

# Folic acid source, usual intake, and folate and vitamin B-12 status in US adults: National Health and Nutrition Examination Survey (NHANES) 2003–2006<sup>1–4</sup>

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## ABSTRACT

**Background:** US adults have access to multiple sources of folic acid. The contribution of these sources to usual intakes above the tolerable upper intake level (UL) (1000  $\mu\text{g}/\text{d}$ ) and to folate and vitamin B-12 status is unknown.

**Objective:** The objective was to estimate usual folic acid intake above the UL and adjusted serum and red blood cell folate, vitamin B-12, methylmalonic acid, and homocysteine concentrations among US adults by 3 major folic acid intake sources—enriched cereal-grain products (ECGP), ready-to-eat cereals (RTE), and supplements (SUP)—categorized into 4 mutually exclusive consumption groups.

**Design:** We used data from the National Health and Nutrition Examination Survey (NHANES) 2003–2006 ( $n = 8258$ ).

**Results:** Overall, 2.7% (95% CI: 1.9%, 3.5%) of adults consumed more than the UL of folic acid. The proportions of those who consumed folic acid from ECGP only, ECGP+RTE, ECGP+SUP, and ECGP+RTE+SUP were 42%, 18%, 25%, and 15%, respectively. Of 60% of adults who did not consume supplements containing folic acid (ECGP only and ECGP+RTE), 0% had intakes that exceeded the UL. Of 34% and 6% of adults who consumed supplements with an average of  $\leq 400$  and  $> 400$   $\mu\text{g}$  folic acid/d,  $< 1\%$  and 47.8% (95% CI: 39.6%, 56.0%), respectively, had intakes that exceeded the UL. Consumption of RTE and/or supplements with folic acid was associated with higher folate and vitamin B-12 and lower homocysteine concentrations, and consumption of supplements with vitamin B-12 was associated with lower methylmalonic acid concentrations ( $P < 0.001$ ).

**Conclusion:** At current fortification levels, US adults who do not consume supplements or who consume an average of  $\leq 400$   $\mu\text{g}$  folic acid/d from supplements are unlikely to exceed the UL in intake for folic acid. *Am J Clin Nutr* 2010;91:64–72.

## INTRODUCTION

Rates of neural tube defects declined in conjunction with the full implementation of fortification of enriched cereal-grain products (ECGP) with 140  $\mu\text{g}$  folic acid/100 g flour in the United States in 1998 (1–5). Serum folate concentrations for all segments of the US population more than doubled between 1988–1994 and 1999–2004 (6). This raised the question of whether or not some subgroups might exceed the tolerable upper intake level (UL) for folic acid, ie, 1000  $\mu\text{g}/\text{d}$  for adults aged  $\geq 19$  y. The UL, which is the highest usual intake level of a nutrient that

is likely to pose no risk of adverse effects in healthy persons, was set by the Institute of Medicine to ensure that the diagnosis of macrocytic anemia due to vitamin B-12 deficiency would not be masked by excess intake of folate from fortified foods or supplements (ie, folic acid) and lead to delays in treatment and an increased risk of developing neurologic complications (7).

During the postfortification era, US adults can consume multiple sources of folic acid, eg, ECGP, ready-to-eat cereals (RTE), and supplements (SUP). The prevalence of US adults whose usual intake exceeds the UL is unknown. Previous studies used one 24-h dietary recall (8) or average data from multiple dietary recalls (9), both of which can bias the estimate of the proportion of adults who exceed 1000  $\mu\text{g}/\text{d}$  (10, 11). One study adjusted for within-individual variation in dietary intake, but estimated total folate, rather than folic acid, intake (12). Data on the associations of source of folic acid with folate and vitamin B-12 status are limited to small nonrepresentative populations or to intake of either dietary or supplement sources of folic acid, but not both (9, 13–15). Results from a previous investigation in US adults in 2001–2004 suggest that the average consumption of folic acid from supplements and from RTE was positively and strongly associated with quintiles of serum folate concentrations (16). In the present study, we determined the proportions of the US adults in 2003–2006 with usual intakes that exceeded the UL and folate and vitamin B-12 status by source of folic acid intake.

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<sup>3</sup> The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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## SUBJECTS AND METHODS

### Study population

Data were obtained from the National Health and Nutrition Examination Survey (NHANES), a stratified multistage probability survey designed to represent the civilian, noninstitutionalized US population. Data for NHANES were collected by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC) via household interviews and physical examinations. Detailed information is available elsewhere (17, 18). The survey was reviewed and approved by the NCHS ethics review board, and participants provided written informed consent before participation. The nonpregnant adult populations aged  $\geq 19$  y from NHANES 2003–2004 and 2005–2006 were selected for this evaluation because the UL for daily folic acid intake is the same for all nonpregnant adults (1000  $\mu\text{g}/\text{d}$ ) (7), and two 24-h dietary recalls were available on survey participants (17, 18).

The overall unweighted examination response rates for adults in NHANES 2003–2004 and 2005–2006 were 69% and 71%, respectively, calculated as the number of examined adults divided by the total number selected for the sample (19, 20). Of the nonpregnant adults aged  $\geq 19$  y who attended the medical examination center (MEC) ( $n = 9478$ ), we excluded 584 participants with incomplete data on the first or second 24-h dietary recall, ie, did not meet the minimum acceptable standards for data quality. We then excluded 627 who were missing information on the second 24-h dietary recall such that we could not code their consumption of RTE with folic acid (*see below*). We excluded an additional 9 who were missing information on use of supplements containing folic acid, which left 8258 participants for analyses.

For the analyses of folate and vitamin B-12 status, we excluded an additional 778 participants who were missing information on serum folate, red blood cell (RBC) folate, or vitamin B-12 concentrations, which left 7480 adults. Finally, methylmalonic acid (MMA) concentrations were not analyzed for NHANES 2005–2006; thus, we present results for MMA concentrations in 3638 participants in NHANES 2003–2004.

### Intakes of folic acid, vitamin B-12, and natural food folate

Information on dietary intake of foods was obtained from two 24-h dietary recalls from NHANES 2003–2004 and 2005–2006. Dietary intake data for day 1 was collected in person in the MEC, and data for day 2 were obtained by telephone 3–10 d later. For NHANES 2003–2004 and 2005–2006, the intake of nutrients [ie, natural food folate, folic acid, and vitamin B-12 (vitamin B-12 includes intake from natural and synthetic sources)] from foods was estimated by using the most current US Department of Agriculture (USDA) Food and Nutrient Databases for Dietary Studies (FNDDS version 2 and FNDDS version 3, respectively) (21, 22). Estimates of folic acid intake are reported in micrograms and were not converted to micrograms of Dietary Folate Equivalents, which adjusts for the higher bioavailability of folic acid than of natural food folate.

The individual food file for each 24-h dietary recall contains the estimated nutrient consumption for every food reported by every participant. From these files, we selected participants who reported consumption of at least one food coded as an RTE (food

codes 57000000–57418000). For each of these participants, we summed the amount of folic acid consumed from RTE in the previous 24 h. A small percentage of participants (<2%) consumed RTE that did not contain folic acid. Participants who reported consumption of RTE that contained folic acid on either day of the two 24-h dietary recalls were classified as consumers of RTE with folic acid.

