). First, some nutrients in foods and DS exist in a variety of chemical forms (e.g., folic acid and folate) that, given their different bioactivities, must be converted to a standard measure before total intake is determined. Second, for the nutrients folic acid, niacin (vitamin B3), and magnesium, the UL only pertain to intakes from DS and from enriched or fortified foods. In such situations, excess consumption may only be identified in a population when nutrient intakes from DS is quantified. The third example pertains to vitamin A. Food and DS labels typically list preformed vitamin A (retinol found in animal-based foods) combined with provitamin A carotenoids (found in plant-based foods). However, the UL only applies to retinol. Therefore, the combination of vitamin A forms on some product labels may not be helpful in determining the proportion of the population exceeding the UL for this nutrient (See **Table 1.1**).

1.8 Methods for Examining Usual Intakes from Food Sources

As mentioned previously, due to within-person variation in dietary intake, direct assessment of usual intake would require many daily observations (36, 91). However, it is impractical to collect such large numbers of replicate 24HR or records. For this reason, several procedures have been developed to estimate the distribution of usual intakes when only a small number of 24HRs are available per individual (92-96). These methods use statistical modeling to approximate the distribution that would be obtained by averaging many 24HRs per person.

When multiple 24HR are not available for all people, and if a replicate is available on a representative subset, usual intake procedures can still be estimated. For example, in the 2016 the Feeding Infants and Toddlers Study, one 24HR was available for all participants and a replicate recall in 25% of participants was used with the NCI method to produce usual total nutrient intakes

(61, 97). When only one 24HR is available, it is possible to use external estimates variance components from a different, but similar group as has been done with different cycles of NHANES data with the ISU method (98). This concept of "borrowing" variance components has also been used to adjust biomarker data from various cycles of NHANES (99, 100).

Usual intake methods vary considerably in their complexity, strengths, limitations, and fitness-for-purpose and they are reviewed in depth elsewhere (66, 96). These methods, typically applied to data from food sources only, generally assume that: (1) 24HRs are prone only to random error and (2) transformations to correct for skewed data will result in normal distributions. Assumption (1) implies that the average of 24HR intakes approximates the mean of the usual intake distribution, but the distribution of intakes from one 24HR per person has more spread than that of the usual intake distribution.

The underlying framework of all of the usual intake methods is illustrated in the four panels of **Figure 1.3**. The distribution of the nutrient exposure from a single day is typically skewed to the right and needs to be transformed to approximate normality (the process from panels A→ B). Transformed single-day intakes are assumed to arise as the result of adding a normally-distributed within-person error term to a normal distribution that exhibits between-person variation. After estimating the within-person and between-person variance components, the within-person variability is removed, "shrinking" the distribution of the data. Shrink is the term that is used because the tails of the usual intake distribution are pulled in closer to the mean relative to the unadjusted distribution with random error (see **Figure 1.1**) (81). Next, the normal distribution, reflecting only between-person variance (panel C), is used as the basis for the remaining step, where a "back transformation" derived from the initial normality transformation and the within-individual variance component, is applied to approximate the distribution of usual intakes in its original, conventional units (the process from panels C→D). In this way the data can be used in the scale which they were collected to provide meaningful comparisons and descriptions. Note that only the top two panels in **Figure 1.3** represent actual observations; the bottom two are based on a hypothetical normal distribution with estimated mean and variance. Estimation of this hypothetical distribution is operationalized by randomly generating 100 simulated individuals for each sample person, sometimes referred to a "pseudo-people", to determine true intakes for the population with this mean and variance. To accommodate more complex modeling, involving covariates (see 1.7.1 below), this simulation approach uses each sample person as the basis for simulated intakes for pseudo-people, which now reflects the usual intakes at the population level based on the distribution of covariates in the population as sampled. The real people represent the real distribution of covariates that exist overall. Thus, it is the population distribution of usual intakes that is estimated from this approach, rather than the distribution of usual intakes for particular individuals.

Table 1.1 Nutrients that have special considerations when applying the Dietary Reference (DRI) Intake framework

		Dietary Reference Intake	
Nutrient	*Conversion Factors*	*EAR, AI*	*UL*
Vitamin A (Retinol and provitamin A carotenoids)[1]	1 IU retinol = 0.3 µg retinol or 0.3 µg retinol activity equivalents (RAE) 1 µg RAE = 12 µg β-carotene, 24 µg α-carotene, or 24 µg β-cryptoxanthin	Includes retinol, α- and β-carotene, and β-cryptoxanthin	Only retinol from all sources
Vitamin E[2]	1 IU = 0.67 mg for d- α-tocopherol (natural form) 1 IU = 0.45 mg for dl- α-tocopherol (synthetic form)	For α-tocopherol alone (the single form that occurs naturally in foods and the four stereoisomeric forms that occur in fortified foods and supplements)	Applies to all forms of α-tocopherol, including the eight stereoisomers present in synthetic vitamin E.
Folate, Folic Acid	1 µg dietary folate equivalents (DFE) = 1 µg food folate = 0.6 µg folic acid from fortified foods or supplements consumed with foods = 0.5 µg folic acid from supplements taken on an empty stomach	Includes DFEs from all source.	Only DFEs from fortified foods and supplements (which is in the form of folic acid)
Niacin Vitamin B3	1 mg niacin equivalents (NE) = 1 mg niacin = 60 mg tryptophan	Includes NEs from all sources	Only niacin from fortified foods and supplements; listed in mg
Magnesium	None; ensure database provides amount of elemental magnesium	Includes mg from all sources	Only magnesium from supplements and pharmacological agents

Table 1.1 continued

Calcium	*None; ensure database provides amount of elemental calcium*	*Includes mg from all sources*	*Calcium from all sources, including food, supplements, water, and pharmacological agents (such as antacids)*

[1,2] New labels on foods and dietary supplements that become mandatory in 2020 will replace the measure of vitamin A in IUs with µg RAE and the measure of vitamin E in IUs with mg.

The first such approach, developed by Beaton, was proposed in 1986 and published in a report by the NRC (92). Future, independent iterations permitted different transformations and included of covariates in the models (see below). These include the bias-corrected best power method, ISU Method, the NCI Method, the European Food Consumption Validation Consortium's MSM, and the SPADE. Currently the ISU and NCI methods are most frequently used by researchers in the United States, and SPADE and MSM are more frequently used in Europe. The ISU method is implemented as a stand-alone program that can run on Linux ® or Windows ® operating systems; whereas the NCI method is implemented in sets of macros that require the SAS ® software. The MSM method is accessed through a dedicated website that performs analysis of user-uploaded data, while SPADE was developed for use with R ® software.

Some of the methods described above can also be of use when interest centers on relating some outcome to (unobservable) usual intake. Using an error-prone measure (e.g., a single 24HR) as a surrogate for usual intake in a (linear, Cox, or logistic) regression model produces biased estimates of the relationship between intake and outcome. Some of the usual intake software implementations can produce inputs to a regression program that yield (approximately, in all but the linear case) unbiased parameter estimates when they are used as the predictor variable. It is crucial to note that these inputs are not intended to approximate individual usual intakes, and thus should not be used to make judgements about particular individuals.

All of the usual intake methods mentioned above can be applied to analyze a single dietary component consumed nearly every day by almost all members of a population. Some of the methods can also handle analysis of an episodically consumed dietary components, where a sizable fraction of the observed data is zero (i.e., no intake is reported). For such analysis, usual intake is conceptualized as the product of the probability to consume on a given day and the usual amount consumed on reported intake days.

1.8.1 Covariates

The ability to explicitly incorporate covariates in to usual intake models is a very powerful addition to usual intake methods that is particularly important when considering DS use. Covariates are generally incorporated into the model for three purposes (94). First, they can be entered to account for factors that may affect intake levels, such as day of the week (commonly weekday vs. weekend). Second, nuisance effects, such as sequence effects or data collection modality of the 24HRs, may also be used as covariates to mitigate their effect. Finally, they may be used to account for individual level effects, such as sex-age groups or supplement consumers compared to non-consumers.

1.9 Methods for Examining Total Usual Nutrient Intakes

Extensions of the usual intake models from foods, as described above, make it possible to estimate not only the group means, but also the distribution of total usual nutrient intakes inclusive of DS. These models are appropriate for estimating total usual intakes at the group level because they more accurately reflect the true distribution of intakes. They can also accommodate additional goals, such as estimating the proportion of the population meeting or exceeding certain DRI cut-points or for estimating intake at certain percentiles of the population distribution.

The methods that exist for incorporating nutrient intakes from DS with nutrient intakes from foods and beverages are provided in **Table 1.2**. Methods exist to examine populations with users and non-users *combined* as a group as well as users and non-users divided o*r stratified* by DS use. The method of choice is dependent on the research question or the purpose of the analysis and the dietary assessment method. The models presented here are intended to be used at the group level.

This section describes the available methods for estimating total usual intakes evoking the 24-HR and DSMQ that are available from NHANES 2007 and beyond; but these methods can be applied with different data sources. Three assumptions are commonly associated with these methods that may not consistently be founded: 1) reported nutrient intakes from food source from

24HR are unbiased, meaning that they capture usual intake with only random error; 2) self-reported DS intake reflects true long-term DS intake; and, 3) label declarations on DS and database estimates are accurate.

1.9.1 Group Mean Method

The group mean method refers to the calculation of the mean of the added nutrients from DS and adding them to nutrient intakes from foods without the use of usual intake procedures. This is *only* appropriate when the goal of the analysis is to estimate the mean intake of a group. For NHANES analysis, to estimate the population mean total intake, we recommend adding the average nutrient intakes from food sources to the average intake of nutrients from DS. Ideally the DS nutrients should be used from the DSMQ because the reported DS use is lower on the 24HR than that of the DSMQ (34), and the DSMQ captures use in a more rigorous way (i.e., home inventory) and thereby facilitates estimation of episodically consumed DS. Ignoring the DSMQ data and relying only on 24HR will introduce an unquantifiable source of bias. For example, if a person uses a calcium supplement 15 of 30 days per month, it is conceivable that the calcium supplement may or may not be consumed on the day(s) the 24HR is performed. Problems also arise when the frequency data on DS use is not collected at all. Indeed, many researchers only have one or two days of 24HR, so decisions must be made about how to calculate the average nutrient intake from DS in such circumstances.

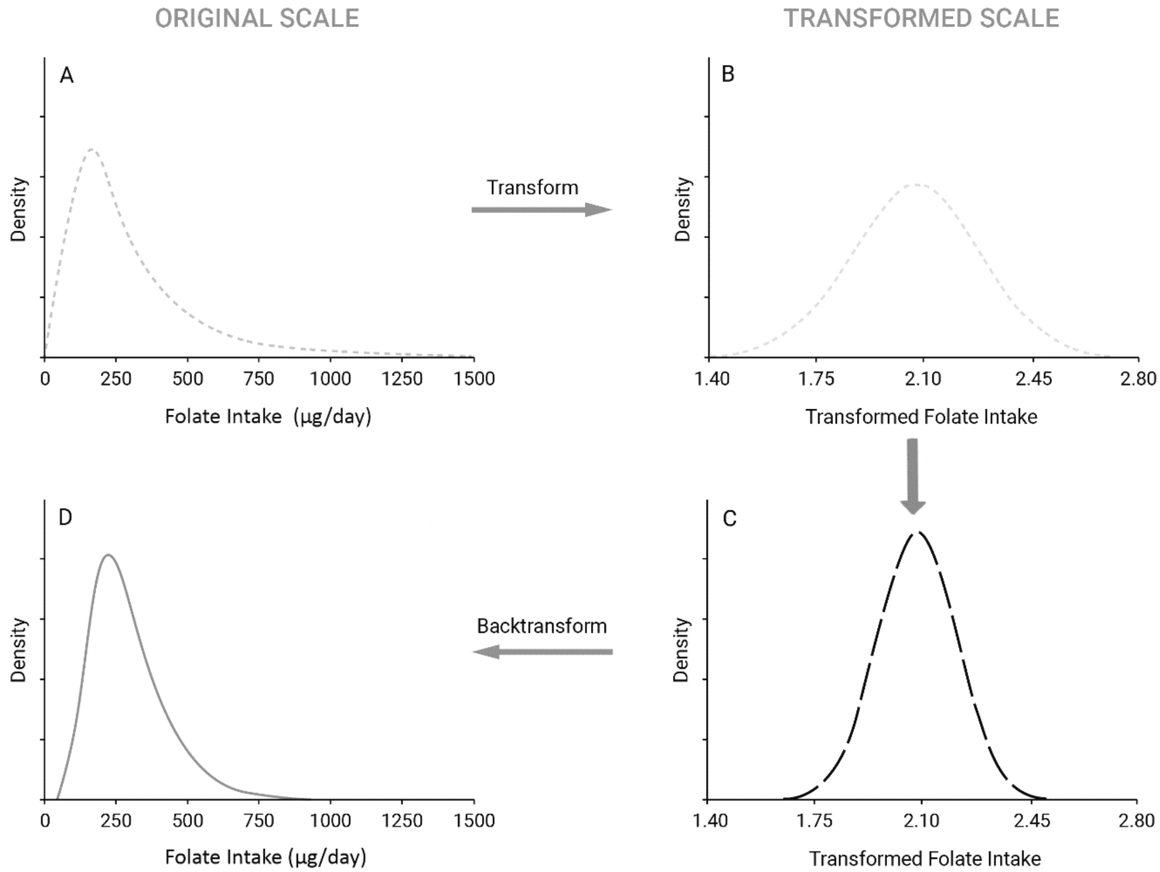


Figure 1.3 The 4-step process in the usual intake estimation framework using a hypothetical folate distribution. Data in the original scale (A) are transformed to normality (B), the within-person variation is removed (C), and a back transformation is applied to approximate the normal scale without within-person variation (D).

