The Journal of Nutrition
Nutritional Epidemiology

The Total Nutrient Index is a Useful Measure for Assessing Total Micronutrient Exposures Among US Adults

Alexandra E Cowan,[1] Regan L Bailey,[1] Shinyoung Jun,[1] Kevin W Dodd,[2] Jaime J Gahche,[3] Heather A Eicher-Miller,[1] Patricia M Guenther,[4] Johanna T Dwyer,[3,5] Nancy Potischman,[3] Anindya Bhadra,[6] Raymond J Carroll,[7] and Janet A Tooze[8]

[1]Department of Nutrition Science, Purdue University, West Lafayette, IN, USA; [2]NIH National Cancer Institute, Bethesda, MD, USA; [3]NIH Office of Dietary Supplements, Bethesda, MD, USA; [4]Department of Nutrition and Integrative Physiology, University of Utah, Salt Lake City, UT, USA; [5]Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA; [6]Department of Statistics, Purdue University, West Lafayette, IN, USA; [7]Department of Statistics, Texas A&M University, College Station, TX, USA; and [8]Wake Forest School of Medicine, Winston-Salem, NC, USA

ABSTRACT

Background: Most dietary indices reflect foods and beverages and do not include exposures from dietary supplements (DS) that provide substantial amounts of micronutrients. A nutrient-based approach that captures total intake inclusive of DS can strengthen exposure assessment.

Objectives: We examined the construct and criterion validity of the Total Nutrient Index (TNI) among US adults (≥19 years; nonpregnant or lactating).

Methods: The TNI includes 8 underconsumed micronutrients identified by the Dietary Guidelines for Americans: calcium; magnesium; potassium; choline; and vitamins A, C, D, and E. The TNI is expressed as a percentage of the RDA or Adequate Intake to compute micronutrient component scores; the mean of the component scores yields the TNI score, ranging from 0–100. Data from exemplary menus and the 2003–2006 (≥19 years; $n = 8861$) and 2011–2014 NHANES (≥19 years; $n = 9954$) were employed. Exemplary menus were used to determine whether the TNI yielded high scores from dietary sources (women, 31–50 years; men ≥ 70 years). TNI scores were correlated with Healthy Eating Index (HEI) 2015 overall and component scores for dairy, fruits, and vegetables; TNI component scores for vitamins A, C, D, and E were correlated with respective biomarker data. TNI scores were compared between groups with known differences in nutrient intake based on the literature.

Results: The TNI yielded high scores on exemplary menus (84.8–93.3/100) and was moderately correlated ($r = 0.48$) with the HEI-2015. Mean TNI scores were significantly different for DS users (83.5) compared with nonusers (67.1); nonsmokers (76.8) compared with smokers (70.3); and those living with food security (76.6) compared with food insecurity (69.1). Correlations of TNI vitamin component scores with available biomarkers ranged from 0.12 (α-tocopherol) to 0.36 (serum 25-hydroxyvitamin D), and were significantly higher than correlations obtained from the diet alone.

Conclusions: The evaluation of validity supports that the TNI is a useful construct to assess total micronutrient exposures of underconsumed micronutrients among US adults. *J Nutr* 2022;152:863–871.

Keywords: total nutrient index, dietary supplement, diet quality, validity, total usual intake estimation

Introduction

The assessment of nutrient exposures is critical for assessing population-level adherence to dietary recommendations and understanding diet and health relationships. Dietary indices offer a robust, reproducible method for examining and comparing diets to a standard across a variety of populations (1). To date, the majority of existing dietary indices have been used to reflect conformance with dietary recommendations based on intakes from foods and beverages alone and do not include nutrients that are obtained from dietary supplements (DS) (2). However, DS provide substantial amounts of micronutrients for the half of adults and one-third of children that use them (3–5). Because the use of DS has been associated with a reduced risk of micronutrient inadequacy in US adults (6–9), excluding them from dietary indices prevents a comprehensive evaluation of nutrient exposures (10).

Manuscript received October 1, 2021. Initial review completed December 6, 2021. Revision accepted December 13, 2021.
First published online December 20, 2021; doi: https://doi.org/10.1093/jn/nxab428.

A validated tool to assess micronutrient intake patterns could be used as a standalone tool or combined with other food-based indexes to provide a more comprehensive exposure assessment than food-based indices alone. To this end, the Total Nutrient Index (TNI) (2) was developed to describe total usual intakes of underconsumed micronutrients among the US population from foods, beverages, and DS relative to the RDA or Adequate Intake (AI). There are 8 micronutrients previously identified as underconsumed among US adults (nonpregnant or lactating) by the Dietary Guidelines for Americans (11): calcium, magnesium, potassium, choline, and vitamins A, C, D, and E comprise the current score. The Food Nutrient Index (FNI), based on foods and beverages alone, is calculated identically to the TNI without the nutrient contributions from DS, making it equivalent to the TNI for individuals who do not use DS (2). When compared to the TNI, the FNI can be used to examine the impact of DS use on adherence to micronutrient intake recommendations for a population.

The purpose of this study is to assess the degree of validity demonstrated by the TNI as a measure of adequacy of intake of underconsumed micronutrients among the US nonpregnant, nonlactating adult population. Construct validity, the extent to which an instrument measures what it intends to measure (12); criterion validity, the performance of a measure against a standard for the population of interest (12); and ceiling effects of the TNI and FNI were evaluated using exemplary menus and national self-report dietary and biomarker data. Specifically, we examined whether index scores were high for diets that were designed to meet recommended nutrient targets and would be expected to be highly adherent to the DRI using exemplary menus. Using national data, known group validity was examined to determine whether the index could distinguish differences in micronutrient intakes between groups that have been demonstrated to differ in this regard. We also examined correlations of the TNI and FNI, including the component scores, with the Healthy Eating Index (HEI) 2015 and its component scores, as well as with nutritional biomarkers. Our expectation was that the index would be weakly to moderately correlated with the HEI-2015, as it represents an overlapping but not identical construct. Similarly, we anticipated weak to moderate correlations with biomarkers, which reflect dietary intakes but are also impacted by other characteristics (e.g., smoking status, obesity) not reflected in the index.