During the household interviews, participants were asked about their use of dietary supplements during the past 30 d. For each supplement, the participant was asked the number of days of consumption and the quantity consumed per day. The interviewer recorded the name of each product and matched it to a list. After the survey, trained nutritionists obtained label information and determined ingredients and serving size (ie, tablets or ounces per dose). A participant was classified as a consumer of supplements containing folic acid if he or she reported consuming any supplement with folic acid during the past 30 d. For each individual, the amount of nutrients was summed across all supplements with folic acid consumed and divided by 30 to yield the average daily amount of supplemental nutrients. The total nutrient intake on each day was calculated as the amount of nutrients from foods on that day plus the average daily amount of nutrients from supplements.

### Biochemical measurements of folate and vitamin B-12 status

Serum folate, RBC folate, and serum vitamin B-12 concentrations were measured by Quantaphase II radioassay (Bio-Rad Laboratories, Hercules, CA). Long-term CVs for NHANES 2003–2006 were 4–7% for serum folate concentrations, 4–6% for RBC folate concentrations, and 3–6% for serum vitamin B-12 concentrations (6). Plasma homocysteine concentrations were measured by a fully automated fluorescence polarization immunoassay on the Abbott AxSym system (Abbott Laboratories, Abbott Park, IL) from 2003 to 2006 (23, 24). Plasma MMA concentrations were measured by gas chromatography–mass spectrometry with cyclohexanol derivatization (23). We arbitrarily defined high serum folate concentration as  $>20$  ng/mL based on the highest calibration point in the Bio-Rad assays before protein diluent is needed, which was similar to the 95th percentile for the US population before fortification, ie, 17 ng/mL (1). We arbitrarily defined vitamin B-12 depletion as  $<300$  pg/mL. Not considered to indicate deficiency, this threshold can indicate the need for further investigation of vitamin B-12 deficiency with MMA and homocysteine (7, 25).

### Covariates

Questionnaire information included sex, age, race-ethnicity, and smoking status. Race-ethnicity was reported by participants based on a list that included an open-ended response. Non-Hispanic blacks and Mexican Americans were oversampled in NHANES. For analysis, race-ethnicity was categorized as non-Hispanic white, non-Hispanic black, and Mexican American. Sample sizes for other race-ethnicity groups were too small for meaningful analysis. Smoking status was based on the response to the following question: “Do you now smoke cigarettes?”

Height and weight were measured by using standard protocols and calibrated equipment in the MEC. Body mass index (BMI)

was calculated as weight (in kg) divided by height squared (in m). Day of the week is the day of the week on which the 24-h dietary recall was collected.

### Statistical analyses

Adults were classified into 4 mutually exclusive folic acid consumption groups: 1) fortified foods excluding RTE or supplements (ECGP only), 2) ECGP plus RTE cereals excluding supplements containing folic acid (ECGP+RTE), 3) ECGP (excluding RTE) plus supplements containing folic acid (ECGP+SUP), and 4) ECGP+RTE+SUP. Participants in groups 3 and 4 consumed supplements containing folic acid. Participants in groups 2 and 4 consumed RTE with folic acid. Proportions and 95% CIs of US adults in each folic acid consumption group were estimated overall and by sex, age, and race-ethnicity group.

Distributions [eg, medians and interquartile ranges (IQRs)] of usual folic acid and vitamin B-12 intakes and the prevalence of folic acid consumption  $>1000$   $\mu\text{g}/\text{d}$  overall and by folic acid consumption group were estimated by using data on total usual folic acid intake from both of the 24-h dietary recalls and Software for Intake Distribution Estimation (PC-SIDE version 1.02, 2003; Department of Statistics, Iowa State University) (26–28). Dietary data from a single 24-h dietary recall does not represent usual intake because of the within individual day-to-day variation in diet and may bias the estimates of the proportion of individuals above or below a certain nutrient intake level (10, 11). PC-SIDE requires that at least some of the respondents have multiple days of nutrient values to estimate the within- and between-individual variation (27). A small percentage ( $<1\%$ ) of participants with an initial 24-h dietary recall had incomplete or no data on the second 24-h dietary recall and their values on the second recall were considered “missing.” The usual natural food folate intake was also estimated by folic acid consumption groups and selected sociodemographic characteristics.

In PC-SIDE, all analyses were adjusted for age, sex, race-ethnicity, interview method (in person or by phone), and day of the week. SEs were estimated by using a set of 60 jackknife repeated replication weights with PC-SIDE. Jackknife replication weights were calculated by using a combination of dietary weights based on the second 24-h dietary recall for most of the participants, and dietary weights were based on the first 24-h dietary recall for the few who did not have a second recall. Multiple linear regression models were used to estimate the geometric means (least-squares means) and 95% CIs for serum and RBC folate, homocysteine, vitamin B-12, and MMA concentrations by folic acid consumption group adjusted for sex, age, race-ethnicity, current smoking status, and BMI. Because the distributions of these biomarkers were skewed, the natural log was used. Satterthwaite-adjusted  $F$  tests were used to examine the statistical significance of differences in the adjusted geometric means. Adjusted relative differences (exponentiated  $\beta$  coefficients) and 95% CIs are reported in the text.

Logistic regression was used to estimate the prevalences (ie, predictive margins) and 95% CIs of high serum folate and vitamin B-12 depletion adjusted for age, sex, race-ethnicity, current smoking status, and BMI. Interactions of folic acid consumption group with age, sex, and race-ethnicity group were tested from the differences in the log-likelihood ratios and df for models with and without the interactions terms in relation to the chi-square distribution.

Differences in the proportions of US adults in folic acid consumption groups by sociodemographic characteristics and prevalences of high serum folate and vitamin B-12 depletion by folic acid consumption groups were evaluated with the chi-square test. All tests were 2-tailed,  $\alpha = 0.05$ . Sample weights were used for all analyses to account for differential nonresponse and noncoverage and to adjust for planned oversampling of some groups. We analyzed all data except, usual intakes (for which we used PC-SIDE as described previously), using SUDAAN statistical software (release 9.0; Research Triangle Institute, Research Triangle Park, NC) to account for the complex sampling design (29).

### RESULTS

Among US adults, 42%, 18%, 25%, and 15% reported consumption of folic acid from ECGP only, ECGP+RTE, ECGP+SUP, and ECGP+RTE+SUP, respectively (**Table 1**). The proportion of US adults in the 4 consumption groups differed by sex, age, and race-ethnicity. Compared with women, a lower proportion of men consumed folic acid from supplements (36.2% compared with 43.0%;  $P < 0.001$ ). Compared with adults aged 19–39 y, a higher proportion aged  $\geq 60$  y consumed folic acid from supplements (51.7% compared with 30.2%;  $P < 0.001$ ). Compared with non-Hispanic white adults, a lower proportion of non-Hispanic black and Mexican American adults consumed folic acid from more than one source (62.6%, 42.1%, and with 41.7%, respectively;  $P < 0.001$ ).

