Total estimated usual nutrient intake and nutrient status biomarkers in women of childbearing age and women of menopausal age

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ABSTRACT

Background: Women of childbearing age (WCBA) and women of menopausal age (WMENO) have distinct nutritional needs. Understanding nutrient intake and status in these life stages is critical for tailoring dietary recommendations.

Objectives: The objectives of this study were to evaluate total estimated usual nutrient intakes from food and food plus supplements and to compare these to established recommendations for WCBA and WMENO life stages and examine associations between self-reported estimated usual intakes and nutrient status biomarkers.

Methods: Twenty-four-hour dietary recall data from 2011–2016 NHANES were used to estimate usual intake of nutrients from food and food plus supplements for WCBA (aged 15–44 y, $n = 4,134$) and WMENO (aged 40–65 y, $n = 3,438$). Estimates of mean usual intake were derived and compared across clinically defined nutrient biomarker categories.

Results: Both young (aged 15–30 y) and older (aged 31–44 y) WCBA had intakes from food below the Estimated Average Requirement (EAR) for calcium (49% and 44%, respectively), magnesium (62%, 44%), and vitamins A (50%, 44%), C (47%, 46%), D (>97%, >97%), and E (92%, 88%). Similarly, perimenopausal (aged 40–50 y) and menopausal (aged 51–65 y) women had intakes from food below the EAR for calcium (48% and 74%, respectively), magnesium (50%, 49%), and vitamins A (44%, 37%), C (44%, 41%), D (>97%, >97%), and E (88%, 86%). Nutrient gaps decreased with supplement usage. For folate, vitamins D and B-12, and DHA, women in the lowest biomarker category (indicating increased risk of deficiency) had significantly lower intake from food (315.2 ± 25.9 compared with 463.8 ± 5.2 µg dietary folate equivalents, 3.5 ± 0.1 compared with 4.2 ± 0.1 µg, 3.6 ± 0.2 compared with 4.3 ± 0.1 µg, and 0.037 ± 0.005 compared with 0.070 ± 0.006 g, respectively; $P < 0.01$) of the corresponding nutrient compared with the highest biomarker category.

Conclusions: Substantial percentages of WCBA and WMENO are not meeting recommendations for multiple nutrients, whereas supplement usage partially fills nutrient gaps. Dietary intake was positively associated with most nutrient status biomarkers. Specific guidance is needed to ensure adequate nutrient intakes and nutrient status during these critical life stages. *Am J Clin Nutr* 2021;113:1042–1052.

Introduction

Adequate nutrient intakes are essential to prevent nutrient deficiencies, optimize health, and limit disease. Individual vitamin and mineral requirements depend on one's age, gender, life stage, and lifestyle (1). For example, women of childbearing age (WCBA) require more iron compared with women of menopausal age (WMENO). Yet, many Americans fall short in obtaining suggested amounts of ≥1 nutrients in their diets (1–3). Notably, the 2015–2020 Dietary Guidelines for Americans identified nutrients that are commonly underconsumed (called "shortfall nutrients"), which include potassium, dietary fiber, choline, magnesium, calcium, and vitamins A, C, D, and E, as well as iron in women aged 19–50 y (1). In addition to healthy eating habits, supplement usage has been shown to help decrease the percentage of the population consuming less than the Estimated Average Requirement (EAR) for all nutrients (2–6). Thus, promotion of age- and gender-specific dietary intake as well as supplements may be advantageous to help women in various life stages meet DRI recommendations (3, 7). Recently, many pregnant women were found to consume inadequate amounts of essential nutrients, although prenatal supplements helped meet their nutritional recommendations (8). However, for key life stages of women including WCBA (aged 15–44 y) and

WMENO (aged 40–65 y), limited data exist on nutrient intakes and dietary supplement use. During these life stages, nutritional requirements change to meet physiological demands, although we have little understanding regarding how nutrient adequacies differ across these stages.

In addition to nutrient intake, biomarker concentrations of a micronutrient or related metabolite in blood or urine are considered indicators of dietary exposure, nutrient bioavailability, and nutritional status (including insufficiencies and deficiencies) (9, 10). In contrast to self-reported nutrient intake data, biomarker status can be more objectively and accurately quantified and provide clinical utility (9). However, little is known about the association between nutrient intakes and biomarker status as measures of nutrient adequacy. In adults, usual total folate intake data estimated a higher prevalence of inadequacy compared with serum and RBC folate biomarker cutoffs (11), supporting the need for a comparison of intake data and biomarker status.

The primary objective of the current study was to utilize the most current NHANES data to determine nutrient gaps in WCBA and WMENO. Our secondary objective was to evaluate nutritional status using nutrient biomarker data. In addition, for nutrients for which data were available, we assessed the association between nutrient intake and biomarkers in women with and without supplement usage. This study is the first to assess nutrient gaps in US WCBA and WMENO and determine the association between dietary intake and biomarker status for key nutrients.

Methods

NHANES data set

NHANES is a continuous survey that uses a complex multistage probability sample designed to be representative of the civilian US population (12). The NHAHES data sets provide nationally representative nutrition and health data and prevalence estimates for nutrition and health status measures in the United States. Data collection for the NHANES includes a household interview and an examination conducted in a mobile examination center. Information on supplement use in the past 30 d was collected by NHANES survey personnel during the household interview. As part of the examination, trained dietary interviewers collected detailed information on all foods and beverages consumed by respondents in the previous 24-h time period (midnight to midnight), which was the first dietary recall interview (day 1). A secondary dietary recall (day 2) is administered by telephone 3–10 d after the first dietary interview but not on the same day of the week as the first interview. In addition, information on supplement use in the previous 24 h is collected during the in-person and telephone dietary recall interviews. The NHANES study protocol was approved by the National Center for Health Statistics Research Ethics Review Board, and all participants provided written informed consent. Biological specimens (blood and/or urine) were collected during the examination for the first dietary recall interview (day 1) for laboratory analysis to provide information about the participants' health and nutritional status. Laboratory analyses conducted on the collected biological specimens varied by survey cycle.

