

# Race-ethnicity differences in folic acid intake in women of childbearing age in the United States after folic acid fortification: findings from the National Health and Nutrition Examination Survey, 2001–2002<sup>1–3</sup>

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## ABSTRACT

**Background:** Neural tube defects are serious birth defects of the brain and spinal cord. Up to 70% of neural tube defects can be prevented by the consumption of folic acid by women before and early during pregnancy.

**Objective:** The objective was to examine folic acid intake in women of childbearing age in the United States.

**Design:** We analyzed nutrient intake data reported by 1685 nonpregnant women aged 15–49 y who participated in the National Health and Nutrition Examination Survey, 2001–2002.

**Results:** The adjusted geometric mean consumption of folic acid from fortified foods was 128  $\mu\text{g}/\text{d}$  (95% CI: 123, 134  $\mu\text{g}/\text{d}$ ) in nonpregnant women. Eight percent (95% CI: 5.8%, 11.0%) of nonpregnant women reported consuming  $\geq 400$   $\mu\text{g}$  folic acid/d from fortified foods. This proportion was lower among non-Hispanic black women (5.0%) than among non-Hispanic white (8.9%) or Hispanic (6.8%) women. A smaller percentage of non-Hispanic black (19.1%) and Hispanic (21%) women than of non-Hispanic white women (40.5%) consumed  $\geq 400$   $\mu\text{g}$  folic acid from supplements, fortified foods, or both, in addition to food folate, as recommended by the Institute of Medicine to reduce the frequency of neural tube defects.

**Conclusions:** Most nonpregnant women of childbearing age in the United States reported consuming less than the recommended amount of folic acid. The proportion with low daily folic acid intake was significantly higher in non-Hispanic black and Hispanic women than in non-Hispanic white women. At the present level of folic acid fortification, most women need to take a folic acid–containing dietary supplement to achieve the Institute of Medicine recommendation. *Am J Clin Nutr* 2007;85:1409–16.

**KEY WORDS** Folic acid, fortification, National Health and Nutrition Examination Survey, NHANES, neural tube defects, race-ethnicity differences, women of reproductive age

## INTRODUCTION

Neural tube defects (NTDs) are serious birth defects of the spinal cord (spina bifida) and brain (anencephaly) (1, 2). Although anencephaly is always fatal, babies born with spina bifida usually survive, albeit with other disabilities (eg, paralysis or bladder and bowel control problems) resulting from nerve damage. NTDs develop within the first few weeks of embryogenesis,

at a time before many women know that they are pregnant (2). Up to 70% of all NTDs can be prevented if women consume a sufficient amount of folic acid around the time of conception and early in pregnancy (1, 3, 4). In 1992, the US Public Health Service issued a recommendation that all women of childbearing age consume 400  $\mu\text{g}$  folic acid/d to reduce the risk of having an infant with an NTD (5). The Institute of Medicine (IOM) made a similar recommendation in 1998—that women of childbearing age consume 400  $\mu\text{g}$  folic acid/d from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet (6).

In 1993, the US Food and Drug Administration (FDA) Folic Acid Subcommittee recommended that folic acid fortification be implemented to ensure that 90% of women of childbearing age consume daily 400  $\mu\text{g}$  folate or folic acid from all sources, but the FDA did not implement fortification at the level required to achieve this because of safety considerations (7). The FDA began requiring folic acid fortification of enriched cereal-grain products in 1998 at a level (140  $\mu\text{g}/100$  g) (8) that was estimated to provide an average person  $\approx 100$   $\mu\text{g}$  additional folic acid/d (7, 9, 10). Some studies have suggested that folic acid intake from fortified foods in the United States may differ from these estimations, providing as much as 200  $\mu\text{g}/\text{d}$  of additional folic acid (11–14).

In any case, average serum folate concentrations increased significantly after the implementation of folic acid fortification (15–17), and the prevalence of NTDs in the United States in 2000 was 26% lower than that before folic acid fortification (18, 19). However, the reduction in NTD prevalence has varied by race

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and ethnicity, which suggests the possibility of racial differences in folic acid intake or in inherent susceptibility to risk reduction. In the study reported here, we used data that contained folic acid dietary intake from fortified foods from the first nationally representative sample to become available since folic acid fortification was made mandatory. Data were used to examine current levels and sources of folic acid intake in women of childbearing age in the United States.

## MATERIALS AND METHODS

### The National Health and Nutrition Examination Survey, 2001–2002

A stratified multistage probability design was used in NHANES 2001–2002 to obtain a nationally representative sample of the noninstitutionalized civilian US population. In NHANES 2001–2002, each survey participant underwent a household interview and a physical examination. For this evaluation, we selected nonpregnant female participants who were 15–49 y old. Analyses were restricted to non-Hispanic white, non-Hispanic black, and Hispanic women. It should be noted that the race-ethnicity categories used in this document reflect those used by the National Health and Nutrition Examination Survey, 2001–2002 (NHANES) at the time the survey was conducted and therefore do not necessarily reflect current US Office of Management and Budget guidelines.

### Estimates of folic acid and food folate intakes

Information on the intakes of folic acid from fortified foods and of food folate was obtained from a single 24-h food recall questionnaire. The US Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies (version 1) was used to calculate nutrient intakes, including folic acid intake from fortified foods (20). Food and Nutrient Database for Dietary Studies, version 1, is the most current nutrient database that contains estimates of folic acid intake from fortified foods. A detailed description of the NHANES 2001–2002 total nutrient intake information was published elsewhere (Internet: [www.ars.usda.gov/Services/docs.htm?docid=7674](http://www.ars.usda.gov/Services/docs.htm?docid=7674)). All participants in NHANES provided written informed consent.