### Usual intake of folic acid, vitamin B-12, and natural food folate

The usual median intake of folic acid differed across folic acid consumption groups (**Table 2**) ( $P < 0.0001$ ). After adjustment for measurement error, age, sex, race-ethnicity, interview method (in person or by phone), and day of the week, usual median intakes) of folic acid for ECGP only, ECGP+RTE, ECGP+SUP, and ECGP+RTE+SUP were 138, 274, 479, and 635  $\mu\text{g}/\text{d}$ , respectively. Differences across consumption groups in usual median intakes were consistent within sex, age, and race-ethnicity groups.

Adjusted usual median intakes of vitamin B-12 for ECGP only, ECGP+RTE, ECGP+SUP, and ECGP+RTE+SUP were 4.3, 7.3, 15.7, and 18.6  $\mu\text{g}/\text{d}$ , respectively (**Table 2**). Differences across consumption groups were consistent within sex, age, and race-ethnicity groups. Across folic acid consumption groups, adjusted usual median intakes of natural food folate varied from 197, 205, and 208 to 212  $\mu\text{g}/\text{d}$ , respectively. Average usual intake of natural food folate differed slightly between supplements users and nonusers (ECGP only and ECGP+RTE compared with ECGP+SUP and ECGP+RTE+SUP;  $P < 0.05$ ) among the total population, among women, and among adults aged 19–39 y, but not among other sex, age, and race-ethnicity groups (*see* Supplemental Table 1 under “Supplemental data” in the online issue).

Of the total US adult population, an estimated 2.7% (95% CI: 1.9%, 3.5%) exceeded the UL for folic acid. Of the 60% of adults who did not consume supplements containing folic acid (ECGP only and ECGP+RTE), 0% exceeded the UL (**Figure 1**). Of the adults who consumed ECGP+SUP and ECGP+RTE+SUP, 5.5%

**TABLE 1**

Proportion of US adults aged  $\geq 19$  y by folic acid consumption group and sociodemographic characteristics: National Health and Nutrition Examination Survey (NHANES) 2003–2006<sup>1</sup>

| Characteristic       | Participants     | Source of folic acid exposure (95% CI) <sup>2</sup> |                   |                   |                   |
|----------------------|------------------|---|-------------------|-------------------|-------------------|
|                      |                  | ECGP only   | ECGP+RTE          | ECGP+SUP          | ECGP+RTE+SUP      |
| Total                | <i>n</i><br>8258 | 42.2 (39.4, 45.1)                                   | 18.0 (16.7, 19.5) | 25.2 (23.2, 27.3) | 14.6 (13.2, 16.1) |
| Sex                  |                  |   |                   | %                 |                   |
| Female               | 4115             | 40.2 (37.3, 43.1)                                   | 16.8 (15.2, 18.4) | 27.2 (24.8, 29.8) | 15.8 (14.2, 17.6) |
| Male                 | 4143             | 44.4 (40.9, 47.9)                                   | 19.4 (17.2, 21.8) | 23.0 (20.7, 25.5) | 13.2 (11.6, 15.1) |
| Age                  |                  |   |                   |                   |                   |
| 19–39 y              | 2932             | 48.2 (44.0, 52.5)                                   | 21.6 (19.4, 24.1) | 18.6 (16.2, 21.3) | 11.6 (9.7, 13.7)  |
| 40–59 y              | 2456             | 43.2 (40.0, 46.4)                                   | 15.1 (13.1, 17.4) | 29.4 (26.4, 32.7) | 12.3 (10.4, 14.6) |
| $\geq 60$ y          | 2870             | 31.4 (28.6, 34.3)                                   | 16.9 (14.8, 19.3) | 29.0 (26.0, 32.2) | 22.7 (20.3, 25.3) |
| Race-ethnicity group |                  |   |                   |                   |                   |
| Non-Hispanic white   | 4304             | 37.4 (33.4, 41.5)                                   | 18.3 (16.7, 20.0) | 27.3 (24.8, 29.9) | 17.1 (15.1, 19.2) |
| Non-Hispanic black   | 1763             | 57.9 (54.5, 61.2)                                   | 17.1 (14.6, 19.9) | 18.3 (15.2, 21.9) | 6.7 (5.3, 8.4)    |
| Mexican American     | 1638             | 58.3 (53.1, 63.3)                                   | 19.9 (16.3, 24.2) | 14.3 (11.0, 18.3) | 7.6 (5.6, 10.2)   |

<sup>1</sup> ECGP only, consumed enriched cereal-grain products only, excluding ready-to-eat cereals and supplements containing folic acid; ECGP+RTE, consumed enriched cereal-grain products plus ready-to-eat cereals; ECGP+SUP, consumed enriched cereal-grain products (excluding ready-to-eat cereals) plus supplements containing folic acid; ECGP+RTE+SUP, consumed enriched cereal-grain products, ready-to-eat cereals, and supplements containing folic acid.

<sup>2</sup> Percentages are weighted, and CIs take into account the complex sampling design.

(95% CI: 3.0%, 8.0%) and 9.4% (95% CI: 5.5%, 13.3%) exceeded the UL, respectively. Except for men and adults aged  $\geq 60$  y, estimates of the proportion above the UL were statistically unreliable across consumption groups when stratified by sex, age, and race-ethnicity and are not shown. Of any population subgroup, usual folic acid intakes of adults aged  $\geq 60$  y who consumed ECGP+RTE+SUP were the most likely to exceed the UL (12.8%; 95% CI: 7.1%, 18.5%).

Because intake above the UL occurred only among supplement users, we further examined average daily intake of folic acid from supplements: 0, 1–200, 201–400, and  $>400$   $\mu\text{g}$  (Figure 2). The estimated proportions of US adults in each group were 60.6%, 10.9%, 23.5%, and 5.9%, respectively. The median total folic acid intakes in the 4 subgroups were 173, 316, 546, and 983  $\mu\text{g}$  folic acid/d, respectively. Less than 1% of adults who consumed an average of  $\leq 400$   $\mu\text{g}$  folic acid/d from supplements exceeded the UL: 0.47% (95% CI: 0.02%, 0.91%) and 0.56% (95% CI: 0.27%, 0.85%) of adults who consumed 1–200 or 201–400  $\mu\text{g}$  folic acid/d from supplements, respectively, and 47.8% (95% CI: 39.5%, 56.0%) of adults who consumed an average of  $>400$   $\mu\text{g}$  folic acid/d from supplements.

#### Serum and RBC folate, serum vitamin B-12, homocysteine, and MMA concentrations

A significant dose-response relation was observed in serum and RBC folate, vitamin B-12, and homocysteine concentrations relative to the usual median intake of folic acid consumption group. Compared with adults who consumed ECGP only, for example, among those who consumed ECGP+RTE, ECGP+SUP, and ECGP+RTE+SUP, the geometric mean serum folate concentrations were 25.3% (95% CI: 22.1%, 28.4%), 44.1% (95% CI: 39.9%, 48.3%), and 80.0% (95% CI: 63.1%, 88.2%) higher, respectively (Table 3). Compared with adults who consumed ECGP only, geometric mean MMA concentrations did not differ

from those of adults who consumed ECGP+RTE ( $P > 0.05$ ) but were 10% lower in adults who consumed ECGP+SUP.

