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## Correlates of intake of folic acid-containing supplements among pregnant women

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### Abstract

**Objective**— This study describes the timing and correlates of folic acid supplement intake among pregnant women.

**Study design**— Data from 2518 women with estimated delivery dates from 1997 to 2000, collected for the National Birth Defects Prevention Study, a population-based case-control study, were analyzed. Multinomial logistic regression was used to identify correlates of supplement intake.

**Results**— Fifty-three percent of women began taking folic acid supplement during the periconceptional period, 35% during early pregnancy, and 8% during late pregnancy (ie, 3 months before through 1 month after conception, 2–3 months after conception, or more than 3 months after conception, respectively). Women who did not take folic acid supplement periconceptionally tended to be nonwhite, speak Spanish, have low education, be younger than 25 years old, be nulliparous, smoke, have no previous miscarriage and no fertility treatments, begin prenatal care and become aware of their pregnancy after the first trimester, have nonplanned pregnancies, and eat less breakfast cereal.

**Conclusion**— This study identifies correlates of folic acid supplement intake, which may contribute to the design of interventions to improve intake during early pregnancy.

### Keywords

Folic acid; Supplements; Pregnancy

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The Public Health Service and the Institute of Medicine recommend that women of child-bearing age consume at least 400 µg/day of synthetic folic acid (FA),<sup>1,2</sup> an amount that is present in most multivitamin/ mineral supplements. The recommendation was originally intended to prevent neural tube defects. FA also may prevent other birth defects,<sup>3–7</sup> other adverse reproductive outcomes,<sup>8</sup> and chronic diseases.<sup>8</sup> Taking FA-containing supplements remains the most likely route of meeting the recommended intake level, even after considering folate intake from fortified foods.<sup>9,10</sup> By the end of pregnancy, most women are taking FA

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supplements,<sup>11</sup> but in the first few weeks, before pregnancy is clinically evident, closer to one third of women take supplements daily.<sup>4,11-14</sup> Intake during early pregnancy is critical because most birth defects occur during the first few weeks of pregnancy. For example, neural tube closure is completed by day 28 after conception, or 6 weeks after the last menstrual period.

Information on patterns of FA supplement intake during pregnancy and correlates of this behavior is critical to the design of effective interventions to improve intake. Few studies have examined correlates of supplement intake during pregnancy in relatively large and diverse study populations and included multivariable analysis.<sup>11,15,16</sup> We are aware of only 1 study that examined whether predictors of supplement intake varied as pregnancy progressed, and its data are from births that occurred in 1988, before the issuance of major public health recommendations regarding FA.<sup>11</sup> This study describes the pattern of intake of FA supplements among pregnant women and examines correlates of FA supplement intake, comparing correlates of intake during the periconceptional period and later during pregnancy, using recent data from a large, multistate, population-based, case-control study.

## Material and methods

This study included data on deliveries that had estimated due dates from October 1997 to December 2000 and were part of the National Birth Defects Prevention Study.<sup>17</sup> This study is an approved activity of the institutional review boards of the participating study centers and the Centers for Disease Control and Prevention. Each study site randomly selected approximately 100 nonmalformed, liveborn controls per study year from birth certificates (Iowa, Massachusetts, and New Jersey) or birth hospitals (Arizona, California, Georgia, New York, and Texas) to represent the population from which the subjects were derived. Live-born infants with major malformations were ineligible as controls. This analysis included data from controls only. Maternal interviews were conducted using a standardized, computer-based questionnaire, primarily by telephone, in English or Spanish. Interviews were conducted with 2594 control mothers, representing 71% of eligibles, on average 8.6 months after delivery. We excluded 76 women who were missing data on supplement intake, leaving 2518 women for analysis.

