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Dietary Supplement Ingredient Database (DSID) and the Application of Analytically Based Estimates of Ingredient Amount to Intake Calculations

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Abstract

During dietary supplement (DS) manufacturing, many ingredients are added at higher than declared-label amounts, but overages are not standardized among manufacturers. As a result, researchers may underestimate nutrient intakes from DSs. The Dietary Supplement Ingredient Database (DSID) provides statistical tools on the basis of the results of chemical analysis to convert label claims into analytically predicted ingredient amounts. These adjustments to labels are linked to DS products reported in NHANES. In this article, we describe the purpose of the DSID, the statistical methodology underlying online calculators of analytically verified supplement content estimates, and the application and significance of DSID label adjustments in nutritional epidemiology. Tables summarizing the numbers of NHANES DS products with ingredient overages and below label content show the importance of DSID adjustments to labels for accurate intake calculations. We show the differences between analytically based estimates and labeled content for vitamin D, calcium, iodine, caffeine, and omega-3 (n–3) fatty acids and their potential impact on the accuracy of intake assessments in large surveys. Analytical overages >20% of label levels are predicted for several nutrients in 50–99% of multivitamin-mineral products (MVMs) reported in NHANES: for iodine and selenium in adult MVMs, for iodine and vitamins D and E in children's MVMs, and for iodine, chromium, and potassium in nonprescription prenatal MVMs. Predicted overages of 10–20% for calcium can be applied to most MVMs and overages >10% for folic acid in the vast majority of adult and children's MVMs. DSID studies are currently evaluating ingredient levels in prescription prenatal MVMs and levels of constituents in botanical DSs. We estimate that the majority of MVM products reported in NHANES have significant overages for several ingredients. It is important to account for nonlabeled additional nutrient exposure from DSs to better evaluate nutritional status in the United States. *J Nutr* 2018;148:1413S–1421S.

Keywords: dietary supplement, reference material, multivitamins, sampling plan, NHANES, quality control, label claim, overage, RDA, US Pharmacopeia

Background and History

Nearly half of the adult US population uses dietary supplements (DSs) (1). As defined by Congress in the Dietary Supplement Health and Education Act (2), which became law in 1994, a DS is a product (other than tobacco) that is intended to supplement the diet; contains ≥1 dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents; is intended to be taken by mouth as a pill, capsule, tablet, or liquid; and is labeled on the front panel as being a DS. Among the most commonly used are multivitamin-mineral products (MVMs), calcium and vitamin D supplements, omega-3 (n–3) FAs, and botanical supplements (1). The use of DSs containing vitamins and minerals contributes significantly to the total intake of many micronutrients. Supplement consumption significantly reduces the number of adults and children with intakes below the Estimated Average Requirement for all analyzed nutrients (3, 4). Even with the wide use of DSs, vitamin D, calcium, and potassium are currently classified as underconsumed nutrients of public health concern (5). Many bioactive compounds, including phytochemicals, do not have established RDAs. A single serving of a botanical extract may provide amounts of bioactive components (e.g., flavonoids) that are equal to or significantly exceed their average intake from foods per day.

Accurate intake estimation of ingredients is problematic; the supplement product-label information is not sufficient

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because of the way the DSs are manufactured and regulated. During manufacturing, some ingredients are added in amounts exceeding the label claims as suggested by the FDA in the DS Good Manufacturing Practices (6) to compensate for losses during shelf life. However, these amounts are not standardized for various ingredients and among different manufacturers. As a result, the actual ingredient amounts are unknown to consumers and researchers. Epidemiologic studies of DSs that use only the manufacturer's label as the source of information on ingredient content can provide misleading information on nutrient intakes and the nutrition status of the US population.

To more accurately estimate total intakes, the USDA Agricultural Research Service/Nutrient Data Laboratory (NDL) and the NIH Office of Dietary Supplements collaborate to optimize and expand the Dietary Supplement Ingredient Database (DSID; https://dietarysupplementdatabase.usda.nih.gov/) (7), an analytically validated database for high-priority ingredients in DS products. Other collaborators include the National Cancer Institute, the National Center for Health Statistics, the Food Composition and Methods Development Laboratory at the USDA Beltsville Human Nutrition Research Center, the National Institute of Standards and Technology, the FDA, and the National Library of Medicine.