This research was funded by a NIH/National Cancer Institute grant (NIH/NCI U01CA215834).
Author disclosures: Unrelated to this submission, RLB has served as a consultant in the past to the NIH Office of Dietary Supplements, Nestlé, the General Mills Bell Institute, RTI International, and Nutrition Impact; is a trustee of the International Food Information Council and a former board member of International Life Sciences Institute–North America; has received travel support to present her research on dietary supplements from the Council of Responsible Nutrition, American Society of Nutrition, and the New York Academy of Sciences. RLB is an Editor of *The Journal of Nutrition* and played no role in the *Journal's* evaluation of the manuscript. JTD has served on advisory boards for McCormick Spice, the Mushroom Council, Bay State Milling, ConAgra Foods (until December 2018), and Nestlé (until 2020); received an honorarium for a single consultation at Motif FoodWorks in 2019 and from Nestle in 2021; receives editorial fees from Lippincott, Williams, and Wilkins/Wolters Kluwer Publishers; and holds stock in several food and drug companies, all unrelated to this study. All other authors report no conflicts of interest.
The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.
Supplemental Box 1, Supplemental Methods, and Supplemental Tables 1–5 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.
Address correspondence to RLB (e-mail: reganbailey@purdue.edu).
Abbreviations used: AI, Adequate Intake; DS, dietary supplement; DSMQ, Dietary Supplement and Prescription Medicine Questionnaire; FNI, Food Nutrient Index; HEI, Healthy Eating Index; NCI, National Cancer Institute; TNI, Total Nutrient Index; 24HR, 24-hour dietary recall; 25(OH)D, 25-hydroxyvitamin D.

Methods

TNI scoring

The total usual intake for each micronutrient is estimated from foods, beverages, and DS and expressed as a percentage of the age- and sex-specific RDA or AI (truncated at 100% of the respective standard), with higher scores (scores range from 0 to 100) reflecting intake more closely aligned with recommendations. The TNI overall score, ranging from 0 to 100, is the average of the 8 micronutrient component scores, with each micronutrient component score weighted equally (2). The scoring algorithm for the FNI and TNI is described in **Supplemental Box 1**; additional details regarding the development and methodology of the FNI and TNI can be found elsewhere (2).

Strategies to evaluate validity

Four strategies were utilized to evaluate the construct and criterion validity of the TNI (**Box 1**). In this case, we sought to determine to what degree the TNI adequately assessed adherence to nutrient adequacy standards by evaluating whether the index *1*) yielded high scores for exemplary menus; *2*) differed between groups with known differences in nutrient intake based on prior knowledge; and *3*) exhibited a relationship with another measure of dietary quality, the HEI-2015; and whether the component scores *4*) were correlated with biomarkers of nutrient intake {e.g., serum 25-hydroxyvitamin D [25(OH)D]}. For the evaluation of the latter points, the TNI was compared to the FNI to elucidate the role of DS use in the utility of the score.

BOX 1.

Questions and strategies used to evaluate the construct and criterion validity of the FNI and the TNI

Question	Strategy
Does the FNI yield high scores for exemplary menus?	Compute FNI scores of sample menus from the USDA Food Patterns, DASH Diet, Harvard Medical School Healthy Eating Guide, and AHA No-Fad Diet for women 31–50 years and men ≥ 70 years
Do the FNI and TNI differentiate between groups with known differences in nutrient intake?	Compare usual FNI and TNI total scores of adult supplement users and nonusers, food-secure and food-insecure adults, and smokers and nonsmokers in the US adult population
What is the relationship between the FNI/TNI and the HEI-2015?	Estimate Pearson correlations of usual total and component HEI-2015 scores and usual total and component FNI and TNI scores, respectively, for the US adult population (≥19 years)
What is the relationship between component scores of the FNI and TNI and their respective nutritional biomarkers?	Estimate Pearson correlations of FNI and TNI component scores and their nutritional biomarkers for the US adult population (≥19 years)

DASH, Dietary Approaches to Stop Hypertension; FNI, Food Nutrient Index; HEI, Healthy Eating Index; TNI, Total Nutrient Index.

As an additional descriptive characteristic, we also evaluated potential ceiling effects by examining the range of scores in the population and the percentage of the population with scores of 100 by component. An a priori criterion of 25% was established to evaluate potential ceiling effects; that is, no more than 25% of the population should have a perfect total score on the TNI.

Data sources

Two types of data were employed: exemplary menus and data from the NHANES, which included two 24-hour dietary recalls (24HR), a dietary supplement inventory, and nutritional biomarkers (NHANES 2003–2006 and NHANES 2011–2014).

Exemplary menus.

Exemplary menus represent eating plans consistent with high-quality diets or adherence to a recommended dietary pattern (i.e., foods and beverages alone) at a given energy level (13). The intent of this analysis was to reflect hypothetical patterns of eating and to determine whether the FNI produces high scores for theoretically high-quality diets (as anticipated). FNI scores were calculated for 4 different exemplary menus: *1*) the 7-day 2000-kcal/d USDA Food Pattern menu (14); *2*) the 7-day 2000-kcal/d National Heart, Lung, and Blood Institute's Dietary Approaches to Stop Hypertension Diet menu (15); *3*) the 7-day 2000-kcal/d Harvard Medical School's Healthy Eating Guide menu (16); and *4*) the 1-day 2000-kcal/d sample menu from the AHA's 2005 No-Fad Diet (17). Complete details on each of the 4 exemplary menus can be found in the **Supplemental Methods**, Section 1.

None of these menu plans include nutrients from DS; thus, for the exemplary menus, we estimated FNI scores using a simple algorithm method. First, the nutrients provided by each menu were calculated by the Purdue University Diet Assessment Center using the USDA Food and Nutrient Database for Dietary Studies, 2017–2018 (18), and summed by day. Next, the mean of the calculated nutrient intakes across the multiple days of menus (if available) was compared to the RDA or AI values for middle-aged women (31–50 years) and also for older men (≥70 years) for each nutrient (11, 19); values above the RDA or AI were truncated at 100, and the mean across all component scores was calculated to yield the FNI score. These groups of adults were chosen for comparison because they have estimated energy requirements of 2000 kcal/day for moderately active women and sedentary men, which is the approximate energy intake used for the menus (20).

Nationally representative data.

The remainder of the analyses used data from the NHANES, a nationally representative, cross-sectional survey of the US noninstitutionalized civilian resident population conducted by the National Center for Health Statistics. In NHANES, data are collected in 2-year, continuous survey cycles at 3 time points: during an in-person household interview, during a dietary interview (i.e., 24HR) and health examination in the Mobile Examination Center, and during a follow-up dietary interview via telephone. Information on foods, beverages, and DS is acquired via up to two 24HRs; DS intake over the previous 30 days is also assessed via the Dietary Supplement and Prescription Medicine Questionnaire (DSMQ). Extensive details of the NHANES methodology are provided in the Supplemental Methods, Section 2. For the purposes of our analysis, 4 survey cycles of NHANES (i.e., 2003–2004, 2005–2006, 2011–2012, and 2013–2014) were examined where relevant demographic, dietary, and nutritional biomarker data were available: NHANES 2003–2006 and 2011–2014 data sets were created. For our primary analytic sample, 9954 US adults (≥19 years) who participated in the 2011–2014 NHANES, had at least one 24HR and a complete DSMQ, and were not pregnant or lactating, were utilized. Select nutritional biomarker (i.e., serum retinol, beta-carotene, vitamin C, and α-tocopherol) analyses were performed using NHANES 2003–2006; demographic, dietary, and biochemical data were collected similarly to those of NHANES 2011–2014 (with the same exclusion criteria applied), resulting in a secondary analytic sample of 8861 US adults (≥19 years).