Study population

For the current analysis, data from the publicly available NHANES data sets for women aged 15–65 y who participated in the What We Eat in America component of NHANES conducted in 2011–2012, 2013–2014, and 2015–2016 (hereafter referred to as 2011–2016) were included (12, 13). Pregnant and/or lactating women were excluded. Only women whose dietary recalls were classified by NHANES as reliable and meeting the minimum criteria set by NHANES (i.e., DR1DRSTZ/DR2DRSTZ = 1) and who completed the dietary supplement questionnaire were included (14). The sample (women aged 15–65 y, excluding pregnant and/or lactating women) consisted of 6894 women. Of these, 6114 women had valid day 1 and day 2 questionnaires, whereas 780 women had a valid day 1 questionnaire only. Women were categorized into 2 non–mutually exclusive age groups, each of which was further divided into 2 subgroups: WCBA (aged 15–30 y and 31–44 y) and WMENO (aged 40–50 y and 51–65 y). There is a small overlap in groups for women aged 40–44 y due to the fact that women at this time may be experiencing different life stages—later-in-life fertility and/or beginning of menopausal transition with perimenopause. During the past 2 decades, first birth rates for women aged 40–44 y increased by 35% (15). The natural menopausal transition can also occur during this time, with US women reaching menopause between ages 40 and 58 y (16).

Nutrient intake

Estimated nutrient intake from food was based on food and beverage consumption records collected during the 24-h recall and nutrient composition from the Food and Nutrient Database for Dietary Studies 2011–2012, 2013–2014, and 2015–2016. Estimated nutrient intake from supplements was based on the 30-d supplement intake data collected during the NHANES household interview. The nutrient intake data provided by NHANES (12) were used. The EAR and/or Adequate Intake (AI) and upper tolerable level (UL), if available, were compiled for nutrients of interest.

Nutrient biomarkers

Data on serum, RBCs, or urinary amounts of 10 biomarkers of interest were compiled from NHANES 2011–2016. Data on the clinically relevant cutoffs for these biomarkers were compiled from the CDC (9), Institute of Medicine (17, 18), and the WHO (19–21). Clinically relevant cutoffs have been established for folate (serum and RBC), vitamin B-12 (serum), iron [serum ferritin and soluble transferrin receptor (sTfR)], and iodine (urinary), whereas for select fatty acids [EPA (20:5n–3), DHA (22:6n–3), and α-linolenic acid (ALA; 18:3n–3)], there are no recognized clinically relevant cutoffs. For vitamin D, cutoffs were based on Endocrine Society recommendations (22). All analyses were restricted to subjects with valid dietary recall on day 1 as biological specimens were collected during the examination for the first dietary recall interview (day 1).

Statistical analyses

Statistical analyses were performed with SAS software (version 9.4; SAS Institute) and Stata (version 12.1; StataCorp).

Usual intake of nutrients from food only was estimated using the 24-h food dietary recall(s), adjusting for day of recall, and indicators for weekday/weekend, age group, and dietary supplement use, using the National Cancer Institute (NCI) method (23) and SAS macros developed by NCI for modeling of a single dietary component. To obtain final distributions of total usual nutrient intakes inclusive of all sources, the "combined" methodology detailed extensively by Bailey et al. (24) was used. In brief, nutrient intake distribution from food source was determined using the NCI method with supplement use as an indicator variable, before adding the usual (30-d average) intake from supplements to the adjusted distribution of intakes from food alone.

The percentage of the population with usual intake below the EAR or above the AI and above the UL (as applicable) was estimated using the cutoff method. Age-specific EAR, AI, and UL were used. For the age groups that overlapped 2 DRI groups, the minimum EAR, AI, and UL were used. This resulted in a conservatively higher estimate of women meeting the dietary requirement for their age group and a conservatively higher estimate of women exceeding the UL for their age group.

For the association analyses, estimates of mean usual intake (and percentage <EAR, percentage >AI, and/or percentage >UL, as appropriate) of respective nutrients from food alone and from food and supplements were derived for women in each of the biomarker categories. Mean (and percentage <EAR, percentage >AI, and/or percentage >UL, as appropriate) intake estimates for women in the lower and mid biomarker categories were compared with the intake estimates derived for the women in the highest biomarker category using a z test ($\alpha = 0.01$, 1-sided z test).

Results

Demographics of the study population

A total of 6894 women were included in the current study; 4134 were WCBA (aged 15–44 y), and 3438 were WMENO (aged 40–65 y). The majority of women (61.3%) were non-Hispanic white, had a poverty income ratio >1.85 (62.3%), and had a household reference education higher than high school (63.7%).

Dietary supplement usage

Of the 6894 women in the study population, 58% (n = 3585) reported using a supplement or antacid during the past 30 d. Antacid usage was considered because antacids can contribute to mineral intake, particularly calcium. The percentage of supplement users among the WCBA and WMENO groups was 47% and 69%, respectively (**Table 1**). The number and percentage of users of supplements containing specific nutrients for each study population are provided in **Table 2**. In general, a higher percentage of women in the WMENO group took supplements compared with women in the WCBA group. However, often within each group, older women reported more supplement use compared with younger women. For example, 25.3% and 36.7% of WCBA aged 15–30 y and 31–44 y and 41.4% and 52.5% of WMENO aged 40–50 y and 51–65 y, respectively, reported using supplements containing vitamin D (D-2 + D-3).

Nutrient intakes from food alone and from food and supplements combined

In both the WCBA and WMENO groups, usual intakes of most nutrients were higher from food and supplements combined than from food alone (**Supplemental Tables 1** and **2**). For example, vitamin D (D-2 + D-3) intake (mean ± SE) from food alone was 3.8 ± 0.1 μg in WCBA aged 15–30 y, 4.0 ± 0.1 μg in WCBA aged 31–44 y, 3.9 ± 0.2 μg in WMENO aged 40–50 y, and 4.2 ± 0.1 μg in WMENO aged 51–65 y. Vitamin D intake from food and supplements was 9.7 ± 0.1 μg in WCBA aged 15–30 y, 14.5 ± 1.4 μg in WCBA aged 31–44 y, 17.8 ± 1.6 μg in WMENO aged 40–50 y, and 26.0 ± 1.5 μg in WMENO aged 51–65 y. Alternatively, for some nutrients not commonly found in supplements (i.e., choline, protein, and carbohydrates; Table 2), few differences were observed between the usual intakes from food alone and food and supplements combined.