In this scenario, imputation techniques, such as hot deck (101) or sequential regression tree (102), should be considered to estimate the group nutrient intakes from DS.

The Group Mean Method can be applied with both the combined and stratified approaches. However, this method is not without limitations and as such researchers should acknowledge potential bias in the interpretation of their results and consider how it may have an impact on application of the findings. With only a limited number of 24HR or records, it is difficult to accurately assess nutrient intakes from episodically consumed DS. Finally, this method assumes that intakes measured from both sources are unbiased, which is generally not the case. Therefore, it is always preferred to use usual intake procedures if they are available.

1.9.2 Group Distribution Methods

When the total usual intake distribution is the primary goal for analysis, rather than just a group mean, it is necessary to move beyond the Group Mean Method and incorporate usual intake procedures. Two temporal procedures have been described to refer to the order in which nutrient intakes are combined relative to the usual intake procedures, referred to here as a "shrink" to the distribution (81). The available methods that exist to estimate usual total intake distributions will be described in this and the following sections: the combined shrink then add method, combined add then shrink method, the stratified add then shrink method, stratified shrink then add method, and a three-part method, which is a hybrid of combined and stratified methods.

Combined Method: Shrink then Add

The preferred application of the combined group approach, where users and non-users of DS are analyzed together as one group, is referred to as the "shrink then add" framework and incorporates DS use as a covariate. In this method, the nutrients from food sources are first processed through the usual intake procedures for the entire sample, employing an indicator variable for reported supplement use (i.e., user or non-user) from the DSMQ or a FBQ, if available. Next, an 'adjustment' incorporates the estimated usual intakes of DS to the adjusted distribution of nutrients from food sources to produce a final distribution of usual total nutrient intake. This adjustment occurs after the model parameters are estimated, during the generation of "pseudo-people." Then, in the second step after the pseudo-people are generated, each one will have a designation from their covariate as to whether or not they are supplement users. If they are supplement users, then the supplement use from the DSMQ is added to each pseudo-person based on covariates employed.

Table 1.2 Analysis strategies and details for methods available to estimate total usual intakes inclusive of nutrients from all sources

	Group Mean Method	Combined Method	Stratified Method	Hybrid Method
Analysis Strategy	Add average 24HR food source intake to average DS intake **OR** Add DS intake to each 24HR food source intake, then average	Adjust nutrient intake distribution from food source first and then add usual DS intake	Adjust nutrient intake distributions separately for DS users and non-users	For DS users, jointly model food source intake and DS frequency from respective 24HRs, add modeled DS dose to adjusted food source intake; for DS nonusers, just adjust food source intake.
DS Assessment[1]	DS FBQ and/or DS amounts from 24HR	DS FBQ and/or DS amounts from 24HR	DS FBQ and/or DS amounts from 24HR	DS user/nonuser Questionnaire, plus DS amounts from 24HR
Shrinkage Procedure	N/A	Shrink then add **OR** Add then shrink[2]	Shrink then add **OR** Add then shrink[2,3]	Shrink then add
Strength	Simplistic	Covariates	Covariates	Covariates
Limitations	Cannot be used to assess the population distribution intakes (i.e., <EAR or >UL)	No publicly available implementation Frequency information may not be available to include as a covariate in some datasets	Small sample sizes for DS users or non-users can lead to highly variable estimates Separate estimation for DS users more likely (but not guaranteed) to meet assumptions	As with Stratified Model, with added complexity and possible instability of joint modeling Rare to only have information on user vs non-user and 24HR Publicly available implementation only for the R® software system[4]

[1] The preferred assessment is always a frequency-based method.
[2] Depending on sample characteristics
[3] Add then shrink should only be used if a covariate is sufficient to reduce the bimodal distribution
[4] This method has not been used with the NHANES data

The “shrink then add” combined approach guarantees that the estimated mean of usual intake will recover a similar mean for the Group Mean Method (81). Additionally, with this method, the prevalence of usual intake <EAR from food sources alone is always greater than or

equal to the estimated prevalence of usual intake <EAR from foods and supplements, which in theory should always be the case (103).

The "shrink then add" combined approach, when applied to methods that utilize covariates, has two advantages that are salient for nutrients from DS. First, it allows for different means of subpopulations to be generated while pooling information about the variance components. This is critical because some (58, 59, 84, 85, 104) but not all reports (60, 105) suggest that DS users have higher intakes of nutrients from their diets alone than non-users. Using this method, adding nutrient intakes from supplements after adjusting the nutrient intake distribution from foods, allows for less-complicated transformations in the usual intake procedures. By avoiding creation of data that violate key assumptions of the shrinkage methods, the "shrink then add" approach is thus preferable to "add then shrink" (81).

Combined Method: Add then Shrink

The "add then shrink" technique, where intakes from foods and DS are added together before shrinkage methods are applied, may not be the correct application at the combined group level and employing it may yield inconsistent population distributions and may evoke a similar group mean to exist for users and non-users of DS (81, 103). The "add then shrink" while easier from a programing standpoint, tends to create a bimodal distribution (one mode for users and one for non-users) that cause the shrinkage methods (i.e., usual intake procedures) to not perform as expected because these methods assume a unimodal distribution. Furthermore, adding the shrink can cause a dramatic widening of the range of the distribution as well as introduce spikes, which impacts the estimate of between-person variation in intake causing it to be too large because the modes artificially inflate the variance. As a result, the "add then shrink" method does not guarantee that the mean will match the Group Mean Method or that the prevalence below the EAR from food sources will be at or below the prevalence from foods and supplements because of the possibility of dramatically different estimates of within- and between-person variance components in the "before-" and "after-summation" data sets. When this distribution is widened, it results in a greater prevalence of intakes below the EAR if a covariate for DS use is not employed (106).

When you stratify users and non-users this problem is eliminated; however, the use of DS as a covariate to the "add then shrink" method, may in some circumstances, also alleviate this problem.

The choice of when to use DS use as a covariate versus when to stratify users and non-users into two groups for analysis depends on many factors, including, but not limited to, the sample size, the proportion of the group that uses DS, and the variance components of nutrient intakes from food sources, which can vary from nutrient to nutrient. If the food source variance components are similar, using the indicator variable from DS use is appropriate; however, if the variance components are different, examining users and non-users with the stratified method is appropriate.

Stratified Methods

Stratifying refers to dividing the group in to supplement users and non-users prior to applying the usual intake methods. Researchers often examine users and non-users of DS as two different groups since their nutrient intakes from food sources can differ. This model has the advantage that the nutrient intakes from the two sources (food and DS) can be distinguished, given the data are good enough (e.g., not too many non-consumers, that is, the "zero inflation" is not too large) (107, 108).

For non-users, because the group is stratified, estimating usual intakes does not differ from the foods alone procedures outlined above. For "users", the safest approach to produce total usual intakes is to proceed with the "shrink then add" approach (81). However, when examining users and non-users as two distinct groups, DS can sometimes be added to the nutrients from foods before usual intake procedures (i.e., "add then shrink") depending on the sample characteristics (81).

For example, because prenatal MVM use is very high in NHANES (~80%) and the formulations are very standardized, it has been treated with the "add then shrink" stratified method without the issues noted above for spikes and skews simply because almost everyone in the group is a user and the nutrient intakes are added almost uniformly to most women in the same amounts. However, because of the reduced between-person variation component that is much higher when these two groups are combined and analyzed as one, the analyst should proceed with caution and examine the group characteristics first, before making a decision on the "add then shrink" method as part of stratified methods.

Three-Part Method

A three-part mixed effect extension of the “shrink then add” approach, developed using a modified NCI method, is currently available in R ® but not in SAS ® (106). This model estimates and combines the usual intake distributions from food alone among non-supplement users (part 1), food alone among supplement users (part 2), and nutrients from DS obtained from a frequency questionnaire with imputed doses from the nutrient distributions from 24HR (part 3).

The three-part model may be thought of as combining elements from the combined and stratified methods. Like the combined “shrink then add” approach and stratified method, it separates DS users from nonusers. In this case, DS users are defined as those who either report intake on a frequency questionnaire in the past 30 days or report intake on either of two survey days from 24HR. The three parts are modeling nutrients from: 1) food sources for nonusers of DS, 2) food sources for users of DS, and 3) DS sources for users of DS. Parts 2 and 3 are modeled jointly, allowing correlation between nutrients from food sources and DS sources (106). Part 1 can be modeled using the food source methods described above to obtain a distribution of usual intakes for pseudo-people who are DS nonusers. Parts 2 and 3 are modeled jointly with correlated random effects to obtain a distribution of pseudo-people with predicted nutrient intake from food sources and *probability* of DS use on a given day. The *amount* of DS use is assumed to be known; specifically, Verkaik-Kloosterman et al. used the mean of DS consumption days to estimate the amount (106). This value was then multiplied by the probability of supplement use, and then added to nutrient intake from food sources to obtain total nutrient usual intake distributions for DS users. Finally, percentiles of total nutrient usual intake for the whole population were obtained from the full set of distribution data for nonusers and users. Because 100 pseudo-people are generated for each actual person in the dataset, the proportions of users and nonusers are represented in the full dataset. The same or different covariates can be added to each part of the model.

1.9.3 Choosing Between Models

There is no one “right” method to model total usual nutrient intakes at the group level. Whatever method is chosen should be driven by the research question and is dependent on the sample characteristics, total sample size, and proportion of that sample that is using DS. The study of a large sample with many supplement users should include a plan with strategies to estimate total usual nutrient intakes, while understanding the caveats that exist (**Box 1**). By avoiding creation of data that violate key assumptions of shrinkage methods, the “shrink then add” approach is preferable to “add then shrink.”

Box 1. Caveats with Dietary Supplements

- There is tremendous variation in the dietary assessment methods used for DS.
- Assessments for DS may query usage over a different time period than those for foods.
- No single comprehensive analytical database exists; ever-evolving marketplace.
- Nutrient amounts in DS databases rely on label declarations, which have varying accuracy and tend toward overages.
- Default product types are typically assigned (depending on assessment method) which may or may not accurately reflect the nutrient content estimates.
- Dissolution and dissolvability are not equivalent to bioavailability, which can bias exposure estimates.
- The form (unit) on the DS label can differ from that of foods.
- Limited database values are available for botanical and herbal DS.
- DS can be consumed daily, episodically, or seasonally.
- Some users take multiple DS with varying frequencies.

In general, the “shrink then add” procedure is the preferred approach for estimating total usual nutrient intakes with the combined group approach. Separation of users from non-users mitigates some the issues that can occur when DS amounts are added to the nutrients from foods before usual intake procedures (i.e., the “add then shrink” procedure). However, even with this separation, it is important to proceed with caution and to examine the group characteristics before using the “add then shrink” method.