It is impossible to provide analytically verified ingredient-content data for every DS manufactured in the United States. Instead, the DSID uses a statistical approach to select products representative of the US market for purchase (8). These products are chemically analyzed, and results are calculated as percentage differences from labeled ingredient amounts. With the use of regression analysis, the DSID establishes relations between the label amounts and percentage differences from labels for a DS category (e.g., adult MVMs).

The DSID project was initiated in 2004 with the identification of priority product categories and ingredients based on prevalence reports from NHANES and other national surveys (9–11). The highest priority category is MVMs, which are reported to be taken by 33% of adult respondents [2003–2006 NHANES (1)]. DS ingredients were prioritized for analysis on the basis of public exposure, public health significance, research needs, and the availability of validated analytical methods and reference materials. The DSID was first published in 2009, and its latest (fourth) release (DSID-4) was in 2017. The DSID currently provides nationally representative supplement-composition data for adult, children's, and prenatal MVMs and for n–3 FAs in fish- and plant-oil supplements. In addition, DSID-4 contains pilot study information about the content of green tea DSs, including information about the levels of constituents that may or may not be labeled.

National sampling plans

MVM supplements were defined for DSID studies as products containing ≥3 vitamins with or without minerals or other bioactive components. Nonprescription prenatal MVM supplements were defined as MVM supplements sold for prenatal use and available for purchase without a health care provider's prescription. Children's MVM supplements were defined as MVM supplements in chewable, liquid, or powder form sold for use by children. n–3 FA DSs were defined for the DSID study as fish oil, plant oil, and fish-/plant-oil blends sold for the primary purpose of increasing intake of n–3 FAs.

To develop national sampling plans for DSs, the NDL consulted with statisticians to modify the statistical sampling plans used to purchase foods for the USDA's food-composition databases (12). Products were identified that represent the US market, with the top selling products and a representative selection of lower market-share products included. The sampling plans used data from NHANES 2001–2008; USDA-commissioned surveys of DS use; *Nutrition Business Journal Supplement Business Reports* (12–15), the Dietary Supplement Label Database, a federally funded label database for DS with >70,000 products (https://dsld.nlm.nih.gov); the Internet; and local and national store surveys.

The basis for identifying and weighting products for each study was the NHANES DS data files. With the use of these files, population weights for all NHANES respondents reporting DS use were summed to obtain a total population weight for all products reported by DS consumers for each DS category [e.g., adult MVMs (8)]. A product's weighted frequency of use was calculated by dividing the summed weights of respondents who reported this product by the total population weight for this category of DS products. For each supplement category, the NHANES' most commonly reported DS products were identified by ranking according to the product weighted frequency of use. The process for identifying and purchasing a representative selection of lower market-share products was modified for each study, taking into account the different types of information available about the products on the market for that supplement category.

Multiple (in the vast majority of cases) lots of the DSs were purchased from mass merchandisers and specialty retailers in 6 US states/counties identified as representative from the most recent US census data. In addition, products were purchased from direct market channels (Internet, multilevel marketing companies, health care providers). The adult MVM-1 products were purchased in 2006–2007, children's MVMs in 2008, prenatal MVMs in 2009–2010, and adult MVM-2 products in 2011. For the n–3 FA DS study, products were purchased and analyzed in 2008–2010 (7). More information on sampling plans can be found in the research summaries for each DSID study.

Laboratory analysis and quality control

After purchase, DS samples were repackaged and sent for analysis to laboratories in defined batches. Quality-control

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Abbreviations used: DS, dietary supplement; DSID, Dietary Supplement Ingredient Database; MVM, multivitamin-mineral; NDL, Nutrient Data Laboratory; QC, quality control; UL, Tolerable Upper Intake Level.