During the household interviews, participants were asked about their use of dietary supplements, including single vitamins, multivitamins, minerals, herbs, and similar nutritional substances. Use in the past month, the number of days a supplement was taken, and the quantities of supplements taken per day were recorded for each reported supplement. The interviewer recorded the name of each product and matched it to a list of known products. After the survey, NHANES staffers obtained label information for each reported supplement to determine the ingredients. A participant was classified as a user of a dietary supplement containing folic acid if she reported taking such a supplement  $\geq 1$  time in the previous month. Folic acid intake was calculated for each supplement on the basis of folic acid content, the number of days a supplement was taken, and the quantity of the supplement taken per day in the previous month. The average daily folic acid intake for each supplement was calculated, and the values were totaled across all supplements taken by each participant to determine the average daily amount of supplemental folic acid consumed.

## Statistical analysis

Because the distributions of folic acid and food folate intakes were not Gaussian, their logarithms were used in the analysis. We calculated geometric means, medians, and 5th and 95th percentiles of reported folic acid and food folate intake in 2 age groups (15–34 and 35–49 y) and by race-ethnicity (non-Hispanic white, non-Hispanic black, and Hispanic). We used linear regression to estimate adjusted geometric means and 95% CIs of reported folic acid and food folate intake by age group and race-ethnicity and to model the age  $\times$  race interaction. We tested for significant differences in adjusted geometric means for folic acid and food folate intakes between age and race-ethnicity groups by using 2-tailed *t* tests with Bonferroni adjustments for multiple comparisons. We estimated the weighted proportion (and 95% CI) of women in each age and race-ethnicity group who daily consumed  $<200$ , 200–399, 400–999, or  $\geq 1000$   $\mu\text{g}$  folic acid and food folate. Using logistic regression, we tested for significant differences by age group and race-ethnicity in the proportion of women who consumed  $\geq 400$   $\mu\text{g}$  folic acid/d, those who consumed folate from foods, and those who reported using supplements containing folic acid, after control for age group, race-ethnicity, and age  $\times$  race-ethnicity interaction. The interaction term was not significant ( $P > 0.084$ ) but was included in the model. To account for multiple comparisons, Bonferroni adjustment was calculated for all *t* test *P* values.

Eighty-one (18%) of the participants who reported using folic acid-containing supplements in the previous month had missing information on the frequency of supplement use. For those participants, we used a multiple imputation technique to estimate the average daily amount of folic acid consumed. In the multiple imputation models, we included age, race-ethnicity, education, marital status, poverty level, smoking status, body mass index, serum vitamin B-12, serum folate concentration, and red blood cell folate concentration as covariates (21).

Some studies have suggested that the actual amount of folic acid in fortified foods differs from that required by the FDA (11–13). To examine the effect of potential underestimates of folic acid intake, we conducted a sensitivity analysis by assuming that folic acid intake from fortified foods was 10% or 25% higher than that estimated from the survey. The results are shown in **Appendix A**. SUDAAN statistical software was used to adjust for the complex sampling design of NHANES 2001–2002 (22).

## RESULTS

NHANES 2001–2002 surveyed 2304 women of childbearing age (15–49 y old). We excluded 78 women of race-ethnicity other than non-Hispanic white, non-Hispanic black, or Hispanic; 372 pregnant women; and 169 women whose dietary interviews did not meet the minimum acceptable standard for data quality (23). The remaining 1685 nonpregnant women were included in the analysis. Of these 1685 women, 69.6% were non-Hispanic white, 13.5% were non-Hispanic black, and 17.0% were Hispanic.

The adjusted geometric mean reported daily consumption of folic acid from fortified foods in women of childbearing age was estimated to be 128  $\mu\text{g}$  (**Table 1**). Folic acid consumption from fortified foods was 18% lower in non-Hispanic black women (109  $\mu\text{g}/\text{d}$ ) than in non-Hispanic white women (133  $\mu\text{g}/\text{d}$ ) ( $P = 0.006$ ). Approximately 8% of women reported consuming



TABLE 1

Folic acid intake from fortified foods alone by age and race-ethnicity in nonpregnant women of childbearing age in the National Health and Nutrition Examination Survey, 2001–2002, United States