Nutrient inadequacy in women of various ages with or without supplement use

The percentages of women in the WCBA and WMENO groups with intakes below the corresponding EAR are presented for shortfall nutrients (1) in **Supplemental Figure 1**. Risk of nutrient inadequacy is defined as intake below the EAR. A substantial percentage of women in both groups had insufficient intakes from food, leading them to be at risk for inadequacy for vitamin D, vitamin E, magnesium, vitamin A, calcium, and vitamin C (Supplemental Figure 1). The prevalence of nutrient inadequacy was lower with supplements. The percentages of women with intakes from food plus supplements at risk for inadequate amounts of nutrients were lower than those for food alone. These results indicate that with supplement usage, fewer women have nutrient intakes below the EAR. The results are fully detailed in **Tables 3** and **4**.

WCBA with usual intakes from food alone were at risk for inadequate intakes of iron, zinc, and copper (Table 3). In general, fewer WMENO were at risk for inadequate intakes of iron, zinc, and copper (Table 4). The addition of dietary supplements did not markedly decrease the percentage of WCBA or WMENO at risk for inadequate intakes of iron, zinc, or copper (Tables 3 and 4). More WMENO were at risk for inadequate intakes of vitamin B-6 compared with WCBA (Tables 3 and 4).

The majority of women with intakes from food alone did not meet the AI for total choline, dietary fiber, or potassium. Similar percentages of women with intakes from food and supplements combined did not meet the AI for these nutrients (Tables 3 and 4). Approximately 43% of WCBA aged 15–30 y and WCBA aged 31–44 y, 40% of WMENO aged 40–50 y, and 37% of WMENO aged 51–65 y did not meet the AI for vitamin K from food alone; 41% of WCBA aged 15–30 y, 40% of WCBA aged 31–44 y, 37% of WMENO aged 40–50 y, and 33% of WMENO aged 51–65 y did not meet the AI for vitamin K from food and supplements combined. The majority of women had total usual intakes that exceeded the AIs for sodium (>97% in all groups).

Prevalence of nutrient intakes higher than the UL in women with or without supplement use

The majority of women in all age groups exceeded the chronic disease risk reduction intake amount for sodium, regardless of

TABLE 1 Study population characteristics[1]

	WCBA (15–44 y)			WMENO (40–65 y)		
	Supplement/antacid use			Supplement/antacid use		
	Total	Yes	No	Total	Yes	No
n	4134	1790	2344	3438	2172	1266
Age, mean $\pm$ SE (y)	29.2 $\pm$ 0.3	30.8 $\pm$ 0.4	27.8 $\pm$ 0.3	52.4 $\pm$ 0.2	53.2 $\pm$ 0.2	50.8 $\pm$ 0.3
Age group, %						
15–30 y	54.7	47.3	61.3	—	—	—
31–44 y	45.3	52.7	38.7	—	—	—
40–50 y	—	—	—	41.6	37.0	51.8
51–65 y	—	—	—	58.4	63.0	48.2
Race/ethnicity, %						
Mexican American	13.1	9.1	16.8	7.4	5.8	11.0
Other Hispanic	7.8	7.1	8.3	5.6	4.8	7.3
Non-Hispanic white	54.9	61.8	48.8	66.8	70.9	57.8
Non-Hispanic black	14.4	11.5	17.1	12.2	10.2	16.7
Other race (including multiracial)	9.7	10.6	9.0	8.0	8.4	7.2
Household income, %						
<1.35 of PIR	33.7	26.3	40.5	21.4	17.2	30.5
1.35–1.85 of PIR	11.3	10.7	11.8	8.0	7.3	9.4
>1.85 of PIR	55.0	63.0	47.7	70.7	75.4	60.1
Household reference education, %						
≤ high school	37.3	29.5	44.3	34.8	30.5	44.1
> high school	62.7	70.5	55.7	65.2	69.5	55.9
BMI, %						
Underweight	2.7	2.5	2.9	1.2	1.1	1.4
Normal	38.8	42.1	35.9	27.2	29.4	22.6
Overweight	24.3	22.7	25.6	28.3	28.1	28.8
Obese	34.3	32.8	35.6	43.3	41.4	47.3
On a special diet						
Yes	15.2	18.7	12.0	20.2	22.6	14.9
No	84.8	81.3	88.0	79.8	77.4	85.1

[1]PIR, poverty income ratio; WCBA, women of childbearing age; WMENO, women of menopausal age.

supplement usage (data not shown). Few women (<3%) of childbearing age exceeded the UL of other studied nutrients from food alone or food and supplements combined. For WMENO, <3% exceeded the UL for vitamin D from food alone, and 2.9% $\pm$ 0.9% and 5.1% $\pm$ 1.0% of women aged 40–50 y and 51–65 y, respectively, exceeded the UL for vitamin D from food and supplements combined. Overall, the addition of supplements did not increase the percentage of women with nutrient intakes that exceeded the UL.

Analysis of nutrient biomarkers

The summary distributions of nutrient biomarkers of interest for each of the age groups are provided in **Supplemental Table 3** and **4**. The distributions were generally skewed. A substantial percentage of women are at risk of deficiency or insufficiency for vitamin D, folate, vitamin B-12, iron, and iodine.

Association of nutrient intakes with biomarkers in women with or without supplement use

Associations between dietary nutrient intake and biomarkers of interest were assessed. Estimates of mean usual intake, percentage <EAR, and percentage >UL of nutrients from food alone or from food and supplements for women in each of the

biomarker categories are summarized in **Table 5**. Each nutrient intake estimate was compared with those in the upper biomarker category or the biomarker category associated with sufficient nutrient status.