(QC) materials were added to each batch of MVM products, including Certified Reference Materials, in-house control materials, and duplicated product samples (8). NDL-qualified analytical contract laboratories analyzed the sample sets with the use of validated sample-handling protocols and appropriate methods (AOAC-approved or other acceptable methods), to obtain analytical information about ingredient levels. Analytical retests for ingredients in specific products were identified to check unusually high or low results, high variability among product lots, or questionable data in batches where QC results were inconsistent (8, 7).

Data analysis

Products obtained from national samplings of multiple lots of 64–124 adult, children's, and nonprescription prenatal MVM supplements and 84 n–3 FA DSs were chemically analyzed. For each sample analyzed, laboratory results were compared with labeled amounts and a percentage difference from the label was calculated: [(analytical value − label value)/label value] × 100. The relations between label-claimed amounts and percentage differences from the label claim across the range of label amounts analyzed were estimated by weighted regression (except for nonprescription prenatal MVMs, which were unweighted) using the SAS mixed-model procedure (SAS Institute). For each ingredient in each study, the label claim was the independent variable and the percentage difference from the label amount was the dependent variable. Three models (mean only, linear, and quadratic) were tested to fit the final laboratory data set, and the most complex, statistically significant model was selected as the final model. The resulting equations predict mean analytical levels for ingredients regardless of product brand names (pooled data) and based only on product category and labeled ingredient amount. The regression equations are implemented in online, interactive calculators (7). Analytically adjusted amounts of 3–22 ingredients are linked to the n–3 FA supplements and MVMs reported in the NHANES 2003–2014.

Recent Developments

Online, interactive DSID calculators generate analytically based label adjustments

The DSID-4 (7, 12) provides research tools to support the assessment of nutrient intake from DSs. These tools complement the USDA-ARS National Nutrient Database for Standard Reference used to support assessment of intake from foods and the USDA modernized food-composition database system, USDA Foods Data System (FooDS; currently under development; https://ndb.nal.usda.gov/) (13, 14). Six online, interactive calculators are provided on the DSID website. These calculators allow the user to enter ingredient label information for a particular supplement category and generate the appropriate predicted mean values, SE, and 95% CI for the mean of the sampled population. For example, DSID studies indicate that adult MVM-2 products labeled at 400 μg folic acid/serving actually contain an average of 483.6 μg folic acid/serving (95% CI: 479.2, 509.4). For all MVM products containing folic acid and reported in NHANES, DSID adjustments are applied in **Tables 1** (>20% of label) and 2 (10–20% of label). DSID results have been considered and their impact discussed in folic acid intake research (15–18).

It is important to note that the DSID is designed to provide mean ingredient values for large-scale surveys where large numbers of responders use many different DS products. For this purpose, DSID ingredient calculators provide mean predicted values for many products at specific labeled amounts with relatively high confidence and small SEs. However, the results are not suitable for individual products, due to their high variability (8). In the example of folic acid (above) with a mean prediction of 483.6 μg/serving, the SE of the mean is 7.61 μg but the SE for an individual observation is 75.4 μg. DSID mean values are not applicable to individual products or products used in clinical trials. Investigative DSs should be chemically analyzed separately in each study.

Examples of how nutrient intake research can be improved with DSID information

Vitamin D in DSs. An accumulating body of evidence suggests that vitamin D may have many roles in human health, and that vitamin D deficiency may contribute to both acute and chronic illnesses (19). Vitamin D is an underconsumed nutrient in the United States, even after accounting for its intake from DSs (5). But the researchers did not account for the actual vitamin D content in DSs. On the basis of DSID findings, the mean vitamin D contents in MVMs are significantly higher than label values for adult, children's, and nonprescription prenatal MVMs (40.5%, 36.3%, and 13.1% above label, respectively) at the most common label levels (7). DSID results have been considered and their impact discussed in vitamin D intake research (20–23). For all children's and prenatal MVMs and a vast majority of adult MVMs containing vitamin D that were reported in NHANES, >20% or 10–20% DSID adjustments are applied (Tables 1 and 2).

