

# Total folate and folic acid intake from foods and dietary supplements in the United States: 2003–2006<sup>1–3</sup>

Regan L Bailey, Kevin W Dodd, Jaime J Gahche, Johanna T Dwyer, Margaret A McDowell, Elizabeth A Yetley, Christopher A Sempos, Vicki L Burt, Kathy L Radimer, and Mary Frances Picciano

## ABSTRACT

**Background:** The term *total folate intake* is used to represent folate that occurs naturally in food as well as folic acid from fortified foods and dietary supplements. Folic acid has been referred to as a double-edged sword because of its beneficial role in the prevention of neural tube defects and yet possible deleterious effects on certain cancers and cognitive function. Previous monitoring efforts did not include folic acid from dietary supplements and are therefore not complete.

**Objective:** Our objective was to combine data on dietary folate (as measured by two 24-h recalls) and folic acid from dietary supplements (collected with a 30-d frequency questionnaire) with the use of the bias-corrected best power method to adjust for within-person variability.

**Design:** The National Health and Nutrition Examination Survey (NHANES) is a nationally representative, cross-sectional survey. Linear contrasts were constructed to determine differences in dietary and total folate intake for age and racial-ethnic groups by sex; prevalence of inadequate and excessive intakes is presented.

**Results:** In 2003–2006, 53% of the US population used dietary supplements; 34.5% used dietary supplements that contained folic acid. Total folate intake (in dietary folate equivalents) was higher for men ( $813 \pm 14$ ) than for women ( $724 \pm 16$ ) and higher for non-Hispanic whites ( $827 \pm 19$ ) than for Mexican Americans ( $615 \pm 11$ ) and non-Hispanic blacks ( $597 \pm 12$ ); 29% of non-Hispanic black women had inadequate intakes. Total folate and folic acid intakes are highest for those aged  $\geq 50$  y, and 5% exceed the Tolerable Upper Intake Level.

**Conclusions:** Improved total folate intake is warranted in targeted subgroups, which include women of childbearing age and non-Hispanic black women, whereas other population groups are at risk of excessive intake. *Am J Clin Nutr* 2010;91:231–7.

## INTRODUCTION

*Total folate* is an umbrella term used to represent the different forms of the B vitamin. Food folate is the form that occurs naturally in food sources. Folic acid is the form of the vitamin found in fortified foods and dietary supplements. The term *dietary folate* is used to represent food folate and folic acid in fortified foods together. Total folate encompasses all dietary and supplemental exposure to folate and folic acid.

Folic acid supplementation in the periconceptional period unequivocally decreases the occurrence of neural tube defects (1, 2). For this reason, the governments of both the United States and

Canada instituted national fortification programs with folic acid to enhance the diets of reproductive-aged women (3–5), and neural tube defect rates decreased in both the United States (6) and Canada (7–9). However, the fortification program increased folic acid intake among virtually all segments of the population. Whereas observational data suggest that increased food folate is beneficial for prevention of some cancers and cardiovascular disease, high folic acid intake may actually increase the risk of colorectal cancers (10, 11) and cognitive impairment (12, 13) among certain individuals. Therefore, careful monitoring of total folate intake from food and dietary supplements is recommended (13, 14).

Data from the National Health and Nutrition Examination Survey (NHANES) can be used to monitor dietary intake and dietary supplement use of folate in the United States. The NHANES data indicate increases in dietary folate intakes from the prefortification (NHANES III) to the postfortification (NHANES 1999–2000) time period, but these data are limited in that they do not include estimates of folic acid from dietary supplements (15). With more than one-half of the US population reporting the use of dietary supplements (16), monitoring folate status without inclusion of this potentially important contributor of nutrients is problematic and incomplete (17, 18).

Some methodologic challenges have precluded the calculation of total nutrient intakes from the NHANES data. First, the data were collected over 2 different periods of time: food intake was measured by two 24-h dietary recalls (ie, single-day estimates), and dietary supplement data were collected through a 30-d frequency questionnaire. Furthermore, both 24-h recalls and frequency methods of dietary assessment are subject to different types of measurement error (19, 20). Thus, nutrient estimates from the 2 instruments may not be directly comparable, and

<sup>1</sup> From the Office of Dietary Supplements (RLB, JTD, EAY, CAS, and MFP) and the National Cancer Institute (KWD), National Institutes of Health, Bethesda, MD; and the National Center for Health Statistics Centers for Disease Control and Prevention, Hyattsville, MD (JYG, MAM, VLB, and KLR).

<sup>2</sup> The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Office of Dietary Supplements, the National Cancer Institute, the National Institutes of Health, the Centers for Disease Control and Prevention/ Agency for Toxic Substances and Disease Registry, or any other entity of the US Government.