Characteristics	Folic acid intake		Weighted percentage distribution (95% CI) by folic acid intake category <sup>2</sup>			
	Geometric mean (95% CI) <sup>1</sup>	Median (5%–95% range)	<200 $\mu\text{g}/\text{d}$	200–399 $\mu\text{g}/\text{d}$	400–999 $\mu\text{g}/\text{d}$	$\geq 1000 \mu\text{g}/\text{d}$
	$\mu\text{g}/\text{d}$			%		
All races-ethnicities						
Age group						
15–34 y	144 (133, 156) [1095] <sup>3,4</sup>	145 (28–545) [1095]	62.7 (58.7, 66.6) [703]	27.1 (23.2, 31.3) [291]	8.7 (5.8, 13.0) [87]	1.5 (0.8, 2.8) [14]
35–49 y	112 (106, 119) [590]	117 (24–410) [590]	79.1 (73.7, 83.6) [472]	15.4 (11.1, 20.9) [92]	5.3 (3.8, 7.5) [24]	0.2 (0.03, 0.9) [2]
Total intake	128 (123, 134) [1685] <sup>5</sup>	131 (25–489) [1685] <sup>5</sup>	70.4 (66.8, 73.7) [1175] <sup>5</sup>	21.6 (17.8, 26.0) [383] <sup>5</sup>	7.1 (5.0, 10.0) [111] <sup>5</sup>	0.9 (0.5, 1.5) [16] <sup>5</sup>
Non-Hispanic white						
Age group						
15–34 y	148 (134, 165) [419]	144 (29–556) [419]	60.4 (53.7, 66.8) [252]	28.7 (23.5, 34.4) [117]	8.9 (5.1, 15.2) [41]	2.0 (1.0, 4.1) [9]
35–49 y	117 (107, 127) [274]	119 (27–462) [274]	77.8 (70.8, 83.5) [215]	15.5 (10.2, 22.9) [41]	6.8 (4.5, 10.1) [18]	0.0 (0.0) [0]
Total intake	133 (124, 142) [693] <sup>5,6</sup>	134 (27–501) [693] <sup>5</sup>	68.9 (63.8, 73.5) [467] <sup>5</sup>	22.2 (17.3, 28.2) [158] <sup>5</sup>	7.9 (5.1, 11.9) [59] <sup>5</sup>	1.0 (0.6, 1.9) [9] <sup>5</sup>
Non-Hispanic black						
Age group						
15–34 y	129 (119, 139) [289]	129 (27–458) [289]	67.4 (61.8, 72.6) [199]	25.4 (20.7, 30.8) [66]	6.4 (3.7, 10.8) [20]	0.8 (0.2, 3.9) [4]
35–49 y	90 (77, 104) [140]	92 (12–343) [140]	83.0 (76.2, 88.2) [117]	14.5 (8.6, 23.5) [20]	1.6 (0.3, 7.1) [2]	0.9 (0.1, 6.2) [1]
Total intake	109 (100, 118) [429] <sup>5</sup>	111 (19–398) [429] <sup>5</sup>	74.7 (70.5, 78.5) [316] <sup>5</sup>	20.3 (16.2, 25.2) [86] <sup>5</sup>	4.1 (2.3, 7.3) [22] <sup>5</sup>	0.9 (0.3, 2.8) [5] <sup>5</sup>
Hispanic						
Age group						
15–34 y	141 (124, 160) [387]	157 (26–501) [387]	67.4 (56.9, 76.3) [252]	22.8 (14.9, 33.1) [108]	9.8 (5.9, 15.8) [26]	0.1 (0.02, 0.9) [1]
35–49 y	115 (96, 138) [176]	125 (16–292) [176]	82.3 (69.6, 90.4) [140]	15.7 (8.0, 28.6) [31]	1.6 (0.4, 6.8) [4]	0.4 (0.04, 3.2) [1]
Total intake	128 (115, 143) [563] <sup>5</sup>	145 (21–453) [563] <sup>5</sup>	73.2 (63.7, 81.0) [392] <sup>5</sup>	20.0 (13.4, 28.7) [139] <sup>5</sup>	6.6 (3.6, 11.6) [30] <sup>5</sup>	0.2 (0.04, 1.1) [2] <sup>5</sup>

<sup>1</sup> Adjusted for age group ( $P < 0.001$ ), race-ethnicity ( $P = 0.005$ ), and age-by-race interaction ( $P = 0.439$ ); 2-tailed  $t$  test was used in the linear regression model to test differences in adjusted geometric means between age group within each race-ethnicity group and between race-ethnicity groups.  $P$  value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>2</sup> Two-tailed  $t$  test was conducted in logistic regression model to test the difference in proportion of women who consumed  $\geq 400 \mu\text{g}$  folic acid/d from fortified foods by race-ethnicity, and  $P$  value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>3</sup> Significantly different from women aged 35–49 y,  $P < 0.001$ .

<sup>4</sup>  $n$  in brackets (all such values).

<sup>5</sup> Total  $n$  in brackets.

<sup>6</sup> Significantly different from non-Hispanic black women,  $P = 0.006$  (Bonferroni-adjusted).

$\geq 400 \mu\text{g}$  folic acid/d from fortified foods; the breakdown by race-ethnicity was 5.0% in non-Hispanic black women ( $P = 0.180$  compared with non-Hispanic white women), 6.8% in Hispanic women ( $P = 0.267$  compared with non-Hispanic white women), and 8.9% in non-Hispanic white women. The average estimated daily folic acid intake from fortified foods was significantly ( $P < 0.001$ ) higher in younger women (aged 15–34 y) than in older women (aged 35–49 y).

A second source of folic acid consumption was dietary supplements. Twenty-six percent of the women surveyed reported taking, on average,  $\geq 400 \mu\text{g}$  folic acid/d from supplements in the previous month (Table 2). The proportion of women who consumed an average of  $\geq 400 \mu\text{g}$  folic acid/d from supplements was significantly ( $P < 0.001$ ) lower in Hispanic women (13.1%) and non-Hispanic black women (14.0%) than in non-Hispanic white women (31.4%).

The adjusted geometric mean, median, and distribution of estimated total daily folic acid intake from fortified foods and folic acid-containing supplements in women by age and race-ethnicity are shown in Table 3. The average estimated daily total folic acid intake was 221  $\mu\text{g}$ . Compared with the intakes of non-Hispanic white women (253  $\mu\text{g}/\text{d}$ ), the intakes of non-Hispanic black women (147  $\mu\text{g}/\text{d}$ ) were 41.7% lower ( $P < 0.001$ ), and the intakes of Hispanic women (175  $\mu\text{g}/\text{d}$ ) were 30.8% lower ( $P = 0.006$ ). Nineteen percent (19.1%) of non-Hispanic black women and 21.0% of Hispanic women reported

consuming daily  $\geq 400 \mu\text{g}$  folic acid from fortified foods and supplements; a significantly ( $P < 0.001$ ) higher proportion (40.5%) of non-Hispanic white women reported that level of consumption. Overall, there were no significant differences between age groups ( $P = 0.184$ ).