In addition, a preliminary DSID analysis of 6 single-ingredient vitamin D_3 DSs representing different source materials, production methods, matrices, and supplement strengths showed significant overages [ranging from 12.8% to 59.5% above the label claim (24)]. A DSID national study of calcium and vitamin D DSs is planned to provide comprehensive national estimates.

Calcium in DSs. Adequate calcium intake is essential for the normal growth and development of the skeleton and teeth and for adequate bone mineralization (20, 25). In adulthood, low calcium intake has been associated with increased risk of osteoporosis, bone fractures, and falls (26). Calcium is an underconsumed nutrient in the United States, even after accounting for its label-based intake from DSs (5). However, DSID findings indicate that the estimated mean analytical content for calcium in adult, children's, and nonprescription prenatal MVMs ranges from 8% to 19% at the most commonly labeled levels. For example, when DSID label adjustments are applied to adult MVMs reported in the 2007–2008 NHANES, 46.2% of products are estimated to have calcium levels ≥10% above the label claim, and 9.2% of products would provide calcium content of ≥20% above the label claim (Tables 1 and 2). Thus, the DSID provides researchers with data to calculate more accurate calcium intake from DSs that may affect previous findings related to calcium intake (20).

Iodine in prenatal MVM DSs. Iodine is essential for the production of thyroid hormones, which, in turn, are important for normal fetal growth and development. Severe iodine deficiency in pregnancy causes cretinism and irreversible brain damage in offspring (27, 28). However, the safe Tolerable Upper Intake Level (UL) in pregnancy is still uncertain because the fetal thyroid is vulnerable to iodine excess (29). DSID studies have shown that iodine intake by pregnant women from

TABLE 1 Ingredients in products from NHANES DS files with DSID-predicted overages >20% above the labeled amount[1]

	2003–2004		2005–2006		2007–2008		2009–2010		2011–2012		2013–2014	
Ingredients, NHANES cycles	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %
Adult MVM-1												
Calcium	51/311 (16.4)	6.83	67/340 (19.6)	7.86	52/347 (16.2)	4.7	—	—	—	—	—	—
Iodine	264/264 (100)	100	280/280 (100)	100	262/262 (100)	100	—	—	—	—	—	—
Selenium	311/311 (100)	100	336/336 (100)	100	338/338 (100)	100	—	—	—	—	—	—
Adult MVM-2												
Chromium	—	—	—	—	—	—	254/324 (78.4)	90.6	256/311 (82.3)	93.7	298/369 (80.8)	91
Folic acid	—	—	—	—	—	—	382/460 (83)	91.9	389/460 (84.6)	93.7	444/524 (84.7)	92
Iodine	—	—	—	—	—	—	259/259 (100)	100	248/248 (100)	100	297/297 (100)	100
Selenium	—	—	—	—	—	—	255/324 (78.7)	87.8	227/306 (74.2)	82.5	250/353 (70.8)	75.7
Vitamin A	—	—	—	—	—	—	207/400 (51.7)	80.6	225/405 (55.6)	80.5	273/461 (59.2)	77.7
Vitamin B-12	—	—	—	—	—	—	459/459 (100)	100	466/466 (100)	100	539/539 (100)	100
Vitamin D	—	—	—	—	—	—	389/394 (98.7)	99.7	389/397 (98.0)	99.5	436/453 (96.3)	98.5
Children's (>4 y old) MVMs												
Calcium	—	—	13/65 (20)	10.2	11/46 (23.9)	6.28	13/35 (37.1)	8.5	—	—	—	—
Iodine	—	—	56/69 (81.2)	92.4	50/60 (83.3)	95.9	55/69 (79.7)	95.6	—	—	—	—
Vitamin A	—	—	31/140 (22.1)	11.9	38/114 (33.3)	28.6	50/114 (43.9)	43.4	—	—	—	—
Vitamin D	—	—	142/142 (100)	100	115/115 (100)	100	126/126 (100)	100	—	—	—	—
Vitamin E	—	—	64/115 (55.7)	50.7	55/90 (61.1)	53.2	71/96 (74)	63.7	—	—	—	—
Nonprescription prenatal MVMs												
Chromium	—	—	—	—	2/2 (100)	100	4/4 (100)	100	5/6 (83.3)	85.2	—	—
Iodine	—	—	—	—	5/5 (100)	100	7/7 (100)	100	9/9 (100)	100	—	—
Potassium	—	—	—	—	2/2 (100)	100	4/4 (100)	100	5/5 (100)	100	—	—