Vitamin D association data.

The Endocrine Society Clinical Practice Guideline (22) has defined cutoffs for vitamin D (Supplemental Table 3). Consequences of vitamin D deficiency include abnormalities in calcium, phosphorus, and bone metabolism (22). Here, we find similar numbers of women in the at risk of deficiency ($n = 1609$), at risk of inadequacy ($n = 1551$), and sufficiency ($n = 1223$) categories (Table 5, Supplemental Table 3). More women in the sufficiency category (~62%) took supplements than those in the deficiency category (~15%). The mean usual intake estimate from food alone was significantly lower for women in the at risk of deficiency category compared with women in the sufficiency category. Correspondingly, the prevalence of nutrient inadequacy was significantly higher for women in the at risk of deficiency category.

Total folate (serum and RBC) association data.

Cutoffs for serum and RBC folate are described in Supplemental Table 3. For serum folate, there were more women

TABLE 2 Number of women reporting using a supplement with the specific nutrient in the previous 30 d, NHANES 2011–2016[1]

Nutrient	No. (%) of women reporting using a supplement with the specific component in the previous 30 d			
	WCBA		WMENO	
	15–30 y ($n = 2396$)	31–44 y ($n = 1738$)	40–50 y ($n = 1477$)	51–65 y ($n = 1961$)
Vitamin A, RAE	465 (22.3)	512 (32.1)	442 (33.6)	607 (35.1)
Retinol	392 (18.7)	443 (27.9)	395 (29.9)	551 (31.3)
Vitamin E as α-tocopherol	481 (23.1)	545 (33.5)	469 (34.5)	665 (38.5)
Vitamin D (D-2 + D-3)	528 (25.3)	600 (36.7)	554 (41.4)	905 (52.5)
Vitamin K	220 (11.2)	311 (19.4)	282 (21.3)	446 (26.1)
Vitamin C	562 (26.9)	593 (36.2)	516 (37.1)	734 (41.5)
Thiamin (vitamin B-1)	358 (18.0)	442 (27.0)	389 (29.5)	569 (32.7)
Riboflavin (vitamin B-2)	359 (18.0)	448 (27.2)	391 (29.1)	576 (33.3)
Niacin	425 (20.9)	497 (30.1)	425 (31.5)	618 (36.3)
Vitamin B-6	488 (24.1)	540 (33.2)	463 (34.3)	640 (37.0)
Folate, DFE	485 (23.7)	535 (33.0)	462 (35.0)	623 (35.7)
Folic acid	485 (23.7)	535 (33.0)	462 (35.0)	623 (35.7)
Vitamin B-12	500 (24.4)	569 (34.9)	497 (36.8)	698 (40.6)
Total choline	148 (7.2)	148 (8.6)	123 (8.4)	112 (7.7)
Calcium	519 (26.8)	589 (36.5)	565 (41.4)	911 (52.5)
Iron	345 (16.3)	410 (24.2)	355 (25.2)	345 (20.2)
Magnesium	292 (15.1)	385 (23.7)	360 (27)	595 (35.8)
Phosphorus	136 (5.9)	130 (8.6)	147 (10.6)	316 (18.8)
Potassium	121 (5.7)	156 (9.8)	145 (10.9)	346 (20.7)
Sodium	134 (7.0)	118 (7.4)	133 (10.0)	213 (11.8)
Zinc	408 (20.5)	467 (28.4)	408 (29.3)	572 (32.9)
Copper	253 (12.5)	357 (21.9)	320 (23.7)	501 (29.6)
Selenium	242 (12.1)	348 (21.7)	323 (24.5)	493 (30.1)
Protein	24 (1.4)	44 (2.5)	44 (3.6)	87 (5.0)
Carbohydrate	274 (13.3)	272 (16.6)	247 (18.6)	315 (19.6)
Total fat	107 (5.1)	171 (10.1)	155 (11.2)	336 (18.4)
Dietary fiber	25 (1.6)	26 (1.3)	34 (3.0)	43 (3.3)
Total SFAs	30 (1.3)	44 (2.4)	39 (2.5)	79 (4.5)
Total MUFAs	12 (0.3)	24 (1.3)	20 (0.9)	34 (1.8)
Total PUFAs	42 (2.1)	73 (4.2)	77 (6.0)	138 (7.8)
PFA EPA	64 (2.5)	90 (5.7)	74 (4.9)	153 (9.5)
PFA DHA	76 (3.2)	101 (6.2)	83 (5.2)	163 (10.3)
Lycopene	27 (1.3)	54 (3.2)	63 (4.5)	168 (10.7)
Lutein + zeaxanthin	73 (3.2)	99 (6.0)	98 (8.0)	284 (17.9)

[1] DFE, dietary folate equivalents; PFA, polyunsaturated fatty acid; RAE, retinol activity equivalents; WCBA, women of childbearing age; WMENO, women of menopausal age.

and supplement users in the sufficiency category than in the folate deficiency category. For RBC folate, there were also more women and supplement users in the sufficiency category than in the insufficiency and deficiency categories. The mean usual intake estimates from both food alone and food and supplements combined were significantly lower for women in the serum folate deficiency category compared with the sufficiency category (Table 5). Similarly, the mean usual intake estimates were significantly lower for women in the RBC folate deficiency and insufficiency categories compared with the sufficiency category. Likewise, the prevalence of nutrient inadequacy was significantly higher for women in the serum folate deficiency category and the RBC folate deficiency and insufficiency categories compared with the respective upper categories for women with intakes from food alone and food and supplements combined. For folic acid (serum and RBC), similar associations were observed for the

mean usual intake estimates from both food alone and food and supplements combined (Table 5).

Vitamin B-12 association data.