For NHANES 2011–2014, DS users were identified based on whether participants responded "yes" to taking any products containing the nutrient of interest on the DSMQ or on 1 or more 24HR. Mean (i.e., average) daily DS intakes were calculated using the proportion of reported days of DS use over the past 30 days, multiplied by the amount the participant reported taking per day, if DS intakes were reported on the DSMQ. If DS intakes were not reported on the DSMQ but were reported on 1 or more 24HR, then the mean nutrient intake from supplemental sources reported on the 24HRs from day 1 and day 2 was used. For NHANES 2003–2006, only data from the DSMQ were used to calculate DS intakes. Therefore, mean (i.e., average) daily DS intakes for all NHANES 2003–2006 nutrient analyses were calculated by *1*) multiplying the number of reported days of DS use over the past 30 days by the amount the participant reported taking per day; and *2*) standardizing the serving size reported on the product label between units of measure to combine DS intakes across products for each participant, as described for vitamins A and E in Supplemental Methods, Section 2.

For all biomarker analyses in NHANES 2003–2006, including serum concentrations of vitamins A (retinol, β carotene), C, E (α tocopherol), and D [serum 25(OH)D] in NHANES 2011–2014, trained phlebotomists collected whole blood and serum samples in the Mobile Examination Center. These samples were then analyzed in a designated nutritional biomarker laboratory at the CDC. Further details describing the laboratory methodology are available elsewhere (21), and additional details pertaining to FNI and TNI component score correlations for vitamins A, C, D, and E with nutritional biomarkers are listed in **Supplemental Table 1**.

Statistical analysis

All analyses of NHANES data used statistical procedures that are appropriate for the complex survey design. SEs for all statistics of interest were approximated using Fay's modified Balanced Repeated Replication technique (22, 23). While a self-reported 24HR can provide rich details about dietary intake on a given day, intake on a single day, even if measured perfectly, does not represent usual (i.e., long-term average) intake, nor does the mean of a small number of days for most nutrients (24–26). The effects of random error in 24HRs, including day-to-day variation, can be accounted for through the use of statistical modeling (27–29). To estimate the distribution of TNI scores of usual intakes, a multivariate extension of the National Cancer Institute (NCI) Method that uses a Markov Chain Monte Carlo approach was applied to NHANES data to model nutrient intakes from foods and beverages for the nutrients included in the TNI (2, 30). The NCI method utilizes a distribution of "pseudo-individuals" that are generated based on estimated model parameters and the covariate distribution (i.e., sex, age, DS use) of dietary data collected in the original study population. To incorporate DS, we added the reported mean daily DS intake amount to the predicted nutrient intakes from foods and beverages in the pseudo-population step. Due to extreme values of reported daily DS intakes, likely reflecting data errors, the DS values were Winsorized; that is, reports above the 98th percentile or below the second percentile were set to the next lowest (98th percentile) or highest (second percentile) value, respectively, to reduce their influence on the total usual intake distributions (10, 31). For each pseudo-person, a ratio of the total usual micronutrient intake to the corresponding age- and sex-specific RDA (if available) or AI (if an RDA was unavailable) was computed and multiplied by 100 for each TNI component, truncated at 100 when necessary. The mean of the component scores comprised the TNI total score, with each micronutrient weighted equally. Estimated population means and percentiles from the first to the 99th percentiles of usual TNI total and components scores were then derived for the pseudo-population. Distributions of FNI scores were computed in an identical fashion without the incorporation of DS information, and therefore reflect usual intakes from foods and beverages alone relative to the RDA or AI.

Estimated mean FNI and TNI scores and distributions were compared between population subgroups with known differences in nutrient intakes, including DS users and DS nonusers (6, 7), smokers and nonsmokers (32, 33), and adults living in households with different

TABLE 1 FNI component and total scores for USDA, DASH, Harvard, and AHA Exemplary Menus[1]

FNI Component	RDA/AI	Maximum FNI Score	USDA[2]	DASH[2]	Harvard[2]	AHA[3]
Total energy, kcal/d	—	—	2030	1980	1962	2002
Men ≥ 70 years						
Calcium, mg	1200	100.0	100.0	100.0	52.5	100.0
Magnesium, mg	420	100.0	100.0	100.0	100.0	100.0
Potassium, mg	3400[4]	100.0	100.0	100.0	100.0	100.0
Choline, mg	550[4]	100.0	70.3	67.1	77.3	71.4
Vitamin A, μg	900	100.0	100.0	100.0	100.0	91.4
Vitamin C, mg	90	100.0	100.0	100.0	100.0	100.0
Vitamin D, μg	20	100.0	52.0	41.6	48.9	26.5
Vitamin E, mg	15	100.0	86.3	100.0	100.0	100.0
FNI Total Score	—	100.0	88.6	86.6	84.8	86.2
Women 31–50 years						
Calcium, mg	1000	100.0	100.0	100.0	63.0	100.0
Magnesium, mg	320	100.0	100.0	100.0	100.0	100.0
Potassium, mg	2600[4]	100.0	100.0	100.0	100.0	100.0
Choline, mg	425[4]	100.0	91.0	86.8	100.0	92.4
Vitamin A, μg	700	100.0	100.0	100.0	100.0	100.0
Vitamin C, mg	75	100.0	100.0	100.0	100.0	100.0
Vitamin D, μg	15	100.0	69.3	55.4	65.2	35.4
Vitamin E, mg	15	100.0	86.3	100.0	100.0	100.0
FNI Total Score	—	100.0	93.3	92.8	91.0	91.0

[1] Exemplary menus for the USDA, DASH, Harvard, and AHA were scored using the RDA or AI to their estimated energy needs per day (i.e., 2000 kcal/day) when assumed to be sedentary (men) or moderately active (women). AI, Adequate Intake; DASH, Dietary Approaches to Stop Hypertension; FNI, Food Nutrient Index; Harvard, Harvard Medical School Healthy Eating Guide; USDA, USDA Food Patterns.
[2] Based on one 7-day 2000 kcal/day sample menu.
[3] Based on one 1-day 2000 kcal/day sample menu.
[4] Indicates an AI rather than an RDA. An AI is used when insufficient scientific evidence is available to establish the RDA.

levels of food security (34). These means were calculated for each stratum (i.e., separately) to eliminate any potential for correlation between subgroups that could occur when using a joint modeling approach. To determine differences in mean TNI and FNI scores, population subgroups were compared using 2-group *t*-tests. This same approach was used to model the mean and distributions for men and women, and ceiling effects were examined by calculating the proportion of the pseudo-population with a perfect score on the TNI.