[1] Ingredients with overages of 0–10% are not included in Tables 1–3. The list of ingredients statistically evaluated by regression varied by product category (7). "*n*/Total *n*" indicates the number of products predicted to exceed 20% of ingredient label value divided by the total number of the products in the DS category for each NHANES cycle (within the DSID regression ranges); "w/W" indicates *n*/total *n* converted to weighted frequency with NHANES weights: the market share of products predicted to have ingredient levels >20% of label divided by the total market share of products in the DS category containing each ingredient per NHANES cycle (within the DSID regression ranges). DS, dietary supplement; DSID, Dietary Supplement Ingredient Database; MVM, multivitamin-mineral; MVM-1, first MVM study; MVM-2, second MVM study.

TABLE 2 Ingredients in products from NHANES DS files with DSID-predicted overages 10–20% above the labeled amount[1]

	2003–2004		2005–2006		2007–2008		2009–2010		2011–2012		2013–2014	
Ingredients, NHANES cycles	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %
Adult MVM-1												
Calcium	203/311 (65.3)	78.5	201/340 (59.1)	74.6	229/347 (66)	76.7	—	—	—	—	—	—
Folic acid	456/456 (100)	100	492/492 (100)	100	497/497 (100)	100	—	—	—	—	—	—
Riboflavin	477/477 (100)	100	518/518 (100)	100	509/509 (100)	100	—	—	—	—	—	—
Adult MVM-2												
Chromium	—	—	—	—	—	—	70/324 (21.6)	9.43	51/311 (16.4)	5.8	67/369 (16.5)	6.79
Copper	—	—	—	—	—	—	118/330 (35.8)	57.5	137/316 (43.3)	53.7	147/354 (41.5)	50.5
Manganese	—	—	—	—	—	—	41/328 (12.5)	5.9	34/314 (10.8)	3.96	43/376 (11.4)	4.46
Phosphorus	—	—	—	—	—	—	71/132 (53.8)	67.6	96/128 (75)	83.8	125/161 (77.6)	83.5
Riboflavin	—	—	—	—	—	—	343/455 (75.4)	86.9	342/464 (73.7)	84	362/504 (71.8)	79.2
Selenium	—	—	—	—	—	—	69/324 (21.3)	12.2	79/306 (25.8)	17.5	103/353 (29.2)	24.3
Vitamin A	—	—	—	—	—	—	116/400 (29)	12.8	102/405 (25.2)	11.7	118/461 (25.6)	13.4
Children's (>4 y old) MVMs												
Calcium	—	—	47/65 (72.3)	83.8	29/46 (63)	91	22/35 (62.9)	91.5	—	—	—	—
Folic acid	—	—	111/111 (100)	100	90/90 (100)	100	96/96 (100)	100	—	—	—	—
Iron	—	—	9/71 (12.7)	3.5	6/51 (11.8)	3.22	13/38 (34.2)	9.78	—	—	—	—
Phosphorus	—	—	14/43 (32.6)	23.4	11/30 (36.7)	20.4	3/17 (17.6)	18.3	—	—	—	—
Vitamin A	—	—	80/140 (57.1)	73.4	65/114 (57)	66.3	54/114 (48.2)	53.8	—	—	—	—
Vitamin B-12	—	—	110/110 (100)	100	90/90 (100)	100	99/99 (100)	100	—	—	—	—
Vitamin B-6	—	—	65/116 (56)	47.5	55/92 (59.8)	53.1	65/96 (67.7)	52	—	—	—	—
Vitamin E	—	—	50/115 (43.5)	49.1	35/90 (38.8)	46.8	25/96 (26.0)	36.3	—	—	—	—
Zinc	—	—	24/75 (32)	35.5	29/65 (44.6)	48	49/75 (65.3)	59.9	—	—	—	—
Nonprescription prenatal MVMs												
Calcium	—	—	—	—	19/20 (95)	95.7	23/25 (92)	97.3	22/24 (91.7)	96.9	—	—
Chromium	—	—	—	—	—	—	—	—	1/6 (16.7)	14.8	—	—
Selenium	—	—	—	—	2/2 (100)	100	3/3 (100)	100	5/5 (100)	100	—	—
Vitamin D	—	—	—	—	21/21 (100)	100	25/25 (100)	100	27/27 (100)	100	—	—

