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Dietary Supplement Use and Folate Status during Pregnancy in the United States¹

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Abstract

Adequate folate and iron intake during pregnancy is critical for maternal and fetal health. No previous studies to our knowledge have reported dietary supplement use and folate status among pregnant women sampled in NHANES, a nationally representative, cross-sectional survey. We analyzed data on 1296 pregnant women who participated in NHANES from 1999 to 2006 to characterize overall supplement use, iron and folic acid use, and RBC folate status. The majority of pregnant women (77%) reported use of a supplement in the previous 30 d, most frequently a multivitamin/-mineral containing folic acid (mean 817 $\mu\text{g}/\text{d}$) and iron (48 mg/d). Approximately 55–60% of women in their first trimester reported taking a folic acid- or iron-containing supplement compared with 76–78% in their second trimester and 89% in their third trimester. RBC folate was lowest in the first trimester and differed by supplement use across all trimesters. Median RBC folate was 1628 nmol/L among users and 1041 nmol/L among nonusers. Among all pregnant women, median RBC folate increased with trimester (1256 nmol/L in the first, 1527 nmol/L in the second, and 1773 nmol/L in the third). Given the role of folic acid in the prevention of neural tube defects, it is notable that supplement use and median RBC folate was lowest in the first trimester of pregnancy, with 55% of women taking a supplement containing folic acid. Future research is needed to determine the reasons for low compliance with supplement recommendations, particularly folic acid, in early pregnancy.

Introduction

Micronutrient needs increase during pregnancy due to changes in physiology and homeostatic control (1,2). Although increased nutrient intake should preferably come from food sources, even within the developed world it may be unlikely that pregnant and child-bearing-age women meet their needs for micronutrients, such as iron and calcium, through

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foods alone (2,3). However, the extent of potential nutrient deficiency during pregnancy may vary by demographic characteristics, such as younger maternal age and lower income and education (1,4). Although general multivitamin supplement use during pregnancy is not formally recommended, clinicians routinely recommend or prescribe prenatal vitamins to potentially compensate for dietary shortfalls (5). However, supplementation with folic acid and iron specifically, either before or during pregnancy, is recommended by several health organizations (1,4–8). In addition to supplementation, the U.S. food supply was fortified with folic acid beginning in 1997 to target reproductive-aged females in order to reduce the incidence of neural tube defects (9). Despite this fortification, women of child-bearing age still have usual folic acid intakes below the recommendations (10,11).

Although prenatal vitamin and mineral supplements are widely recommended as a standard of care in clinical practice, little is known about the national prevalence of supplement use during pregnancy and the characteristics of pregnant women who take dietary supplements. In addition, folic acid and iron supplement use and folate status have not, to our knowledge, been examined among a nationally representative sample of pregnant women in the US. Previous studies of dietary supplement use in pregnancy using national data are now outdated because of changes in folic acid awareness and fortification (12,13), are specific to only one micronutrient (14), or are not specific beyond multivitamin use (15). Therefore, the purpose of this analysis is to describe the prevalence and correlates of dietary supplement use as well as iron and folic acid supplement use and to describe RBC folate status during pregnancy using data from the NHANES (1999–2006).

Subjects and Methods

We used data from the 1999–2006 NHANES for this analysis. NHANES is a nationally representative, cross-sectional sample of the U.S. civilian, noninstitutionalized population administered by the National Center for Health Statistics (16). Since 1999, NHANES has been operated as a continuous survey and includes a household interview component followed by a physical examination in the mobile examination center (MEC)⁶. During the 1999–2006 NHANES, response rates for the household interview averaged 81% and averaged 77% for the MEC exam. During this same period, NHANES oversampled pregnant women (17). This analysis of secondary data was not subject to institutional review by any of the participating organizations.

Pregnancy status for NHANES participants is assessed during both the household interview and the MEC examination. In addition to being asked about current pregnancy status at the time of the household screening, women ages 8–59 y who were examined in the MEC were also given a urine pregnancy test before undergoing an examination (17). Only women who were seen in the MEC were included in this analysis. In addition, questions about currently being pregnant and month of pregnancy were asked during the MEC examination as part of the reproductive health questionnaire (RHQ) (18). From 1999 to 2006, we initially identified 1274 women who were pregnant at the time of their MEC participation according to the RIDEXPRG variable, which indicates pregnancy status in NHANES. Twenty-two additional

⁶Abbreviations used: MEC, mobile examination center; PIR, poverty income ratio; RHQ, reproductive history questionnaire.

women had a missing pregnancy status according to the RIDEXPRG variable but stated they were currently pregnant and had information on month of pregnancy in the RHQ. We therefore reassigned their status to “pregnant,” resulting in 1296 pregnant women available for analysis. Of these, all women had data on dietary supplement use.