For vitamin B-12, the cutoffs are described in Supplemental Table 3. Here, we find more women supplement users were in the sufficient category than in the low normal or moderately low/deficient categories (Table 5). The mean usual intake estimates from both food alone and food and supplements combined were significantly lower for women in the low normal and moderately low/deficient categories compared with the sufficient category. The prevalence of nutrient inadequacy was significantly higher for women in the low normal group with intakes from both food alone and food and supplements, whereas the prevalence of nutrient inadequacy was only higher for the

TABLE 3 Percentage of WCBA aged 15–44 y with usual intake from food only and food and supplements <EAR or >AI, NHANES 2011–2016[1]

Nutrient	WCBA age group 15–30 y (n = 2396)		31–44 y (n = 1738)	
	Food only	Food + supplements	Food only	Food + supplements
% <EAR				
Vitamin A, RAE (μg)	50.1 ± 2.3	42.3 ± 2.1	44.2 ± 2.2	33.6 ± 1.9
Vitamin E as α-tocopherol (mg)	92.2 ± 1.0	76.1 ± 1.6	87.9 ± 1.4	63.4 ± 1.7
Vitamin D (D-2 + D-3) (μg)	>97	80.7 ± 1.5	>97	68.9 ± 1.7
Vitamin C (mg)	46.9 ± 2.2	38.9 ± 1.9	45.9 ± 2.2	34.4 ± 1.9
Thiamin (vitamin B-1) (mg)	3.2 ± 0.8	2.9 ± 0.7	<3	<3
Riboflavin (vitamin B-2) (mg)	5.3 ± 0.7	4.8 ± 0.6	2.6 ± 0.4	<3
Niacin (mg)	<3	<3	<3	<3
Vitamin B-6 (mg)	7.1 ± 1.1	6.1 ± 0.9	8.1 ± 0.8	6.4 ± 0.7
Folate, DFE (μg)	19.7 ± 1.5	16.7 ± 1.3	17.5 ± 1.6	13.4 ± 1.3
Vitamin B-12 (μg)	7.8 ± 1.1	6.4 ± 0.9	7.1 ± 0.9	5.1 ± 0.7
Calcium (mg)	49.2 ± 1.6	44.2 ± 1.6	43.7 ± 1.9	35.7 ± 1.8
Iron (mg)	11.5 ± 1.1	10.1 ± 1.0	9.5 ± 1.1	7.6 ± 1.0
Magnesium (mg)	61.7 ± 1.9	58.5 ± 1.9	43.7 ± 1.8	39.5 ± 1.8
Phosphorus (mg)	<3	<3	<3	<3
Zinc (mg)	20.1 ± 1.6	17.6 ± 1.4	14.5 ± 1.3	11.8 ± 1.2
Copper (mg)	16.7 ± 1.3	15.7 ± 1.2	9.4 ± 0.8	8.3 ± 0.7
Selenium (μg)	<3	<3	<3	<3
Protein (g)	3.3 ± 0.5	3.3 ± 0.5	<3	<3
Carbohydrate (g)	<3	<3	<3	<3
% >AI				
Vitamin K (μg)	57.3 ± 1.9	59.1 ± 1.9	57.1 ± 2.2	60.5 ± 2.1
Total choline (mg)	4.0 ± 0.7	4.2 ± 0.7	5.7 ± 0.9	6.2 ± 0.8
Potassium (mg)	33.5 ± 1.9	33.7 ± 1.9	32.0 ± 1.6	32.3 ± 1.6
Sodium (mg)	>97	>97	>97	>97
Dietary fiber (g)	4.2 ± 0.6	4.3 ± 0.6	7.8 ± 0.9	7.9 ± 0.9
PFA ALA (g)	77.4 ± 1.8	NA	81.9 ± 1.8	NA

[1]Values are means ± SEs unless otherwise indicated. AI, Adequate Intake; ALA, α-linolenic acid; DFE, dietary folate equivalents; EAR, Estimated Average Requirement; NA, not available; PFA, polyunsaturated fatty acid; RAE, retinol activity equivalents; WCBA, women of childbearing age.

moderately low/deficient category for women with intakes from both food and supplements.

Iron (ferritin and transferrin receptor) association data.

The cutoffs for serum ferritin are described in Supplemental Table 3. Serum ferritin is sensitive to iron deficiency but does not indicate severity of deficiency (9). Serum sTfR is a better indicator of iron status during functional iron deficiency (9). Cutoffs for serum ferritin and sTfR are specific to age and gender. For ferritin, more women were in the sufficient category than in the depleted iron stores and risk of overload categories. However, similar percentages of women used supplements in each biomarker category. Likewise, for sTfR, more women were in the sufficiency category than in the deficiency category, whereas each group had similar percentages of women reporting supplement use. As shown in Table 5, for both intakes from food alone and food and supplements combined, there were no significant differences in mean intake, percentage <EAR, or percentage >UL for women in the depleted iron stores category or risk of overload ferritin biomarker category compared with the sufficient category, or in the sufficient serum sTfR category compared with the deficiency category.

For vitamin D, folate, and vitamin B-12, we find that higher mean intake, lower percentage <EAR, and a minimal increase in percentage >UL are all associated with supplement usage and a decreased risk of nutrient deficiency by biomarker status.

However, similar associations were not observed for iron (ferritin and sTfR) biomarker status. This may be due to the limitations of iron biomarkers for determining iron status at the population extent.

Fatty acid association data.

No clinically defined cutoffs have been defined for fatty acids; therefore, women were grouped based on the distribution tertiles (Table 5, Supplemental Table 4). For DHA, similar numbers of women were in the <117 μmol/L, 117 to <172 μmol/L, and ≥172 μmol/L categories. More women in the ≥172 μmol/L category took supplements than in the 117 to <172 and <117 μmol/L categories. The mean usual intake estimate from food alone was significantly lower for women in the <117 μmol/L category, and the mean usual intake estimates from food plus supplements were significantly lower for women in both the <117 and 117 to <172 μmol/L categories compared with the ≥172 μmol/L category. For other fatty acids, EPA and ALA (an essential fatty acid), comparisons across biomarker tertiles were not significantly different (Table 5).