These relations appeared to be consistent and significant across age, sex, and race-ethnicity groups, with the exception of serum vitamin B-12 and MMA concentrations among Mexican Americans and MMA concentrations among non-Hispanic black adults and adults aged 19–39 y. The differences in these concentrations by folic acid consumption groups were not statistically significant ( $P > 0.05$ ).

#### Prevalence of high serum folate and vitamin B-12 depletion

The absolute differences in the adjusted prevalence of high serum folate concentration by folic acid consumption group were modified by sex, age group, and race-ethnicity ( $P < 0.05$ ), but the prevalence ratios were similar across sociodemographic groups (Table 4). Compared with adults who consumed ECGP only, adults who consumed ECGP+RTE+SUP were  $\approx 10$  times more likely to have high serum folate concentrations and 70% less likely to have vitamin B-12 depletion.

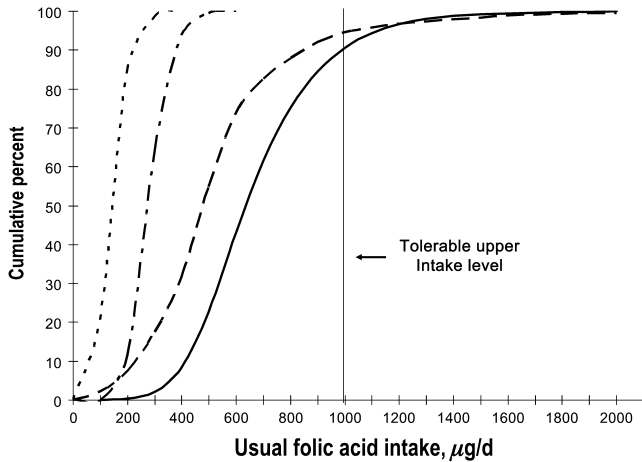
#### DISCUSSION

Since the initiation of fortification,  $<3\%$  of US adults have exceeded the UL for folic acid. We estimated that nearly 60% of US adults consumed folic acid from RTE and/or supplements and 15% from both. Compared with the consumption of ECGP only, regular consumption of RTE with folic acid was associated with about a 100% higher usual intake, and use of supplements with folic acid with about a 200% higher intake. Despite the contributions to median folic acid intakes of ECGP, RTE, and supplements, the 94% of US adults who do not consume supplements or consume  $\leq 400$   $\mu\text{g}$  folic acid/d from supplements are unlikely to exceed the UL for folic acid.

**TABLE 2**  
 Median (interquartile range) usual folic acid intakes and usual vitamin B-12 intakes by folic acid consumption group and sociodemographic characteristics among US adults aged  $\geq 19$  y: National Health and Nutrition Examination Survey (NHANES) 2003–2006<sup>1</sup>

|   | Usual folic acid intake |                |                |                |                |       | Usual vitamin B-12 intake |                  |                   |                   |                  |  |
|---|-------------------------|----------------|----------------|----------------|----------------|-------|---------------------------|------------------|-------------------|-------------------|------------------|--|
|   | ECGP only               | ECGP+RTE       | ECGP+SUP       | ECGP+RTE+SUP   | Total          | Total | ECGP only                 | ECGP+RTE         | ECGP+SUP          | ECGP+RTE+SUP      | Total            |  |
| Total ( $\mu\text{g}/\text{d}$ )              | 138 (106, 176)          | 274 (230, 324) | 479 (360, 610) | 635 (512, 797) | 288 (160, 462) | 8258  | 4.3 (3.2, 6.9)            | 7.3 (5.6, 12.4)  | 15.7 (9.1, 31.0)  | 18.6 (11.1, 42.2) | 8.5 (4.6, 20.6)  |  |
| <i>n</i>                                      | 3731                    | 1546           | 1894           | 1087           | 8258           | 3731  | 1546                      | 1894             | 1087              | 8258              |                  |  |
| Sex   |                         |                |                |                |                |       |                           |                  |                   |                   |                  |  |
| Male ( $\mu\text{g}/\text{d}$ )               | 161 (123, 204)          | 314 (266, 370) | 493 (372, 628) | 687 (552, 849) | 301 (178, 466) | 4143  | 5.4 (4.0, 8.5)            | 8.2 (6.6, 12.5)  | 18.3 (10.6, 32.2) | 22.4 (13.2, 44.6) | 9.6 (5.5, 21.7)  |  |
| <i>n</i>                                      | 1978                    | 805            | 866            | 494            | 4143           | 1978  | 805                       | 866              | 494               | 4143              |                  |  |
| Female ( $\mu\text{g}/\text{d}$ )             | 117 (90, 148)           | 236 (196, 282) | 465 (351, 603) | 621 (504, 787) | 277 (142, 463) | 4115  | 3.4 (2.5, 5.9)            | 6.8 (4.8, 12.2)  | 14.3 (7.9, 29.6)  | 16.5 (9.8, 37.0)  | 7.5 (3.9, 19.4)  |  |
| <i>n</i>                                      | 1753                    | 741            | 1028           | 593            | 4115           | 1753  | 741                       | 1028             | 593               | 4115              |                  |  |
| Age   |                         |                |                |                |                |       |                           |                  |                   |                   |                  |  |
| 19–39 y ( $\mu\text{g}/\text{d}$ )            | 162 (124, 207)          | 304 (256, 359) | 478 (340, 658) | 608 (489, 754) | 276 (171, 423) | 2932  | 4.6 (3.5, 5.7)            | 7.3 (6.8, 8.0)   | 12.6 (8.5, 22.1)  | 16.7 (9.9, 34.8)  | 7.4 (4.6, 12.80) |  |
| <i>n</i>                                      | 1524                    | 647            | 472            | 289            | 2932           | 1524  | 647                       | 472              | 289               | 2932              |                  |  |
| 40–59 y ( $\mu\text{g}/\text{d}$ )            | 130 (101, 164)          | 256 (215, 303) | 474 (347, 602) | 640 (537, 762) | 272 (151, 453) | 2456  | 4.4 (3.1, 6.8)            | 10.6 (5.5, 22.7) | 16.5 (9.1, 35.6)  | 18.8 (11.2, 40.8) | 8.7 (4.2, 22.9)  |  |
| <i>n</i>                                      | 1179                    | 376            | 648            | 253            | 2456           | 1179  | 376                       | 648              | 253               | 2456              |                  |  |
| $\geq 60$ y ( $\mu\text{g}/\text{d}$ )        | 104 (79, 133)           | 238 (208, 286) | 490 (396, 611) | 672 (538, 845) | 349 (163, 526) | 2870  | 4.8 (2.6, 21.7)           | 8.7 (5.4, 21.0)  | 21.2 (9.9, 37.3)  | 24.1 (13.3, 50.8) | 10.3 (5.2, 37.6) |  |
| <i>n</i>                                      | 1028                    | 523            | 774            | 545            | 2870           | 1028  | 523                       | 774              | 545               | 2870              |                  |  |
| Race-ethnicity group                          |                         |                |                |                |                |       |                           |                  |                   |                   |                  |  |
| Non-Hispanic white ( $\mu\text{g}/\text{d}$ ) | 139 (106, 179)          | 276 (233, 326) | 486 (372, 615) | 648 (522, 896) | 316 (167, 507) | 4304  | 4.5 (3.2, 7.6)            | 7.6 (5.6, 17.2)  | 16.7 (9.3, 31.5)  | 18.8 (11.2, 42.9) | 9.2 (4.8, 22.7)  |  |
| <i>n</i>                                      | 1551                    | 799            | 1153           | 801            | 4304           | 1551  | 799                       | 1153             | 801               | 4304              |                  |  |
| Non-Hispanic black ( $\mu\text{g}/\text{d}$ ) | 118 (93, 147)           | 237 (197, 283) | 472 (303, 599) | 578 (447, 746) | 188 (116, 294) | 1763  | 3.9 (2.9, 5.6)            | 7.1 (6.1, 8.6)   | 13.3 (7.7, 23.8)  | 17.8 (11.1, 35.8) | 5.9 (3.4, 12.3)  |  |
| <i>n</i>                                      | 971                     | 343            | 333            | 115            | 1763           | 971   | 343                       | 333              | 116               | 1763              |                  |  |
| Mexican American ( $\mu\text{g}/\text{d}$ )   | 114 (149, 190)          | 290 (245, 342) | 442 (302, 585) | 583 (454, 737) | 220 (134, 358) | 1638  | 4.2 (3.1, 6.3)            | 7.2 (6.1, 8.8)   | 14.4 (7.9, 32.9)  | 14.5 (10.0, 22.4) | 6.1 (3.5, 11.5)  |  |
| <i>n</i>                                      | 922                     | 316            | 250            | 126            | 1638           | 922   | 316                       | 274              | 126               | 1638              |                  |  |