Supplement use, folate status, and covariates

Dietary supplement use was assessed as part of the household interview for all NHANES participants. Survey participants were asked to complete the dietary supplement questionnaire that examines use of dietary supplements in the previous 30 d. If a person reported use of supplements, they were asked to provide the container and/or label of the products, which were then quantified and verified by survey personnel through examination of the supplement labels or by otherwise obtaining information from the supplement manufacturers (19). In the NHANES dietary supplement data, antacid use is considered separately from other dietary supplement use. If a pregnant woman answered “no” to the question regarding dietary supplement use but “yes” to the question on antacid use, she was not counted in this analysis as a dietary supplement user. This was done to avoid over-representing true dietary supplement use by including women who might have used antacids only for medicinal purposes (e.g., to relieve heartburn) instead of to obtain minerals such as calcium and magnesium, which antacids commonly contain. Because of this, if a pregnant respondent answered “yes” to the dietary supplement question and reported taking antacids in addition to other supplements, the antacids were included and analyzed as their own group to distinguish them from other mineral supplements.

For the more general analysis on supplement intake, we classified supplements according to the following categories: 1) combined multivitamin/-mineral: supplement containing mainly both vitamins and minerals; 2) single or multivitamin: supplement contains one or more vitamins with no minerals; 3) single or multimineral: supplement contains one or more minerals with no vitamins and is not otherwise classified as an antacid; 4) botanical/herbal/other: supplement contains mainly botanical or other non-vitamin or mineral ingredients; 5) antacid: supplement may contain multiple minerals but is classified as an antacid; and 6) unknown: supplement reported but name and ingredients were unknown. The categories of herbal/botanical/other and unknown had too few reported to make reliable estimates and therefore results are not shown. For the specific folic acid and iron supplement intake analysis, we identified supplements by their inclusion of folic acid or iron as noted by their respective ingredient identification codes on the appropriate dietary supplement analytic file.

We examined RBC folate (nmol/L), which is collected and analyzed as part of the standard venipuncture performed during the MEC examination (20). For all the years included in this analysis, we measured serum and RBC folate using the Bio-Rad Laboratories assay; however, it has been shown that this assay underestimates RBC folate when compared to the gold-standard microbiological assay (21). Therefore, we adjusted RBC folate values using regression equations as recommended by the National Center for Health Statistics (22). Data on RBC folate were missing for 92 (7.1%) of pregnant women. We examined only RBC folate in this analysis, because it is a better indicator of long-term folate storage than serum folate and not subject to hemodilution that occurs during pregnancy (23).

Covariates of interest included age (<25, 25 y), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, and other, including other Hispanic), marital status (married or unmarried), education (high school graduate or less, some college or more), parity (first pregnancy or second or greater pregnancy), trimester of pregnancy coded according to the month of pregnancy reported by the respondent on the RHQ, health insurance coverage status, and socioeconomic status. Socioeconomic status was assessed using poverty income ratio (PIR), which is the ratio of income to the appropriate poverty threshold, developed and updated regularly by the U.S. Census Bureau (24). A ratio of <1 designates a family or individual as being “poor” or falling below the federal poverty threshold. For the current analysis, the PIR was categorized as poor (<1), near-poor (1 to <2), and not poor (≥2).

Statistical analysis

Weighted frequencies of the socio-demographic characteristics were examined for pregnant women taking and not taking supplements. Percentages and SEs were estimated using PROC DESCRIPT in SUDAAN (25). We present results in text as percentages ± SE. Significant differences in percentages within variable categories were assessed using pairwise comparisons generated by the PRED_EFF statement in PROC RLOGIST at the $P < 0.05$ level (25). Because supplement use was highly prevalent in these data, resulting in ORs substantially higher than the RR, we calculated model-adjusted prevalence ratios and 95% CIs for each covariate using the PREDMARG statement in PROC RLOGIST (26). Model-adjusted methods were used to further examine these associations after adjusting for the effect of the other variables and determining the most parsimonious model. The logistic regression models do not include missing data. We also estimated the percent of pregnant women reporting dietary supplement use according to the broader categories of supplements and specifically folic acid and iron using PROC SURVEYFREQ in SAS (27). The mean intake of folic acid and iron intake via dietary supplements (mean ± SE) was calculated using an algorithm and program provided by National Center for Health Statistics (28). Mean and percentiles of RBC folate were estimated according to supplement use and trimester of pregnancy using PROC DESCRIPT. All results were weighted using the MEC examination weights, which were combined and recalculated for all years of NHANES used in analysis per NHANES guidance (29).