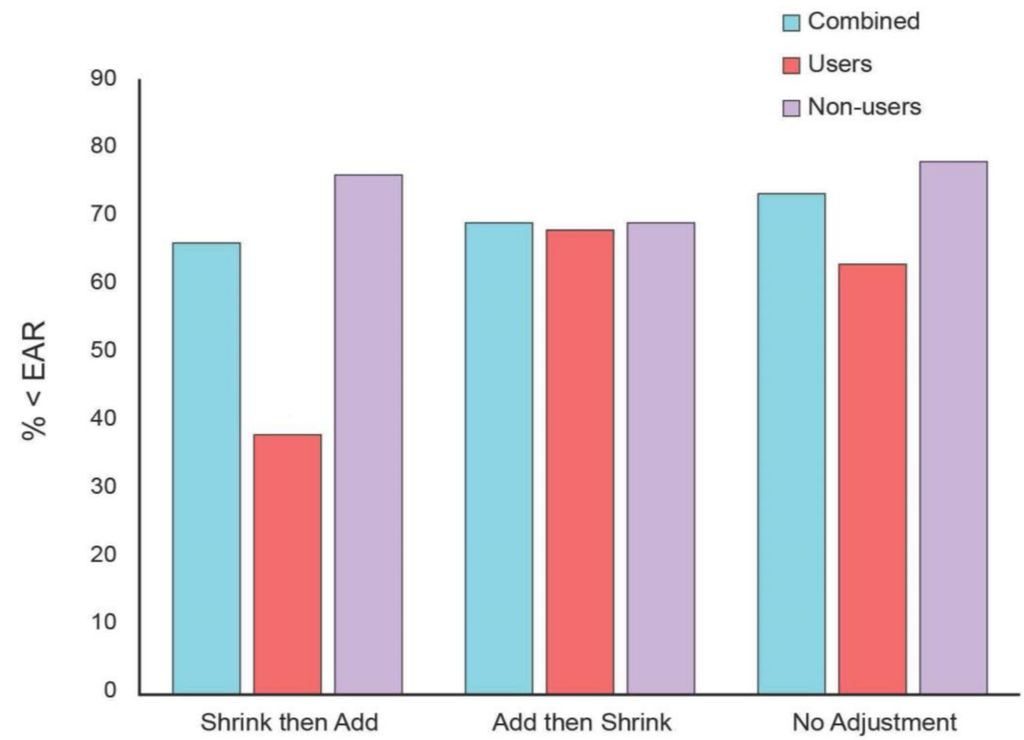
Figure 1.4 compares the Group Mean Method (i.e., “no adjustment) with the combined and stratified group approach for both the “add then shrink” and “shrink then add” procedures utilizing the NCI method to estimate calcium intake among 14-18-y-old girls from NHANES 2007-2008 (11). The mean intakes from users and non-users combined are generally consistent for all 3 approaches; however, the “add then shrink” procedure forces the group means to be similar, resulting in the same total mean intake for those who take and those who do not take calcium supplements, and, as a result, produces similar prevalence of the group <EAR. Importantly, the Group Mean Method (i.e., “no adjustment”) overestimates the proportion <EAR for the group and for DS users because there is no adjustment for the random error of within-person variation. While each nutrient behaves differently, it should be noted that this phenomenon has also been observed for vitamin D (106) and vitamin C (81).

The "shrink then add" approach at the combined group level, when applied to methods that utilize covariates, has two advantages that are relevant for nutrients from DS. First, it allows for different means of subpopulations to be generated while pooling information about the variance components, which is salient because DS users tend to have higher nutrient intakes from their diets alone than non-users. Using this procedure, adding nutrient intakes from supplements after adjusting the nutrient intake distribution from foods, allows for less complicated transformations. The "shrink then add" procedure has been used with the NCI method in NHANES, incorporating research-specific covariates, like income and DS use, at the combined group level (62).

However, it should be noted that few method comparisons have been published comparing usual intake methods with inclusion of nutrients from DS with the NCI method; but, the ISU and SPADE reports have issued similar recommendations as we do for the NCI method (81, 106).

1.10 Summary and Conclusions

Assessment of nutrient intakes from both diet and DS is essential for determining prevalence of nutrient inadequacies or excesses in a population and for estimating true exposures to relate to health outcomes. However, currently no standardized methods are available to assess the prevalence of use and nutrient exposures from DS. Researchers and policymakers should be aware of the fact that when comparing estimates of DS and MVM use between NHANES and other studies, important differences in methodology and product definitions can impact those prevalence estimates obtained (5). FBQs and FFQs vary considerably on the types/brands and frequency of consumption questions from one questionnaire to another, making comparisons difficult if not impossible (19). Furthermore, online surveys used for assessing DS use tend to report much higher prevalence estimates when compared with NHANES (109, 110).



Total Nutrient Intakes, *Mean* (mg)

	Shrink then Add	Add then Shrink	No Adjustment
Combined	905	871	887
Users	1165	871	1099
Non-users	810	870	801

Figure 1.4 Mean total usual calcium intakes and prevalence (%) less than the EAR among US girls, aged 14-18y, combined and stratified by use of dietary supplements containing calcium using 3 different analytical approaches.

This review described the major challenges that should be considered when estimating usual total nutrient intakes, including DS, in research studies; described statistical approaches that have been used; and offers a lessons-learned approach to help researchers handle many issues that may arise when working with DS data. Understanding the major challenges in working with DS will provide insights to improving methods to estimate usual total nutrient intakes. Challenges with supplements differ from those with foods so we cannot simplistically assume that what is good for measuring foods is equally good for measuring DS. Furthermore, the measurement error from traditional dietary assessment for foods and beverages (e.g., energy under-reporting, difficulty in estimating portion size, and issues of social desirability) is likely to differ considerably from error in measuring DS use. DS add nutrients to the diet that are not bound by energy intakes, leading to severely skewed multimodal distributions with spikes corresponding to discrete doses delivered in DS, complicating traditional methods to estimate usual intakes.

1.10.1 Future Directions

Future directions in this field should include studies to identify and characterize the structure of measurement error of nutrient intakes from DS. Standardized FBQ are needed both as standalone DS assessment methods, but also as part of FFQs. Comprehensive databases with analytically-derived values are also needed, and best practices for the appropriate handling of assigning default values is critical; this is especially important for FFQ and FBQ methods of DS assessment. Examination of the total usual intake methods discussed should be further investigated for nutrients beyond what has been observed for calcium, vitamin D, and vitamin C. Future work should also seek to develop new methods to estimate total usual nutrient intakes at both the group level with both combined and stratified approaches. In that vein, the previous models developed to incorporate episodically-consumed foods (107, 108), conditional on being a consumer, may possibly be applied to a DS.

Finally, a note of caution, because so little is known properties and measurement error associated specifically with DS at present it is simply premature to assume that the use of 24HR alone without a FBQ is sufficient to adequately capture DS use. Challenges with DS are different than those with foods it is inappropriate to assume that best practices from measuring foods and beverages is equivalent for measuring DS.

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CHAPTER 2. PREVALENCE OF DIETARY SUPPLEMENT USE BY SOCIOECONOMIC AND HEALTH-RELATED CHARACTERISTICS AMONG U.S. ADULTS, NHANES 2011-2014

Cowan AE, Jun S, Gahche JJ, Tooze JA, Dwyer JT, Eicher-Miller HA, Bhadra A, Guenther PM, Potischman N, Dodd KW, et al. Dietary Supplement Use Differs by Socioeconomic and Health-Related Characteristics among U.S. Adults, NHANES 2011-2014. Nutrients 2018;10(8). doi: 10.3390/nu10081114.

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2.1 Abstract

The objective of this study was to estimate the prevalence of use and types of DS used by U.S. adults (≥19 years) by sociodemographic characteristics: PIR, food security status, and SNAP participation using NHANES 2011–2014 data (n = 11,024). DS use was ascertained via a home inventory and a retrospective 30-day questionnaire. Demographic and socioeconomic differences related to DS use were evaluated using a univariate t statistic. Half of U.S. adults (52%) took at least one DS during a 30-day period; MVM products were the most commonly used (31%). DS and MVM use was significantly higher among those with a household income of ≥ 350% of the poverty level, those who were food secure, and SNAP income-ineligible nonparticipants across all sex, age, and race/ethnic groups. Among women, prevalence of use significantly differed between SNAP participants (39%) and SNAP income-eligible nonparticipants (54%). Older adults (71+ years) remained the highest consumers of DS, specifically among the highest income group (82%), while younger adults (19–30 years), predominantly in the lowest income group (28%), were the lowest consumers. Among U.S. adults, DS use and the types of products consumed varied with income, food security, and SNAP participation.

2.2 Introduction

The DGA states that nutrient needs should be met primarily from nutrient-dense foods because, in addition to vitamins and minerals, they contain fiber and other naturally occurring substances with beneficial health effects. The DGA also state that in certain cases, fortified foods and DS may be useful (1). In 2003–2006, about half of adults in the U.S. used at least one dietary supplement daily (2). Adults at the highest adjusted income have higher micronutrient intakes and lower risk of dietary inadequacy than those with lower incomes (3).

The prevalence of food insecurity has increased overtime (4). In 2016, 40.6 million Americans lived in poverty, an increase from 33.3 million in 2000 (5, 6). Since dietary choices and nutrient intakes are commonly influenced by income, people with lower incomes are more likely to have lower quality, less nutrient-dense diets (7, 8). Nutrient adequacy in adults is related to income (3, 9); however, little is known about DS use patterns according to income indicators among U.S. adults. Therefore, the objectives of this study were to provide updated estimates of DS use and to examine the relationship between DS use and demographic, socioeconomic, and health-related characteristics among U.S. adults, using data from the NHANES 2011–2014.

2.3 Methods

The NHANES, conducted by the National Center for Health Statistics, is a nationally representative, continuous cross-sectional survey of the noninstitutionalized, civilian residents of the U.S. (10). NHANES employs a complex, multistage probability sampling design. The NHANES protocol includes an in-person household interview as well as a follow-up health examination in a mobile examination center for each participant. All data presented in this report were collected during the in-person household interview, with the exception of body mass index. Persons who were less than 19 years of age (n = 7939), pregnant or lactating (n = 184), or had unknown or missing data on the use of dietary supplements (n = 4) were excluded, yielding a final analytic sample size of 11,024 U.S. adults. Written informed consent was obtained for all participants or proxies and NHANES survey protocol was approved by the Research Ethics Review Board at the Centers for Disease Control and Prevention, National Center for Health Statistics.

All questionnaire data used for this analysis, including the demographic and lifestyle data on age, sex, race and Hispanic origin, educational attainment, income, smoking status, alcohol use, self-reported health status, and health insurance coverage were collected from participants using the computer-assisted personal interview system during the in-person household interview. In NHANES, race and Hispanic origin is categorized as non-Hispanic white, non-Hispanic black, non-Hispanic Asian, or Hispanic. Age groupings were constructed using the Dietary Reference Intake age categories (11). Educational attainment was categorized as completion of less than high school, high school diploma or general equivalency diploma, or more than high school. Current health status was classified as excellent/very good, good, or fair/poor. Health insurance coverage of the participant at the time of the survey was categorized as either public, private (including those covered under both private and public plans), or uninsured (12). Current smoking status was determined based on whether participants were never smokers (smoked < 100 cig/lifetime), former smokers (>100 cig/lifetime but do not currently smoke), or current smokers. Current smokers were then further classified based on whether they smoked cigarettes daily (current, daily) or whether they classified themselves as a smoker, but did not smoke cigarettes daily (current, occasional) (13). Alcohol consumption was assessed using three questions from the NHANES Alcohol Use Questionnaire that measured use in the last 12 months, frequency, and number of drinks. A standard drink was defined at the time of the interview as a 12 fl. oz. (354 mL) glass of beer, a 5 fl. oz. (148 mL) glass of wine, or 1.5 fl. oz. (44 mL) of liquor (12). The mean daily drink number was calculated as the number of days a participant reported drinking in the past 12 months multiplied by the usual number of drinks that were consumed divided by the total number of days, and was categorized as 0, 1, 2, or ≥3 drinks/day (12).