Correlations between TNI and FNI component scores and HEI-2015 component scores (35, 36) were examined. The HEI-2015 is a density-based measure that encompasses 9 adequacy and 4 moderation components (from foods and beverages only), evaluated for the minimum standard. Additional details pertaining to the HEI-2015 are available in Supplemental Methods, Section 3. Pearson correlations were estimated after applying Box-Cox transformations to each TNI and HEI component score, and differences between correlations for the FNI and TNI were tested after applying the Fisher's Z-transformation (SEs of differences in Z-transformed correlations were estimated via Balanced Repeated Replication and used to obtain *P* values for the *t*-tests of the differences). Food and nutrient intakes of the HEI-2015 dietary components were modeled simultaneously with the FNI nutrient intakes in a multivariate model as described above, and then HEI-2015 scores were calculated using the scoring described by Reedy et al. (36). TNI vitamin D and calcium component scores were correlated with the HEI-2015 dairy component score, and the TNI vitamin A and C component scores were correlated with both the HEI-2015 total fruit and total vegetable component scores.

Pearson correlation coefficients were also computed to evaluate the relationships between the TNI and the FNI component scores and the respective biomarker for each nutrient of interest (i.e., vitamins A, C, D, and E) using the same procedure described above. In the present analysis, correlation coefficients less than 0.3 were considered to be low; those from 0.3 to 0.5 were considered to be moderate; and those >0.5 were considered to be high (37). These cut points were determined a priori. All statistical analyses were performed using SAS software (version 9.4; SAS Institute Inc.). Statistical significance was set at a *P* value of <0.05.

Results

Exemplary menus

The USDA, Dietary Approaches to Stop Hypertension, Harvard, and AHA exemplary menus received high scores on the FNI, with scores ranging from 84.8 to 93.3 (Table 1). Scores for middle-aged women (31–50 years; FNI scores, 91.0–93.3) were similar to those of older men (≥70 years; FNI scores, 84.8–88.6). Among the FNI components, all 4 menus consistently received the maximum scores for magnesium, potassium, and vitamin C, but none scored perfectly for vitamin D (26.5–52.0) or choline (67.1–77.3). While all menu plans were developed for 2000 kcal/d, slight variations were observed for some plans (range, 1962–2030 kcal/d), and some variation in FNI scores may be in small part due to these differences in energy.

Nationally representative data among US adults

Groups with known differences in nutrient intake.

Mean TNI scores were significantly different ($P < 0.001$) for DS users and nonusers (83.5 compared with 67.1, respectively), for nonsmokers and smokers (76.8 compared with 70.3, respectively), and by household food security status among adults (food-secure and food-insecure adults; 76.6 compared with 69.1, respectively; Figure 1). For the TNI component scores, large differences were observed (i.e., 10 points or more) for DS users and nonusers for calcium (10), magnesium (14), and vitamins A (19), C (24), D (51.4), and E (17.9). Similar noteworthy differences were found for vitamins A (10.8), C (13.9), and D (12.6) among smokers and nonsmokers and for

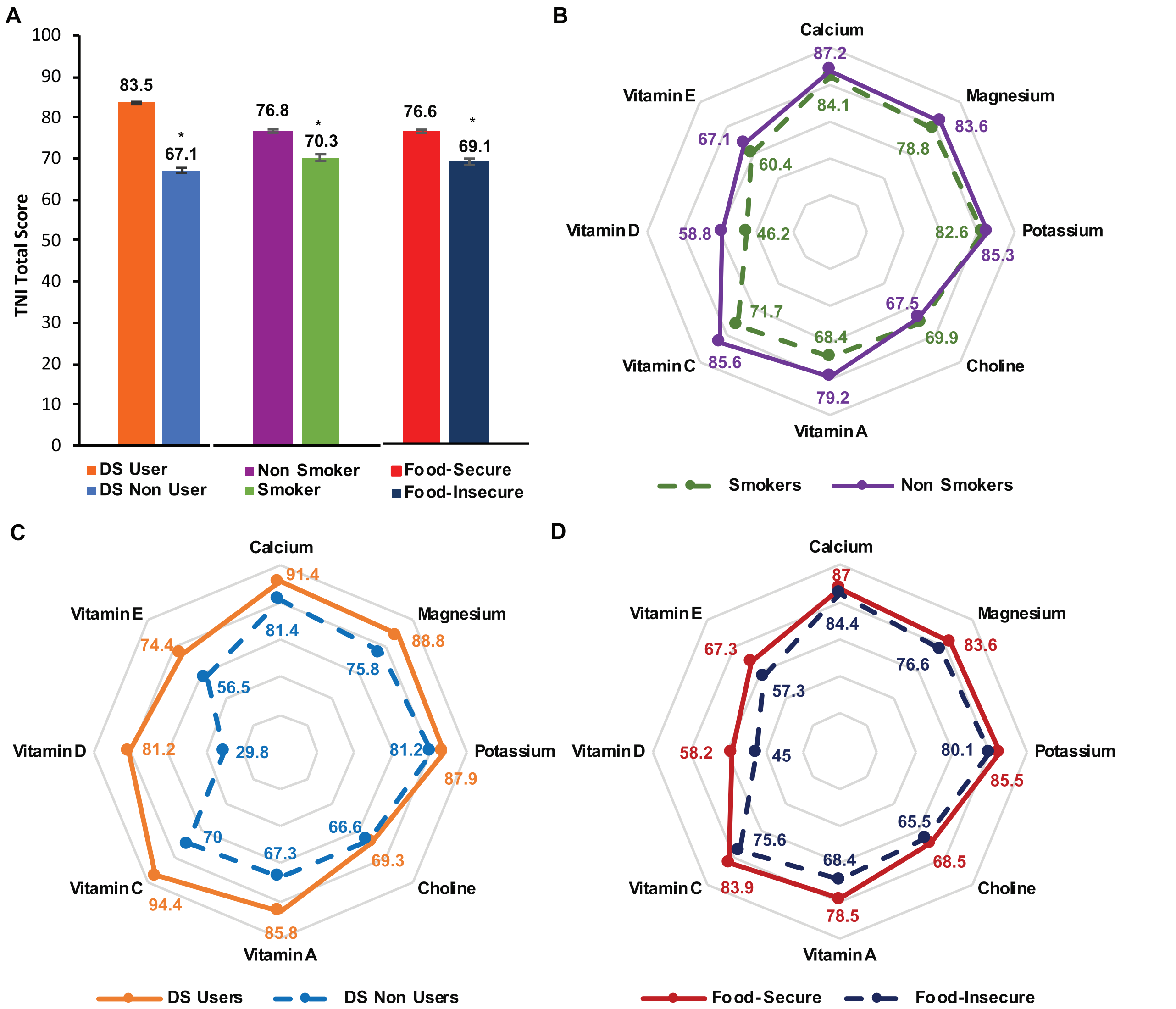

FIGURE 1 Estimated total nutrient index total and component scores among US adults (≥19 years), by household food security status, DS use, and smoking status, NHANES 2011–2014. (A) Estimated TNI total scores for DS users and nonusers, smokers and nonsmokers, and food-secure and food-insecure US adults. Estimated TNI component scores among US adults by (B) household food security status, (C) DS use, and (D) smoking status. DS, Dietary Supplement; TNI, Total Nutrient Index.