Results

Of pregnant women, $78\% \pm 2$ reported supplement use in the previous 30 d (**Table 1**). Pregnant women using supplements differed from women not using supplements by nearly every characteristic. Compared with those not taking supplements, pregnant women reporting supplement use were more likely to be 25 y of age or older, have at least some college education, and were more likely to be non-Hispanic white. Eighteen percent of supplement users were unmarried compared with 47% among supplement nonusers. Pregnant women who reported supplement use were more likely to be in their third trimester, whereas women reporting no supplement use were more likely in their first trimester. Whereas most supplement users and nonusers had some type of health insurance, nonusers were more likely to be uninsured than women who reported supplement use.

Finally, pregnant women reporting supplement use were more likely to have a PIR of 2 (indicating higher income) compared with those not taking supplements.

In the crude bivariate analysis (**Table 2**), significant associations supported the results shown in Table 1. Due to the correlation among education, income, and health insurance, only education was included in the adjusted model, along with the other demographic characteristics. Education was selected due to its previously shown association with nutritional habits (30). Health insurance was then added to this model to assess whether it had an additional impact on the correlates of supplement use; however, addition of insurance did not change the model fit or substantially alter the associations with the other correlates. The results of that model are shown in Table 2. Addition of income did not change model fit and is not presented here. After adjusting for all variables, except income, only trimester and education were significantly associated with supplement use.

The majority of pregnant women reported taking a multivitamin/mineral (**Table 3**). In addition, 74% reported taking a supplement, either a multivitamin or multimineral containing folic acid, and 73% reported taking an iron-containing supplement. Most pregnant women reporting supplement use reported taking only one supplement ($72\% \pm 3$), but values ranged from 1 to 12 with a mean of 1.4 ± 0.1 . We examined and compared the characteristics of women reporting folic acid and iron supplementation with those not reporting use, but the results were very similar to those of supplement use overall and are not reported here.

Finally, we examined the percent of women taking iron and folic acid by trimester of pregnancy (**Table 4**) and percentiles of RBC folate by supplement use and trimester (**Table 5**). Approximately 55–60% of women in their first trimester reported taking a folic acid- or iron-containing supplement compared with 76–78% in their second trimester and 89% in their third trimester. In general, RBC folate was lower among supplement nonusers and lowest among women in their first trimester.

Discussion

The majority of pregnant women in the US are using a dietary supplement at some time during their pregnancy, most frequently a multivitamin/-mineral product. However, ~20% reported not using a dietary supplement during pregnancy, although this may vary by trimester; women in their third trimester of pregnancy were more likely to report using supplements compared with women in their first trimester. In addition, use of supplements in pregnancy was related to education, income, health insurance status, age, race/ethnicity, and marital status similar to findings in other life-stage groups and other reports (15,17). However, after multivariate adjustment, only education and trimester of pregnancy were significantly associated with supplement use during pregnancy in the US. We also found that the majority of pregnant women were taking a supplement containing folic acid and/or iron and that supplement use was associated with improved RBC folate status. Finally, RBC folate status varied by trimester, indicating potential shortfalls in folic acid intake in early pregnancy even during an era of increased awareness of folic acid use in pregnancy and fortification of the food supply.

To our knowledge, only one previous study has examined iron supplement use among a nationally representative sample of pregnant women in the US. Using NHANES III (1988–1994), Cogswell et al. (14) reported that 72% of pregnant women sampled reported taking a dietary supplement containing iron. Although the unweighted sample size ($n = 295$) was less than in the current study, our results of 73% closely match. However, this may indicate that iron supplementation has not improved among pregnant women in the US in the last decade. In addition, we report a lower mean intake of iron from supplements (48 mg/d) compared with the 78 mg/d that Cogswell et al. (14) reported. The reason for this difference is not clear, although the estimates from the current study are more closely aligned with the Tolerable Upper Intake Limit for iron of 45 mg/d (31). A recent analysis using the same NHANES sample as the current study reported that the overall prevalence of iron deficiency was 18% among pregnant women, which still exceeds the Healthy People 2010 baseline measure of 16% and the target goal of 14.5% iron deficiency during pregnancy (32,33). This indicates that more strides may need to be made to improve iron supplementation to help reduce iron deficiency during pregnancy.

We are not aware of any other study that reported findings on the prevalence of folic acid supplementation or folate status among a nationally representative sample of pregnant women in the US, although studies have reported on folate status and folic acid intake among nonpregnant women using NHANES data (11,34,35). An analysis of women of childbearing age sampled in the 2001–2002 NHANES revealed low intake of folic acid via supplementation (26% of women 15–49 y old taking $>400 \mu\text{g/d}$) (11). Similarly, an analysis of folic acid intake from supplements and foods from the 2003–2006 NHANES demonstrated that only 24% of nonpregnant women overall consumed the recommended 400 $\mu\text{g/d}$ (34); however, when stratified by supplement use, 72% of women reporting supplement use were found to consume 400 $\mu\text{g/d}$ folic acid, thus illustrating the role supplements play in helping women obtain the recommended daily amount. In addition, studies have shown that dietary supplement users have better dietary quality, including higher fruit and vegetable consumption, and have higher folic acid intakes from food alone compared with supplement nonusers (36,37); therefore, the pregnant women reporting supplement use in this sample could also be obtaining the recommended amount of folic acid due to improved diets as well. Although we did not assess dietary intake of this group of pregnant women, future research could determine if there are differences in dietary quality associated with supplement use during pregnancy.