[1] Ingredients with overages of 0–10% are not included in Tables 1–3. The list of ingredients statistically evaluated by regression varied by product category (7). "*n*/Total *n*" indicates the number of products predicted to have ingredients amounts 10–20% above label value divided by the total number of the products in the DS category for each NHANES cycle (within the DSID regression ranges); "w/W" indicates *n*/total *n* converted to weighted frequency with NHANES weights: the market share of products predicted to have ingredient levels 10–20% of label divided by the total market share of products in the DS category containing each ingredient per NHANES cycle (within the DSID regression ranges). DS, dietary supplement; DSID, Dietary Supplement Ingredient Database; MVM, multivitamin-mineral; MVM-1, first MVM study; MVM-2, second MVM study.

nonprescription prenatal MVM products is underestimated if we rely on label information instead of analytically verified estimates. Nonprescription prenatal MVM products labeled at 150 μg I/serving are estimated to contain an average of 26% above the label claim, or 189 μg I/serving (95% CI: 175, 203 μg). For all MVM products containing iodine reported in NHANES, DSID adjustments are applied at >20% or 10–20% of label (Tables 1 and 2). Thus, the DSID provides researchers with data to calculate more accurate iodine intake from DSs that may affect previous findings on iodine status (30, 31). A pilot study measuring the nutrient content of prescription prenatal MVMs is now underway.

n–3 FA content in DSs. Sales of fish oil and animal oil for use by the nutritional supplement industry are a $1 billion industry in the United States (32). The evidence for health effects of n–3 FA supplementation, however, is still controversial and not conclusive [see, e.g., the most recent science advisory report and recommendations from the American Heart Association (33)]. A DSID national study of multiple lots of 84 DSs containing n–3 FAs focused on the results for products labeled for the 3 major n–3 FAs: α-linolenic acid (18:3n–3), EPA (20:5n–3), and DHA (22:6n–3). Eighty-five percent of products were labeled (voluntarily) for ≥1 of these 3 major n–3 FAs. An evaluation of analytical results indicated that ingredients in these products did not have the overages seen in MVMs (in fact, many products were slightly below label levels), and the results were less variable than for most vitamins and minerals in MVMs. DHA and α-linolenic acid mean estimates were not significantly different from label levels. The estimated mean percentage differences from label were significant only for EPA, which was below label (–5.4%; **Table 3**).

Caffeine in DSs. FDA regulations require that caffeine be listed on a DS product label if added, but listing the amount of caffeine is not required. Two DSID pilot studies have analyzed the caffeine content in DSs. The first study evaluated multiple lots of 53 products and found that there was a wide range of caffeine present in these samples, which were sold predominantly for the purposes of losing weight or increasing energy (34). The study also found that the products with voluntary label information about the amount of caffeine ($n = 28$) had significantly higher levels than those not labeled for quantity. Twenty-five of these products had analytically based caffeine levels per day of between −16% and +16% of the claimed levels. This trend for a wide range of caffeine levels and higher levels for products labeled for caffeine content was also seen in a recent study of 32 DSs with green tea as the only or primary ingredient (7).

DSID applications to NHANES DS product data files. One of the major applications of the DSID data is for large-population studies that take into account the intake of nutrients and other bioactive components from DSs, in addition to their intake from foods. The DSID-4 provides tables with linking codes to products reported in the NHANES cycles 2003–2014. DSID adjustments for specific products and ingredients are linked to the NHANES cycles preceding, coinciding with, and after the products' purchase date for each study.