The source of folic acid for non-Hispanic white women was split almost evenly between fortified foods and supplements (Figure 1). The most striking difference in the folic acid intake of non-Hispanic black, Hispanic, and non-Hispanic white women was the amount obtained from supplements. On average, non-Hispanic black and Hispanic women obtained  $\approx 26\%$  and non-Hispanic white women obtained 47.5% of their folic acid intake from supplements. These differences were highly significant ( $P < 0.001$ ).

A third source of folate (not folic acid) consumption was dietary folate. Women of childbearing age consumed daily an average of 151  $\mu\text{g}$  of dietary folate from foods (Table 4), with 95.2% of women consuming  $< 400 \mu\text{g}/\text{d}$ . In contrast to folic acid intake from fortified foods, the average daily food folate intake was significantly higher in older women than in younger women ( $P = 0.005$ ).

## DISCUSSION

Despite both the IOM recommendation that women of reproductive age consume 400  $\mu\text{g}$  folic acid/d and the FDA's mandate

TABLE 2

Folic acid intake reported in the previous month from folic acid–containing supplements alone by average daily amount consumed, age, and race-ethnicity in nonpregnant women of childbearing age in the National Health and Nutrition Examination Survey, 2001–2002, United States<sup>1</sup>

Characteristics	Weighted percentage distribution (95% CI) by average folic acid intake category		
	None	<400 $\mu\text{g}/\text{d}$	$\geq 400 \mu\text{g}/\text{d}$
		%	
All races-ethnicities			
Age group			
15–34 y	69.1 (63.5, 74.2) [867] <sup>2</sup>	8.0 (5.6, 11.4) [73]	22.9 (19.1, 27.2) [155]
35–49 y	56.8 (51.6, 61.9) [375]	13.7 (10.7, 17.4) [66]	29.5 (25.2, 34.1) [149]
Total intake	63.3 (60.2, 66.4) [1242] <sup>3</sup>	10.7 (8.6, 13.3) [139] <sup>3</sup>	26.0 (23.1, 29.0) [304] <sup>3</sup>
Non-Hispanic white			
Age group			
15–34 y	62.3 (53.9, 69.9) [281]	9.4 (6.1, 14.3) [41]	28.3 (23.3, 34.0) [97]
35–49 y	49.6 (42.4, 56.9) [139]	15.7 (11.8, 20.5) [42]	34.7 (29.1, 40.8) [93]
Total intake	56.1 (51.5, 60.6) [420] <sup>3</sup>	12.5 (10.0, 15.5) [83] <sup>3</sup>	31.4 (27.5, 35.6) [190] <sup>3,4</sup>
Non-Hispanic black			
Age group			
15–34 y	82.3 (72.9, 89.0) [253]	4.7 (2.0, 10.8) [10]	13.0 (7.7, 21.1) [26]
35–49 y	78.9 (67.5, 87.1) [111]	6.1 (3.6, 10.1) [8]	15.1 (8.9, 24.4) [21]
Total intake	80.7 (74.1, 86.0) [364] <sup>3</sup>	5.3 (3.0, 9.3) [18] <sup>3</sup>	14.0 (10.3, 18.6) [47] <sup>3,4</sup>
Hispanic			
Age group			
15–34 y	83.5 (76.3, 88.9) [333]	5.6 (2.8, 11.0) [22]	10.9 (5.4, 20.6) [32]
35–49 y	72.4 (64.1, 79.5) [125]	11.0 (5.2, 21.7) [16]	16.6 (9.7, 26.8) [35]
Total intake	79.2 (73.5, 83.9) [458] <sup>3</sup>	7.7 (4.6, 12.7) [38] <sup>3</sup>	13.1 (8.1, 20.6) [67] <sup>3,4</sup>

<sup>1</sup> Two-tailed *t* test was conducted in logistic regression model, adjusted for age group ( $P = 0.0514$ ), race-ethnicity ( $P < 0.001$ ), and age-by-race interaction ( $P = 0.8741$ ), to test the difference in percentage of dietary supplements use between age group within each race-ethnicity group and between race-ethnicity groups. *P* value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>2</sup> *n* in brackets (all such values).

<sup>3</sup> Total *n* in brackets.

<sup>4</sup> Significantly different between non-Hispanic white, non-Hispanic black, and Hispanic women,  $P < 0.001$  (Bonferroni-adjusted).

of folic acid fortification of enriched cereal-grain products, approximately two-thirds of US women of reproductive age continue to report consuming less than the amount recommended by the IOM. Of those women who did consume  $\geq 400 \mu\text{g}$  folic acid/d, 76% used folic acid–containing supplements. Moreover, the proportion of women who daily consumed  $\geq 400 \mu\text{g}$  folic acid from fortified foods or supplements (or both) varied significantly by race-ethnicity, ranging from 19.1% in non-Hispanic black women to 21.0% in Hispanic women and 40.5% in non-Hispanic white women. These findings are consistent with a recent study suggesting that the total folate intake of women of reproductive age after folic acid fortification in the United States varied significantly by age and race-ethnicity (24).

There are several potential sources of imprecision in the estimates of dietary folate and folic acid intake used in our study. Although NHANES 2001–2002 used the most recent USDA Food and Nutrient Database for Dietary Studies to calculate intakes, the accuracy of folic acid intakes estimated from consumption of fortified food has not been independently validated. There is some evidence that the actual amount of folic acid in fortified foods may differ from that required by FDA, and this difference may lead to underestimates of folic acid intake (10–13).

NHANES provides nutrient intakes from a single 24-h recall of food consumption. Estimates from a single day may not be representative of a woman's usual folate consumption, and multiple days of food records would provide more stable estimates (25, 26). A second day's subsample of 24-h food recalls was

included in the 2002 NHANES data; however, this information is not publicly available and was not used in this analysis. Because our data are from a single 24-h recall and may not truly reflect a woman's usual intake, they should be interpreted cautiously.