Our results also demonstrate that folic acid supplement use was associated with improved folate status, similar to a recent population-based study of Canadian women (38). In that study, Colapinto et al. (39) reported that for supplement nonusers, at least 25% of pregnant women did not have RBC folate concentrations $>906 \text{ nmol/L}$, which is one cutoff value that has been defined to prevent neural tube defects. Our results showed that among all pregnant women, the 25th percentile value of 953 nmol/L for women in their first trimester was not much above this particular cutoff value. We found that the RBC folate concentration was lowest during the first trimester, a time when folic acid is critical; however, the median RBC folate in the first trimester was still greater among the pregnant supplement takers in our study compared with nonpregnant women ages 15–44 y from NHANES 1999–2010 as

reported by Pfeiffer et al. (40). In addition, the majority of folic acid supplements reported in this analysis contained higher dosages of folic acid (800 μg), which indicates that most women were taking prenatal doses of folic acid rather than the lower standard multivitamin dosages (400 μg). Small numbers did not permit us to conduct a more formal analysis by folic acid dose by trimester. Although we report a mean daily folic acid intake from supplements of double the recommended amount and that 72% of pregnant women reported taking a folic-acid supplement, we were not able to assess when women began using folic acid. However, folic acid supplementation, as well as overall dietary supplement use, was lowest in the first trimester of pregnancy, a finding not explained by sociodemographic characteristics.

Although multivitamin and folic acid supplementation is recommended during early pregnancy, these findings could reflect the difficulties some women encounter with tolerance of supplementation, particularly iron supplements, due to nausea and vomiting in early pregnancy (41,42). In addition, it is possible that women who were sampled while in their first trimester may have recently become aware of their pregnancy and therefore were not taking supplements. However, because folic acid is recommended prior to pregnancy for women of child-bearing age, this may also corroborate the low compliance of these recommendations as reported by Yang et al. (11). More research is needed on the potential for lower-than-recommended nutrient intakes, particularly in early pregnancy, and to determine the reasons for noncompliance in early pregnancy.

It is important to note, however, that the pregnant women in NHANES were not evenly distributed by trimester. Of the women with data on month of current pregnancy (81% of women coded as pregnant), 20% were in the first trimester, with 41 and 38% in the second and third trimesters, respectively (unweighted and weighted data yielded similar distributions). Women who were missing data on trimester were similar to all pregnant women in NHANES, with respect to race/ethnicity, education, and marital status, and ~72% of women missing information on trimester reported taking supplements; however, it is possible that some bias may have been incurred by this unequal distribution of pregnancy by trimester. We did perform a sensitivity analysis to try to assess this potential bias where all pregnant women missing information on month of pregnancy were reassigned to the first trimester group and the data were reanalyzed. Although this resulted in a more even distribution of women by trimester among supplement users, it did not change the results of the percent of pregnant women taking supplements by trimester or the logistic regression.

In the current study, education was associated with supplement use in pregnancy, which is similar to findings from studies of multivitamin use in the general population using NHANES data (43,44). In addition, education as well as age and race/ethnicity is associated with intention to be become pregnant, which in turn is associated with multivitamin and folic acid use (45,46). Though this could help explain the findings related to education, information on intention of pregnancy is not available in NHANES. Further research is needed to understand potential interactions between intention of pregnancy and demographic characteristics as they relate to multivitamin and dietary supplement use.

Our study relies upon self-reported interview data; however, NHANES interviewers ask to see the dietary supplement containers that each participant reports using to verify the reported supplements. Furthermore, although we had a nationally representative sample, the unweighted sample sizes were too small to perform more stratified analyses by supplement type and examine potential interactions (e.g., race/ethnicity by education). We were not able to assess other potential factors related to dietary supplement use in pregnancy, such as pregnancy intention. Furthermore, physiological changes in pregnancy may alter RBC folate concentrations. With these caveats in mind, the strengths of our study should not be overlooked. This study documents supplement use and is the first to our knowledge to examine folate status in pregnancy in a nationally representative population of pregnant women who were sampled at different times throughout pregnancy. The detailed information on supplement use allowed us to explore dietary supplements beyond multivitamins and minerals among a nationally representative group of pregnant women, which to the best of our knowledge, has not been previously done.