<sup>3</sup> Address correspondence to RL Bailey, 6100 Executive Boulevard, 2B03, Bethesda, MD 20892-7517. E-mail: baileyrl@mail.nih.gov.

Received July 23, 2009. Accepted for publication October 27, 2009.

First published online November 18, 2009; doi: 10.3945/ajcn.2009.28427.

simply adding them together may not be a satisfactory approach. Previous methods have described how to adjust dietary estimates from 24-h recalls to decrease within-person variation (21–25), but little is known about the derivation of total nutrient intakes with the use of adjusted dietary data. Carriquiry (26) has published strategies to combine diet and supplemental sources of nutrients; in this article, we use this methodologic framework to combine dietary folate intake estimates from the 24-h dietary recall data and the 30-d frequency questionnaire of dietary supplement use to derive total folate intakes with the use of the 2003–2006 NHANES data.

## SUBJECTS AND METHODS

The NHANES is a nationally representative, cross-sectional survey that samples noninstitutionalized, civilian US residents with the use of a complex, stratified, multistage, probability cluster sampling design. All data were collected by the National Center for Health Statistics of the Centers for Disease Control and Prevention. Briefly, participants were asked to complete 3 components: an in-person household interview, a health examination in a mobile examination center (MEC)  $\approx$ 3 wk later, and a phone interview to collect additional dietary data. At the household interview, demographic information, dietary supplement use, and some health-related data were collected. The MEC visit consisted of clinical tests, laboratory studies, a dietary recall, and a health interview. Written informed consent was obtained from all participants or proxies, and the survey protocol was approved by the Research Ethics Review Board of the National Center for Health Statistics.

The NHANES data are publicly available and are released in 2-y data sets to ensure confidentiality of the participants and to allow for adequate sample size for statistical analysis. However, the combination of 4 y of data may be necessary to produce reliable estimates with the statistical methods required with the complex sample design for more detailed analyses of population subgroups. For this reason, the 2003–2004 and 2005–2006 NHANES data sets were combined.

The unweighted examination response rate for all participants, which was calculated as the number of participants divided by the total number selected for the sample, was 79% for the interview component and 76% for the examination component in NHANES 2003–2004 and 80% for the interview component and 77% for the examination component in NHANES 2005–2006. Only participants over the age of 14 y were included in this analysis ( $n = 13,468$ ); pregnant and lactating women were excluded ( $n = 764$ ), which left the analytic sample at 12,704. Of this sample, 12,119 completed both the interview and examination components. From this sample, participants with incomplete dietary recall data were excluded ( $n = 657$ ); thus, this report includes data for 11,462 participants.

### Dietary data

#### 24-h Recalls

All survey participants were eligible for the dietary interview and dietary supplement use interview questions. During the MEC examination, a 24-h dietary recall was administered by trained interviewers. A second dietary recall was collected via telephone  $\approx$ 3–10 d after the MEC examination. Both 24-h recalls were

collected with the use of the US Department of Agriculture's Automated Multiple-Pass Method (27, 28).

#### Folate bioequivalence

The bioavailability of food folate is much lower than that of folic acid added to fortified foods and dietary supplements. The dietary folate equivalent (DFE) conversion was developed to reflect this differential bioavailability (29). Equation 1 shows the conversion to the DFE metric:

$$1 \text{ DFE} = 1 \mu\text{g food folate} = 0.6 \mu\text{g folic acid from supplements and fortified foods} \quad (1)$$

#### Dietary supplement use

Dietary supplement use information was collected during the household interview as part of the Dietary Supplement Questionnaire. The questionnaire was used to determine a sample person's use of vitamins, minerals, herbs, and other dietary supplements over the past 30 d. Detailed information about type, consumption frequency, duration, and amount taken was collected for each reported dietary supplement. The average daily intake of folic acid was calculated for individuals with the use of the number of days that the supplement was reported to have been taken, the reported amount taken per day, and the serving size unit from the product label. Missing information was assigned a default value of the most commonly reported serving size, dose, or frequency of intake.

#### Total folate intakes

The dietary folate intakes reported on the 24-h dietary recalls were adjusted for within-person variability with the use of the bias-corrected best power method to obtain a set of intermediary values that reflected the distribution of usual nutrient intake from food sources (22, 25). Each of the intermediary values was based on data from a particular individual, for whom additional data that concerned supplement use were available. Each individual's reported average daily dose of folic acid from dietary supplements was added to his or her intermediary value to produce a final set of adjusted values that reflected the distribution of usual intake of folate in DFE and folic acid separately in micrograms (25, 26). Thus, dietary and total nutrient intakes were estimated in 2 ways: 1) dietary and total folate in DFE and 2) dietary and total folic acid in micrograms, because the Dietary Reference Intakes are constructed in this manner. The estimated average requirement (EAR) is for folate in DFE, but the Tolerable Upper Intake Level (UL) is for folic acid in micrograms. Folic acid in fortified foods, when converted to DFEs, can be used to meet the EAR recommendations. However, the analysis that compared mean intakes of the groups with the UL is for synthetic folic acid only, ie, food folate does not contribute toward the UL.