<sup>1</sup> Median usual folic acid and vitamin B-12 intakes and interquartile ranges (25th and 75th percentiles) were estimated from PC-SIDE (Department of Statistics, Iowa State University) with jackknife replicate weights and were adjusted for participant ID, age, sex, race-ethnicity, interview method (in person or by phone), and day of the week. *n* values are unweighted. ECGP only, consumed enriched cereal-grain products only, excluding ready-to-eat cereals and supplements containing folic acid; ECGP+RTE, consumed enriched cereal-grain products plus ready-to-eat cereals; ECGP+SUP, consumed enriched cereal-grain products (excluding ready-to-eat cereals) plus supplements containing folic acid; ECGP+RTE+SUP, consumed enriched cereal-grain products, ready-to-eat cereals, and supplements containing folic acid.



**FIGURE 1.** The cumulative distribution of usual intake of folic acid for US adults who consumed enriched cereal-grain products with folic acid (ECGP) only [ $n = 3731$ ; 0.0% exceeded the tolerable upper intake level (UL); .....], ECGP plus ready-to-eat cereals with folic acid (RTE) ( $n = 1546$ ; 0.0% exceeded the UL; - - -), ECGP plus supplements with folic acid (SUP) [ $n = 1894$ ; 5.5% (95% CI: 3.0%, 8.0%) exceeded the UL; \_ \_ \_], or ECGP+RTE+SUP [ $n = 1087$ ; 9.4% (95% CI: 5.5%, 13.3%) exceeded the UL; \_\_\_\_].

The median usual daily intake of folic acid among adults who consumed ECGP only (138  $\mu\text{g}$ ) was slightly higher than the Food and Drug Administration's estimated range of 70 to 130  $\mu\text{g}$  (2). Among adults who consumed ECGP only, higher usual mean folic acid intakes occurred in men than in women, in adults aged  $<60$  y than in those aged  $\geq 60$  y, and in non-Hispanic whites than in non-Hispanic blacks ( $t$  tests,  $P < 0.01$  for all). These associations are consistent with differences in the estimated postfortification changes in folate intake from a previous study (12), but not with mean serum or RBC folate concentrations in the current study. This finding may be related to differences across population subgroups in natural food folate intake or folic acid metabolism.

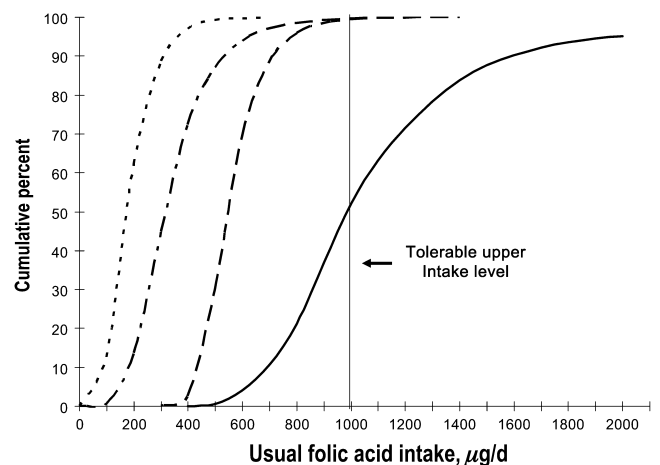
Our results, in agreement with previous studies, indicate that the consumption of RTE and/or supplements contributes significantly to intakes of folic acid and that supplements or RTE are associated with higher serum folate and/or lower homocysteine concentrations (9, 13–15). Our study also indicates that the consumption of RTE and/or supplements with folic acid is associated with higher usual vitamin B-12 intakes and concentrations among US adults. More than 95% of RTE and supplement consumers also consumed vitamin B-12 from these sources (data not shown).

The masking of vitamin B-12 deficiency is a concern among older adults (6). Among US adults aged  $\geq 60$  y, a higher prevalence of high folate concentrations and a lower prevalence of vitamin B-12 depletion were positively associated with intake of RTE and/or supplements with folic acid. The estimated joint prevalence of low vitamin B-12 status (defined as  $<300$  pg/mL) and usual intake exceeding the UL of folic acid is 0.1% (95% CI: 0.04%, 0.26%) among all US adults and 0.1% (95% CI: 0.01%, 0.71%) among US adults aged  $>60$  y. These estimates are statistically unreliable because of the small number of US adults in our sample who both consumed  $>1000$   $\mu\text{g}$  folic acid and had low vitamin B-12 concentrations (unweighted  $n = 11$  adults,  $n = 3$  adults aged  $> 60$  y). Lower MMA concentrations

were associated with consumption of supplements with folic acid ( $t$  test,  $P < 0.001$  for differences in adjusted geometric means for ECGP+SUP or ECGP+SUP+RTE compared with ECGP only), but not RTE ( $t$  test,  $P = 0.116$  for difference in adjusted geometric means for ECGP+RTE compared with ECGP only). Because the vast majority of RTE and supplements with folic acid also contain vitamin B-12, consumption may reduce the risk of vitamin B-12 deficiency among older adults. As did another recent report (30), our data suggest that US adults aged  $\geq 60$  y who do not consume supplements with vitamin B-12 may be at increased risk of vitamin B-12 deficiency, even those with median usual vitamin B-12 intakes of  $\approx 3$   $\mu\text{g}/\text{d}$  from RTE (greater than the Recommended Dietary Allowance of 2.4  $\mu\text{g}/\text{d}$ ) (7).