Although the majority of U.S. pregnant women appear to be taking a dietary supplement during pregnancy, ~20% are not. While young women, those of race/ethnicity other than non-Hispanic white, and/or those who have less education are at potential risk for nutritional deficiencies in pregnancy, more research is needed to understand why supplement use may still be low in early pregnancy. In addition, the results of this analysis suggest that the desired compliance with folic acid supplement recommendations for women of child-bearing age are still not being fully met, as indicated by relatively low RBC folate status of women in early pregnancy.

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Literature Cited

1. Institute of Medicine. Nutrition during pregnancy. Part I: weight gain. Part II: nutrient supplements. National Academy of Sciences; Washington, DC: 1990. Subcommittee on Nutritional Status and Weight Gain during, Pregnancy..
2. Picciano MF. Pregnancy and lactation: physiological adjustments, nutritional requirements and the role of dietary supplements. *J Nutr.* 2003; 133:S1997–2002.
3. Turner RE, Langkamp-Henken B, Littell RC, Lukowski MJ, Suarez MF. Comparing nutrient intake from food to the estimated average requirements shows middle- to upper-income pregnant women lack iron and possibly magnesium. *J Am Diet Assoc.* 2003; 103:461–6. [PubMed: 12669009]
4. Kaiser L, Allen LH, American Dietetic Association. Position of the American Dietetic Association: nutrition and lifestyle for a healthy pregnancy outcome. *J Am Diet Assoc.* 2008; 108:553–61. [PubMed: 18401922]
5. American Academy of Pediatrics, American College of Obstetricians and Gynecologists. Guidelines for prenatal care. 6th ed.. American Academy of Pediatrics; Elk Grove (IL): 2007.
6. The American College of Obstetricians and Gynecologists. [2012 Sep 18] Frequency asked questions: pregnancy. Available from: <http://www.acog.org/~media/For%20Patients/faq001.pdf?dmc=1&ts=20120823T1027301297>
7. CDC.. [2012 Sept 18] National Center for Birth Defects and Developmental Disabilities. During pregnancy. Available from: http://www.cdc.gov/ncbddd/pregnancy_gateway/during.html

8. March of Dimes. [2012 Sept 18] Eating healthy during pregnancy. Available from: http://www.marchofdimes.com/pregnancy/nutrition_in-depth.html
9. FDA. Food additives permitted for direct addition to food for human consumption; folic acid (folacin), final rule. Fed Regist. 1996; 61:8797–807.
10. Bailey RL, Dodd KW, Gahche JJ, Dwyer JT, McDowell MA, Yetley EA, Sempos CA, Burt VL, Radimer KL, Picciano MF. Total folate and folic acid intake from foods and dietary supplements in the United States: 2003–2006. Am J Clin Nutr. 2010; 91:231–7. [PubMed: 19923379]
11. Yang QH, Carter HK, Mulinare J, Berry RJ, Friedman JM, Erickson JD. 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. Am J Clin Nutr. 2007; 85:1409–16. [PubMed: 17490980]
12. Timbo B, Altekruse S, Hyman F, Klontz K, Tollefson L. Vitamin and mineral supplementation during pregnancy. Mil Med. 1994; 159:654–8. [PubMed: 7870324]
13. Yu SM, Keppel KG, Singh GK, Kessel W. Preconceptional and prenatal multivitamin-mineral supplement use in the 1988 National Maternal and Infant Health Survey. Am J Public Health. 1996; 86:240–2. [PubMed: 8633743]
14. Cogswell ME, Kettel-Khan L, Ramakrishnan U. Iron supplement use among women in the United States: science, policy, and practice. J Nutr. 2003; 133:S1974–7.
15. Sullivan KM, Ford ES, Azrak MF, Mokdad AH. Multivitamin use in pregnant and nonpregnant women: results from the Behavioral Risk Factor Surveillance System. Public Health Rep. 2009; 124:384–90. [PubMed: 19445414]
16. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey.. About NHANES. Available from: www.cdc.gov/nchs/nhanes.htm
17. Mirel, LB.; Curtin, LR.; Gahche, J.; Burt, V. JSM Proceedings, Section on Government Statistics. American Statistical Association; Alexandria (VA): 2009. Characteristics of pregnant women from the 2001–06 National Health and Nutrition Examination Survey.; p. 2592–601.
18. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey.. Reproductive Health Questionnaire. Available from: <http://www.cdc.gov/nchs/nhanes/nhanes1999-2000/RHQ.htm>
19. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey.. Dietary supplement use. Available from: http://www.cdc.gov/nchs/data/nhanes/nhanes_99_00/dsqdoc.pdf
20. National Center for Health Statistics. National Health and Nutrition Examination Survey. 1999–2000 Data documentation, codebook, and frequencies [cited 2012 Sept 18].. Nutritional biochemistries. Available from: <http://www.cdc.gov/nchs/nhanes/nhanes1999-2000/LAB06.htm>
21. Fazili Z, Pfeiffer CM, Zhang M, Jain RB, Koontz D. Influence of 5,10-methylenetetrahydrofolate reductase polymorphism on whole-blood folate concentrations measured by LC-MS/MS, microbiologic assay, and bio-rad radioassay. Clin Chem. 2008; 54:197–201. [PubMed: 18160726]
22. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey 2007–2008 Data Documentation. Available from: http://www.cdc.gov/nchs/nhanes/nhanes2007-2008/FOLATE_E.htm
23. Yetley EA, Pfeiffer CM, Phinney KW, Fazili Z, Lacher DA, Bailey RL, Blackmore S, Bock JL, Brody LC, Carmel R, et al. Biomarkers of folate status in NHANES: a roundtable summary. Am J Clin Nutr. 2011; 94:S303–12.
24. U.S. Census Bureau. [2012 Sept 18] Current Population Survey (CPS) definitions and explanations. 2003. Available from: <http://www.census.gov/cps/>
25. Research Triangle Institute. SUDAAN language manual, release 10.0. Research Triangle Institute; Research Triangle Park (NC): 2008.
26. Bieler GS, Brown GG, Williams RL, Brogan DJ. Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. Am J Epidemiol. 2010; 171:618–23. [PubMed: 20133516]
27. SAS Institute Inc.. SAS 9.2 Help and documentation. SAS Institute Inc.; Cary (NC): 2008.
28. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey. Dietary NHANES tutorial.. Estimate population mean intakes. Task 3: estimate mean