#### Statistical analysis

All statistical analyses were performed with the use of SAS software (version 9; SAS Institute Inc, Cary, NC). Sample weights were used to account for differential nonresponse and noncoverage, and to adjust for planned oversampling of some

groups. Mean and percentiles of dietary and total folate (DFE) and dietary and total folic acid (micrograms) were estimated. Mean dietary and total folate intake were compared with EAR, and mean dietary and total folic acid were compared with the UL (29, 30), to determine the proportion of the population that meets or exceeds these recommendations, respectively.

Linear contrasts were constructed to determine differences between mean folate intake for age and racial-ethnic groups by sex. The referent group for the age comparisons was 19–30 y for both men and women. For racial-ethnic groups, the referent group was non-Hispanic white for both men and women. The SEs for all statistics of interest (means, medians, proportions with usual intake below or above EAR-UL, and linear contrasts) was approximated by Fay's modified balanced repeated replication technique (31, 32) with the use of 32 sets of replicate weights constructed with an initial perturbation factor of 0.7. Each set of replicate weights was poststratified to control totals computed from the initial sample weights. For the linear contrasts, a *t* statistic was computed by the division of the estimate of each contrast by its estimated SE.

## RESULTS

The use of dietary supplements was reported by 53.4% of NHANES 2003–2006 participants, and 34.5% reported the use of supplements that contained folic acid. Non-Hispanic whites (39%) reported a higher prevalence of use of folic acid dietary supplements than did non-Hispanic blacks (19%) and Mexican Americans (18%). Use and mean contribution from dietary supplements that contained folic acid was highest for 51–70-y-

olds, with 47% of men and 53% of women in this age group reporting use. In this age group, the mean ( $\pm$ SE) contribution of folic acid from supplements was  $436 \pm 21.4 \mu\text{g}$ , and 5% were above the UL from dietary supplements alone when the sexes were examined together.

In general, dietary folate intakes were relatively stable for women across age groups (Table 1). In contrast, total folate intakes (diet plus supplements) were higher in those aged  $>51$  y. Among men, no differences were noted in age groups for dietary folate intakes. Men  $>51$  y had significantly higher total folate intakes compared with the referent group. Among both sexes, non-Hispanic whites had higher total folate intakes than did non-Hispanic blacks and Mexican Americans. Across all age and racial-ethnic groups, men had higher mean dietary and total folate intakes than did women (between-sex differences not statistically compared). However, women had a higher percentage than men of total intake contributed by dietary supplements (37% compared with 28%, respectively; data not shown).

Mean dietary and total folate intakes were compared with the Dietary Reference Intake recommendations. The use of dietary supplements as reflected in total folate intakes lowered the prevalence of individuals who did not meet the EAR. More women than men had inadequate intakes (ie, they did not meet the EAR) for both dietary and total folate. Even with the use of dietary supplements, 19% of 14–18-y-old and 17% of 19–30-old women did not meet the EAR. A significantly higher prevalence of inadequate intakes of total folate was observed for non-Hispanic black women (23%) than for non-Hispanic white women (13%). Similarly, a significantly higher prevalence of inadequate total folate intakes was observed for non-Hispanic

**TABLE 1**

Energy, dietary folate, and total folate intakes [in dietary folate equivalents (DFE)] compared with the estimated average requirement (EAR) stratified by sex, age group, and race-ethnicity in the United States, 2003–2006<sup>1</sup>