The strengths of this study include its use of a large nationally representative sample of US adults, its oversampling of population subgroups by age and race-ethnicity, its adjustment for potential confounders, its use of folate and vitamin B-12 biomarkers to evaluate dose response across groups, and its application of an established statistical method by using two 24-h dietary recalls in most of the sample to estimate usual folic acid and vitamin B-12 intakes.

Potential limitations include the inability to examine temporal associations due to the cross-sectional design of the survey. Dietary data were self-reported and were collected at the time of the medical examination or shortly thereafter, and supplement data were collected over the 30 d before the survey, thus requiring that we combined intake data obtained with the 2 different instruments. The 24-h dietary recall underestimates calorie intake by  $\approx 11\%$  (31), but this does not indicate that micronutrient intake is also underestimated by the same amount. Actual folic acid and vitamin B-12 in foods may be higher or lower than that estimated in the nutrient database. Average nutrient intakes from supplements do not reflect irregular patterns of intake for some individuals; therefore, the within-person variability in total folic acid intake may be underestimated. The amount of folic acid and



**FIGURE 2.** The cumulative distribution of usual intake of folic acid for US adults who consumed no supplements containing folic acid [ $n = 5277$ ; 0.0% exceeded the tolerable upper intake level (UL); .....], an average of 1–200  $\mu\text{g}$  folic acid/d from supplements [ $n = 703$ ; 0.47% (95% CI: 0.02%, 0.91%) exceeded the UL; - - -], an average of 201–400  $\mu\text{g}$  folic acid/d from supplements [ $n = 1776$ ; 0.56% (95% CI: 0.27%, 0.85%) exceeded the UL; \_ \_ \_], or an average of  $>400$   $\mu\text{g}$  folic acid/d from supplements [ $n = 441$ ; 47.8% (95% CI: 39.5%, 56.0%) exceeded the UL; \_\_\_\_].

**TABLE 3**

Serum folate, red blood cell (RBC) folate, homocysteine, vitamin B-12, and methylmalonic acid concentrations by folic acid consumption group and by sociodemographic characteristics among US adults aged  $\geq 19$  y: National Health and Nutrition Examination Survey (NHANES) 2003–2006<sup>1</sup>