vitamins A (10.1), D (13.2), and E (10) among adults with different levels of household food security. Consistent with these findings, DS users (71.8), nonsmokers (70.0), and adults from food-secure households (69.9) also scored significantly higher on the FNI when compared with their DS nonuser (66.1), smoker (65.8), and food-insecure adult (64.9) counterparts (**Supplemental Table 2**).

HEI-2015 correlations.

The TNI (r = 0.48) and FNI (r = 0.46) total scores were moderately correlated with the HEI-2015 total score (Table 2). The FNI component scores exhibited higher correlations with HEI-2015 components compared with those of the TNI, ranging from 0.41 to 0.63. Total fruits and vitamin C exhibited the highest correlation at 0.63, followed by dairy and vitamin D (r = 0.55), dairy and calcium (r = 0.48), total vegetables and vitamin C (r = 0.43), total fruits and vitamin A (r = 0.41), and, lastly, total vegetables and vitamin A (r = 0.30). Correlations of TNI component scores with HEI-2015 component scores ranged from low to moderate (r = 0.23 to r = 0.53), with the highest correlations observed for total fruits and vitamin C (r = 0.53); dairy and calcium (r = 0.44), total fruits and vitamin A (r = 0.38), total vegetables and vitamin C (r = 0.38), total vegetables and vitamin A (r = 0.29), and dairy and vitamin D (r = 0.23) all subsequently followed. Differences in correlations between the FNI and TNI component scores with the HEI-2015 components scores were most notable for vitamins C ($P < 0.001$) and D ($P < 0.001$).

Correlations with biomarker data.

Correlations of TNI component scores with the biomarkers for retinol and beta-carotene (vitamin A; $P < 0.001$), vitamin C ($P < 0.001$), vitamin D ($P < 0.001$), and vitamin E ($P = 0.03$) were significantly higher than those observed for the FNI (Table 3). Overall TNI correlations ranged from 0.12 for vitamin E and α-tocopherol to 0.36 for vitamin D and 25(OH)D, with both vitamins A (r = 0.17 with serum retinol; r = 0.21 with serum β-carotene) and C (r = 0.22 with serum vitamin C) exhibiting low correlations with their respective

TABLE 2 Estimated Pearson correlations of FNI and TNI total and component scores with HEI-2015 scores: NHANES 2011–2014 ($n = 9954$)[1]

	HEI-2015	HEI-2015 Total Dairy & Calcium Score	HEI-2015 Total Dairy & Vitamin D Score	HEI-2015 Total Fruit & Vitamin A Score	HEI-2015 Total Fruit & Vitamin C Score	HEI-2015 Total Vegetable & Vitamin A Score	HEI-2015 Total Vegetable & Vitamin C Score
FNI, foods/beverages	0.46	0.48	0.55	0.41	0.63	0.30	0.43
TNI, foods/beverages + DS	0.48	0.44	0.23	0.38	0.53	0.29	0.38
P value,[2] FNI vs. TNI	0.016	<0.001	<0.001	0.041	<0.001	0.238	0.006

[1]DS, dietary supplements; FNI, Food Nutrient Index; HEI, Healthy Eating Index; TNI, Total Nutrient Index.
[2]*P* values are for *t*-tests of differences in Z-transformed correlations.

biomarkers. However, correlations were even lower (all r values ≤ 0.10) when DS were not included.

Evaluation of ceiling effects.
The estimated mean total TNI score was 76.1 among men and 75.2 among women in the United States, with approximately 0.9% of men and 2.7% of women reaching perfect total scores (i.e., TNI score of 100; **Supplemental Table 3**). Among the TNI components, less variation was observed, with 5 out of 8 nutrients in men (all except choline and vitamins D and E) and 6 out of 8 nutrients in women (all except choline and vitamin E) exceeding the 25% criterion established to evaluate potential ceiling effects. The distribution of TNI total scores across the percentiles ranged from 44.7 (first percentile) to 98.6 (99th percentile) among men and from 45.4 (first percentile) to 96.7 (99th percentile) among women, and nearly all TNI components had reached a perfect score (all except choline in men) by the 95th percentile. These patterns were also consistent when evaluating the distributions of TNI total and component scores by sex and age (**Supplemental Table 4**). The same index from foods and beverages only, the FNI, resulted in a mean total score of 69.0 out of 100. The distribution of FNI scores ranged from 31.5 at the first percentile to 97.0 at the 99th percentile (**Supplemental Table 5**).

Discussion

The TNI is a useful tool to reflect population-level adherence to nutrient standards of total usual intakes of underconsumed micronutrients among US adults. We examined the validity of the FNI and TNI using multiple approaches. First, the FNI yielded high scores on exemplary menus developed to meet healthy eating guidelines while achieving micronutrient adequacy, supporting the construct validity of the FNI from foods and beverages. However, for some nutrients it is challenging to meet nutrient recommendations from foods alone. Indeed, even with extensive food pattern modeling for choline and vitamin D, achieving targets across most energy levels in adults is unlikely (38). The Harvard menus had the lowest scores for calcium and vitamin D because, by design, they omit dairy foods that are rich sources of these nutrients. Thus, perfect scores on exemplary menus are not expected across all nutrients examined. Moreover, given differences in DRI values by sex and life stage, we anticipated higher FNI scores for middle-aged women when compared with older men because older menhave higher RDAs or AIs for all nutrients examined, with the exception of vitamin E. The higher overall scores obtained for the FNI by women indeed reflected this underlying construct we intended to capture.