DS use in the previous 30 days prior to the household interview was collected via the Dietary Supplement Questionnaire. Trained NHANES interviewers asked the participant about their use of vitamins, minerals, herbals, and other DS. Participants were asked to show interviewers the containers for all products taken in the past 30 days. For each DS reported, interviewers recorded label information including the product name, manufacturer, form (e.g., tablet), and strengths per serving. Participants were also asked about the consumption frequency, dose, and duration of use, for all products reported. Containers were examined for 83% of products reported. If containers were not available, participants were asked to recall in detail the product that they had taken. NHANES nutritionists at the National Center for Health Statistics then matched products reported by participants to product labels, obtained from several sources. More information on the NHANES DS component protocol can be found elsewhere (14, 15). For the analyses presented in this report, the specific types of products were chosen for presentation due to their high frequency of use among U.S. adults (2). Single nutrient containing DS categories were constructed based on whether the DS contained any amount of the specific nutrient (i.e., calcium, iron, zinc, magnesium, selenium, folate, and vitamins D, C, B12, B6, K) (2, 16). DS use was also examined for three mutually exclusive product classes: multivitamin-minerals (MVM), multivitamins, and botanicals. MVM use was defined as a product containing three or more vitamins and one or more mineral counts per supplement (2). Similarly, multivitamins were defined as vitamin combinations without minerals that were not categorized as MVM (17), and use of a botanical ingredient product was determined by the botanical count variable (2). Further details regarding analysis methods have been described elsewhere (2, 12, 18).

PIR, SNAP participation status, and food security were also assessed during the household interview. PIR is a measure of income that was established by the Department of Health and Human Services to represent the ratio of household income to the poverty guidelines, after adjusting for inflation and family size (19). The poverty guidelines are updated annually and differ by geographical location (with different cutoffs for the 48 contiguous states, the District of Columbia, Puerto Rico, Alaska, and Hawaii). A PIR ≤ 130% is the cutoff to determine financial eligibility for SNAP, the largest federally funded nutrition assistance program that provides vouchers for food purchases with the objective of reducing hunger and improving the health of low-income individuals and families (20, 21). Three PIR categories were constructed for this analysis: ≤130%, 131–350%, and >350%. The Food Security Questionnaire was used to collect information on both SNAP participation and adult food security. SNAP participation was assessed based on information collected on whether the respondent was currently a beneficiary. Individuals classified as SNAP income-eligible nonparticipants consisted of individuals who are not currently a beneficiary of SNAP yet are financially eligible (PIR ≤ 130%) to receive SNAP benefits. Individuals classified as SNAP income-ineligible nonparticipants are individuals who are not currently a beneficiary of SNAP nor are they financially eligible to receive SNAP benefits, due to a PIR > 130%. Adult food security was assessed using 10 questions in the USDA’s Food Security Survey Module (22). A dichotomous adult food security variable was constructed from the four options included in the module: adults who were considered to have full food security (no affirmative responses) or marginal food security (1–2 affirmative responses) were classified as food secure, while those with low food security (3–5 affirmative responses) or very low food security (6–10 affirmative responses) were classified as food insecure.

BMI, obtained from height and weight measured during the health examination, was calculated as kg/m^2. The classifications for BMI were as follows: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), and obese (≥30) (23). BMI data are only available for participants who attended the mobile examination center (n = 10,863).

All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA) and SAS-callable SUDAAN software (version 11; Research Triangle Institute, Raleigh, NC, USA). For data obtained via the household questionnaire, all analyses were conducted using the NHANES interview weights to account for differential nonresponse and noncoverage, and to adjust for oversampling and post-stratification. In contrast, NHANES examination weights were used to account for nonresponse and oversampling in all analyses that included BMI, since that data was collected in the mobile examination center. A Taylor Series Linearization approach was used to approximate SEs for all estimates, and statistical comparisons of DS use were evaluated using a univariate t statistic. A Bonferroni-corrected p-value of 0.0167 was considered statistically significant.

2.4 Results

About half of all U.S. adults (52%) took at least one DS in a 30-day period. DS use was higher among women (59%) than men (45%), and use increased linearly with age (**Table 2.1**). Specifically, older (71+ years) women had the highest prevalence of DS use (79%), while younger (19–30 years) men had the lowest (32%). Non-Hispanic whites (58%) and non-Hispanic Asians (53%) had a higher use of DS than non-Hispanic blacks (40%) or Hispanics (35%). Participants categorized as obese reported less DS use than those categorized as normal or overweight. Other differences were also evident; prevalence of use was higher among those who were former smokers (61% vs. 39%), those who had a self-reported health status of excellent or very good (58% vs. 49%), those with private health coverage (57% vs. 35%), or who typically consumed a moderate amount of alcohol (1 drink/day; 63% vs. 35%) compared to their counterparts. Patterns of MVM use generally followed these same general trends (**Table 2.1**).

Overall DS use, type, and number of products consumed differed by income, with consistent patterns for DS use observed across all levels of income and food security and by SNAP participation. Higher income (SNAP income-ineligible and PIR > 350%) and food-secure populations particularly were more likely to consume one or more DS compared to those who were less affluent (**Table 2.2**). The prevalence of DS use significantly increased in a stepwise fashion for adults across all age categories of PIR. Older adults (71+ years) remained the highest consumers of DS, specifically among the PIR > 350% group (82%), while younger adults (19–30 years), predominantly those in the PIR ≤ 130% group, were the lowest DS consumers (28%). Similarly, the food insecure compared to the food secure, SNAP participants and SNAP income-eligible nonparticipants had lower DS prevalence of use than income-ineligible nonparticipants.

The prevalence of MVM use also differed by income. SNAP income-ineligible, PIR > 350%, and food-secure groups used MVMs the most. MVM use was highest among older adults (71+ years), non-Hispanic whites, and women (**Table 2.3**). Interestingly, half of older adults (71+ years) with a PIR > 350% commonly took a MVM (51%), whereas patterns of MVM use were significantly lower among those with a PIR ≤ 130%. Also those with a PIR ≤ 130%, younger adults (19–30 years), and Hispanics were the least likely to take an MVM when compared to other PIR groups. Similar patterns of use were evident across food security categories; those who were food insecure (19%) had a significantly lower prevalence of MVM use when compared to their food-secure counterparts (33%). Across all poverty indicators, SNAP participants, specifically men (12%), had the lowest prevalence of MVM use, substantially lower than men who were SNAP income-ineligible nonparticipants (34%).

MVM, multivitamin, and botanical users tended to have higher incomes than non-users. Of these three DS product categories, MVMs were the most commonly consumed DS (31%), followed by botanicals (7%) and multivitamins (6%) (data not shown). Approximately 2% of dietary supplement users take all three supplements (MVM, multivitamin, and botanical), and 8% of users commonly take both a MVM and a botanical (data not shown). About 7% of U.S. adults take a botanical supplement; botanical use is highest among older adults (71+ years; 10%), primarily older women (9%), with those over the age of 51 accounting for 20% of botanical users (data not shown). Interestingly, non-Hispanic whites were more likely to take a botanical than non-Hispanic blacks, non-Hispanic Asians, or Hispanics (data not shown). Those who were food-secure, SNAP income-eligible nonparticipants, and those who had a PIR > 350% were more likely to take an MVM, multivitamin, and botanical than those who were food insecure, SNAP participants, or who had a PIR ≤ 130%, in that order (**Figure S2.1**). MVM and botanical use was significantly different between categories across all three poverty indicators. However, this was not the case with multivitamin use. Those with a PIR > 350% had a significantly higher prevalence of multivitamin use than their lower income counterparts, while those with a PIR between 131–350% did not significantly differ in use of a multivitamin than those with a PIR ≤ 130%. Likewise, SNAP income-eligible nonparticipants and SNAP participants did not significantly differ in multivitamin use; however, SNAP income-ineligible nonparticipants were significantly more likely to take a multivitamin. On average, the majority of U.S. adult DS users (66%) took one or two supplements daily (**Table 2.4**). During a 30-day period, 61% of DS users took their supplements every day, 12% took them on 20–29 days, 11% took them on 10–19 days, and 15% took DS on fewer than 10 days (data not shown). Among DS users, use of products containing one or more selected vitamins ranged from 45 to 75% (**Table S2.1**). These vitamins included vitamins B-6, B-12, C, D, or K. Vitamin K use was the lowest overall (45%), while vitamin D use was the highest (75%). Likewise, between 33 and 71% of DS users took a supplement containing calcium, iron, zinc, magnesium, selenium, or folate during a 30-day period. Supplements containing iron were the least commonly consumed DS (33%), while supplements containing calcium (71%) were the most commonly consumed DS over the 30-day period. These vitamins and minerals were selected for presentation based on whether the vitamin or mineral reported was taken by at least 30% of consumers.

Table 2.1 Estimated prevalence (%) of any dietary supplement (DS) use and multivitamin-mineral (MVM) use by demographic, anthropometric, and lifestyle characteristics among U.S. adults (≥19 years), NHANES 2011–2014 [1,2,3].

		Any DS			**MVM**		
Characteristic	***n***	**Total % (SE)**	**Men (*n* = 5425)**	**Women (*n* = 5599)**	**Total % (SE)**	**Men (*n* = 5425)**	**Women (*n* = 5599)**
Total	**11,024**	**52.1 (1.0)**	**45.4 (1.1)**	**58.6 (1.2) ***	**31.2 (0.8)**	**28.3 (0.7) [1]**	**34.0 (1.1) [2]**
Age range, years							
19–30	2284	35.5 (1.9) [a]	31.6 (2.1)	40.0 (2.6) *	22.6 (1.5) [a]	19.5 (1.7)	26.1(2.2) *
31–50	3686	45.2 (1.0) [b]	38.4 (1.5)	51.7 (1.7) *	29.1 (0.9) [b]	25.1 (1.0)	33.0 (1.4) *
51–70	3524	63.3 (1.6) [c]	56.3 (1.8)	69.8 (1.8) *	35.4 (1.4) [c]	34.5 (1.6)	36.2 (1.7)
≥71	1530	74.9 (1.2) [d]	69.3 (1.7)	79.0 (1.5) *	42.7 (1.3) [d]	40.9 (2.1)	44.0 (1.8)
Race/ethnicity	11,024						
Non-Hispanic White	4346	58.2 (1.1) [a]	51.3 (1.3)	64.8 (1.4) *	35.7 (1.0) [a]	32.8 (0.9)	38.5 (1.3) *
Non-Hispanic Black	2605	40.3 (1.4) [b]	33.9 (1.8)	45.5 (1.8) *	22.6 (1.0) [b]	20.3 (1.3)	24.6 (1.3)
Hispanic	2362	35.3 (1.1) [c]	27.5 (1.4)	43.2 (1.5) *	19.7 (1.0) [b]	15.3 (1.1)	24.2 (1.6) *
Non-Hispanic Asian	1388	53.5 (2.1) [a]	47.3 (2.3)	58.9 (2.5) *	28.8 (1.6) [c]	28.2 (1.8)	29.2 (2.0)
Educational Attainment	10,710						
Less than high school	2436	37.8 (1.1) [a]	30.2 (1.4)	45.9 (1.5) *	20.6 (1.1) [a]	17.7 (1.3)	23.7 (1.6) *
High school diploma/GED	2343	47.2 (1.5) [b]	36.7 (1.8)	58.2 (2.1) *	25.2 (1.2) [b]	19.2 (1.7)	31.6 (2.1) *
More than high school	5931	58.1 (1.1) [c]	53.5 (1.3)	62.3 (1.4) *	36.3 (0.9) [c]	35.0 (1.2)	37.5 (1.3)
BMI (kg/m^2)	10,863						
<18.5	217	46.8 (5.1) [a,b]	35.2 (7.4)	52.9 (7.2)	25.6 (4.4) [a,b]	16.3 (6.2)	30.5 (5.3)
18.5–24.9	3220	54.2 (1.7) [a]	44.1 (1.7)	62.5 (2.1) *	32.8 (1.6) [a]	27.0 (1.4)	37.6 (2.1) *
25.0–29.9	3454	54.6 (1.5) [a]	50.0 (1.8)	60.5 (1.8) *	34.0 (1.4) [a]	31.8 (1.6)	36.8 (1.6) *
≥30	3972	48.5 (0.9) [b]	41.5 (1.3)	54.5 (1.4) *	27.7 (0.9) [b]	26.0 (1.3)	29.2 (1.2)
Smoking Status	10,858						
Never	6161	53.5 (1.1) [a]	47.7 (1.6)	58.0 (1.3) *	32.5 (0.9) [a]	30.2 (1.2)	34.3 (1.2)
Former	2484	61.0 (1.5) [b]	53.5 (1.8)	70.8 (2.2) *	37.8 (1.6) [b]	34.9 (1.8)	41.5 (2.3) *
Current, occasional	412	40.3 (3.0) [c]	34.2 (3.1)	49.6 (3.6) *	23.2 (2.4) [c]	21.7 (2.4)	25.5 (4.2)
Current, daily	1801	38.8 (1.6) [c]	30.9 (1.6)	47.7 (2.6) *	19.9 (1.3) [c]	15.6 (2.0)	24.7 (2.0) *
Alcohol use, drinks/day	9898						
0	3212	54.7 (1.8) [a]	47.7 (2.0)	60.0 (2.4) *	29.5 (1.5) [a]	26.8 (1.9)	31.6 (2.2)
1	2368	62.6 (1.3) [b]	56.3 (2.4)	66.3 (1.6) *	39.0 (1.5) [b]	36.9 (1.8)	40.2 (1.8)
2	2801	53.0 (1.4) [a]	49.2 (1.7)	57.2 (2.1) *	32.0 (1.2) [a]	30.7 (1.4)	33.5 (2.2)
≥3	1517	35.5 (2.0) [c]	32.8 (2.1)	43.3 (3.4) *	23.4 (1.8) [c]	22.1 (1.9)	26.9 (2.6)
Self-reported health status	9951						
Excellent or very good	3591	57.8 (1.3) [a]	50.5 (1.8)	65.1 (1.6) *	36.7 (1.2) [a]	32.4 (1.3)	41.0 (1.7) *
Good	4030	49.4 (1.3) [b]	42.8 (1.5)	56.4 (1.9) *	29.3 (1.0) [b]	27.2 (1.2)	31.5 (1.6) *
Fair or poor	2330	49.0 (1.5) [b]	43.1 (2.3)	54.1 (1.7) *	25.0 (1.5) [b]	24.0 (2.2)	25.9 (2.1)
Health insurance coverage	10,977						
Private	5580	57.5 (1.1) [a]	51.1 (1.5)	63.7 (1.4) *	35.1 (1.0) [a]	32.4 (1.1)	37.7 (1.3) *
Public	2913	53.1 (1.6) [a]	46.8 (1.9)	58.1 (2.3) *	29.3 (1.4) [b]	28.1 (1.8)	30.3 (2.0)
Uninsured	2484	34.7 (1.5) [b]	28.7 (1.9)	41.8 (2.1) *	21.1 (1.1) [c]	17.3 (1.3)	25.6 (1.9)