	<i>n</i>	Energy intake	Folate intake			
			Diet only	Below the EAR <sup>2</sup>	Total intake	Below the EAR <sup>2</sup>
		<i>kcal</i>	<i>DFE</i>	%	<i>DFE</i>	%
<b>Women</b>						
14–18 y	1250	1926 $\pm$ 31 <sup>3</sup>	496 $\pm$ 14	22.4 $\pm$ 2.7	577 $\pm$ 24	19.0 $\pm$ 2.6
19–30 y	914	1902 $\pm$ 31	460 $\pm$ 12	21.8 $\pm$ 2.3	645 $\pm$ 17	16.9 $\pm$ 2.4
31–50 y	1350	1861 $\pm$ 23	470 $\pm$ 12	22.9 $\pm$ 2.1	714 $\pm$ 29	14.6 $\pm$ 1.7
51–70 y	1251	1662 $\pm$ 21 <sup>4</sup>	460 $\pm$ 11	22.8 $\pm$ 2.5	900 $\pm$ 39 <sup>4</sup>	12.7 $\pm$ 1.9
$\geq 71$ y	787	1539 $\pm$ 24 <sup>4</sup>	454 $\pm$ 10	23.7 $\pm$ 2.3	797 $\pm$ 26 <sup>4</sup>	14.4 $\pm$ 1.9
Non-Hispanic white	2540	1775 $\pm$ 12	476 $\pm$ 9.0	22.2 $\pm$ 1.4	811 $\pm$ 25	13.0 $\pm$ 1.1
Non-Hispanic black	1406	1803 $\pm$ 33	402 $\pm$ 9.4 <sup>4</sup>	28.7 $\pm$ 2.9 <sup>4</sup>	544 $\pm$ 18 <sup>4</sup>	23.2 $\pm$ 2.5 <sup>4</sup>
Mexican American	1200	1838 $\pm$ 46	457 $\pm$ 7.9	20.2 $\pm$ 2.8	593 $\pm$ 15 <sup>4</sup>	12.6 $\pm$ 1.2
<b>Men</b>						
14–18 y	1351	2687 $\pm$ 60	674 $\pm$ 19	9.5 $\pm$ 2.0	745 $\pm$ 24	9.2 $\pm$ 2.0
19–30 y	1097	2752 $\pm$ 48	652 $\pm$ 16	5.9 $\pm$ 1.7	774 $\pm$ 28	5.2 $\pm$ 1.6
31–50 y	1439	2733 $\pm$ 27	633 $\pm$ 11	4.1 $\pm$ 0.8	843 $\pm$ 23	3.6 $\pm$ 0.8
51–70 y	1215	2319 $\pm$ 35 <sup>4</sup>	583 $\pm$ 14	8.2 $\pm$ 1.5	938 $\pm$ 37 <sup>4</sup>	6.3 $\pm$ 1.3
$\geq 71$ y	808	1922 $\pm$ 31 <sup>4</sup>	558 $\pm$ 8.2	9.3 $\pm$ 1.4	935 $\pm$ 24 <sup>4</sup>	5.5 $\pm$ 1.1
Non-Hispanic white	2707	2600 $\pm$ 18	644 $\pm$ 8.9	5.3 $\pm$ 0.8	909 $\pm$ 23	4.3 $\pm$ 0.7
Non-Hispanic black	1479	2412 $\pm$ 40 <sup>4</sup>	522 $\pm$ 13 <sup>4</sup>	12.7 $\pm$ 2.4 <sup>4</sup>	651 $\pm$ 156 <sup>4</sup>	10.6 $\pm$ 2.1 <sup>4</sup>
Mexican American	1341	2487 $\pm$ 39	570 $\pm$ 12 <sup>4</sup>	7.8 $\pm$ 1.7	670 $\pm$ 22 <sup>4</sup>	7.3 $\pm$ 1.6 <sup>4</sup>

<sup>1</sup> Different sample sizes were available for the age groups and racial-ethnic groups by sex because the “all other” racial category was included in the age group analysis. Dietary folate represents the combination of food folate and folic acid in fortified foods. Total folate encompasses dietary folate and folic acid from dietary supplements combined. Both dietary and total folate are in the DFE metric.

<sup>2</sup> The EAR for individuals aged 14–18 y is 330 DFE and is 320 DFE for individuals aged  $\geq 19$  y.

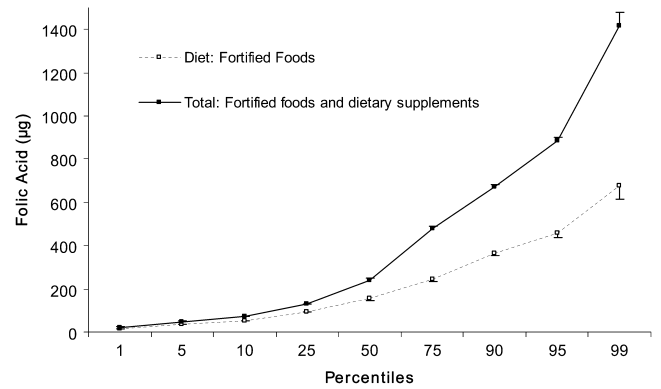
<sup>3</sup> Mean  $\pm$  SE (all such values). SEs were calculated with the use of Fay's modified balanced repeated replication technique.

<sup>4</sup> Significantly different from the referent age group (19–30 y) or the referent racial group (non-Hispanic whites),  $P \leq 0.003$  (Bonferroni-adjusted).

black and Mexican American men than for non-Hispanic white men.

Mean intakes of folic acid from the diet (ie, fortified foods) and from all sources (ie, fortified foods and dietary supplements) are presented in **Table 2**. Women aged 50–70 y and  $\geq 71$  y had significantly higher total folic acid intakes than the referent group. The prevalence of excessive intakes of folic acid from food alone was  $<1\%$  for women and  $<2\%$  for men; dietary supplement use increased the prevalence of intakes above the UL. Non-Hispanic white women and men had a significantly higher prevalence of excessive total folate intakes than their counterparts in other racial-ethnic groups. Approximately 5% of women aged 51–70 y and men in the 50–70-y and  $\geq 71$ -y age group had total folic acid intake above the UL.