Adults classified as current smokers (39) and those who are food insecure (34) not only have a lower prevalence of use of DS, but also tend to have lower overall diet quality when compared to nonsmokers and those with food security. Adults living in households with food insecurity had lower total TNI (8 points) and component scores for all nutrients except calcium and choline. This is consistent with previous work that found a significantly higher prevalence of the risk of inadequacy, using the Estimated Average Requirement (EAR), across most micronutrients but did not identify differential risks for calcium or choline (34). Previous studies have documented lower serum concentrations of several nutrients (folate, iron, and vitamins A and E) among adults living in food-insecure households when compared with those living in food-secure households (40, 41), and have concluded that food insecurity is associated with iron deficiency anemia in pregnant as well as reproductive-aged women (42, 43), as well as many other negative health outcomes, such as depression and risk of chronic disease (44). Nutrient intakes from foods and beverages tend to be higher in DS users than nonusers; the TNI and FNI were consistent with these findings. The magnitude of differences in the overall (~16 points) and component scores (range, 3–51 points) by DS use were particularly notable for most nutrients examined, with the exceptions of potassium and choline, both of which are not routinely found in DS. The ability of the TNI to distinguish between population subgroups with known

TABLE 3 Estimated Pearson correlations of FNI and TNI component scores for vitamins A, C, D, and E with their respective biomarkers: NHANES 2003–2006 ($n = 8861$) and 2011–2014 ($n = 9954$)[1]

Dietary Exposure	Vitamin A Score[2]		Vitamin C Score[2]	Vitamin D Score[3]	Vitamin E Score[2]
Serum biomarker	Retinol	β-Carotene	Vitamin C	25(OH)D	α-Tocopherol
FNI, foods/beverages	0.09	0.10	0.07	0.04	0.01
TNI, foods/beverages + DS	0.17	0.21	0.22	0.36	0.12
P value,[4] FNI vs. TNI	<0.001	<0.001	<0.001	<0.001	0.031

[1]DS, dietary supplements; FNI, Food Nutrient Index; TNI, Total Nutrient Index; 25(OH)D, 25-hydroxyvitamin D.
[2]NHANES 2003–2006 data were utilized for this analysis.
[3]NHANES 2011–2014 were utilized for this analysis.
[4]*P* values are for *t*-tests of differences in Z-transformed correlations.

differences in nutrient intake supports the construct validity of the TNI and demonstrates that the measure performs equally well in a variety of contexts (e.g., in population subgroups with different nutrient intakes).

Our findings evaluating the relationship between the HEI-2015 and the TNI demonstrated that the 2 indices are moderately correlated. The HEI-2015 is a density-based measure that encompasses both adequacy and moderation components, evaluated for the minimum standard. In contrast, the TNI is focused solely on intakes of underconsumed micronutrients. Therefore, we expected these 2 related constructs—adherence to the Dietary Guidelines for Americans and adherence to the DRIs for underconsumed micronutrients—to be moderately correlated, reflecting their overlapping but distinct purposes. Combining the use of the TNI with other indices has the potential to more fully capture multiple dimensions of dietary exposures.

The correlations of nutrient component scores with concentration biomarkers of status or exposure were consistently higher with the TNI than the FNI for all 4 nutrients examined (vitamins A, C, D, and E), suggesting that the TNI exhibits a stronger relationship with biochemical indicators of nutrient intake when inclusive of DS. This is also consistent with findings from previous studies that have shown that DS users tend have to higher serum concentrations of nutritional biomarkers when compared with DS nonusers (45–48).

The distributions of TNI and FNI total scores exhibited a sufficient level of variation to detect meaningful differences in scores among individuals in the population, meeting our criterion for ceiling effects. The variation of TNI scores was lower than that of FNI scores, reflecting the contribution that DS make toward most nutrients examined in this analysis. We established this arbitrary criterion of 25% a priori; however, other disciplines have used a 15% definition for ceiling effects (49, 50). Applying the TNI framework to other nutrients or other population subgroups may result in different estimates of ceiling effects.

Limitations and strengths

A number of caveats are associated with the validity approaches employed in the present analysis. Self-reported dietary data are prone to measurement error. The dietary data in NHANES are collected by trained interviewers using the USDA's automated multiple-pass method, a research-based, multiple-pass approach that employs 5 steps of recall designed to enhance complete and accurate food recall and reduce the respondent burden. However, little is known about the measurement error structure of DS reporting, and it is likely to differ from that of foods and beverages (10). Future work improving our understanding of DS assessments and associated measurement errors is warranted (10).

We chose to compare the TNI to nutritional biomarkers, given that a measure of dietary intake should, theoretically, be correlated with a measure of nutritional status in the body (51). Recovery biomarkers only exist for energy, protein, sodium, and potassium, substantially limiting the ability to obtain biomarker estimates that are not prone to measurement error for other nutrients (52, 53). Consequently, concentration biomarkers were employed in this analysis, which reflect both exposure dose and bioavailability and are subject to metabolic differences and/or personal characteristics. Correlation coefficients estimated in this analysis were adjusted for random error in the self-report dietary assessment by use of the NCI method, but we were unable to adjust for random error in the biomarkers. Correlation coefficients between error-prone measures may reflect correlations of systematic errors or biases associated both with misreporting of dietary intakes (e.g., obesity) and the use of biomarkers to reflect dietary intake rather than nutrient status [e.g., 25(OH)D levels are related to adiposity and sun exposure], and not true intakes. With systematic error, the impact of these errors is unpredictable, and could lead to higher or lower estimated correlation coefficients.

Finally, in order for a novel index to be of utility, validation studies are needed to assess how well the measure accurately reflects its construct (i.e., construct validity) and how well the test or measure performs against a criterion (i.e., criterion validity) (12). In an ideal validation study, both construct and criterion validity would be assessed using gold-standard measures, which provide an exact estimate of the "true" diet (e.g., usual micronutrient intake). However, in nutrition research, truth is nearly impossible to obtain; at best, one can use an unbiased tool, such as a recovery biomarker, to obtain an estimate of truth plus random error.

A strength of this study is that a broad range of strategies with several different comparison measures were employed to fully assess the construct and criterion validity of the TNI. By constructing the FNI in addition to the TNI, we were able to isolate the contribution of including DS in total intakes on adherence to the DRIs. Another strength is that we used NHANES data in our evaluation of TNI, which is reflective of the US adult population, suggesting broad applicability of the TNI. The TNI was developed to reflect long-term usual intake; applications of the TNI with the use of usual intake methods for foods and beverages is recommended when using the TNI scoring system.

Conclusions and future applications

Tools that can be used to more completely describe nutrient exposures and how those relate to biomarkers of nutritional status and health outcomes are greatly needed. This validation study illustrates that the TNI is a useful tool for comprehensively representing total nutrient exposures of underconsumed micronutrients among the US adult population. While the same index limited to dietary sources (i.e., FNI) can be applied in applications where foods and beverages alone are of interest, the preferred application of the TNI is to capture intake from all sources.