Abbreviations: BMI, body mass index (calculation as weight in kilograms divided by height in meters squared); SE, standard error. [1] Different superscript letters (a, b, c) indicate significant differences within a column at a Bonferroni corrected $p < 0.0167$, determined by using a univariate t statistic. [2] An asterisk "*" indicates significant differences between sex within a row at a Bonferroni corrected $p < 0.0167$, determined by using a univariate t statistic. [3] Data are presented as percentages (SE); sample size is 11,024 unless otherwise noted.

Table 2.2 Estimated prevalence (%) of dietary supplement (DS) use by selected poverty and demographic indicators, among U.S. adults, 2011–2014

	Any DS								
		PIR			Food Security		SNAP Participation		
	Total (*n* = 11,024)	**PIR ≤ 130% (*n* = 3661)**	**131–350% (*n* = 3430)**	**≥350% (*n* = 3040)**	**Food-Insecure (*n* = 8829)**	**Food-Secure (*n* = 2115)**	**SNAP Participant (*n* = 2267)**	**Income-Eligible Nonparticipant (*n* = 2030)**	**Income-Ineligible Nonparticipant (*n* = 5963)**
All	52.1 (1.0)	38.6 (1.5) [a]	50.3 (1.0) [b]	63.5 (1.3)[c]	36.4 (1.7) [a]	55.1 (1.0) [b]	32.1 (1.3) [a]	44.4 (1.9) [b]	59.0 (0.9) [c]
Sex									
Men	45.4 (1.1)	30.2 (1.4) [a]	41.9 (1.4) [b]	58.3 (1.6)[c]	29.1 (2.2) [a]	48.3 (1.3) [b]	23.7 (1.5) [a]	34.1 (2.0) [b]	52.8 (1.2) [c]
Women	58.6 (1.2)	45.7 (2.0) [a]	58.3 (1.6) [b]	69.1 (1.7)[c]	43.2 (1.9) [a]	61.6 (1.2) [b]	38.9 (1.8) [a]	54.1 (2.5) [b]	65.2 (1.2) [c]
Age									
19–30 y	35.8 (1.9)	27.6 (2.5) [a]	36.3 (2.5) [b]	46.3 (3.7)[b]	30.7 (3.1)	36.9 (2.1)	22.0 (2.2) [a]	32.0 (2.5) [b]	42.2 (2.6) [b]
31–50 y	45.2 (1.0)	34.7 (2.0) [a]	43.4 (1.8) [b]	55.2 (1.5)[c]	34.8 (2.3) [a]	47.6 (1.1) [b]	26.3 (1.8) [a]	41.7 (3.1) [b]	51.7 (1.2) [c]
51–70 y	63.3 (1.6)	47.7 (1.8) [a]	57.0 (2.3) [b]	73.9 (1.9)[c]	41.6 (3.1) [a]	66.2 (1.6) [b]	44.1 (2.4) [a]	52.7 (2.5) [b]	68.5 (1.6) [c]
71+ y	74.9 (1.2)	66.3 (3.1) [a]	75.0 (1.7) [a]	82.1 (2.1)[c]	59.8 (4.6) [a]	75.7 (1.2) [b]	59.5 (4.2) [a]	69.3 (4.5) [a,b]	78.7 (1.3) [b]
Race									
Non-Hispanic White	58.2 (1.1)	44.9 (1.7) [a]	55.3 (1.7) [b]	66.2 (1.3)[c]	41.5 (2.8) [a]	60.4 (1.0) [b]	35.9 (2.4) [a]	51.6 (2.2) [b]	62.9 (1.1) [c]
Non-Hispanic Black	40.3 (1.4)	33.0 (2.2) [a]	42.0 (1.9) [b]	49.2 (3.0)[b]	30.7 (2.0) [a]	43.0 (1.5) [b]	30.9 (2.1) [a]	37.4 (3.2) [a,b]	46.5 (2.1) [b]
Hispanic	35.3 (1.1)	29.6 (2.1) [a]	36.4 (1.9) [a]	49.4 (2.9)[b]	31.7 (2.2)	37.0 (1.2)	26.1 (2.0) [a]	32.6 (2.8) [a]	42.3 (1.7) [b]
Non-Hispanic Asian	53.5 (2.1)	43.3 (4.3) [a]	48.7 (3.5) [a]	62.6 (2.7)[b]	38.7 (6.0) [a]	54.6 (2.2) [b]	41.3 (6.5) [a,b]	45.6 (4.1) [a]	57.1 (2. 3) [b]

Abbreviations: PIR, poverty–income ratio; SNAP, Supplemental Nutrition Assistance Program. [1] Different superscript letters (a, b, c) indicate significant differences within a row at a Bonferroni corrected $p < 0.0167$, determined by using a univariate t statistic. Missing superscripts indicate that the difference between groups within a category was not statistically significant. [2] Data are presented as percentages (SE); sample size is 11,024 unless otherwise noted.

Table 2.3 Estimated prevalence (%) of multivitamin-mineral (MVM) use by selected poverty and demographic indicators, among U.S. adults, 2011–2014 [1,2].

	MVM								
		PIR			Food Security		SNAP Participation		
	Total (*n* = 11,024)	**PIR ≤ 130%** (*n* = 3661)	**131–350%** (*n* = 3430)	**≥350%** (*n* = 3040)	**Food-Insecure** (*n* = 8829)	**Food-Secure** (*n* = 2115)	**SNAP Participant** (*n* = 2267)	**Income-Eligible Nonparticipant** (*n* = 2030)	**Income-Ineligible Nonparticipant** (*n* = 5963)
All	31.2 (0.8)	20.5 (1.2) [a]	29.1 (1.0) [b]	40.7 (1.2) [c]	18.9 (1.6)[a]	33.5 (0.8) [b]	16.4 (1.0) [a]	24.6 (1.5) [b]	36.6 (0.9) [c]
Sex									
Men	28.3 (0.7)	15.5 (1.2) [a]	25.4 (1.1) [b]	38.8 (1.3) [c]	15.5 (1.8)[a]	30.6 (0.8) [b]	12.4 (1.3) [a]	18.1 (1.5) [b]	34.1 (0.9) [c]
Women	34.0 (1.1)	24.6 (1.7) [a]	32.6 (1.4) [b]	42.9 (1.8) [c]	22.1 (1.8)[a]	36.3 (1.1) [b]	19.5 (1.3) [a]	30.6 (2.2) [b]	39.1 (1.2) [c]
Age									
19–30 y	22.6 (1.5)	15.4 (1.8) [a]	22.4 (1.5) [a,b]	32.4 (3.5) [b]	17.7 (2.6)	23.9 (1.8)	12.8 (1.6) [a]	18.5 (2.0) [b]	27.8 (2.3) [c]
31–50 y	29.1 (0.9)	19.5 (1.4) [a]	28.0 (1.6) [b]	37.9 (1.9) [c]	18.6 (2.4)[a]	31.5 (1.1) [b]	14.1 (1.3) [a]	23.8 (1.9) [b]	35.0 (1.3) [c]
51–70 y	35.4 (1.4)	23.0 (2.1) [a]	29.1 (2.1) [a]	44.5 (1.9) [b]	19.5 (2.6)[a]	37.6 (1.5) [b]	21.7 (2.1) [a]	26.2 (2.6) [a]	39.3 (1.7) [b]
71+ y	42.7 (1.3)	34.4 (2.6) [a]	42.3 (2.6) [a,b]	50.9 (3.1) [b]	27.3 (6.0)[a]	43.7 (1.4) [b]	21.7 (3.9) [a]	40.1 (3.7) [b]	46.7 (1.8) [b]
Race									
Non-Hispanic White	35.7 (1.0)	24.3 (2.0) [a]	32.4 (1.6) [b]	42.9 (1.4) [c]	22.1 (2.9)[a]	37.5 (1.0) [b]	18.5 (2.0) [a]	28.9 (2.3) [b]	39.6 (1.1) [c]
Non-Hispanic Black	22.6 (1.0)	17.0 (2.1) [a]	24.0 (1.4) [b]	30.9 (2.0) [c]	15.5 (2.0)[a]	24.7 (1.1) [b]	15.3 (1.8) [a]	21.7 (3.3) [a,b]	27.5 (1.1) [b]
Hispanic	19.7 (1.0)	15.5 (1.8) [a]	20.7 (1.3) [a]	31.1 (2.7) [b]	16.0 (2.0)[a]	21.2 (1.0) [b]	13.1 (1.5) [a]	17.7 (2.4) [a]	25.1 (1.3) [b]
Non-Hispanic Asian	28.8 (1.6)	19.8 (3.1) [a]	25.4 (2.7) [a]	36.5 (2.1) [b]	16.0 (4.3)[a]	29.7 (1.6) [b]	15.9 (4.0) [a]	21.8 (3.6) [a]	32.4 (1.9) [b]

Abbreviations: PIR, poverty–income ratio; SNAP, Supplemental Nutrition Assistance Program. [1] Different superscript letters (a, b, c) indicate significant differences within a row at a Bonferroni corrected $p < 0.0167$, determined by using a univariate t statistic. Missing superscripts indicate that the difference between groups within a category was not statistically significant. [2] Data are presented as percentages (SE); sample size is 11,024 unless otherwise noted.