Discussion

This is the first analysis of NHANES data to *1*) examine nutrient status of women in distinct life stages of childbearing [young reproductive age (15–30 y) and later-in-life fertility

TABLE 4 Percentage of WMENO aged 40–65 y with usual intake from food only and food + supplements <EAR or >AI, NHANES 2011–2016[1]

Nutrient	WMENO age group 40–50 y (n = 1477)		51–65 y (n = 1961)	
	Food only	Food + supplements	Food only	Food + supplements
% <EAR				
Vitamin A, RAE (µg)	43.8 ± 2.7	33.0 ± 2.1	36.5 ± 2.1	27.1 ± 1.6
Vitamin E as α-tocopherol (mg)	88.1 ± 1.6	62.7 ± 2.0	86.3 ± 1.8	57.3 ± 1.9
Vitamin D (D-2 + D-3) (µg)	>97	64.1 ± 1.9	>97	51.4 ± 1.5
Vitamin C (mg)	43.6 ± 2.5	32.5 ± 2.1	41.4 ± 1.7	28.6 ± 1.3
Thiamin (vitamin B-1) (mg)	<3	<3	<3	<3
Riboflavin (vitamin B-2) (mg)	3.1 ± 0.5	2.6 ± 0.5	2.6 ± 0.4	<3
Niacin (mg)	<3	<3	2.6 ± 0.4	<3
Vitamin B-6 (mg)	10.6 ± 1.3	8.3 ± 1.0	20.8 ± 1.8	15.2 ± 1.4
Folate, DFE (µg)	19.9 ± 2.3	15.0 ± 1.7	18.9 ± 1.9	14.0 ± 1.4
Vitamin B-12 (µg)	8.8 ± 1.2	6.2 ± 0.9	7.3 ± 1.2	4.9 ± 0.8
Calcium (mg)	47.6 ± 2.1	37.3 ± 2.0	73.9 ± 1.5	50.9 ± 1.5
Iron (mg)	11.5 ± 1.5	9.2 ± 1.3	<3	<3
Magnesium (mg)	49.8 ± 2.0	44.6 ± 2.0	48.7 ± 1.8	40.7 ± 1.8
Phosphorus (mg)	<3	<3	<3	<3
Zinc (mg)	16.6 ± 1.6	13.5 ± 1.4	16.2 ± 1.6	12.6 ± 1.3
Copper (mg)	10.1 ± 1.0	8.9 ± 0.9	9.3 ± 1.2	7.7 ± 1.0
Selenium (µg)	<3	<3	<3	<3
Protein (g)	<3	<3	<3	<3
Carbohydrate (g)	<3	<3	<3	<3
% >AI				
Vitamin K (µg)	59.8 ± 2.5	63.2 ± 2.3	63.0 ± 2.2	67.5 ± 2.0
Total choline (mg)	5.4 ± 0.9	5.8 ± 0.9	5.8 ± 0.8	6.4 ± 0.8
Potassium (mg)	33.7 ± 1.7	34.1 ± 1.7	38.4 ± 1.5	39.4 ± 1.5
Sodium (mg)	>97	>97	>97	>97
Dietary fiber (g)	7.1 ± 0.7	7.5 ± 0.7	9.4 ± 12.7	9.7 ± 12.8
PFA ALA (g)	81.7 ± 2.0	NA	83.0 ± 1.6	NA

[1]Values are means ± SEs unless otherwise indicated. AI, Adequate Intake; ALA, α-linolenic acid; DFE, dietary folate equivalents; EAR, Estimated Average Requirement; NA, not available; PFA, polyunsaturated fatty acid; RAE, retinol activity equivalents; WMENO, women of menopausal age.

(31–44 y)] and menopause [perimenopausal (40–50 y) and menopausal (51–65 y)] and *2*) to perform association analysis of nutrient intakes and nutrient status biomarkers. Women in these critical life stages have distinct and specific nutritional needs. Not only is adequate nutrition important for the health of women of childbearing age but also crucial for infants' neurodevelopment from conception through pregnancy and for the first 2 y of life (8, 25). Key nutrients that support neurodevelopment include zinc, choline, folate, iodine, and vitamins A, D, B-6, and B-12 (25). Adequate intake of DHA is also critical for infants' brain development during the intrauterine period (26). In addition, WCBA require more iron than do WMENO due to menstrual iron losses in fertile women and increased blood volume in pregnant women (27). As women age, there is an association between nutritional intakes with ovarian reserve and the timing of menopause (28). For WMENO, the decline in estrogen production and increase in resorption of calcium can increase risk of bone fractures (18). Thus, adequate intakes of calcium and vitamin D are essential for optimal bone health in women at this life stage (18, 29). Given specific nutritional needs for WCBA and WMENO, understanding nutritional intakes for women in these life stages is critical to best tailor dietary recommendations for optimal health.

Despite dietary guidance, the majority of Americans have inadequate intakes of at least 1 vitamin or mineral in their diet (1–3). Of emphasis, the 2015–2020 Dietary Guidelines for Americans identified "shortfall nutrients" with high prevalence of inadequate intakes (1). Analysis of NHANES nutrient intake data (2009–2012) showed that ≥25% of adults aged 19–70 y consume (from food only) below the EAR or AI for choline, calcium, magnesium, and vitamins A, C, D, and E (7). Similarly, our data show that WCBA and WMENO are not meeting the dietary recommendations for calcium, magnesium, and vitamins A, C, D, and E. A separate study found that in addition to these shortfall nutrients, a significant number of pregnant women are not meeting nutritional recommendations for iron (8). Here, we found that more WCBA are at risk for inadequate amounts of iron compared with WMENO. In contrast, we found that as women transitioned from early perimenopause (ages 40–50 y) to postmenopause (ages 51–65 y), nutrient gaps were higher for vitamin B-6 and calcium, suggesting specific guidance is needed for WMENO to meet nutritional needs. Thus, we conclude that women of various ages are not obtaining the vital nutrients they need from their diets alone.