nutrient intake from supplements. Available from: <http://www.cdc.gov/nchs/tutorials/Dietary/Basic/PopulationMeanIntakes/intro.htm>

29. National Center for Health Statistics. [2012 Sept 18] National Health and Nutrition Examination Survey. Continuous NHANES tutorial. Specifying weighting parameters. Task 2: constructing weights for combined NHANES survey cycles. Available from: <http://www.cdc.gov/nchs/tutorials/NHANES/SurveyDesign/Weighting/intro.htm>
30. Variyam JN, Blaylock J. Unlocking the mystery between nutrition knowledge and diet quality. *FoodRev.* 1998; 21:21–8.
31. Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. National Academy Press; Washington, DC: 2001.
32. Mei Z, Cogswell ME, Looker AC, Pfeiffer CM, Cusick SE, Lacher DA, Grummer-Strawn LM. Assessment of iron status in US pregnant women from the National Health and Nutrition Examination Survey (NHANES), 1999–2006. *Am J Clin Nutr.* 2011; 93:1312–20. [PubMed: 21430118]
33. Healthy People 2020 Topics and Objectives. [2012 Sept 18] Nutrition and weight status. Objective NWS-22.. Reduce iron deficiency among pregnant females. Available from: <http://www.healthypeople.gov/2020/topicsobjectives2020/objectiveslist.aspx?topicId=29>
34. Tinker SC, Cogswell ME, Devine O, Berry RJ. Folic acid intake among U.S. women aged 15–44 years, National Health and Nutrition Examination Survey, 2003–2006. *Am J Prev Med.* 2010; 38:534–42. [PubMed: 20347553]
35. Centers for Disease Control and Prevention. Use of supplements containing folic acid among women of childbearing age: United States, 2007. *MMWR Morb Mortal Wkly Rep.* 2008; 57:5–8. [PubMed: 18185493]
36. Foote JA, Murphy SP, Wilkens LR, Hankin JH, Henderson BE, Kolonel LN. Factors associated with dietary supplement use among healthy adults of five ethnicities: the Multiethnic Cohort Study. *Am J Epidemiol.* 2003; 157:888–97. [PubMed: 12746241]
37. Bailey RL, Fulgoni VL III, Keast DR, Dwyer JT. Examination of vitamin intakes among US adults by dietary supplement use. *J Acad Nutr Diet.* 2012; 112:657–63. [PubMed: 22709770]
38. Colapinto CK, O'Connor DL, Dubois L, Tremblay MS. Folic acid supplement use is the most significant predictor of folate concentrations in Canadian women of childbearing age. *Appl Physiol Nutr Metab.* 2012; 37:284–92. [PubMed: 22452580]
39. Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects. Implications for prevention. *JAMA.* 1995; 274:1698–702. [PubMed: 7474275]
40. Pfeiffer CM, Hughes JP, Lacher DA, Bailey RL, Berry RJ, Zhang M, Yetley EA, Rader JI, Sempos CT, Johnson CL. Estimation of trends in serum and RBC folate in the U.S. population from pre- to postfortification using assay-adjusted data from the NHANES 1988–2010. *J Nutr.* 2012; 142:886–93. [PubMed: 22437563]
41. Nguyen P, Nava-Ocampo A, Levy A, O'Connor DL, Einarson TR, Taddio A, Koren G. Effect of iron content on the tolerability of prenatal multivitamins in pregnancy. *BMC Pregnancy Childbirth.* 2008; 8:17. [PubMed: 18482454]
42. Nguyen P, Thomas M, Koren G. Predictors of prenatal multivitamin adherence in pregnant women. *J Clin Pharmacol.* 2009; 49:735–42. [PubMed: 19386624]
43. Bailey RL, Gahche JJ, Lentino CV, Dwyer JT, Engel JS, Thomas PR, Betz JM, Sempos CT, Picciano MF. Dietary supplement use in the United States, 2003–2006. *J Nutr.* 2011; 141:261–6. [PubMed: 21178089]
44. Radimer K, Bindewald B, Hughes J, Ervin B, Swanson C, Picciano MF. Dietary supplement use by US adults: data from the National Health and Nutrition Examination Survey, 1999–2000. *Am J Epidemiol.* 2004; 160:339–49. [PubMed: 15286019]
45. Chuang CH, Hillemeier MM, Dyer AM, Weisman CS. The relationship between pregnancy intention and preconception health behaviors. *Prev Med.* 2011; 53:85–8. [PubMed: 21539855]
46. D'Angelo D, Williams L, Morrow B, Cox S, Harris N, Harrison L, Posner SF, Hood JR, Zapata L, CDC. Preconception and interconception health status of women who recently gave birth to a live-