Possible future applications of the TNI include testing the effectiveness of a dietary intervention or serving as a complementary index to food-based and dietary pattern–based indices such as the HEI. Although the TNI was validated for representing total nutrient exposures of 8 underconsumed micronutrients among US adults, the TNI framework utilizes the mean of equally weighted subscores and, therefore, could easily be expanded to include different nutrients that are appropriate for different populations. As the applications of the TNI expand, additional efforts related to validation should be considered to demonstrate its robust use for assessing total intakes of underconsumed nutrients and examining the roles of nutrients on health outcomes across a variety of populations.

Acknowledgments

The authors' responsibilities were as follows – AEC, RLB, KWD, JJG, JAT: designed the research and concepts presented; AEC, RLB, JAT, KWD: wrote sections of the paper; HAE-M, PMG: proposed the evaluation plan; SJ, RLB, JAT, JJG, HAE-M, PMG, JTD, NP, AB, RJC, KWD: provided critical review and presented

insights; AEC, RLB, JAT: had primary responsibility for the final content; and all authors: read and approved the final manuscript.

References

1. Dietary Guidelines Advisory Committee. Scientific report of the 2015 Dietary Guidelines Advisory Committee: Advisory report to the Secretary of Health and Human Services and the Secretary of Agriculture. Washington, DC: USDA, Agricultural Research Service; 2015.
2. Cowan AE, Jun S, Tooze JA, Dodd KW, Gahche JJ, Eicher-Miller HA, Guenther PM, Dwyer JT, Potischman N, Bhadra A, et al. A narrative review of nutrient based indexes to assess diet quality and the proposed total nutrient index that reflects total dietary exposures. Crit Rev Food Sci Nutr 2021. [Accessed September 2, 2021]. doi: 10.1080/10408398.2021.1967872.
3. Bailey RL, Gahche JJ, Lentino CV, Dwyer JT, Engel JS, Thomas PR, Betz JM, Sempos CT, Picciano MF. Dietary supplement use in the United States, 2003–2006. J Nutr 2011;141(2):261–6.
4. Bailey RL, Gahche JJ, Miller PE, Thomas PR, Dwyer JT. Why US adults use dietary supplements. JAMA Intern Med 2013;173(5):355–61.
5. Bailey RL, Gahche JJ, Thomas PR, Dwyer JT. Why US children use dietary supplements. Pediatr Res 2013;74(6):737–41.
6. Bailey RL, Fulgoni VL, 3rd, Keast DR, Dwyer JT. Dietary supplement use is associated with higher intakes of minerals from food sources. Am J Clin Nutr 2011;94(5):1376–81.
7. Bailey RL, Fulgoni VL, 3rd, Keast DR, Dwyer JT. Examination of vitamin intakes among US adults by dietary supplement use. J Acad Nutr Diet 2012;112(5):657–663.e4.
8. Fulgoni VL, 3rd, Keast DR, Bailey RL, Dwyer J. Foods, fortificants, and supplements: Where do Americans get their nutrients? J Nutr 2011;141(10):1847–54.
9. Blumberg JB, Balz FB, Fulgoni VL, Weaver CM, Zeisel SH. Impact of frequency of multi-vitamin/multi-mineral supplement intake on nutritional adequacy and nutrient deficiencies in U.S. adults. Nutrients 2017;9(8):849.
10. Bailey RL, Dodd KW, Gahche JJ, Dwyer JT, Cowan AE, Jun S, Eicher-Miller HA, Guenther PM, Bhadra A, Thomas PR, et al. Best practices for dietary supplement assessment and estimation of total usual nutrient intakes in population-level research and monitoring. J Nutr 2019;149(2):181–97.
11. US Department of Health and Human Services and USDA. Dietary guidelines for Americans 2015–2020. In: Department of Agriculture Department of Health and Human Services, editor. 8th ed. Washington, DC: US Government Printing Office; 2015.
12. Trochim W, Donnelly J, Kanika A. Research methods: The essential knowledge base [Internet]. Cengage Learning; 2016. [cited April 2020]. Available from: http://www.cengage.com.
13. Guenther PM, Reedy J, Krebs-Smith SM, Reeve BB. Evaluation of the Healthy Eating Index–2005. J Am Diet Assoc 2008;108(11):1854–64.
14. U.S. Department of Health and Human Services and U.S. Department of Agriculture. Dietary Guidelines for Americans 2010 – 2015 [Internet]. 7th Ed. Washington, D.C.: U.S. Government Printing Office 2010;2010. Appendix 10, Sample menus for a 2000 calorie food pattern. Available from: http://www.choosemyplate.gov/food-groups/downloads/Sample_Menus-2000Cals-DG2010.pdf
15. Your guide to lowering your blood pressure with DASH [Internet]. U.S. Department of Health And Human Services, National Institutes of Health National Heart, Lung, and Blood Institute; 2006. Available from: https://www.nhlbi.nih.gov/files/docs/public/heart/new_dash.pdf
16. Willett W, Skerrett PJ. Eat, drink, and be healthy: The Harvard Medical School guide to healthy eating. New York, New York: Simon and Schuster; 2017.
17. American Heart Association. American Heart Association No-Fad Diet: A Personal Plan for Healthy Weight Loss. New York, New York: Crown Publishers; 2011.
18. U.S. Department of Agriculture. USDA Food and Nutrient Database for Dietary Studies 2017–2018 [Internet]. 2018 [cited August 2021]. Available from: http://www.ars.usda.gov/ba/bhnrc/fsrg
19. Food and Nutrition Board. Dietary reference intakes: Applications in dietary assessment. Washington, DC: Institute of Medicine; 2000.
20. U.S. Department of Agriculture Center for Nutrition Policy and Promotion. Estimated calorie needs per day–Energy levels used for assignment of individuals to USDA food patterns [Internet]. 2015. [cited September 2021]. Available from: https://fns-prod.azureedge.net/sites/default/files/usda_food_patterns/EstimatedCalorieNeedsPerDay.pdf
21. National Center for Health Statistics. NHANES laboratory data [Internet]. 2020. [cited August 2021]. Available from: https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Laboratory
22. Burt VL, Cohen SB. A comparison of methods to approximate standard errors for complex survey data. Rev Public Data Use. 1984;12:159–68.
23. Shao J, Rao J. Modified balanced repeated replication for complex survey data. Biometrika 1999;86:403–15.
24. Kipnis V, Subar AF, Midthune D, Freedman LS, Ballard-Barbash R, Troiano RP, Bingham SA, Schoeller DA, Schatzkin A, Carroll RJ. Structure of dietary measurement error: Results of the OPEN biomarker study. Am J Epidemiol 2003;158(1):14–21.
25. Subar AF, Kipnis V, Troiano RP, Midthune D, Schoeller DA, Bingham SA, Sharbaugh CO, Trabulsi J, Runswick S, Ballard-Barbash R, et al. Using intake biomarkers to evaluate the extent of dietary misreporting in a large sample of adults: The OPEN study. Am J Epidemiol 2003;158(1):1–13.
26. Park Y, Dodd KW, Kipnis V, Thompson FE, Potischman N, Schoeller DA, Baer DJ, Midthune D, Troiano RP, Bowles H, et al. Comparison of self-reported dietary intakes from the automated self-administered 24-h recall, 4-d food records, and food-frequency questionnaires against recovery biomarkers. Am J Clin Nutr 2018;107(1):80–93.
27. Dodd KW, Guenther PM, Freedman LS, Subar AF, Kipnis V, Midthune D, Tooze JA, Krebs-Smith SM. Statistical methods for estimating usual intake of nutrients and foods: A review of the theory. J Am Diet Assoc 2006;106(10):1640–50.
28. Tooze JA, Midthune D, Dodd KW, Freedman LS, Krebs-Smith SM, Subar AF, Guenther PM, Carroll RJ, Kipnis V. A new statistical method for estimating the usual intake of episodically consumed foods with application to their distribution. J Am Diet Assoc 2006;106(10): 1575–87.
29. Tooze JA, Kipnis V, Buckman DW, Carroll RJ, Freedman LS, Guenther PM, Krebs-Smith SM, Subar AF, Dodd KW. A mixed-effects model approach for estimating the distribution of usual intake of nutrients: The NCI method. Stat Med 2010;29(27):2857–68.
30. Zhang S, Midthune D, Guenther PM, Krebs-Smith SM, Kipnis V, Dodd KW, Buckman DW, Tooze JA, Freedman L, Carroll RJ. A new multivariate measurement error model with zero-inflated dietary data, and its application to dietary assessment. Ann Appl Stat 2011;5(2B):1456–87.
31. Cowan AE, Jun S, Tooze JA, Dodd KW, Gahche JJ, Eicher-Miller HA, Guenther PM, Dwyer JT, Moshfegh AJ, Rhodes DG, et al. Comparison of 4 methods to assess the prevalence of use and estimates of nutrient intakes from dietary supplements among US adults. J Nutr 2020;150(4):884–93.
32. Dallongeville J, Marécaux N, Fruchart JC, Amouyel P. Cigarette smoking is associated with unhealthy patterns of nutrient intake: A meta-analysis. J Nutr 1998;128(9):1450–57.
33. Touvier M, Niravong M, Volatier JL, Lafay L, Lioret S, Clavel-Chapelon F, Boutron-Ruault MC. Dietary patterns associated with vitamin/mineral supplement use and smoking among women of the E3N-EPIC cohort. Eur J Clin Nutr 2009;63(1):39–47.
34. Cowan AE, Jun S, Tooze JA, Eicher-Miller HA, Dodd KW, Gahche JJ, Guenther PM, Dwyer JT, Potischman N, Bhadra A, et al. Total usual micronutrient intakes compared to the dietary reference intakes among U.S. adults by food security status. Nutrients 2019;12(1):38.
35. Krebs-Smith SM, Pannucci TE, Subar AF, Kirkpatrick SI, Lerman JL, Tooze JA, Wilson MM, Reedy J. Update of the Healthy Eating Index: HEI-2015. J Acad Nutr Diet 2018;118(9):1591–602.
36. Reedy J, Lerman JL, Krebs-Smith SM, Kirkpatrick SI, Pannucci TE, Wilson MM, Subar AF, Kahle LL, Tooze JA. Evaluation of the Healthy Eating Index–2015. J Acad Nutr Diet 2018;118(9):1622–33.
37. Hinkle DE, Wiersma W, Jurs SG. Applied statistics for the behavioral sciences. Boston, Massachusetts: Houghton Mufflin; 2003.
38. Dietary Guidelines Advisory Committee.Scientific report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture. Washington, DC: U.S. Department of Agriculture, Agricultural Research Service; 2020.