The use of dietary supplements has been shown to help increase nutrient intake, reduce inadequacies, and is associated with more favorable health and lifestyle choices (2, 4–6, 30). Indeed, more than half of American adults use dietary supplements (30) to improve and/or maintain overall health (31). Regular supplement usage is associated with higher nutrient intakes and lower inadequacies, particularly for vitamins A, B-6, B-12, C, D, and E (4–6, 32). Importantly, supplement usage does not substantially increase the risk of nutrient overconsumption (6). Therefore, addition of nutrient supplements to one's diet

TABLE 5 Usual intake of nutrients from food or food + supplements per biomarker amount category in all women aged 15–65 y, NHANES 2011–2016[1]

	Biomarker amount category		
25(OH)D$_2$ + 25(OH)D$_3$ (nmol/L) (NHANES 2011–2014)	<50	50 to <75	75–250[2]
Vitamin D (D-2 + D-3) (µg)[3]			
n	1609	1551	1223
% taking supplement	15.2 ± 1.4	36.4 ± 1.8	62.6 ± 1.8
	Intake from food only		
Mean	3.5 ± 0.1*	3.8 ± 0.2	4.2 ± 0.1
% <EAR	>99*	98.4 ± 0.4	97.7 ± 0.5
% >UL	<1	<1	<1
	Intake from food + supplements		
Mean	5.5 ± 0.3*	10.6 ± 0.7*	28.9 ± 2.2
% <EAR	89.2 ± 1.1*	70.8 ± 1.9*	43.1 ± 1.9
% >UL	<1*	<1*	5.6 ± 1.4
Serum total folate (nmol/L) (NHANES 2011–2016)	<10[4]	≥10[2]	—
Folate, DFE (µg)			
n	48	6447	—
% taking supplement	1.7 ± 1.3	31.6 ± 1.0	—
	Intake from food only		
Mean	315.2 ± 25.9*	463.8 ± 5.2	—
% <EAR	56.9 ± 8.8*	18.4 ± 1.7	—
	Intake from food + supplements		
Mean	321.6 ± 24.9*	663.5 ± 8.8	—
% <EAR	56.2 ± 8.5*	14.2 ± 1.3	—
Folic acid (µg)			
n	48	6447	—
% taking supplement	1.7 ± 1.3	31.6 ± 1.0	—
	Intake from food only		
Mean	99.2 ± 12.6*	157.7 ± 2.4	—
% >UL	<1	<1	—
	Intake from food + supplements		
Mean	103.0 ± 12.2*	275.2 ± 4.5	—
% >UL	<1*	4.1 ± 0.3	—
RBC folate (nmol/L) (NHANES 2011–2016)	<340[5]	340–906	≥906[2]
Folate, DFE (µg)			
n	39	2380	4128
% taking supplement	6.4 ± 3.8	15.6 ± 0.9	38.9 ± 1.1
	Intake from food only		
Mean	314.9 ± 32.0*	408.3 ± 7.9*	487.8 ± 5.7
% <EAR	57.8 ± 10.7*	28.7 ± 2.5*	13.7 ± 1.4
	Intake from food + supplements		
Mean	380.2 ± 55.5*	482.3 ± 9.6*	742.6 ± 10.9
% <EAR	54.6 ± 9.8*	25.2 ± 2.1*	9.3 ± 1.0
Folic acid (µg)			
n	39	2380	4128
% taking supplement	6.4 ± 3.8	15.6 ± 0.9	38.9 ± 1.1
	Intake from food only		
Mean	96.0 ± 13.3*	137.6 ± 3.3*	166.2 ± 2.9
% >UL	<1	<1	<1
	Intake from food + supplements		
Mean	134.4 ± 34.1*	181.1 ± 4.5*	316.1 ± 5.7
% >UL	4.2 ± 3.4	0.7 ± 0.1*	5.4 ± 0.5
Vitamin B-12 (pmol/L) (NHANES 2011–2014)	<201[6]	201–301	>301[2]
Vitamin B-12 (µg)			
n	290	789	2642
% taking supplement	16.9 ± 3.0	26.7 ± 2.8	42.2 ± 1.5
	Intake from food only		
Mean	3.6 ± 0.2*	3.7 ± 0.1*	4.3 ± 0.1
% <EAR	12.4 ± 3.0	10.9 ± 1.9*	5.3 ± 1.0
	Intake from food + supplements		
Mean	7.8 ± 1.9*	21.2 ± 3.1*	110.7 ± 15.6
% <EAR	10.3 ± 2.7*	8.4 ± 1.4*	3.3 ± 0.7
Ferritin (µg/L)	<15	15–150[2]	>150
Iron (mg)			
n	305	1121	74
% taking supplement	16.5 ± 3.9	17.7 ± 2.3	23.3 ± 3.9

(Continued)

TABLE 5 (*Continued*)