The shift in the folic acid intake distribution from the use of dietary supplements as measured in micrograms with sex and all age groups combined is shown in **Figure 1**. Dietary supplements supply large amounts of folic acid, and the variability increases as mean intake increases. The percentile distributions for dietary intakes alone and for total folate intakes in DFE are shown in **Table 3**. The difference in the percentiles of dietary folate and total folate shows the effect of the amount of folic acid that is added from dietary supplements. In general, for dietary and total folate intakes, means were higher than medians for all age and sex groups examined. This is suggestive of a significant skew to the intake distributions and indicates that some persons have a relatively high total folate intake. The magnitude of the difference between the percentiles of folate from the diet alone and total folate intake increases as the percentiles increase.



**FIGURE 1.** Mean ( $\pm$ SE) percentiles of dietary and total folic acid intake in the United States, 2003–2006. The SEs were calculated with the use of Fay’s modified balanced repeated replication technique and are presented below the diet intakes and above total intakes. Dietary folic acid is from fortified foods. Total folic acid is from fortified foods combined with folic acid from dietary supplements.

## DISCUSSION

This study used a strategy to derive total folate intakes, which is based on previous work by Carriquiry (26) with modifications suggested by Dodd et al (25). This method produced distributions of total folate intakes by the addition of person-specific dietary supplement intakes to adjusted dietary intake estimates of folate with the use of a nationally representative data set for 2003–2006. To our knowledge, this is the first effort to describe the population

**TABLE 2**

Dietary folic acid and total folic acid intake (in  $\mu\text{g}$ ) stratified by sex, age group, and race-ethnicity in the United States, 2003–2006<sup>1</sup>

	n	Folic acid intake			
		Diet only	Above the UL	Total intake	Above the UL
		$\mu\text{g}$	%	$\mu\text{g}$	%
<b>Women</b>					
14–18 y	1250	201 $\pm$ 7.5 <sup>2</sup>	0.0 $\pm$ 0.0	248 $\pm$ 13.1	0.4 $\pm$ 0.2 <sup>3</sup>
19–30 y	914	165 $\pm$ 5.6	0.0 $\pm$ 0.0	274 $\pm$ 9.5	2.2 $\pm$ 0.6
31–50 y	1350	154 $\pm$ 6.7	0.3 $\pm$ 0.2 <sup>3</sup>	297 $\pm$ 16.1	2.7 $\pm$ 0.7
51–70 y	1251	148 $\pm$ 5.7	0.0 $\pm$ 0.0	407 $\pm$ 22.2 <sup>d</sup>	5.2 $\pm$ 0.8 <sup>d</sup>
$\geq 71$ y	787	156 $\pm$ 6.0	0.0 $\pm$ 0.0	358 $\pm$ 15.8 <sup>d</sup>	3.2 $\pm$ 0.8
Non-Hispanic white	2540	162 $\pm$ 4.8	0.1 $\pm$ 0.01	359 $\pm$ 14.0	3.8 $\pm$ 0.5
Non-Hispanic black	1406	136 $\pm$ 4.9	0.0 $\pm$ 0.0	220 $\pm$ 10.2 <sup>d</sup>	1.4 $\pm$ 0.2 <sup>d</sup>
Mexican American	1200	152 $\pm$ 4.3	0.0 $\pm$ 0.0	232 $\pm$ 8.6 <sup>d</sup>	1.3 $\pm$ 0.3 <sup>d</sup>
<b>Men</b>					
14–18 y	1351	280 $\pm$ 9.5	1.2 $\pm$ 0.5 <sup>3</sup>	322 $\pm$ 12.4	2.3 $\pm$ 0.7 <sup>d,5</sup>
19–30 y	1097	245 $\pm$ 9.0	0.5 $\pm$ 0.3 <sup>3</sup>	317 $\pm$ 16.1	2.1 $\pm$ 0.9 <sup>3</sup>
31–50 y	1439	217 $\pm$ 5.6	0.0 $\pm$ 0.0	341 $\pm$ 12.8	2.1 $\pm$ 0.4
51–70 y	1215	197 $\pm$ 7.6	0.5 $\pm$ 0.2 <sup>3</sup>	406 $\pm$ 21.5 <sup>d</sup>	4.8 $\pm$ 0.8
$\geq 71$ y	808	200 $\pm$ 5.2	0.0 $\pm$ 0.0	421 $\pm$ 15.5 <sup>d</sup>	5.0 $\pm$ 0.7
Non-Hispanic white	2707	233 $\pm$ 4.7	0.4 $\pm$ 0.1	389 $\pm$ 12.7	3.9 $\pm$ 0.4
Non-Hispanic black	1479	185 $\pm$ 5.9 <sup>d</sup>	0.2 $\pm$ 0.1 <sup>3</sup>	261 $\pm$ 8.4 <sup>d</sup>	1.3 $\pm$ 0.5 <sup>d,5</sup>
Mexican American	1341	190 $\pm$ 5.7 <sup>d</sup>	0.3 $\pm$ 0.1 <sup>5</sup>	248 $\pm$ 11.3 <sup>d</sup>	1.3 $\pm$ 0.3 <sup>d</sup>