Approximately 18% of women who reported taking folic acid–containing supplements in the previous month had missing information on frequency of use. When our analyses were restricted to include data only on participants with complete supplement use information, the geometric mean and distribution of folic acid intake were unchanged (data not shown).

Our calculation of adjusted geometric mean daily folic acid intake from fortified foods in US women of childbearing age—128  $\mu\text{g}$ —was slightly greater than the estimated intake in some studies (7, 9, 10) and substantially less than that of others (11–13, 27). Sensitivity analysis (see Appendix) indicated that potential underestimates of folic acid intake from fortified foods would affect the values estimated for women with lower folic acid intakes more than it would affect the values for women who had higher folic acid intakes. For example, if the folic acid intake from fortified foods was 25% higher than that calculated from the USDA Food and Nutrient Database, the percentage of women who consumed  $< 200 \mu\text{g}$  folic acid/d from fortified foods decreased from 70.4% (95% CI: 66.8%, 73.7%) to 60.3% (56.9%, 65.5%). In contrast, the percentage of women who consumed  $\geq 400 \mu\text{g}/\text{d}$  increased from 8.0% (5.8%, 11.0%) to 12.5% (9.9%, 15.5%) (see Appendix).

**TABLE 3**

Average total folic acid intake from fortified foods plus folic acid–containing supplements by age and race-ethnicity in nonpregnant women of childbearing age in the National Health and Nutrition Examination Survey, 2001–2002, United States

Characteristics	Folic acid intake		Weighted percentage distribution (95% CI) by total folic acid intake category <sup>2</sup>			
	Geometric mean (95% CI) <sup>2</sup>	Median (5%–95% range)	<200 µg/d	200–399 µg/d	400–999 µg/d	≥1000 µg/d
	µg/d		%			
<b>All races-ethnicities</b>						
Age group						
15–34 y	225 (203, 249) [1095] <sup>3</sup>	215 (36–1047) [1095]	45.9 (41.9, 50.0) [579]	22.3 (18.4, 26.8) [264]	24.8 (20.3, 30.0) [207]	7.0 (5.0, 9.6) [45]
35–49 y	217 (198, 238) [590]	220 (31–906) [590]	46.9 (41.8, 52.1) [313]	15.9 (12.8, 19.6) [93]	33.0 (29.4, 36.7) [166]	4.2 (2.4, 7.3) [18]
Total intake	221 (209, 232) [1685] <sup>4</sup>	217 (35–1020) [1685] <sup>4</sup>	46.4 (43.2, 49.6) [892] <sup>4</sup>	19.3 (16.3, 22.8) [357] <sup>4</sup>	28.6 (25.4, 32.1) [373] <sup>4</sup>	5.7 (4.0, 8.1) [63] <sup>4</sup>
<b>Non-Hispanic white</b>						
Age group						
15–34 y	252 (220, 288) [419]	252 (40–1075) [419]	40.3 (33.7, 47.2) [177]	22.3 (17.3, 28.2) [96]	28.1 (21.2, 36.1) [114]	9.4 (6.7, 13.0) [32]
35–49 y	255 (227, 286) [274]	309 (44–1043) [274]	40.5 (33.6, 47.7) [115]	15.8 (12.2, 20.1) [42]	38.4 (33.4, 43.6) [103]	5.4 (3.0, 9.5) [14]
Total intake	253 (233, 275) [693] <sup>4,6</sup>	268 (43–1058) [693] <sup>4</sup>	40.3 (35.5, 45.4) [292] <sup>4</sup>	19.1 (15.2, 23.8) [138] <sup>4</sup>	33.1 (28.4, 38.1) [217] <sup>4,7</sup>	7.4 (5.1, 10.7) [46] <sup>4</sup>
<b>Non-Hispanic black</b>						
Age group						
15–34 y	167 (144, 193) [289]	148 (35–835) [289]	58.3 (50.6, 65.6) [181]	21.8 (18.3, 25.8) [60]	17.4 (11.7, 25.1) [40]	2.5 (1.0, 6.0) [8]
35–49 y	128 (110, 150) [140]	118 (17–632) [140]	65.9 (55.9, 74.7) [94]	15.8 (10.3, 23.6) [21]	16.6 (10.2, 25.9) [23]	1.6 (0.4, 6.4) [2]
Total intake	147 (135, 160) [429] <sup>4</sup>	136 (21–790) [429] <sup>4</sup>	61.9 (55.7, 67.7) [275] <sup>4</sup>	19.0 (15.6, 22.9) [81] <sup>4</sup>	17.0 (13.3, 21.6) [63] <sup>4,7</sup>	2.1 (1.0, 4.5) [10] <sup>4</sup>
<b>Hispanic</b>						
Age group						
15–34 y	179 (147, 217) [387]	185 (27–823) [387]	56.8 (42.9, 69.7) [221]	22.6 (15.6, 31.5) [108]	18.9 (11.9, 28.7) [53]	1.8 (0.4, 7.1) [5]
35–49 y	170 (135, 214) [176]	172 (15–614) [176]	61.9 (49.8, 72.8) [104]	16.6 (9.3, 28.0) [30]	20.7 (14.5, 28.5) [40]	0.8 (0.1, 4.0) [2]
Total intake	175 (147, 208) [563] <sup>4</sup>	177 (25–824) [563] <sup>4</sup>	58.8 (47.9, 68.9) [325] <sup>4</sup>	20.3 (14.5, 27.6) [138] <sup>4</sup>	19.6 (14.3, 26.2) [93] <sup>4,7</sup>	1.4 (0.4, 4.5) [7] <sup>4</sup>

<sup>1</sup> Two-tailed *t* test was conducted in logistic regression model to test the difference in proportion of women who consumed ≥400 µg total folic acid/d from fortified foods plus folic acid–containing supplement use between race-ethnicity groups. *P* value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>2</sup> Geometric mean was adjusted for age group (*P* = 0.660), race-ethnicity (*P* = 0.001), and age-by-race interaction (*P* = 0.084); 2-tailed *t* test was used in linear regression model to test difference in adjusted geometric means between age groups within each race-ethnicity group and between race-ethnicity groups. *P* value was adjusted by Bonferroni correction to account for multiple comparisons.