39. 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):1114.
40. Dixon LB, Winkleby MA, Radimer KL. Dietary intakes and serum nutrients differ between adults from food-insufficient and food-sufficient families: Third National Health and Nutrition Examination Survey, 1988–1994. J Nutr 2001;131(4):1232–46.
41. Bhattacharya J, Currie J, Haider S. Poverty, food insecurity, and nutritional outcomes in children and adults. J Health Econ 2004;23(4):839–62.
42. Fischer NC, Shamah-Levy T, Mundo-Rosas V, Méndez-Gómez-Humarán I, Pérez-Escamilla R. Household food insecurity is associated with anemia in adult Mexican women of reproductive age. J Nutr 2014;144(12):2066–72.
43. Park CY, Eicher-Miller HA. Iron deficiency is associated with food insecurity in pregnant females in the United States: National Health and Nutrition Examination Survey 1999–2010. J Acad Nutr Diet 2014;114(12):1967–73.
44. Food insecurity and health outcomes. Health Aff 2015;34(11): 1830–9.
45. Ford ES, Schleicher RL, Mokdad AH, Ajani UA, Liu S. Distribution of serum concentrations of α-tocopherol and γ-tocopherol in the US population. Am J Clin Nutr 2006;84(2):375–83.
46. Schleicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003–2004 National Health and Nutrition Examination Survey (NHANES). Am J Clin Nutr 2009;90(5):1252–63.
47. Schleicher RL, Sternberg MR, Lacher DA, Sempos CT, Looker AC, Durazo-Arvizu RA, Yetley EA, Chaudhary-Webb M, Maw KL, Pfeiffer CM, et al. The vitamin D status of the US population from 1988 to 2010 using standardized serum concentrations of 25-hydroxyvitamin D shows recent modest increases. Am J Clin Nutr 2016;104(2):454–61.
48. Herrick KA, Storandt RJ, Afful J, Pfeiffer CM, Schleicher RL, Gahche JJ, Potischman N. Vitamin D status in the United States, 2011–2014. Am J Clin Nutr 2019;110(1):150–7.
49. McHorney CA, Tarlov AR. Individual-patient monitoring in clinical practice: Are available health status surveys adequate? Qual Life Res 1995;4(4):293–307.
50. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, Bouter LM, de Vet HC. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60(1):34–42.
51. Potischman N, Freudenheim JL. Biomarkers of nutritional exposure and nutritional status: An overview. J Nutr 2003;133(3):873S–4S.
52. Thompson FE, Kirkpatrick SI, Subar AF, Reedy J, Schap TE, Wilson MM, Krebs-Smith SM. The National Cancer Institute's dietary assessment primer: a resource for diet research. J Acad Nutr Diet 2015;115(12):1986–95.
53. National Institutes of Health, National Cancer Institute. The measurement error webinar series. The measurement error webinar series [Internet]. 2011 [cited May 2021]. Available from: http://riskfactor.cancer.gov/measurementerror/