	Biomarker amount category		
	Intake from food only		
Mean	12.4 ± 0.7	12.1 ± 0.2	11.5 ± 0.7
% <EAR	10.1 ± 4.2	11.9 ± 2.4	14.5 ± 5.6
% >UL	<1	<1	<1
	Intake from food + supplements		
Mean	17.9 ± 1.7	15.6 ± 0.7	19.4 ± 3.4
% <EAR	9.1 ± 3.7	10.5 ± 2.0	12.3 ± 4.3
% >UL	5.2 ± 2.0	2.2 ± 0.6	6.5 ± 2.8
Transferrin receptor (mg/L) (NHANES 2015–2016)	≤4.4[2]	>4.4	—
Iron (mg)			
n	1118	355	—
% taking supplement	18.1 ± 1.7	15.5 ± 3.2	—
	Intake from food only		
Mean	12.2 ± 0.2	11.9 ± 0.7	—
% <EAR	11.5 ± 2.3	13.1 ± 4.5	—
% >UL	<1	<1	—
	Intake from food + supplements		
Mean	15.8 ± 0.7	17.0 ± 0.9	—
% <EAR	10.1 ± 1.9	11.6 ± 4.0	—
% >UL	2.2 ± 0.6	4.3 ± 0.9	—
EPA (μmol/L) (NHANES 2011–2012)	<38	38 to <64.7	≥64.7[2]
PFA EPA (g)			
n	376	306	298
% taking supplement	1.2 ± 0.6	3.3 ± 1.6	7.0 ± 1.6
	Intake from food only		
Mean	0.016 ± 0.002	0.015 ± 0.002	0.018 ± 0.002
	Intake from food + supplements		
Mean ± SE	0.017 ± 0.002	0.020 ± 0.002	0.031 ± 0.005
DHA (μmol/L) (NHANES 2011–2012)	<117	117 to <172	≥172[2]
PFA DHA (g)			
n	309	338	330
% taking supplement	1.5 ± 1.0	2.2 ± 0.8	8.8 ± 2.4
	Intake from food only		
Mean	0.037 ± 0.005*	0.050 ± 0.006	0.070 ± 0.006
	Intake from food + supplements		
Mean	0.038 ± 0.005*	0.052 ± 0.006*	0.080 ± 0.006
ALA (μmol/L) (NHANES 2011–2012)	<65.6	65.6 to <91.0	≥91.0[2]
PFA ALA (g)			
n	361	297	319
% taking supplement	NA	NA	NA
	Intake from food only		
Mean	1.48 ± 0.05	1.59 ± 0.06	1.66 ± 0.06
% <EAR	76.7 ± 5.1	83.4 ± 4.0	85.9 ± 2.8

[1]Values are means ± SEs unless otherwise indicated. *Significantly different [$P < 0.01$ ($\alpha = 0.01$, 1-sided z test)] from highest biomarker category; ALA, α-linolenic acid; EAR, Estimated Average Requirement; NA, not available; PFA, polyunsaturated fatty acid; UL, upper tolerable limit; 25(OH)D, 25-hydroxyvitamin D.

[2]Reference category for statistical comparisons.

[3]For vitamin D, the woman in the "risk of excess" category (>250 nmol/L; $n = 1$) was removed from the analysis.

[4]For serum folate, the women in the "risk of megaloblastic anemia" category (<7 nmol/L; $n = 10$) were combined with those in the "possible deficiency" category (7–9 nmol/L).

[5]For RBC folate, the women in the "risk of megaloblastic anemia" category (<305 nmol/L; $n = 25$) were combined with those in the "possible deficiency" category (306–339 nmol/L).

[6]For vitamin B-12, the women in the "deficient" category (<100 pmol/L; $n = 18$) were combined with those in the "moderately low" category (101–200 pmol/L).

may help bridge nutrient gaps and improve overall health (33). Here, we assessed the prevalence of supplement usage among women and found that most WMENO (69%) use supplements. Supplement usage helped partially fill nutrient gaps, resulting in fewer women with nutrient intakes below the EAR, particularly for shortfall nutrients. In addition, with supplement usage, fewer WCBA and WMENO had iron or vitamin B-6 intakes below the

EAR, respectively. Our findings, along with published literature, show that dietary supplement usage may be one important way of overcoming nutrient inadequacies in women of various life stages (4, 8). Even with supplement use, nutrient gaps remained for both WCBA and WMENO, indicating additional dietary guidance is needed to help women during these life stages to meet their nutrient needs, including considering all contributions to total

intake (food and supplements) and how to adjust appropriately to completely fill nutrient gaps.

Assessment of nutrient intake is essential to evaluate intake adequacy. Although dietary intake data are a convenient approximation of nutrient status, they are prone to measurement errors. Nutrient status biomarkers are a physiological alternative to validate intake data (9). Clinically relevant cutoffs have been identified to align with health-related conditions and reflect an individual's health status (9). Thus, nutrient biomarkers reflect the relation between biochemical indicators and health outcomes. We associated intakes and biomarker status for vitamin D, folate, vitamin B-12, iron, and DHA (9). Bailey et al. (11) performed an analysis for folate in adults and found a higher prevalence for inadequate folate intake by intake estimates compared with biomarker amounts. Here, dietary intake estimates were associated with nutrient status biomarkers for most studied nutrients, which supports the value of self-reported dietary intake data for assessing nutritional status. Notably, iron intake did not significantly associate with biomarker status (serum ferritin and sTfR), suggesting that further work is needed to assess intakes of this critical nutrient. Similarly, the majority of previous cross-sectional studies have not been able to demonstrate an association between iron intake and iron status (34). Differences in bioavailability of heme compared with nonheme iron as well as various dietary factors that affect iron absorption may be responsible for this lack of association. It is also possible that limitations of iron status biomarkers for determining iron status at the population extent led to the lack of association observed here. The strength of this study is that it is the first such analysis in a nationally representative sample of WCBA and WMENO. The main limitation is the use of self-reported usual dietary intake. Self-reported dietary intake is subject to measurement errors as a result of memory and limitations related to estimating quantities, social desirability bias, and the assumption that self-reported intake is representative of longer term intakes.

In conclusion, we found that a high percentage of WCBA and WMENO do not meet the dietary recommendations for calcium, magnesium, and vitamins A, C, D, and E. Supplement usage helped fill some of these nutrient gaps, although it did not lead to nutrient intakes above the UL. The effect of filling these nutrient gaps can be substantial for the health of WCBA and the development of their future offspring and health before, during, and after pregnancy. For WMENO, nutrient gaps were higher for vitamin B-6 and calcium. For certain nutrients not commonly found in food or supplements, there is a need for education and additional dietary guidance. Although dietary intake was associated with nutrient status biomarkers for folate, vitamin D, vitamin B-12, and DHA, future work is needed to identify alternative approaches for assessing iron intake and status at the population extent, particularly for WCBA. Because most WCBA and WMENO are not meeting nutrient intake recommendations, specific guidance is needed to help these populations meet nutrient needs.

Data Availability

Data described in the manuscript will be made available upon request pending approval.

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