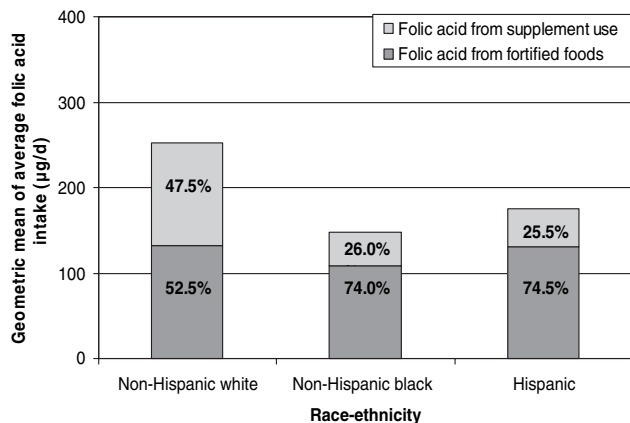
<sup>3</sup> *n* in brackets (all such values).

<sup>4</sup> Total *n* in brackets.

<sup>5</sup> Significantly different from non-Hispanic black women, *P* < 0.001 (Bonferroni-adjusted).

<sup>6</sup> Significantly different from non-Hispanic black women, *P* = 0.006 (Bonferroni-adjusted).

<sup>7</sup> Significantly different between non-Hispanic black, non-Hispanic white, and Hispanic women at consumption levels of ≥400 µg/d, *P* < 0.001 (Bonferroni-adjusted).



**FIGURE 1.** Weighted and adjusted geometric mean and composition of folic acid intake by race-ethnicity among nonpregnant women of childbearing age, National Health and Nutrition Examination Survey, 2001–2002, USA. The numbers given inside each bar indicate the percentage of folic acid from fortified foods and the percentage from use of dietary supplements. A 2-tailed *t* test was conducted to test the difference in percentage of folic acid intake from use of dietary supplements by race-ethnicity group, and *P* value was adjusted by Bonferroni correction to account for multiple comparisons. The percentage of folic acid intake from use of dietary supplements among non-Hispanic white women was significantly higher than that among non-Hispanic black and Hispanic women, Bonferroni adjusted *P* < 0.001.

We found significant differences in the average daily folic acid intake from fortified foods between non-Hispanic black and non-Hispanic white women. The low proportion of non-Hispanic black women who consumed the recommended amount of folic acid from all sources may explain the absence of a significant reduction in the prevalence of spina bifida and anencephaly in the newborns of non-Hispanic black women participating in a recent study (19). Women who were 15–34 y old were also more likely to consume fortified foods than were women aged 35–49 y. This difference could be due to an increased consumption of ready-to-eat cereals by 15–34 y-old women. The USDA’s 1994–1996 Continuing Survey of Food Intakes by Individuals found that women who were 12–29 y old had higher intakes of ready-to-eat cereals than did women who were 30–49 y old (28). Ready-to-eat cereals were the third-highest contributor to total folate intake in NHANES 1999–2000 (14). Fortification at 140 µg folic acid/100 g enriched cereal-grain product enabled ≈8% of women to obtain the recommended daily intake of folic acid (≥400 µg) from fortified foods alone (Table 1).

Taking supplements was the most important factor in achieving the recommended daily folic acid intake for women of childbearing age, but the rate of supplement use was lower among non-Hispanic black women (19.3%) and Hispanic women (20.8%) than among non-Hispanic white women (43.9%) (Table 2). This difference in folic acid supplement use accounted for 78% of the difference in total folic acid intake between

TABLE 4

Food folate intake alone by age and race-ethnicity in nonpregnant women of childbearing age in the National Health and Nutrition Examination Survey, 2001-2002, United States