<sup>1</sup> Different sample sizes were available for the age groups and racial-ethnic groups by sex because the “all other” racial category was included in the age group analysis. Dietary folic acid represents folic acid from fortified foods. Total folic acid represents folic acid from fortified foods combined with folic acid from dietary supplements. The Tolerable Upper Intake Level (UL) is 800  $\mu\text{g}$  synthetic folic acid for individuals aged 14–18 y and 1000  $\mu\text{g}$  for individuals aged  $\geq 19$  y.

<sup>2</sup> Mean  $\pm$  SE (all such values). SEs were calculated with the use of Fay’s modified balanced repeated replication technique.

<sup>3</sup> The relative SE is  $>40\%$ ; this estimate is unreliable.

<sup>4</sup> Significantly different from the referent age group (19–30 y) or the referent racial group (non-Hispanic whites),  $P \leq 0.003$  (Bonferroni-adjusted).

<sup>5</sup> The relative SE is  $>30\%$  and  $<40\%$ .

**TABLE 3**Percentiles of dietary folate and total folate intakes [in dietary folate equivalents (DFE)] stratified by sex, age group, and race-ethnicity in the United States, 2003–2006<sup>1</sup>

	Percentiles of folate intake						
	1st	5th	25th	50th	75th	95th	99th
<b>Diet alone</b>							
<b>Women</b>							
14–18 y	128	205	342	451	607	888	1237
19–30 y	141	212	335	427	545	884	1076
31–50 y	119	215	246	437	562	834	1137
51–70 y	134	223	331	429	554	810	1165
≥71 y	159	221	258	417	532	852	1088
Non-Hispanic white	123	213	334	437	568	875	1183
Non-Hispanic black	120	198	307	383	472	663	874
Mexican American	126	222	348	437	543	755	1021
<b>Men</b>							
14–18 y	151	283	145	620	807	1316	1893
19–30 y	232	301	471	609	777	1148	1470
31–50 y	210	339	479	607	755	1047	1271
51–70 y	208	286	421	538	686	1035	1477
≥71 y	183	277	324	529	670	924	1144
Non-Hispanic white	220	317	467	602	769	1127	1472
Non-Hispanic black	180	263	392	489	625	870	1135
Mexican American	201	285	429	538	670	932	1198
<b>Diet and dietary supplements</b>							
<b>Women</b>							
14–18 y	138	218	358	495	710	1149	1592
19–30 y	147	228	363	490	812	1642	2275
31–50 y	162	234	387	574	954	1577	2489
51–70 y	145	250	419	765	1133	1940	4854
≥71 y	161	255	396	641	1104	1626	2726
Non-Hispanic white	158	245	407	635	1083	1762	2777
Non-Hispanic black	131	216	324	416	609	1204	1870
Mexican American	133	222	367	487	686	1258	1869
<b>Men</b>							
14–18 y	171	283	468	666	911	1564	2083
19–30 y	232	313	487	678	946	1506	2178
31–50 y	248	355	520	709	1073	1665	2177
51–70 y	214	305	495	746	1202	1938	2981
≥71 y	217	307	504	762	1227	1914	2875
Non-Hispanic white	232	334	532	755	1153	1823	2661
Non-Hispanic black	180	270	416	541	753	1350	2008
Mexican American	214	290	443	576	780	1329	2005

<sup>1</sup> Dietary folate represents the combination of food folate and folic acid in fortified foods. Total folate encompasses the combination of dietary folate and folic acid from dietary supplements. Both dietary and total folate are in the DFE metric.

status of total folate intake from foods, fortified foods, and dietary supplements.

Several methodologic concerns must be acknowledged. First, all estimates of dietary intake were adjusted for within-individual variation, and these estimates reflect usual intake and assume that reported nutrient intake from food sources on any given 24-h recall day are unbiased and that the self-reported supplement intake reflects true long-term supplement intake. Second, estimates of folate in food depend largely on label declarations rather than analytic values. Actual amounts are often higher than label values (33). Third, the folic acid content of dietary supplements is also based on label values; recent analytic data suggest that label values also may exceed actual amounts (34, 35).