| Folic acid consumption group  | Participants <sup>3</sup> | Adjusted geometric mean concentration (95% CIs) <sup>2</sup> |                |                   |                    |                      |
|-------------------------------|---------------------------|--|----------------|-------------------|--------------------|----------------------|
|                               |                           | Serum folate   | RBC folate     | Homocysteine      | Serum vitamin B-12 | Methylmalonic acid   |
|                               | <i>n</i>                  | ng/mL  | ng/mL          | $\mu\text{mol/L}$ | pg/mL              | $\mu\text{mol/L}$    |
| <b>Total</b>                  |                           |  |                |                   |                    |                      |
| ECGP only                     | 3337 (1653)               | 9.4 (9.2, 9.6)   | 234 (230, 239) | 8.8 (8.6, 8.9)    | 412 (401, 423)     | 0.143 (0.138, 0.149) |
| ECGP+RTE                      | 1385 (629)                | 12.1 (11.7, 12.5)  | 273 (266, 279) | 8.3 (8.1, 8.4)    | 462 (449, 475)     | 0.146 (0.137, 0.156) |
| ECGP+SUP                      | 1754 (870)                | 14.6 (14.1, 15.2)  | 309 (303, 315) | 7.9 (7.7, 8.1)    | 530 (514, 548)     | 0.131 (0.126, 0.135) |
| ECGP+RTE+SUP                  | 1004 (486)                | 16.9 (16.2, 17.6)  | 329 (321, 337) | 7.7 (7.5, 7.8)    | 547 (525, 570)     | 0.129 (0.123, 0.136) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | <0.001               |
| <b>Sex</b>                    |                           |  |                |                   |                    |                      |
| <b>Male</b>                   |                           |  |                |                   |                    |                      |
| ECGP only                     | 1755 (866)                | 8.9 (8.7, 9.2)   | 229 (225, 236) | 9.4 (9.2, 9.7)    | 417 (405, 429)     | 0.145 (0.138, 0.152) |
| ECGP+RTE                      | 713 (328)                 | 11.6 (11.2, 12.1)  | 272 (266, 279) | 9.1 (8.8, 9.4)    | 462 (443, 481)     | 0.151 (0.140, 0.163) |
| ECGP+SUP                      | 807 (399)                 | 13.9 (13.3, 14.6)  | 299 (291, 307) | 8.6 (8.4, 8.8)    | 518 (500, 538)     | 0.134 (0.128, 0.139) |
| ECGP+RTE+SUP                  | 466 (226)                 | 16.1 (15.1, 17.2)  | 319 (309, 330) | 8.2 (8.1, 8.4)    | 544 (518, 571)     | 0.126 (0.120, 0.132) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | <0.001               |
| <b>Female</b>                 |                           |  |                |                   |                    |                      |
| ECGP only                     | 1562 (787)                | 9.8 (9.5, 10.1)  | 239 (234, 245) | 8.2 (8.0, 8.4)    | 408 (394, 423)     | 0.142 (0.136, 0.148) |
| ECGP+RTE                      | 672 (301)                 | 12.5 (12.0, 13.1)  | 272 (263, 281) | 7.6 (7.3, 7.8)    | 458 (441, 477)     | 0.142 (0.133, 0.152) |
| ECGP+SUP                      | 947 (471)                 | 15.2 (14.6, 16.0)  | 318 (309, 327) | 7.3 (7.2, 7.5)    | 540 (518, 565)     | 0.127 (0.121, 0.134) |
| ECGP+RTE+SUP                  | 538 (260)                 | 17.7 (16.9, 18.6)  | 338 (327, 350) | 7.2 (6.9, 7.4)    | 550 (521, 581)     | 0.131 (0.122, 0.141) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | 0.004                |
| <b>Age</b>                    |                           |  |                |                   |                    |                      |
| <b>19–39 y</b>                |                           |  |                |                   |                    |                      |
| ECGP only                     | 1304 (636)                | 8.7 (8.5, 8.9)   | 216 (211, 222) | 7.6 (7.5, 7.7)    | 419 (408, 430)     | 0.123 (0.117, 0.129) |
| ECGP+RTE                      | 553 (231)                 | 11.0 (10.5, 11.6)  | 250 (240, 260) | 7.1 (6.9, 7.3)    | 481 (457, 508)     | 0.124 (0.113, 0.136) |
| ECGP+SUP                      | 425 (194)                 | 12.5 (11.8, 13.2)  | 272 (261, 282) | 7.1 (6.9, 7.3)    | 518 (493, 546)     | 0.113 (0.107, 0.120) |
| ECGP+RTE+SUP                  | 258 (115)                 | 13.5 (12.8, 14.4)  | 282 (269, 297) | 6.8 (6.6, 7.0)    | 502 (474, 531)     | 0.118 (0.109, 0.129) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | 0.170                |
| <b>40–59 y</b>                |                           |  |                |                   |                    |                      |
| ECGP only                     | 1090 (507)                | 9.2 (8.9, 9.6)   | 237 (232, 243) | 8.7 (8.5, 8.9)    | 411 (397, 426)     | 0.142 (0.134, 0.150) |
| ECGP+RTE                      | 354 (171)                 | 11.7 (11.2, 12.2)  | 274 (263, 287) | 8.2 (7.9, 8.5)    | 453 (434, 474)     | 0.141 (0.132, 0.150) |
| ECGP+SUP                      | 611 (283)                 | 14.3 (13.6, 15.0)  | 306 (296, 317) | 8.0 (7.7, 8.3)    | 523 (497, 550)     | 0.130 (0.123, 0.138) |
| ECGP+RTE+SUP                  | 239 (105)                 | 16.7 (15.1, 18.3)  | 320 (317, 341) | 7.8 (7.6, 8.0)    | 566 (528, 607)     | 0.129 (0.117, 0.142) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | 0.048                |
| <b><math>\geq 60</math> y</b> |                           |  |                |                   |                    |                      |
| ECGP only                     | 943 (510)                 | 10.6 (10.2, 11.0)  | 256 (247, 264) | 11.1 (10.6, 11.5) | 401 (384, 419)     | 0.187 (0.178, 0.195) |
| ECGP+RTE                      | 478 (227)                 | 14.7 (14.1, 15.3)  | 307 (299, 315) | 10.5 (10.0, 11.0) | 439 (409, 471)     | 0.208 (0.182, 0.238) |
| ECGP+SUP                      | 718 (393)                 | 18.9 (18.1, 19.7)  | 376 (364, 388) | 9.4 (9.2, 9.6)    | 555 (536, 574)     | 0.164 (0.154, 0.175) |
| ECGP+RTE+SUP                  | 507 (266)                 | 22.5 (21.6, 23.5)  | 398 (384, 414) | 9.3 (8.9, 9.6)    | 567 (542, 593)     | 0.158 (0.148, 0.168) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | <0.001               |
| <b>Race-ethnicity</b>         |                           |  |                |                   |                    |                      |
| <b>Non-Hispanic white</b>     |                           |  |                |                   |                    |                      |
| ECGP only                     | 1396 (726)                | 9.6 (9.4, 9.9)   | 242 (236, 236) | 9.0 (8.8, 9.2)    | 393 (384, 404)     | 0.152 (0.144, 0.159) |
| ECGP+RTE                      | 726 (337)                 | 12.6 (12.1, 13.1)  | 286 (278, 278) | 8.5 (8.2, 8.7)    | 446 (432, 460)     | 0.157 (0.145, 0.169) |
| ECGP+SUP                      | 1081 (555)                | 15.2 (14.6, 15.9)  | 322 (314, 330) | 8.1 (7.9, 8.3)    | 519 (487, 517)     | 0.137 (0.131, 0.143) |
| ECGP+RTE+SUP                  | 741 (369)                 | 17.6 (16.7, 18.4)  | 342 (333, 351) | 7.9 (7.7, 8.1)    | 531 (522, 576)     | 0.137 (0.129, 0.145) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | <0.001             | <0.001               |
| <b>Non-Hispanic black</b>     |                           |  |                |                   |                    |                      |
| ECGP only                     | 844 (386)                 | 8.3 (8.1, 8.7)   | 196 (191, 201) | 8.5 (8.3, 8.8)    | 484 (467, 501)     | 0.116 (0.109, 0.122) |
| ECGP+RTE                      | 294 (125)                 | 9.9 (9.5, 10.3)  | 215 (205, 225) | 8.3 (8.0, 8.7)    | 524 (501, 549)     | 0.114 (0.103, 0.127) |
| ECGP+SUP                      | 298 (132)                 | 12.5 (11.9, 13.3)  | 255 (243, 267) | 7.7 (7.4, 8.0)    | 582 (545, 620)     | 0.119 (0.111, 0.128) |
| ECGP+RTE+SUP                  | 109 (40)                  | 15.2 (13.7, 17.0)  | 280 (257, 305) | 7.9 (7.5, 8.3)    | 647 (588, 712)     | 0.112 (0.104, 0.121) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | 0.001             | <0.001             | 0.768                |
| <b>Mexican American</b>       |                           |  |                |                   |                    |                      |
| ECGP only                     | 837 (400)                 | 8.8 (8.6, 9.1)   | 226 (219, 233) | 7.4 (7.3, 7.5)    | 497 (466, 530)     | 0.113 (0.106, 0.120) |
| ECGP+RTE                      | 286 (132)                 | 10.7 (10.2, 11.3)  | 255 (244, 269) | 7.1 (6.9, 7.3)    | 514 (486, 545)     | 0.107 (0.098, 0.117) |
| ECGP+SUP                      | 251 (127)                 | 13.3 (12.6, 14.0)  | 294 (280, 309) | 7.0 (6.7, 7.2)    | 536 (506, 567)     | 0.117 (0.106, 0.130) |
| ECGP+RTE+SUP                  | 114 (56)                  | 13.5 (12.5, 14.6)  | 288 (270, 307) | 6.6 (6.2, 6.9)    | 527 (469, 593)     | 0.115 (0.097, 0.137) |
| <i>P</i> value <sup>4</sup>   |                           | <0.001   | <0.001         | <0.001            | 0.246              | 0.545                |

<sup>1</sup> ECGP only, consumed enriched cereal-grain products only, excluding ready-to-eat cereals and supplements containing folic acid; ECGP+RTE, consumed enriched cereal-grain products plus ready-to-eat cereals; ECGP+SUP, consumed enriched cereal-grain products (excluding ready-to-eat cereals) plus supplements containing folic acid; ECGP+RTE+SUP, consumed enriched cereal-grain products, ready-to-eat cereals, and supplements containing folic acid.

<sup>2</sup> Adjusted for age, sex, race-ethnicity, current smoking status, and BMI (calculated in weight in kilograms divided by height squared in meters) in multiple linear regression models. Analyses were weighted and took into account the complex sampling design.

<sup>3</sup> Unweighted *n*; unweighted *n* with methylmalonic acid measurements in the NHANES 2003–2004 in parentheses.

<sup>4</sup> *P* values for testing differences in adjusted concentrations across different folic acid exposure groups based on Satterthwaite-adjusted *F* tests.