born infant–Pregnancy Risk Assessment Monitoring System (PRAMS), United States, 26 reporting areas, 2004. *MMWR Surveill Summ.* 2007; 56:1–35. [PubMed: 18075488]

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TABLE 1

Characteristics of supplement users and nonusers among pregnant women in NHANES 1999–2006

	Supplement users, <i>n</i> = 1007		Supplement nonusers, <i>n</i> = 289		Chi-square <i>P</i> value
	<i>n</i>	weighted % ¹	<i>n</i>	weighted %	
All pregnant women	1007	77.6 ± 2.2	289	22.4 ± 2.2	<0.0001
Age					
<25 y	364	28.3 ± 2.7	181	56.7 ± 5.3	<0.0001
≥25 y	643	71.7 ± 2.7	108	43.2 ± 5.3	
Race/ethnicity					
Non-Hispanic white	508	62.5 ± 2.7	54	27.7 ± 5.7	<0.0001
Non-Hispanic black	129	12.3 ± 1.5	78	27.0 ± 4.6	
Mexican-American	266	11.7 ± 1.4	125	23.6 ± 3.7	
Other	104	13.5 ± 2.3	32	21.7 ± 6.4	
Marital status					
Unmarried	201	17.9 ± 2.5	126	46.5 ± 5.2	<0.0001
Married	772	76.0 ± 2.9	153	45.3 ± 4.7	
Missing ³	34	–	10	–	
Parity					
First birth	297	29.5 ± 2.7	58	17.0 ± 4.1	NS ⁴
Second birth or higher	635	63.2 ± 3.3	193	69.5 ± 5.6	
Missing	75	–	38	–	
Trimester					
First	141	16.3 ± 2.2	97	44.4 ± 6.1	<0.01
Second	372	34.7 ± 3.2	86	40.8 ± 5.3	
Third	370	32.9 ± 3.1	50	14.8 ± 3.7	
Missing	124	16.1 ± 2.6	56	25.7 ± 4.4	
Health insurance					
No	130	9.4 ± 1.4	110	34.8 ± 4.3	<0.0001
Yes	875	90.5 ± 1.4	173	63.8 ± 4.5	
Missing	2	–	6	–	
Poverty-income ratio					
<1	286	15.2 ± 1.6	142	41.4 ± 6.7	<0.0001
1–1.9	202	16.5 ± 2.4	76	21.2 ± 4.9	
≥2	519	59.4 ± 3.4	71	29.1 ± 5.9	
Missing		70		25	
Education					
High school or less	480	33.9 ± 2.9	231	75.5 ± 4.5	<0.0001
Some college or more	526	66.0 ± 2.9	58	24.5 ± 4.5	
Missing		1		0	

¹Values are percentage ± SE based on weighted data.

²Denote unreliable estimates.

³Missing denotes women who were missing data for the variable of interest.

⁴ P value = 0.05.