Table 2.4 Estimated prevalence (%) of dietary supplement use by number of dietary supplements taken and selected poverty indicators among U.S. adult supplement users, 2011–2014 [1,2]

	Total	PIR			Food Security		SNAP Participation		
	Total (*n* = 5375)	**PIR ≤ 130% (*n* = 1438)**	**131–350% (*n* = 1678)**	**≥350% (*n* = 1867)**	**Food-Insecure (*n* = 769)**	**Food-Secure (*n* = 4573)**	**SNAP Participant (*n* = 755)**	**Income-Eligible Nonparticipant (*n* = 913)**	**Income-Ineligible Nonparticipant (*n* = 3358)**
Number of supplements									
1	42.7 (1.1)	53.9 (2.3) [a]	43.1 (1.5) [b]	37.2 (1.5) [c]	58.7 (2.7) [a]	40.8 (1.2) [b]	57.8 (2.1) [a]	50.8 (2.8) [a]	39.1 (1.1) [b]
2	22.9 (0.8)	19.8 (1.1) [a]	22.3 (1.3) [a,b]	25.3 (1.8) [b]	19.5 (1.8)	23.3 (0.9)	19.7 (1.7) [a]	20.2 (1.3) [a,b]	24.0 (1.0) [b]
3	14.6 (0.5)	11.8 (1.0) [a]	12.8 (1.2) [a,b]	16.3 (1.0) [b]	10.0 (1.5) [a]	15.1 (0.5) [b]	9.9 (1.6) [a]	12.9 (1.5) [a,b]	15.1 (0.6) [b]
4	7.6 (0.5)	5.4 (0.1) [a]	7.6 (0.7) [a,b]	8.9 (0.8) [b]	4.3 (0.8) [a]	8.0 (0.6) [b]	4.3 (0.8) [a]	6.5 (1.4) [a,b]	8.5 (0.6) [b]
5 or more	12.2 (0.7)	9.1 (1.3) [a]	14.1 (1.1) [b]	12.6 (1.1) [a,b]	7.3 (1.3) [a]	12.8 (0.7) [b]	8.4 (1.6) [a]	9.5 (1.4) [a]	13.1 (0.7) [b]

Abbreviations: MVM, multivitamin-mineral; PIR, poverty–income ratio; SNAP, Supplemental Nutrition Assistance Program. [1] Different superscript letters (a, b, c) indicate significant differences within a row at a Bonferroni corrected $p < 0.0167$, determined by using a univariate t statistic. Missing superscripts indicate that the difference between groups within a category was not statistically significant. [2] Data are presented as percentages (SE); sample size is 5375 unless otherwise noted.

2.5 Discussion

Results from this analysis indicate that over half of U.S. adults (52%) take one or more DS, particularly MVMs, and income is associated with DS use, type, and number of supplements taken. Many characteristics of DS use were also observed in other recent reports (2, 12, 24), such as comparable patterns of age, sex, and racial differences between U.S. population subgroups. DS use has remained relatively stable overtime. While 52% of the U.S. adult population used supplements in 2000 (25), a similar percentage of U.S. adults (52%) reported taking a supplement in the present study. Likewise, DS use among adults (≥19 years) was estimated to be 54% in 2003–2006 (2). Similar to previous studies, use of DS in adults was also associated with characteristics associated with good health, such as lower BMIs, moderate alcohol use, abstinence from smoking, having private health insurance, and higher educational attainment (12, 18, 26). This study provides additional, updated information on DS use in relationship to family income, food security and SNAP participation status. To our knowledge, this study is the first to use NHANES to provide updated information assessing the relationship between dietary supplement use and indicators of participants' economic status in U.S. adults.

According to the 2015 DGA Advisory Committee, food insecurity, or living without "consistent, dependable access to enough food for active healthy living" has the potential to limit an individual's capacity to choose a healthy diet (27, 28). Although over 40 million people currently receive SNAP benefits (20), 40.6 million people live in poverty, and approximately 13% of U.S. households are food-insecure (28), suggesting that some of these persons may be at increased risk of dietary inadequacy. Adults in poor socioeconomic status have a higher prevalence of micronutrient inadequacies based on total nutrient intakes from both diet and DS (3, 7).

Previous studies have shown that compliance with federal nutrition recommendations is especially problematic among the lower income populations (9). In part, this may be because nutrient rich foods tend to be more expensive than lower-quality foods (29, 30). However, studies have also shown that despite having a high-income status (PIR > 350%) and access to better-quality foods, some population subgroups continue to have inadequate micronutrient intakes, suggesting that the relationship between micronutrient status and income remains unclear (3).

2.6 Strengths and Limitations

The strengths and limitations of the present study should be noted. Although MVMs are the most commonly reported supplement used, no legal regulatory definition exists for MVMs (31). Despite the self-reported nature of NHANES, DS containers and labels were seen 83% of the time by interviewers to verify accuracy. NHANES is a nationally representative survey of the U.S. noninstitutionalized population. However, the response rates for the years 2011–2012 and 2013–2014 for adults were 66% and 65%, respectively (32, 33). We cannot completely rule out the potential for self-selection bias; that is, people who are more health-conscious may have been more interested in participating in NHANES. Furthermore, given the cross-sectional nature of the data we cannot infer causality between income and DS use.

2.7 Conclusions

In conclusion, DS are used by over half (52%) of U.S. adults, ≥19 years; MVM supplements are the most frequently consumed supplement across all adult age groups. All of the income indicators used in this analysis were also related to the prevalence of DS use and with the type and number of products consumed.

2.8 Acknowledgements

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CHAPTER 3. CONTRIBUTION OF DIETARY SUPPLEMENTS TO TOTAL MICRONUTRIENT INTAKES AMONG U.S. ADULTS, NHANES 2011-2014

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3.1 Abstract

This study examined the contribution of DS to total usual micronutrient intakes relative to the DRI, among U.S. adults (≥19y) by sex, age, PIR, and race/Hispanic origin using the 2011-2014 NHANES (n=9,954). Dietary data were collected using two 24-hour recalls; DS data were collected via an in-home interview. The NCI method was used to estimate the distribution of mean total usual intakes. DS contributed to total intakes for calcium, magnesium, zinc, and vitamins B6, C, D. Nevertheless, many population subgroups were at risk of inadequacy for these nutrients. The majority of nutrients came from food sources, except for vitamin D. The contributions of DS to total intakes increased with age for vitamin C, calcium, magnesium, and zinc. Vitamin D from DS contributed most to total intakes, with the largest contribution to total intakes among older women (84%). Large proportions of adults still had total intakes that were lower than the EAR for vitamin D (63%), magnesium (45%), and vitamins C (35%); similar patterns were observed across sex, age, income, and race/Hispanic origin groups. Women with the lowest incomes (PIR ≤ 130%) were at risk for inadequate vitamin D (73%), magnesium (56%), and/or vitamin C (42%); that is, their usual intakes were more likely to be below their requirements compared to women in higher income groups. However, many supplement users, especially those who were middle-aged and older adults, had total usual intakes that exceeded the UL for folic acid, vitamin D, calcium, and iron. Thus, while DS contribute substantially to meeting, and at times, exceeding requirements, some shortfall nutrients continue to exist in U.S. adults.

3.2 Introduction

Micronutrient intakes that align with the DRI are optimal for health promotion and reducing the risk of some chronic diseases (1). The DGA 2015-2020 identified a number of micronutrients, including calcium, magnesium, potassium and vitamins A, C, D, and E, as being under consumed by the U.S. population relative to the EAR or AI (2). DS have the potential to lower the prevalence of inadequate intakes for some micronutrients (3, 4). However, their use may also increase the risk of intakes above the UL (3-6). Total micronutrient intakes, inclusive of DS, have been shown to vary by age, sex, income, and race/Hispanic origin (6-8). Therefore, this study's objective was to examine the contributions of DS to total usual micronutrient intakes relative to the DRIs for adequacy (i.e., the EAR or AI) and excess (i.e., the UL) among U.S. adults by these demographic characteristics, using data from the NHANES, 2011-2014.

3.3 Methods

The NHANES is a nationally representative, continuous cross-sectional survey of noninstitutionalized, civilian residents of the U.S., conducted by the National Center for Health Statistics (9). The NHANES protocol includes an in-person household interview that queries health information and demographics as well as a follow-up health examination in a MEC for each participant. Written informed consent was obtained for all participants or their proxies, and the NHANES survey protocol was approved by the Research Ethics Review Board at the CDC/National Center for Health Statistics. For the purposes of this analysis, data on dietary and DS intakes from the NHANES 2011-2012 and 2013-2014 cycles were combined to form a sample of 19,151 participants. Participants who were <19 years of age (n=7,939), did not complete or had incomplete 24-h dietary recall or dietary supplement questionnaire data (n=1,088), or who were pregnant and/or lactating (n=170) were excluded, yielding a final analytic sample size of 9,954 adults.

All demographic data used for this analysis, including data on sex, age, income, race and Hispanic origin, were collected from participants using the Computer-Assisted Personal Interview system during the household interview. Race and Hispanic origin is categorized as non-Hispanic (NH) White, NH Black, NH Asian, or Hispanic according to NHANES protocol. Age was categorized to be consistent with the DRI age groups (10). Income was classified using PIR, a measure of income established by the Department of Health and Human Services representing the ratio of family income to the poverty guidelines, a variable that is available in NHANES (11). Three PIR categories were used in this analysis: ≤ 130%, 131% to 350%, and > 350%. A PIR <130% is the income eligibility criterion for participation in SNAP, and these cutoff points have been shown to be associated with various health-related characteristics, DS use, and nutrition indicators among subgroups in previous NHANES analyses (5, 12, 13).

DS use in the previous 30 days was collected during the household interview via the DSQ. Participants were asked to show interviewers the containers for all products taken in the past 30 days. For each DS reported, interviewers recorded the name, manufacturer, form of the products (e.g. tablet) and dose per serving for selected single nutrient products from the label. Detailed information on the consumption frequency, amount, and duration of DS use were also collected for all products reported. Mean daily nutrient intakes from supplemental sources for each individual were calculated using the total number of reported days, amount taken per day, and the dose per serving of each product from the label. More information on the NHANES dietary supplement component protocol can be found elsewhere (13-16).

Dietary intake was self-reported in the MEC using an in-person 24-hour dietary recall. A second 24-hour dietary recall was completed via telephone approximately 3-10 days after the MEC exam. Both 24-hour recalls were collected by trained interviewers using a computer-assisted multiple-pass method (17, 18). The U.S. Department of Agriculture, Food and Nutrient Database for Dietary Studies and the NHANES Dietary Supplement Database were used to convert foods, beverages, and dietary supplements as reported, to their respective nutrient values (19, 20). DS information for vitamins A and E were not available in NHANES 2011-2012, thus total usual nutrient intakes could not be estimated and usual intakes are reflective of food sources only for these nutrients. Sodium and potassium were excluded from the analyses since negligible amounts are found in DS (21). Written informed consent was obtained for all participants or proxies and the NHANES survey protocol was approved by the Research Ethics Review Board at the CDC/National Center for Health Statistics.

An adaptation of the NCI Method (22, 23) was used to estimate (1) distributions of usual micronutrient intakes (from foods alone and total) by men and women and (2) the proportions of the subpopulations (i.e. sex, age, income, race/Hispanic origin) whose usual intakes were <EAR, >AI, and >UL. The NCI method is used to estimate the distributions of “usual” or “long-term mean daily" intakes by accounting for random measurement error (i.e., within-person variation). It was adapted to estimate the contributions of DS to usual micronutrient intake estimates through the incorporation of reported DS intakes from the DSQ using the method described by Bailey et al. (5). Covariates that were used to adjust the usual intake models included day of the week of the dietary recall (weekend/weekday), interview sequence (first or second dietary recall), and DS use, as well as categorical variables for income, age, and race/Hispanic origin for each individual subgroup analysis. Mean daily nutrient intakes from DS and their relative contribution to total intakes were estimated by adding nutrients from supplemental sources to the adjusted usual intake from dietary sources to estimate total usual micronutrient intake among the adult total population (DS users and nonusers combined) (21, 24). The relative contribution of DS to total micronutrient intakes by men and women was calculated by dividing the mean usual micronutrient intake from dietary supplements by the mean total usual micronutrient intake from all sources at the group level.

Total usual micronutrient intake distributions were compared to age and sex-specific DRIs established by the National Academies of Science, Engineering, and Mathematics in order to compute total usual micronutrient intakes relative to the DRIs for adequacy and excess; including the %<EAR, %> AI, and %>UL using the cut-point method (1, 10). The EAR cut-point method assumes that the DRI nutrient requirement distribution is symmetric, and therefore, is unable to be applied to iron since the DRI requirement distribution for iron is skewed in reproductive-aged women.

All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA) accounting for the NHANES complex survey design and sampling weights to adjust for differential nonresponse and noncoverage, and oversampling and post-stratification. Standard errors for all statistics of interest were approximated using Fay's modified Balanced Repeated Replication technique (25, 26).