The percentages of products in the NHANES database affected by the DSID-predicted overages or below label-ingredient content were calculated. Tables 1–3 show the percentages of products in adult MVM-1 and 2, children's MVMs, nonprescription prenatal MVMs, and n–3 FA DS categories reported in NHANES in 2003–2014 that are affected by DSID estimates of ≥10% above label- or below label-ingredient content. Products with ingredients whose predicted overages range from 0% to 10% above label are not reported.

Ingredients with >20% overages and with more than half of the NHANES products affected are iodine and selenium in adult MVM-1 products; chromium, folic acid, iodine, selenium, vitamin A, vitamin B-12, and vitamin D in adult MVM-2 products; iodine and vitamins D and E in children's MVMs; and chromium, iodine, and potassium in nonprescription prenatal MVMs. Ingredients with overages of 10–20% applied to more than half of NHANES products are calcium, folic acid, and riboflavin in adult MVMs; copper, phosphorus, and riboflavin in adult MVM-2 products; calcium, folic acid, vitamin A, vitamin B-12, and vitamin B-6 in children's MVMs; and calcium, selenium, and vitamin D in nonprescription prenatal MVMs. DSID overages of 10–20% for calcium are predicted for all MVMs (except for adult MVM-2) and >10% overages for folic acid in the vast majority of adult and children's MVMs.

Ingredients with content predicted to be below label and with more than half of NHANES products affected are thiamin in adult MVM-1 products; magnesium and thiamin in adult MVM-2 products; niacin, thiamin, vitamin B-6, and zinc in nonprescription prenatal MVMs and EPA in n–3 FA supplements (Table 3). In all 3 tables, the results for product categories across the 3 NHANES cycles are similar, which indicates stability in the label-level distributions.

In order to more accurately assess the effect on intake calculations, the percentages of products in the NHANES database affected by predicted overages or below-label ingredient content were compared with their summed relative NHANES product weight percentages. These 2 percentages were generally similar for the ingredients with high (>50%) numbers of affected products but could differ significantly for ingredients with lower numbers of affected products [1–20%; e.g., for calcium (Table 1), manganese (Table 2), and vitamin A (Table 3)]. In summary, predicted ingredient estimates in NHANES products may differ between the product categories but are similar for each product category across the 3 NHANES cycles.

Overages in combination with label levels above the RDA or UL. The analytically determined nutrient content of a nationally representative sample of DS can be used to evaluate the risk of exposure to levels in excess of the RDA, and, particularly, the UL (26). For example, most of the products for the adult MVM study (purchased in 2006–2007) had label levels at or above the RDA (but not exceeding the UL) for 12 nutrients (copper, iodine, iron, zinc, folic acid, niacin, riboflavin, thiamin, vitamin B-12, vitamin B-6, vitamin C, and vitamin E). For niacin, 30% of products were labeled above the UL and for folic acid, 8% were labeled above the UL. If the DSID estimated mean overages and the intake from food sources are added, these nutrients (except for thiamin) might be the most probable candidates for population nutrient overexposure (12). To determine and monitor nutrients in DSs with labeled levels at or above RDA and UL in a more comprehensive way than simply relying on label information, the DSID is a valuable resource. US Pharmacopeia researchers utilized the DSID data in a stimuli article reviewing factors affecting the optimization of US Pharmacopeia standards for the DS industry. This article also raises awareness about label accuracy and the potential risks associated with excessive intakes of vitamins and minerals, especially if a product contains any vitamins or minerals above the UL (35).