Characteristics	Food folate intake		Weighted percentage distribution (95% CI) by food folate intake category <sup>1</sup>			
	Geometric mean (95% CI) <sup>2</sup>	Median (5%–95% range)	<200 μg/d	200–399 μg/d	400–999 μg/d	≥1000 μg/d
	μg/d		%			
All races-ethnicities						
Age group						
15–34 y	142 (131, 154) [1095] <sup>3</sup>	143 (46–360) [1095]	69.2 (62.3, 75.4) [776]	27.6 (22.5, 33.4) [288]	3.2 (1.8, 5.5) [31]	0.0 (0.0) [0]
35–49 y	162 (154, 171) [590] <sup>4</sup>	167 (56–438) [590]	64.1 (60.1, 67.9) [380]	29.2 (25.3, 33.5) [170]	6.3 (4.3, 9.3) [36]	0.4 (0.1, 1.6) [4]
Total intake	151 (144, 159) [1685] <sup>5</sup>	152 (49–392) [1685] <sup>5</sup>	66.8 (62.9, 70.6) [1156] <sup>5</sup>	28.4 (24.9, 32.1) [458] <sup>5</sup>	4.6 (3.6, 5.9) [67] <sup>5</sup>	0.2 (0.04, 0.7) [4] <sup>5</sup>
Non-Hispanic white						
Age group						
15–34 y	145 (132, 161) [419]	146 (46–365) [419]	66.9 (57.8, 74.9) [290]	30.1 (23.6, 37.6) [117]	3.0 (1.4, 6.4) [12]	0.0 (0.0) [0]
35–49 y	171 (160, 182) [274]	173 (59–435) [274]	62.2 (56.7, 67.3) [172]	30.9 (26.1, 36.1) [82]	7.0 (4.4, 11.0) [20]	0.0 (0.0) [0]
Total intake	157 (147, 167) [693] <sup>5,6</sup>	158 (52–393) [693] <sup>5</sup>	64.6 (59.3, 69.5) [462] <sup>5</sup>	30.5 (26.1, 35.2) [199] <sup>5</sup>	4.9 (3.5, 7.0) [32] <sup>5</sup>	0.0 (0.0) [0] <sup>5</sup>
Non-Hispanic black						
Age group						
15–34 y	123 (110, 137) [289]	123 (38–332) [289]	75.5 (64.0, 84.2) [219]	23.5 (15.2, 34.4) [65]	1.1 (0.3, 3.3) [5]	0.0 (0.0) [0]
35–49 y	139 (126, 153) [140]	132 (38–528) [140]	71.0 (64.2, 76.9) [99]	21.9 (17.1, 27.6) [31]	4.5 (1.9, 10.1) [6]	2.6 (0.8, 8.8) [4]
Total intake	130 (120, 141) [429] <sup>5</sup>	128 (39–366) [429] <sup>5</sup>	73.4 (66.4, 79.3) [318] <sup>5</sup>	22.7 (17.5, 29.1) [96] <sup>5</sup>	2.7 (1.4, 5.1) [11] <sup>5</sup>	1.2 (0.4, 4.2) [4] <sup>5</sup>
Hispanic						
Age group						
15–34 y	143 (129, 159) [387]	142 (57–396) [387]	73.0 (65.4, 79.4) [267]	21.8 (16.0, 29.0) [106]	5.2 (2.7, 9.8) [14]	0.0 (0.0) [0]
35–49 y	150 (136, 165) [176]	152 (56–387) [176]	67.5 (51.7, 80.2) [109]	27.8 (17.1, 41.9) [57]	4.7 (1.9, 11.1) [10]	0.0 (0.0) [0]
Total intake	146 (136, 158) [563] <sup>5</sup>	147 (57–395) [563] <sup>5</sup>	70.8 (63.2, 77.5) [376] <sup>5</sup>	24.2 (18.9, 30.4) [163] <sup>5</sup>	5.0 (2.7, 9.8) [24] <sup>5</sup>	0.0 (0.0) [0] <sup>5</sup>

<sup>1</sup> Two-tailed *t* test was conducted in logistic regression model to test the difference in proportion of women who consumed  $\geq 400$  μg food folate/d from foods between race-ethnicity groups, and *P* value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>2</sup> Geometric mean was adjusted for age group (*P* = 0.005), race-ethnicity (*P* = 0.003), and age-by-race interaction (*P* = 0.409); 2-tailed *t* test was used in linear regression model to test difference in adjusted geometric means between age group within each race-ethnicity group and between race-ethnicity groups. *P* value was adjusted by Bonferroni correction to account for multiple comparisons.

<sup>3</sup> *n* in brackets (all such values).

<sup>4</sup> Significantly different from women aged 15–34 y, *P* = 0.005.

<sup>5</sup> Total *n* in brackets.

<sup>6</sup> Significantly different from non-Hispanic black women, *P* = 0.002 (Bonferroni-adjusted).

non-Hispanic black and non-Hispanic white women and for 98% of the difference between Hispanic and non-Hispanic white women (Tables 1 and 3). Because folic acid from supplements was the largest contributor to folic acid intake, the racial and ethnic differences in supplement use may have been key factors in determining whether women consumed adequate amounts of folic acid every day.


We found that 5.7% of all women of childbearing age in the United States reported consuming supplements and fortified foods that provided  $>1000$  μg folic acid/d, the tolerable upper level (UL) set by the IOM (Table 3). The UL is the highest usual intake of a nutrient that poses no risk of adverse effects (29). The IOM established the UL for folic acid intake at 1000 μg/d to ensure that persons with undiagnosed vitamin B-12 deficiency would have no risk of developing neurologic complications (6). On the basis of multiple case reports of persons with pernicious anemia, the IOM determined that the lowest observed adverse effect level (known as LOAEL) for individual consumption of folic acid was 5000 μg/d, and the UL was arbitrarily set at one-fifth of that value. The IOM also noted that the prevalence of vitamin B-12 deficiency among women of childbearing age was very low and that consuming folic acid at or above the UL is unlikely to have adverse effects (6). Additional studies have discussed other potential benefits and risks of folic acid in relation to several types of cancer, cardiovascular disease, stroke,

dementia, and osteoporosis (30–39). However, further research is needed to determine the range of folic acid intake that provides optimal overall health benefits for the population as a whole.

The IOM has recommended that all women of childbearing age consume 400 μg/d of folic acid from supplements, fortified foods, or both, in addition to the food folates contained in a varied diet (6). Our combined estimates of folic acid from fortified foods (128 μg/d) and dietary folate (151 μg/d) are similar to those reported for total folate intake (dietary folate and fortified foods) from NHANES 1999–2000 (292 μg/d) (14). Nevertheless, NHANES 2001–2002 data indicate that only one-third of women in the United States are meeting the IOM recommendation and that only 8% of women do so through consumption of fortified foods alone. In addition, a large disparity was found among the racial-ethnic groups, with 40.5% of non-Hispanic white women but only 19.1% of non-Hispanic black women and 21% of Hispanic women meeting the recommendations.