The fortification of the food supply with folic acid was intended to enhance the diets of reproductive-age women. In this study, ≈22% of reproductive-age women did not meet the EAR

through diet alone. When dietary supplements and foods were examined (ie, total folate intake), 19% of 14–18-y-olds, 17% of 19–30-y-olds, and 15% of 31–50-y-olds did not meet the EAR recommendations. Non-Hispanic black women also had a high prevalence of inadequate intakes, with 29% who did not meet the EAR through diet alone and 23% who did not meet the EAR for total intakes. However, the NHANES data indicate that, whereas some groups have inadequate intakes, other groups are at risk of excessive intakes. It is important to note that when examined separately, 4% of dietary supplement users exceeded the UL simply from the use of the supplements alone. Approximately 5% of US women and men aged ≥50 y had total folic acid intakes above the UL. Given accumulating data that suggest high folic acid intakes in those with preexisting lesions may increase cancer risk, older adults and those who use folic acid supplements in addition to a high folic acid diet certainly

should be cautious about intake amounts. Our results support the earlier conclusions of Lewis et al (36) that a need exists to improve total folate intake in targeted subgroups, which include women of childbearing age and non-Hispanic black women, while not putting other population groups at risk of excessive intakes. In this article, we present the estimates for folate and folic acid exposure from dietary and supplemental sources. Given the underreporting of energy intake (37) and limitations of both the dietary and dietary supplements composition tables, careful examination of the biomarker data of folate status, in addition to the dietary data, is a crucial next step to inform nutrition policy.

Dietary supplements constitute an important source of nutrients for large segments of the population, and more than one-half of the US population reports usage. Previous research indicates that dietary supplement users also tend to have high dietary intakes of nutrients (38). Thus, the relation between nutrient intakes from food and from dietary supplements is complex and one that should not be ignored in human studies. Furthermore, distributions of usual total nutrient intakes are necessary to accurately monitor the population's nutritional status and compliance with federal recommendations for supplemental folic acid (39, 40).

The methods applied in this study provide a relatively uncomplicated means to account for dietary supplement use in NHANES. The methods described here could easily be applied to other nutrients or other samples. This method does not require special statistical software; we performed all analyses in SAS. Simulation studies (not shown here) suggest that the method produces unbiased estimates of usual intake percentiles (41). Our results indicate that  $\approx 40\%$  of the US population uses a dietary supplement that contains folic acid. These data contribute to national efforts to monitor folate in the postfortification era.

The authors' responsibilities were as follows—RLB, JTD, EAY, CAS, MAM, VLB, KLR, and MFP: concept development and manuscript preparation; and KWD and JIG: methodologic and statistical aspects of the work and manuscript review. None of the authors had a personal or financial conflict of interest.