Differences in demographic variables, mean usual micronutrient intakes (from food sources alone and total) and in total usual micronutrient intakes relative to the DRIs for adequacy and excess were compared using a univariate t-test statistic; a Bonferroni-corrected *p*-value of 0.0167 was considered statistically significant. In order to evaluate the micronutrient density per calorie consumed, an energy-adjusted dietary intake value was calculated to adjust for differences in total energy intake when comparing differences in mean total usual nutrient intakes between men and women (27). This energy-adjusted dietary intake value was further used in the NCI models to estimate adjusted usual micronutrient intake from dietary sources with the addition of nutrients from supplemental sources to estimate energy-adjusted total usual micronutrient intake. For differences among age and race/Hispanic origin groups of men and women, Hsu's procedure (28) was used to determine the highest and lowest values for mean total usual micronutrient intakes and DRI comparisons (29), rather than a series of multiple comparison of all pairs to minimize the probability of Type I error, with a *p*-value set at 0.025.

3.4 Results

The relative contributions of DS to total usual intakes varied by nutrient, with the highest contributions from DS for calcium, magnesium, zinc, and vitamins D, C, and B6 **(Figure 3.1).** The proportion of micronutrients contributed by DS increased with age for vitamin C, calcium, magnesium, and zinc. In general, the proportion of nutrients from dietary sources was greater than the proportion from DS. However, the proportion of total micronutrient intake contributed by DS was large for some nutrients, especially for vitamin D in older women (84%), vitamin B6 among women 51-70y+ (80%), and DS accounted for over half of total intakes among adults over 50y, although the proportions differed by age, race, and income groups **(Figure 3.1).**

DS contributed substantially to meeting the EAR and AI for several key nutrients, including calcium, magnesium, zinc, and vitamins B6, C, D, and K in both men and women **(Table 3.1).** Differences in total usual nutrient intake and usual intake from foods alone were apparent in both men and women and within each sex, for calcium, magnesium, zinc, and vitamins C and D. Among women, significant differences between food alone and total nutrient intakes indicating the contribution of DS were also present for vitamins B6 and K **(Table 3.1).** After adjustment for energy, women had higher intakes of calcium, magnesium, iron, and vitamins B12, D, and K from both foods alone and total intakes than men (**Table 3.2**). A small proportion of the total population had total usual nutrient intakes below the EAR for vitamin B6 (6%), folate (8%), thiamin (4%), riboflavin (2%), niacin (1%), vitamin B12 (3%), phosphorous (1%), selenium (1%), and copper (5%, data not shown).

In spite of DS contributing substantially to total intakes of several nutrients, many adults still had total usual intakes that were lower than the EARs for magnesium (45%), vitamins C (35%), D (63%), regardless of whether they were DS users or nonusers, and similar patterns were also evident by sex, age, income, and race/Hispanic origin groups. Specifically, many older men (58%, 70+y, **Table S3.1)** and women with the lowest incomes (56%, PIR ≤130%, **Table S3.2)** had intakes below requirements for magnesium, while women with lower incomes (42%, PIR ≤130%) were also less likely to meet their requirements for copper (14%, and vitamin C (42%) than any higher income women **(Table S3.2).** About half (51%) of Hispanic women exceeded the AI for vitamin K, while only 13% of NH Asian did so **(Table S3.3).** Significant differences in vitamin D intake were also apparent by race/Hispanic origin; NH Black and Hispanic adults were more likely to have intakes of vitamin D below requirements than NH Whites and Asians **(Table S3.3).** The prevalence of exceeding the UL was low for most nutrients from food alone (data not shown). However, many supplement users, especially those who were middle-aged and older adults, had total usual intakes that exceeded the UL for folic acid, vitamin D, calcium, or iron **(Figure 3.2).** About 22% of older women and 18% of older men who took DS exceeded the UL for iron, while 16% of middle-aged (51-70y) women exceeded the UL for calcium. However, the same was not true for folic acid. About 10% of women 19-30y exceeded the UL for folic acid; whereas about 6% of women in each of the older groups did so **(Figure 3.2).**

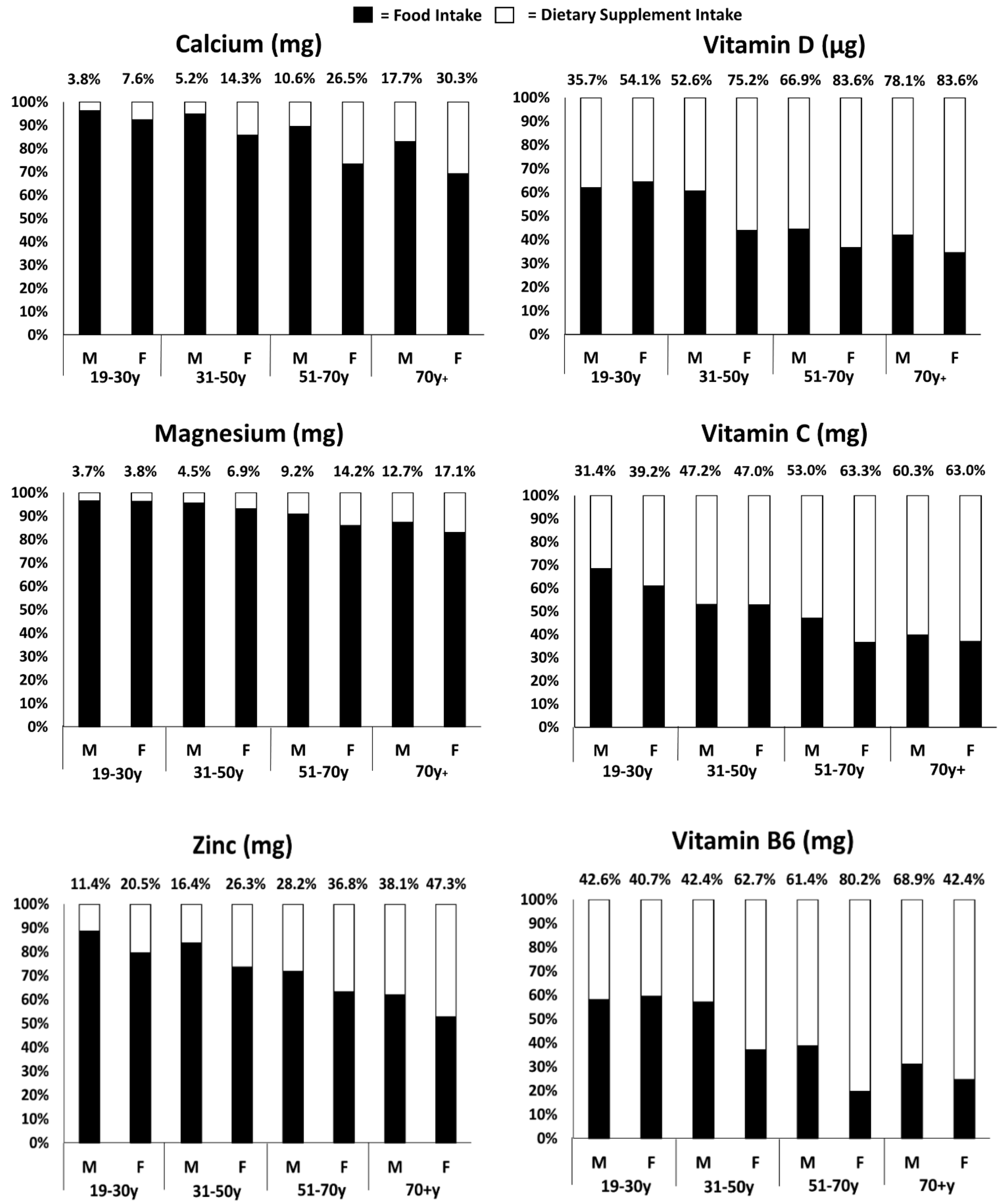

Figure 3.1 Relative contribution of foods/beverages and dietary supplements to total usual intakes for selected nutrients by age group among men and women (≥19y) in the U.S., NHANES 2011-2014[1]

[1] The analytic sample includes individuals ≥19 years old that were not pregnant or lactating with complete information for age and the day 1 and 2, 24-hour dietary recalls. Percentages above each bar represent the relative contribution from dietary supplements.

Table 3.1 Estimated percent (% (SE)) of men and women (≥19y) with total usual micronutrient intakes below the Estimated Average Requirement (EAR) in the U.S., 2011-2014[1,2]

	% < EAR (SE), Usual Intakes from Foods Alone		*P*-value	% < EAR (SE), Total Usual Intakes		*P*-value
	Men (A)	Women (B)	A v B	Men (A)	Women (B)	A v B
Calcium (mg)	26.0 (1.2)	58.0 (1.6)	<0.0001	21.0 (1.0)*	41.0 (1.3)*	<0.0001
Magnesium (mg)	52.0 (1.3)	50.7 (1.3)	0.48	46.0 (1.2)*	43.6 (1.2)*	0.16
Iron (mg)[3]	--	--	--	--	--	--
Phosphorous (mg)	1.0 (0.2)	0.0 (0.0)	<0.0001	1.0 (0.2)	0.0 (0.0)	<0.0001
Selenium (µg)	0.0 (0.0)	1.0 (0.2)	<0.0001	0.0 (0.0)	0.8 (0.2)	<0.0001
Zinc (mg)	16.3 (1.4)	17.3 (1.2)	0.59	12.7 (1.1)	13.2 (1.1)*	0.75
Copper (mg)	2.5 (0.4)	10.3 (0.7)	<0.0001	2.2 (0.4)	8.5 (0.7)	<0.0001
Vitamin A (µg RAE)[4]	48.0 (2.3)	41.0 (2.0)	0.02	--	--	--
Vitamin C (mg)	50.8 (1.7)	44.0 (1.4)	<0.0001	39.0 (1.7)*	32.0 (1.2)*	0.0007
Vitamin D (µg)	91.5 (0.9)	98.4 (0.3)	<0.0001	66.4 (1.0)*	59.1 (1.8)*	0.0005
Vitamin E (mg ATE)[5]	70.5 (1.4)	88.2 (1.1)	<0.0001	--	--	--
Thiamin (mg)	2.6 (0.5)	9.3 (1.1)	<0.0001	2.1 (0.4)	7.0 (0.9)	<0.0001
Riboflavin (mg)	2.2 (0.3)	2.8 (0.4)	0.23	1.9 (0.3)	2.3 (0.3)	0.35
Niacin (mg)	0.2 (0.1)	1.9 (0.3)	<0.0001	0.2 (0.1)	1.5 (0.2)	<0.0001
Folate (DFE, µg)[6]	6.0 (0.8)	15.9 (1.6)	<0.0001	5.0 (0.6)	12.0 (1.2)	<0.0001
Vitamin B6 (mg)	2.6 (0.6)	14.4 (1.0)	<0.0001	1.9 (0.5)	10.6 (0.8)*	<0.0001
Vitamin B12 (µg)	1.1 (0.4)	6.7 (0.8)	<0.0001	1.0 (0.3)	5.0 (0.6)	<0.0001
Vitamin K (µg)[7]	41.6 (1.7)	59.0 (2.0)	<0.0001	45.9 (1.7)	63.0 (1.8)	<0.0001

Table 3. 2 Mean (SE) energy-adjusted total usual micronutrient intakes by sex among men and women (≥ 19 y) in the U.S., 2011-2014[1]

	Mean (SE)		*P*-value
	Men (A)	Women (B)	A v B
Calcium (mg)	551.9 (8.0)	705.2 (10.0)	<0.0001
Magnesium (mg)	173.5 (2.6)	188.4 (2.3)	<0.0001
Iron (mg)	9.0 (0.2)	11.9 (0.3)	<0.0001
Phosphorous (mg)	679.6 (4.8)	675.6 (4.9)	0.56
Selenium (µg)	75.5 (0.9)	73.3 (5.3)	0.69
Zinc (mg)	9.4 (0.3)	9.8 (0.2)	0.26
Copper (mg)	0.9 (0.0)	0.9 (0.0)	1.00
Vitamin A (µg RAE)[2]	302.2 (9.1)	346.4 (9.1)	0.0006
Vitamin C (mg)	122.7 (6.9)	141.9 (8.3)	0.08
Vitamin D (µg)	10.7 (0.6)	17.4 (0.9)	<0.0001
Vitamin E (mg ATE)[3]	4.2 (0.1)	4.5 (0.1)	0.03
Thiamin (mg)	6.0 (1.3)	6.0 (0.7)	1.00
Riboflavin (mg)	3.3 (0.2)	3.6 (0.2)	0.29
Niacin (mg)	23.0 (1.3)	22.2 (0.9)	0.61
Folate (DFE, µg)[4]	621.3 (258.9)	618.7 (144.5)	0.99
Vitamin B6 (mg)	4.1 (0.2)	5.4 (1.1)	0.26
Vitamin B12 (µg)	54.1 (7.6)	86.8 (7.9)	0.0029
Vitamin K (µg)	60.0 (1.2)	83.1 (5.8)	0.0001

[1] The analytic sample includes individuals ≥19 years old that were not pregnant/lactating with complete information for age and the day 1 and 2, 24-hour dietary recalls. A Bonferonni-corrected p-value < 0.0167 was considered statistically significant.
[2] As retinol activity equivalents (RAEs). 1 RAE = 1 mg retinol, 12 mg b-carotene, 24 mg a-carotene, or 24 mg b-cryptoxanthin. Total usual intakes are from food sources only.
[3] As a-tocopherol. a-Tocopherol includes *RRR*-a-tocopherol, the only form of a-tocopherol that occurs naturally in foods, and the *2R*-stereoisomeric forms of a-tocopherol (*RRR*-, *RSR*-, *RRS*-, and *RSS*-a-tocopherol) that occur in fortified foods and supplements. Total usual intakes are from food sources only.
[4]As dietary folate equivalents (DFEs). 1 DFE = 1 µg food folate = 0.6 µg of folic acid from fortified food or as a supplement consumed with food = 0.5 µg of a supplement taken on an empty stomach.