Nearly half of the pregnancies that occur in the United States are unintended (40), and the use of folic acid supplements is significantly lower among women with unintended pregnancies than among those with planned pregnancies (41). Fortification helps women of childbearing age to increase their folic acid intake and prevent the occurrence of NTDs in their infants. However, with the present level of fortification, approximately

two-thirds of nonpregnant American women of childbearing age are not consuming the recommended amount of folic acid. Low consumption is a greater problem among Hispanic and non-Hispanic black women than among non-Hispanic white women. Hispanic women have the highest prevalence and non-Hispanic black women have the lowest prevalence of NTD-affected pregnancies (19). These differences in NTD prevalence must involve genetic or environmental factors in addition to the differences in folic acid intake that we observed.

Although average serum folate concentrations have more than doubled, and red blood cell folate concentration has increased by 59% across race-ethnicity groups after folic acid fortification in the United States (16, 17), our findings show that most women need to consume a supplement to obtain the recommended amount of folic acid every day. To meet the *Healthy People 2010* goals (Objectives 16-15 and 16-16a) of reducing NTDs by 50% and increasing the proportion of nonpregnant 15–44-y-old women who consume 400  $\mu\text{g}$  folic acid/d to 80% (42), public health programs should continue to encourage women of reproductive age to take dietary supplements containing folic acid. These programs should target younger women and especially Hispanic and non-Hispanic black women, to reduce their risks of having a pregnancy that is affected by spina bifida or anencephaly. 

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### Appendix A

Sensitivity analysis of effect of increasing folic acid content of fortified foods by 10% or 25% over that estimated from the survey on folic acid intake from fortified foods alone, by age and race-ethnicity in all nonpregnant women of childbearing age (15–49 y old) in the National Health and Nutrition Examination Survey (NHANES), 2001–2002, United States

Characteristics	Folic acid intake		Weighted percentage distribution (95% CI) by folic acid intake category			
	Geometric mean (95% CI) <sup>1</sup>	Median (5%–95% range)	<200 µg/d	200–399 µg/d	400–999 µg/d	≥1000 µg/d
	µg/d		%			
All races-ethnicities						
Observed	128 (123, 134) [1685] <sup>2</sup>	131 (25–489) [1685]	70.4 (66.8, 73.7) [1175]	21.6 (17.8, 26.0) [383]	7.1 (5.0, 10.0) [111]	0.9 (0.5, 1.5) [16]
10% higher than observed	141 (135, 147) [1685]	144 (27–438) [1685]	66.7 (62.9, 70.4) [1105]	23.6 (19.6, 28.2) [422]	8.7 (6.3, 11.8) [140]	1.0 (0.5, 1.9) [4]
25% higher than observed	160 (154, 167) [1685]	164 (31–611) [1685]	60.3 (56.9, 63.5) [997]	27.3 (23.5, 31.4) [475]	11.2 (8.8, 14.0) [191]	1.3 (0.7, 2.6) [22]
Non-Hispanic white						
Observed	133 (124, 142) [693]	134 (27–501) [693]	68.9 (63.8, 73.5) [467]	22.2 (17.3, 28.2) [158]	7.9 (5.1, 11.9) [59]	1.0 (0.6, 1.9) [9]
10% higher than observed	146 (136, 156) [693]	148 (30–551) [693]	66.0 (60.6, 71.0) [448]	23.8 (18.5, 30.1) [168]	9.0 (6.2, 12.9) [67]	1.2 (0.6, 2.5) [10]
25% higher than observed	166 (155, 177) [693]	168 (34–627) [693]	60.0 (55.0, 64.7) [410]	27.1 (22.2, 32.6) [185]	11.4 (8.7, 14.9) [86]	1.6 (0.7, 3.4) [12]
Non-Hispanic black						
Observed	109 (100, 118) [429]	111 (19–398) [429]	74.7 (70.5, 78.5) [316]	20.3 (16.2, 25.2) [86]	4.1 (2.3, 7.3) [22]	0.9 (0.3, 2.8) [5]
10% higher than observed	120 (110, 130) [429]	122 (21–438) [429]	71.2 (66.4, 75.6) [302]	21.3 (16.5, 26.9) [90]	6.7 (4.4, 10.0) [32]	0.9 (0.3, 2.8) [5]
25% higher than observed	136 (125, 148) [429]	139 (24–498) [429]	67.0 (62.9, 70.8) [283]	22.1 (17.4, 27.6) [96]	9.7 (6.5, 14.2) [43]	1.3 (0.5, 3.5) [7]
Hispanic						
Observed	128 (115, 143) [563]	145 (21–453) [563]	73.2 (63.7, 81.0) [392]	20.0 (13.4, 28.7) [139]	6.6 (3.6, 11.6) [30]	0.2 (0.04, 1.1) [2]
10% higher than observed	141 (126, 157) [563]	160 (23–499) [563]	66.1 (57.7, 73.6) [355]	24.7 (18.9, 31.4) [164]	9.0 (5.1, 15.3) [41]	0.3 (0.06, 1.0) [3]
25% higher than observed	160 (143, 179) [563]	181 (26–567) [563]	56.2 (50.0, 62.3) [304]	32.3 (27.3, 37.2) [194]	11.3 (7.0, 17.7) [62]	0.3 (0.06, 1.0) [3]

<sup>1</sup> Geometric mean was adjusted for age group ( $P < 0.001$ ), race-ethnicity ( $P = 0.005$ ), and age-by-race interaction ( $P = 0.439$ ). “Observed” values represent the estimates of folic acid intake from fortified foods provided by the NHANES 2001–2002 datasets; 10% higher than observed assumed that each woman’s folic acid intake from fortified foods was 10% higher than the observed value, and 25% higher than observed assumed that each woman’s folic acid intake from fortified foods was 25% higher than the observed value.

<sup>2</sup>  $n$  in brackets (all such values).