Exposures to many factors were assessed, relative to the woman's estimated date of conception, which was derived by subtracting 266 days from the woman's expected due date (EDD). The EDD was based on mother's self-report; if unknown, the EDD was estimated from information in the medical record (less than 2% of subjects). A shortened version of the Willett Food Frequency Questionnaire (FFQ) assessed frequency of intake of 58 food items during the year before pregnancy.<sup>18</sup> Separate, more detailed questions assessed intakes of breakfast cereals, tea and coffee, sodas, and food supplements (ie, products that are sometimes mixed into drinks, like protein powder) during the 3 months before pregnancy. The U.S. Department of Agriculture version 16 nutrient database served, as the source of nutrient values.<sup>19</sup> Final nutrient values incorporate data from the FFQ, cereals, beverages, and food supplements combined. The dietary data were treated as missing for 78 women with more than 1 missing food item in the FFQ (n = 31) and/or average daily kilocalorie consumption less than 500 or more than 5000 (n = 63).

Women were queried about their intake of vitamin and mineral dietary supplements during the 12 weeks before conception through the date of delivery. For each supplement product, they reported start and stop dates and frequency of intake; women who did not know the exact start or stop date of intake reported duration of intake; this information was recoded to correspond to month-long (ie, 30-day) increments before or after the date of conception. All products were hand reviewed to assess whether they contained FA. Women were divided into four groups: (1) periconceptional intake, in which intake began during the 3 months before conception (or

earlier) or during the first month after conception; (2) early pregnancy intake, in which intake began during the second or third month after conception; (3) late intake, in which intake began during the fourth month or later during pregnancy; or (4) no intake during the 3 months before conception or during pregnancy. Within these groups, we identified women as having continuous or sporadic intake (ie, intake was continued until delivery or was discontinued before delivery).

Potential correlates of supplement intake included mother's race-ethnicity; nativity; language of interview; education; household income; employment during the 3 months before conception through the time of delivery; age; prepregnancy body mass index; number of previous live births; previous miscarriage; fertility treatments (based on a positive response to any of the following three questions: "Did you have any surgical procedures... [to help you become pregnant]?"; "in the 2 months before you became pregnant with [baby's name], did you take any medications to help you become pregnant?"; or "did you have any other procedures to help you become pregnant...?"); nausea or vomiting during the first trimester; cigarette smoking, alcohol consumption, and recreational drug use during the 3 months before conception through the time of delivery; trimester of first prenatal care visit; trimester when pregnancy was recognized; pregnancy wantedness (defined below); daily intake of dietary folate equivalents<sup>19</sup>; daily servings of ready-to-eat breakfast cereal; daily servings of fruits and vegetables (to reflect diet quality); and study site. Pregnancy wantedness was categorized as: (1) wanted to become pregnant then, (2) wanted to wait until later, (3) did not want to become pregnant at all, (4) no preference, and (5) became pregnant while using contraception consistently. The first 4 categories were taken directly from a question about pregnancy wantedness. The final category was derived from a question about use of contraception because women who became pregnant while using contraception were not asked about pregnancy wantedness.

We examined correlates of FA supplement intake during each defined time period. We estimated odds ratios (ORs) and 95% confidence intervals (CIs) from multinomial logistic regression models in SAS using PROC CATMOD (version 9.1, 2002-2003, SAS Institute, Cary, NC). Periconceptual users served as the reference group for all comparisons because they represent the ideal behavior. We first put all potential covariates into a single model and excluded 1 variable at a time, based on the highest *P* value, until all variables in the model had *P* values less than .20. The overall *P* values reflect whether any of the groups being compared differed from periconceptual users. Multivariable analyses were conducted separately for women with continuous and sporadic intake.

## Results

Among the 2518 women interviewed, 53% (1324) began taking FA supplements before or during the periconceptual period, 35% (879) during early pregnancy, and 8% (208) during late pregnancy, such that overall, 96% (2411) took FA supplements at some time during the 3 months before pregnancy or during pregnancy (Table I). Two percent of the women (39) took only non-FA-containing supplements, and 3% (68) took no supplements during this time period. Among women who took FA supplements, 94% (2256) reported daily intake, 97% (2346) reported intake of prenatal multivitamin/mineral formulations, and 84% (2021) continued intake through delivery.

The main multivariable analysis included 1948 women with continuous (ie, nonsporadic) FA intake or no supplement intake. Table II shows the distribution of each of the variables included in the final multivariable model, within each of the 4 supplement use groups. Table III shows the adjusted ORs associated with each variable, and each supplement use group, relative to periconceptual users. The following variables were not predictive of periconceptual FA

intake (overall *P* values of .20 or greater): maternal nativity, income, employment, body mass index, nausea during the first trimester, pregnancy wantedness, dietary folate intake, and daily servings of fruits and vegetables.