**TABLE 4**

Adjusted prevalence (95% CI) of high serum folate, low vitamin B-12 by folic acid consumption group and sociodemographic characteristics among US adults aged  $\geq 19$  y: National Health and Nutrition Examination Survey (NHANES) 2003–2006<sup>1</sup>

| Characteristic              | Folic acid consumption group |                             |                   |                            | P value <sup>2</sup> |
|-----------------------------|------------------------------|-----------------------------|-------------------|----------------------------|----------------------|
|                             | ECGP only                    | ECGP+RTE                    | ECGP+SUP          | ECGP+RTE + SUP             |                      |
| Total (n) <sup>3</sup>      | 3337                         | 1385                        | 1754              | 1004                       |                      |
| Serum folate >20 ng/mL (%)  | 2.5 (1.7, 3.4)               | 8.5 (6.5, 10.6)             | 20.1 (17.1, 23.1) | 29.6 (25.4, 33.7)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 21.9 (19.1, 24.7)            | 12.9 (10.6, 15.1)           | 9.3 (7.2, 11.4)   | 5.8 (3.7, 7.9)             | <0.001               |
| Sex                         |                              |                             |                   |                            |                      |
| Male (n)                    | 1775                         | 713                         | 807               | 466                        |                      |
| Serum folate >20 ng/mL (%)  | 1.6 (0.9, 2.4)               | 6.4 (4.2, 8.6)              | 15.5 (12.6, 18.5) | 22.3 (17.8, 26.8)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 18.8 (15.7, 21.9)            | 11.8 (8.8, 14.7)            | 8.7 (6.1, 11.2)   | 4.1 (2.2, 6.0)             | <0.001               |
| Female (n)                  | 1562                         | 672                         | 947               | 538                        |                      |
| Serum folate >20 ng/mL (%)  | 3.4 (2.1, 4.8)               | 10.7 (7.7, 13.7)            | 23.9 (19.5, 28.2) | 36.1 (30.6, 41.6)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 24.8 (21.0, 28.5)            | 14.1 (10.7, 17.5)           | 10.0 (7.4, 12.6)  | 7.4 (4.2, 10.6)            | <0.001               |
| Age                         |                              |                             |                   |                            |                      |
| 19–39 y (n)                 | 1304                         | 553                         | 425               | 258                        |                      |
| Serum folate >20 ng/mL (%)  | 0.5 (0.1, 1.0) <sup>4</sup>  | 4.6 (1.1, 8.0) <sup>4</sup> | 9.0 (1.3, 6.8)    | 12.7 (8.2, 17.3)           | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 19.4 (15.9, 22.8)            | 10.9 (7.1, 14.7)            | 8.3 (4.9, 11.7)   | 7.7 (4.1, 11.3)            | <0.001               |
| 40–59 y (n)                 | 1090                         | 354                         | 611               | 239                        |                      |
| Serum folate >20 ng/mL (%)  | 2.0 (0.8, 3.3)               | 4.5 (1.6, 7.3)              | 17.4 (14.1, 20.8) | 27.3 (19.1, 35.6)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 22.2 (18.7, 25.7)            | 10.9 (7.1, 14.8)            | 9.8 (5.6, 13.9)   | 5.0 (1.8, 8.1)             | <0.001               |
| $\geq 60$ y (n)             | 943                          | 478                         | 718               | 507                        |                      |
| Serum folate >20 ng/mL (%)  | 6.7 (4.6, 8.8)               | 21.0 (17.0, 24.9)           | 40.8 (36.0, 45.5) | 58.1 (52.7, 63.5)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 26.6 (23.1, 30.2)            | 19.0 (14.8, 23.1)           | 10.0 (7.5, 12.5)  | 5.1 (2.6, 7.7)             | <0.001               |
| Race-ethnicity group        |                              |                             |                   |                            |                      |
| Non-Hispanic white (n)      | 1396                         | 726                         | 1081              | 741                        |                      |
| Serum folate >20 ng/mL (%)  | 2.9 (1.7, 4.1)               | 10.2 (7.4, 13.0)            | 22.4 (18.7, 26.2) | 33.2 (28.2, 38.2)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 24.9 (21.6, 28.2)            | 14.8 (12.1, 17.5)           | 10.1 (7.6, 12.7)  | 6.5 (3.9, 9.1)             | <0.001               |
| Non-Hispanic black (n)      | 844                          | 294                         | 298               | 109                        |                      |
| Serum folate >20 ng/mL (%)  | 1.5 (0.6, 2.4)               | 2.3 (1.2, 3.5)              | 11.6 (8.1, 15.2)  | 24.0 (15.5, 32.5)          | <0.001               |
| Vitamin B-12 <300 pg/mL (%) | 11.7 (9.5, 14.0)             | 5.4 (2.4, 8.4)              | 6.6 (3.5, 9.6)    | 3.3 (0, 7.0) <sup>4</sup>  | <0.001               |
| Mexican American (n)        | 837                          | 286                         | 251               | 114                        |                      |
| Serum folate >20 ng/mL (%)  | 1.2 (0.5, 1.9)               | 3.6 (1.4, 5.9)              | 10.1 (5.2, 14.9)  | 12.1 (5.9, 18.3)           | 0.001                |
| Vitamin B-12 <300 pg/mL (%) | 11.5 (7.9, 15.1)             | 10.7 (7.4, 13.9)            | 9.8 (5.1, 14.4)   | 5.2 (0, 11.1) <sup>4</sup> | <0.001               |

<sup>1</sup> Prevalences of high serum folate (>20 ng/mL) and low vitamin B-12 (<300 pg/mL) were adjusted for age, sex, race or ethnicity, smoking status, and BMI in multiple logistic regression models. Analyses were weighted and took into account the complex sampling design. ECGP only, consumed enriched cereal-grain products only, excluding ready-to-eat cereals and supplements containing folic acid; ECGP+RTE, consumed enriched cereal-grain products plus ready-to-eat cereals; ECGP+SUP, consumed enriched cereal-grain products (excluding ready-to-eat cereals) plus supplements containing folic acid; ECGP+RTE+SUP, consumed enriched cereal-grain products, ready-to-eat cereals, and supplements containing folic acid.

<sup>2</sup> P values for testing differences in adjusted prevalences across different folic acid exposure groups by using a chi-square test.

<sup>3</sup> Unweighted n values.

<sup>4</sup> Does not meet the standard of statistical reliability and presentation (relative SE > 30%).

vitamin B-12 intake from supplement labels may be an underestimate (32). The sample size was inadequate in some groups, which resulted in unstable estimates of prevalence of excessive usual intakes. Nonresponse bias may result in an over- or underestimate of the total folic acid intake among US adults; however, estimates are weighted according to nonresponse.

Compared with the consumption of ECGP only, consumption of RTE and/or supplements with folic acid is associated with higher folate and vitamin B-12 intakes and concentrations among US adults. Less than 3% of US adults exceeded the UL for folic acid in 2003–2006. Almost all of these adults consumed an average of >400  $\mu$ g folic acid/d from supplements. As recommended by the Institute of Medicine, persons aged  $\geq 51$  y should consume the required amount of vitamin B-12 from synthetic sources (7). Our results and others (30) suggest that further investigation of the average daily amount of synthetic vitamin B-12 required to prevent deficiency among older adults is warranted.

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