TABLE 3 Ingredients in products from NHANES DS files with DSID-predicted content below the labeled amount[1]

	2003–2004		2005–2006		2007–2008		2009–2010		2011–2012		2013–2014	
Ingredients, NHANES cycles	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %	*n*/Total *n* (%)	w/W, %
Adult MVM-1												
Thiamin	417/466 (89.5)	93.8	447/504 (88.7)	93.7	446/494 (90.3)	93.9	—	—	—	—	—	—
Vitamin B-6	108/480 (22.5)	10.9	130/527 (24.7)	13.3	137/533 (25.7)	13	—	—	—	—	—	—
Adult MVM-2												
Magnesium	—	—	—	—	—	—	333/333 (100)	100	328/328 (100)	100	382/382 (100)	100
Phosphorus	—	—	—	—	—	—	45/132 (34.1)	29.3	15/128 (11.7)	11.8	19/161 (11.8)	13.5
Thiamin	—	—	—	—	—	—	459/459 (100)	100	470/470 (100)	100	504/504 (100)	100
Vitamin A	—	—	—	—	—	—	58/400 (14.5)	4.57	62/405 (15.3)	5.5	50/461 (10.9)	4.46
Nonprescription prenatal MVMs												
Niacin	—	—	—	—	19/20 (95)	99.1	23/25 (92)	97.4	26/27 (96.3)	97.9	—	—
Thiamin	—	—	—	—	20/20 (100)	100	25/25 (100)	100	26/26 (100)	100	—	—
Vitamin B-6	—	—	—	—	20/20 (100)	100	25/25 (100)	100	27/27 (100)	100	—	—
Zinc	—	—	—	—	17/20 (85)	94.7	17/23 (73.9)	86.8	16/26 (61.5)	84.3	—	—
n–3 FA supplements												
EPA	—	—	62/62 (100)	100	96/96 (100)	100	89/89 (100)	100	—	—	—	—

[1] Ingredients with overages of 0–10% are not included in Tables 1–3. The list of ingredients statistically evaluated by regression varied by product category (7). "*n*/Total *n*" indicates the number of products predicted to have ingredient amounts below the label value divided by the total number of the products in the DS category for each NHANES cycle (within the DSID regression ranges); "w/W" indicates *n*/total *n* converted to weighted frequency with NHANES weights: the market share of products predicted to have ingredient levels below the label divided by the total market share of products in the DS category containing each ingredient per NHANES cycle (within the DSID regression ranges). DS, dietary supplement; DSID, Dietary Supplement Ingredient Database; MVM, multivitamin-mineral; MVM-1, first MVM study; MVM-2, second MVM study.

Future Directions

DSID pilot studies are currently evaluating ingredient amounts in prescription prenatal MVMs and in botanical supplements containing green tea (where many products do not provide information about phytochemical concentration). A primary goal of the DSID botanical initiative is to identify gaps in the labeling requirements for botanical DSs. We plan to evaluate whether information about the weight of extracts (currently required by the FDA unless it is part of a proprietary blend) without the constituent concentration is actually sufficient for researchers to closely monitor phytochemical intakes and for consumers to make informed choices.

A national study of the analytical content in calcium and vitamin D supplements, including nonprescription calcium-containing antacids, is planned. DSID research has also expanded to include the evaluation of in vitro disintegration and dissolution methods to assess the performance and quality of DSs. The efficacy of a DS is determined not only by the amount of the active ingredient but also by the formulation design. The design of a DS, including the excipients and capsule materials, can greatly influence the rate of ingredient release from supplement dosage forms for absorption and utilization by the body.

Conclusions

Through the use of statistical sampling plans, validated analytical methods, and statistical evaluation of analytical ingredient data, the DSID project provides nationally representative data about the nutrient and other bioactive contents of MVMs and n–3 FA DSs. DSID data can be used to address a variety of research questions and concerns. In many cases, ingredient overages appear to be applied by manufacturers in products labeled below and above the RDA and UL. We show that mean ingredient estimates may differ for specific ingredients and categories of DSs and for DSs targeting different consumer categories. The intake of some underconsumed nutrients, such as calcium and vitamin D, may be underestimated if DSID adjustments to label claims are not applied. For some ingredients, a high proportion of products with DSID adjustments >20% of label or below label indicate the importance of DSID corrections to label values for epidemiologic research of intakes and their relations to health.

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