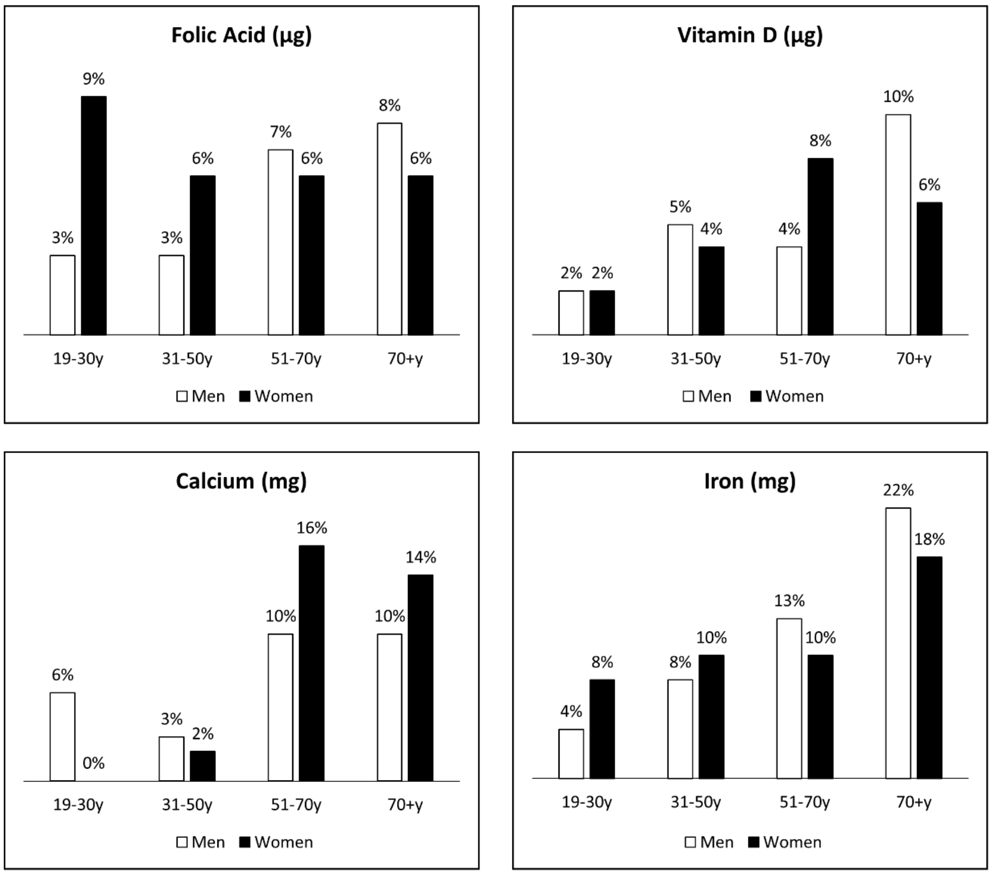

Figure 3.2 Estimated percent (%) of total micronutrient intakes above the Tolerable Upper Intake Level (UL) by age group among adult (≥19y) supplement users in the U.S., 2011-2014[1]

[1] The analytic sample includes individuals ≥19 years old that were not pregnant or lactating with complete information for age and the day 1 and 2, 24-hour dietary recalls. Percentages above each bar represent the estimated proportion of the population with intakes greater than the U

3.5 Discussion

This study's findings suggest that the use of micronutrient containing DS significantly contributed to total nutrient intakes and reduced the risk of inadequacy for several micronutrients across all sex, age, race, and income groups in the US population. DS contributed to over a quarter (≥ 25%) of total usual nutrient intakes for calcium, zinc, and vitamins B6, C, and D, and to a lesser extent magnesium for most age and sex groups.

Understanding the contribution of micronutrients from DS to total intakes is important, because they have the potential to fill nutrient gaps in the diet. Although many Americans still have inadequate intakes of some micronutrients even with the inclusion of DS, our findings suggest that DS aid in bridging the nutrient gap and in reducing the proportion of the population at risk for inadequate intakes especially for calcium, zinc, and vitamins B6, C and D. Strong scientific evidence supports the need for sufficient nutrient intakes to meet optimal health (1, 30). Since calcium, magnesium and vitamins C and D are under-consumed nutrients relative to the EAR, shifting dietary patterns towards increased intake of these nutrients through a healthier dietary pattern, fortified foods and/or DS may move population level estimates closer to DRI recommendations, and, it is to be hoped, improve nutritional health (2).

Some previous reports (3, 4) have suggested that DS users have an increased likelihood of intakes above the UL for several nutrients, including iron, calcium, and folic acid and that this might be prejudicial to health. Our analysis also showed that total usual intakes of those nutrients as well as zinc were above the UL for some DS users. However, the proportion of the population consuming levels above the UL was relatively low among DS users; the highest proportion above the UL in any age/sex subgroup of users being: 22% for iron, 16% for calcium, 9% for folic acid, and 10% for vitamin D. Nevertheless, caution is indicated for using high doses of iron, calcium, folic acid, and vitamin D since they have adverse health effects (31). Taken together, our findings suggest that while DS can be helpful in meeting nutrient requirements for many persons, nutrient excess may also be of concern for certain nutrients in a relatively small proportion of users, suggesting that moderation in their use is in order. While a relatively large proportion of those with the greatest need (i.e., who are at the greatest risk for nutrient inadequacy) may not be using these micronutrient-containing DS and are thus at risk, a minority of those who are using DS may not be at risk for nutrient inadequacy, posing risk for adverse effects among DS users if their intakes exceed the UL.

Differences between men and women were apparent with women having higher total usual nutrient intakes for most micronutrients per calorie when compared to men after adjusting for total energy, suggesting a more micronutrient dense diet. In previous analyses of DS use among U.S. adults in these survey years, women had higher prevalence of DS use that is likely to have contributed to higher total nutrient intakes among women (14).

This NHANES analysis and those of others (6-8) suggested that significant differences in total usual nutrient intakes and in the prevalence of inadequacy were present by sex, age, race/Hispanic origin, and income. Even after adjusting for these demographic characteristics, NH whites had a significantly lower prevalence of inadequacy for most micronutrients included in our analysis than those in other race/Hispanic origin groups, which is likely accounted for by NH whites' higher prevalence of DS use (14). In contrast, NH blacks had the lowest mean total usual nutrient intakes and thus the highest prevalence of inadequacy for most micronutrients, particularly calcium and vitamin D, which are "nutrients of public health concern." The lower micronutrient intakes observed in these race/Hispanic origin groups may partially contribute to the increased prevalence of some diet-related chronic diseases among them (32, 33). Specifically for calcium and vitamin D, inadequate intakes are associated with a number of adverse effects, including increased fracture risk, osteoporosis, inflammatory bowel disease, metabolic syndrome, and colorectal and breast cancer, among others (32, 33). Those in the highest income category (PIR > 350%) had significantly higher proportions of the population meeting EAR requirements for several micronutrients when compared to the lowest income category (PIR ≤ 130%). Previous studies have shown that nutrient inadequacy is more common in lower income populations (34).

3.6 Strengths and Limitations

The strengths and limitations of the present study should be noted. A strength of this analysis is that the models applied to examine total usual intakes adjust for the effects of within-person variation measurement error, in addition to using the recommended method of adding mean daily nutrient intakes from supplemental sources to the adjusted usual nutrient intake from dietary sources (24). The USDA's AMPM is a state of the art method for dietary data collection that ensures the quality of DS collection is exceptionally high, as is the FNDDS database that supports it. However, self-reported dietary data are prone to systematic errors. Furthermore, we assume that the DS intake reported for the past 30 days on the in-home interview reflected long-term DS intake;

but little is known about the measurement error structure of DS reporting (21). NHANES is a nationally representative survey of the U.S. noninstitutionalized population. However, the response rates for the years 2011–2012 and 2013–2014 for adults were 66% and 65%, respectively (35, 36), and total usual nutrient intakes could not be estimated for vitamins A and E due to unavailable NHANES 2011-2012 data. We cannot completely rule out the potential for self-selection bias; that is, people who participate in nutrition and health related research tend to differ by sociodemographic factors and may have been more interested in participating in NHANES (37).

3.7 Conclusions

In summary, our findings are consistent with previous reports that demonstrate that many U.S. adults have inadequate intakes of potassium, magnesium, calcium, vitamin D, vitamin A, and/or vitamin C and that the proportions of the population having intakes below their requirements for micronutrients differ by sex, age, and race/Hispanic origin, and income. Use of DS substantially reduced the prevalence of inadequate intakes for calcium and vitamins D and C, but not for the other 17 micronutrients assessed.

3.8 Acknowledgements

All authors designed the research and concepts presented, wrote sections of the paper, and provided critical review and insights presented.

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CHAPTER 4. SUMMARY AND FUTURE DIRECTIONS

4.1 Summary

About half of U.S. adults currently take a DS, particularly products containing vitamins and minerals. DS use, the number of supplements taken, and the type of DS are associated with income status. Higher income populations are not only more likely to take any DS, but also more likely to take multiple of them. In general, DS use in adults differs by demographic subgroup, but it is also associated with a number of health-related characteristics, including abstinence from smoking, lower BMIs, private health insurance, and moderate alcohol use.

The use of micronutrient containing DS can contribute to over a quarter (>25%) of total usual nutrient intakes and reduce the risk of inadequacy for calcium, zinc, and vitamins B6, C, and D and to a lesser extent magnesium for most age and sex groups. Thus, understanding the contribution of micronutrients from DS to total intakes is important because they have the potential to fill nutrient gaps in the diet. However, the proportions of the population with intakes below micronutrient recommendations differ by sex, age, and race/Hispanic origin, and income; many Americans still have inadequate intakes of some micronutrients even with the inclusion of DS. Some DS users exceed the UL for iron, calcium, folic acid, and vitamin D. Taken together, our findings suggest that while DS can be helpful in meeting nutrient recommendations for adequacy for many adults, but risk of inadequate intakes exist for potassium, magnesium, calcium, vitamin D, vitamin A, and/or vitamin C, and nutrient excess may also be of concern for certain nutrients in a relatively small proportion of DS users.

The research findings presented in this thesis contribute key evidence to the growing body of scientific literature on total nutrient exposures in U.S. adults and highlight the importance of assessing nutrient exposures from supplemental sources, in addition to dietary sources.

4.2 Future Directions

Future research investigating the standardization of methods to assess the prevalence of use and nutrient exposures from DS is needed. Specifically, standardized measurement tools and analysis methods that are designed to accurately classify nutrient exposures from DS and investigate and characterize the measurement error structure of DS reporting. Currently, the accuracy, reliability, and measurement error structure of DS assessment methods is unknown, and likely to differ from the measurement error structure for dietary assessment methods. Since current strategies are unable to adequately capture nutrient exposures from all sources, and no standardized methods that produce accurate and reproducible results exist, there is a significant need for such a method.