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TABLE 2

Percentages of pregnant women taking dietary supplements and crude and adjusted prevalence ratios for the association between characteristics and supplement use in NHANES 1999–2006¹

	Taking supplements	Crude PR (95% CI)	Model-adjusted PR (95% CI)
	<i>weighted %</i>		
Age			
<25 y	63.3 ± 4.5	Ref	Ref
≥ 25 y	85.1 ± 2.4	1.34 (1.15, 1.57)	1.10 (0.97, 1.24)
Race/ethnicity			
Non-Hispanic white	88.6 ± 2.2	Ref	Ref
Non-Hispanic black	61.2 ± 4.1	0.69 (0.60, 0.79)	0.86 (0.73, 1.01)
Mexican-American	63.1 ± 4.2	0.71 (0.62, 0.82)	0.90 (0.78, 1.02)
Other	68.3 ± 7.0	0.77 (0.62, 0.95)	0.82 (0.66, 1.02)
Marital status			
Unmarried	57.0 ± 4.4	Ref	Ref
Married	85.3 ± 1.9	1.50 (1.27, 1.76)	1.11 (1.00, 1.24)
Parity			
First pregnancy	85.7 ± 3.2	Ref	Ref
Second pregnancy or more	75.9 ± 3.2	0.89 (0.79, 1.00)	0.93 (0.85, 1.02)
Trimester			
First trimester	63.0 ± 6.7	Ref	Ref
Second trimester	79.8 ± 3.5	1.27 (1.01, 1.59)	1.16 (0.99, 1.35)
Third trimester	91.3 ± 2.2	1.45 (1.16, 1.82)	1.30 (1.11, 1.51)
Health insurance			
No	48.3 ± 4.8	Ref	Ref
Yes	83.0 ± 2.2	1.72 (1.41, 2.09)	1.11 (0.95, 1.30)
Poverty-income ratio			
<1.0	56.0 ± 6.0	Ref	Ref
1.0–1.9	72.9 ± 5.6	1.30 (0.97, 1.75)	2
≥ 2.0	87.6 ± 2.8	1.56 (1.25, 1.96)	2
Education			
High school or less	60.8 ± 3.7	Ref	Ref
Some college or more	90.3 ± 2.1	1.48 (1.31, 1.69)	1.17 (1.05, 1.30)

¹Values are percentage ± SE and PR (95% CI) based on weighted data. Ref, reference group.

²Variable not in adjusted model.

TABLE 3

Percentage of pregnant women taking supplements by supplement type and intakes of folic acid and iron supplementation among pregnant women in NHANES 1999–2006¹

	Unweighted <i>n</i>	Weighted %
Any folic acid-containing supplement	970	73.9 ± 2.6
Any iron-containing supplement	949	72.5 ± 2.5
Single vitamin	107	8.4 ± 1.5
Single mineral	183	11.1 ± 1.6
Multivitamin/mineral	962	74.7 ± 2.4
Antacid	301	28.4 ± 2.4
		<i>µg/d</i>
Supplemental folic acid intake	761	817 ± 27.6
Supplemental iron intake ²	754	47.7 ± 4.2

¹Values are percentage ± SE or mean ± SE based on weighted data.

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TABLE 4

Percent of pregnant women taking a folic acid or iron-containing supplement by trimester of pregnancy in NHANES 1999–2006¹

Trimester	Unweighted <i>n</i>	Iron	Folic acid
		<i>unweighted %</i>	
First	238	56.1 ± 6.7	60.0 ± 7.0
Second	458	76.4 ± 3.8	78.8 ± 3.5
Third	420	89.9 ± 2.3	89.2 ± 2.5
Missing ²	180	56.4 ± 6.4	56.5 ± 6.4

¹ Values are percentage ± SE based on weighted data.

² Missing denotes women who were missing information on month of pregnancy.

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TABLE 5

Percentiles of RBC folate by supplement use and trimester of pregnancy among pregnant women in NHANES 1999–2006¹

	RBC folate percentile					
	Unweighted n ²	10th	25th	50th	75th	90th
				<i>nmol/L</i>		
Supplement users	935	1002 (887, 1111)	1360 (1257, 1442)	1628 (1589, 1695)	1968 (1849, 2096)	2420 (2226, 2968)
Supplement nonusers	269	622 (547, 792)	855 (704, 950)	1041 (962, 1184)	1359 (1191, 1540)	1905 (1521, 2590)
First trimester ³	217	808 (725, 900)	953 (904, 1109)	1255 (1048, 1525)	1632 (1447, 1916)	2051 (1631, 2412)
Second trimester ³	434	1015 (884, 1124)	1231 (1167, 1366)	1527 (1449, 1630)	1781 (1656, 1990)	2253 (1956, 2603)
Third trimester ³	391	1146 (1079, 1331)	1467 (1400, 1600)	1773 (1694, 2012)	2159 (2019, 2301)	2536 (2297, 3815)

¹ Percentile value (95% CI) based on weighted data.

² Unweighted sample size of pregnant women with measured RBC folate.

³ Includes both supplement users and nonusers.

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