## REFERENCES

1. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 1991; 338:131–7.
2. Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med* 1992;327:1832–5.
3. US Food and Drug Administration. Food additives permitted for direct addition to food for human consumption; folic acid (folacin). *Fed Regist* 1996;61:8798–807.
4. US Food and Drug Administration. Food labeling: health claims and label statements; folate and neural tube defects. *Fed Regist* 1996;61: 8752–81.
5. US Food and Drug Administration. Food standards: amendment of standards of identity for enriched grain products to require addition of folic acid. *Fed Regist* 1996;61:8781–97.
6. Centers for Disease Control and Prevention. Spina bifida and anencephaly before and after folic acid mandate—United States, 1995–1996 and 1999–2000. *MMWR Morb Mortal Wkly Rep* 2004;53:362–5.
7. Persad VL, Van den Hof MC, Dube JM, Zimmer P. Incidence of open neural tube defects in Nova Scotia after folic acid fortification. *CMAJ* 2002;167:241–5.
8. Ray JG, Meier C, Vermeulen MJ, Boss S, Wyatt PR, Cole DE. Association of neural tube defects and folic acid food fortification in Canada. *Lancet* 2002;360:2047–8.
9. De Wals P, Rusen ID, Lee NS, Morin P, Niyonsenga T. Trend in prevalence of neural tube defects in Quebec. *Birth Defects Res A Clin Mol Teratol* 2003;67:919–23.
10. Mason JB, Dickstein A, Jacques PF, et al. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. *Cancer Epidemiol Biomarkers Prev* 2007;16:1325–9.
11. Hirsch S, Sanchez H, Albala C, et al. Colon cancer in Chile before and after the start of the flour fortification program with folic acid. *Eur J Gastroenterol Hepatol* 2009;21:436–9.
12. Morris MC, Evans DA, Bienias JL, et al. Dietary folate and vitamin B12 intake and cognitive decline among community-dwelling older persons. *Arch Neurol* 2005;62:641–5.
13. Yetley EA, Rader JI. Modeling the level of fortification and post-fortification assessments: U.S. experience. *Nutr Rev* 2004;62:S50–9; discussion S60–1.
14. Rader JI, Yetley EA. Nationwide folate fortification has complex ramifications and requires careful monitoring over time. *Arch Intern Med* 2002;162:608–9.
15. Dietrich M, Brown CJ, Block G. The effect of folate fortification of cereal-grain products on blood folate status, dietary folate intake, and dietary folate sources among adult non-supplement users in the United States. *J Am Coll Nutr* 2005;24:266–74.
16. Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999–2000. *Am J Epidemiol* 2004;160: 339–49.
17. Murphy SP, White KK, Park SY, Sharma S. Multivitamin-multimineral supplements' effect on total nutrient intake. *Am J Clin Nutr* 2007;85: 280S–4S.
18. Park SY, Murphy SP, Martin CL, Kolonel LN. Nutrient intake from multivitamin/mineral supplements is similar among users from five ethnic groups: the Multiethnic Cohort Study. *J Am Diet Assoc*. 2008; 108:529–33.
19. Carroll RJ, Freedman LS, Kipnis V. Measurement error and dietary intake. *Adv Exp Med Biol* 1998;445:139–45.
20. Kipnis V, Midthune D, Freedman L, et al. Bias in dietary-report instruments and its implications for nutritional epidemiology. *Public Health Nutr* 2002;5:915–23.
21. National Research Council. Nutrient adequacy. Washington, DC: National Academy Press, 1986.
22. Nusser SM, Carriquiry AL, Dodd KW, Fuller WA. A semiparametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 1996;91:1440–9.
23. Subar AF, Dodd KW, Guenther PM, et al. The food propensity questionnaire: concept, development, and validation for use as a covariate in a model to estimate usual food intake. *J Am Diet Assoc*. 2006;106: 1556–63.
24. Toozee JA, Midthune D, Dodd KW, et al. A new statistical method for estimating the usual intake of episodically consumed foods with application to their distribution. *J Am Diet Assoc* 2006;106:1575–87.
25. Dodd KW, Guenther PM, Freedman LS, et al. Statistical methods for estimating usual intake of nutrients and foods: a review of the theory. *J Am Diet Assoc* 2006;106:1640–50.
26. Carriquiry AL. Estimation of usual intake distributions of nutrients and foods. *J Nutr* 2003;133:601S–8S.
27. Blanton CA, Moshfegh AJ, Baer DJ, Kretsch MJ. The USDA Automated Multiple-Pass Method accurately estimates group total energy and nutrient intake. *J Nutr* 2006;136:2594–9.
28. Moshfegh AJ, Rhodes DG, Baer DJ, et al. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *Am J Clin Nutr* 2008;88:324–32.
29. Food and Nutrition Board. Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B<sub>6</sub>, folate, vitamin B<sub>12</sub>, pantothenic acid, biotin, and choline. Washington, DC: National Academy Press, 1998.
30. Food and Nutrition Board. Dietary reference intakes applications in dietary assessment. Washington, DC: National Academy Press, 2000.
31. Burt VL, Cohen SB. A comparison of methods to approximate standard errors for complex survey data. *Rev Public Data Use* 1984;12:159–68.
32. Rao JNK, Shao J. Modified balanced repeated replication for complex survey data. *Biometrika* 1999;86:403–15.
33. Rader JI, Weaver CM, Angyal G. Total folate in enriched cereal-grain products in the United States following fortification. *Food Chem* 2000; 70:275–89.

34. Dwyer JT, Holden J, Andrews K, et al. Measuring vitamins and minerals in dietary supplements for nutrition studies in the USA. *Anal Bioanal Chem* 2007;389:37–46.
35. Roseland JM, Holden JM, Andrews KW, et al. Dietary supplement ingredient database (DSID): preliminary USDA studies on the composition of adult multivitamin/mineral supplements. *J Food Compos Anal* 2008;21:S69–77.
36. Lewis CJ, Crane NT, Wilson DB, Yetley EA. Estimated folate intakes: data updated to reflect food fortification, increased bioavailability, and dietary supplement use. *Am J Clin Nutr* 1999;70:198–207.
37. Subar AF, Kipnis V, Troiano RP, 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;158:1–13.
38. Rock CL. Multivitamin-multimineral supplements: who uses them? *Am J Clin Nutr* 2007;85:277S–9S.
39. US Preventive Services Task Force, Agency for Healthcare Research and Quality. Folic acid for the prevention of neural tube defects: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009;150:626–31.
40. US Preventive Services Task Force, Agency for Healthcare Research and Quality. Summaries for patients. Folic acid for the prevention of infant neural tube defects: U.S. Preventive Services Task Force recommendation. *Ann Intern Med* 2009;150:1–50.
41. Dodd K, Bailey R, Wilger J, et al. Estimating distributions of usual total nutrient intake: a comparison of available methods. *FASEB J* 2009; 23:341.6