Relative to non-Hispanic white women, who were more likely to be periconceptual supplement users than women in other racial-ethnic groups, women with other race-ethnicities were about 2 times more likely to begin taking FA supplements during early pregnancy than they were to take supplements during the periconceptual period. Relative to non-Hispanic white women, they tended to be even more likely to begin supplement intake later during pregnancy or not at all (ORs ranged from 2.0 to 5.0). A similar pattern was observed for women with less than 4 years of college. Women interviewed in Spanish were at increased risk of nonpericonceptual supplement intake (OR range 2.0 to 7.2), compared with women interviewed in English. Women younger than 20 years old were more likely to begin FA intake after the periconceptual period or not at all (OR range 2.3 to 2.9).

Women who had 2 or more previous live births were at increased risk of no intake (OR 3.1, 95% CI 1.3 to 7.0). The ORs among women who had any fertility treatments ranged from 0.2 to 0.4, suggesting that they were 2.5 to 5.0 times more likely to be periconceptual users.

Relative to women who began prenatal care in the first trimester, women who began care in the second trimester were at increased risk of nonpericonceptual intake (OR range 1.5 to 24.9). Results were mixed for women who began prenatal care in the third trimester or not at all, probably because of the small number of women in this category. Women who became aware of their pregnancy after the first trimester were more likely to report late or no supplement intake than periconceptual intake (OR range 1.3 to 9.3).

In general, the factors that were associated with early pregnancy FA intake had even stronger associations with late pregnancy intake. Associations with no intake were less consistent, perhaps due to the small number of women who did not take any FA supplements.

Among the 390 women with sporadic patterns of intake, 50% (195) began taking supplements in the periconceptual period, 38% (149) in early pregnancy, and 12% (46) in late pregnancy. Most of them (67%) stopped taking supplements during late pregnancy. Multinomial logistic regression results were similar as for women with continuous FA intake, with 1 exception: the addition of pregnancy wantedness (data not shown). Women who were not trying to get pregnant tended to be more likely to be nonpericonceptual users, with most of the estimated ORs around 1.5.

## Comment

This study indicates that most (96%) women from several regions of the United States took FA supplements during pregnancy. However, only 53% took FA around the time of neural tube closure, which is completed by 4 weeks after conception.

Women who were not taking FA supplements during the first few weeks after conception (ie, the periconceptual period) tended to be nonwhite and younger than 25 years old, have low education, begin prenatal care and become aware of their pregnancy after the first trimester, and have nonplanned pregnancies, findings that parallel several previous studies.<sup>11,12,15,16,20–22</sup> Women who had fertility treatments were much more likely to take FA supplements around the time of conception than women who did not have any treatments. Women who had a previous live birth, especially women with 2 or more live births, had an increased risk of no intake.

Unique contributions of this study include its description of when women began taking FA supplements by month of pregnancy, multivariable analysis of a wide variety of potential correlates of supplement intake, and comparison of correlates among different groups of women based on when they began taking FA. Additional advantages are that it includes a recent, population-based, multistate sample, and data on supplement intake were detailed with regard to timing and frequency and types of supplements taken. Nonetheless, our ability to estimate the contribution of correlates may be compromised by certain study design features. Individuals may have been misclassified with regard to type, timing, and frequency of supplement intake. The validity of self-reported supplement intake is likely to be high,<sup>23,24</sup> especially with regard to FA content, given the predominant intake of prenatal supplements, which have relatively standard FA content. The extent of error in the reported dates of intake, or in reported estimated dates of delivery, is unknown. The relatively small number of women who did not take any FA-containing supplements limited the precision with which we could estimate risks within this group. The potential impact of selection bias is unknown.

A recent study using data from the Pregnancy Risk Assessment Monitoring System reported prevalences of FA supplement intake at least 4 times per week during the month before pregnancy from 25% to 41% across 19 states.<sup>14</sup> A recent case-control study, based on data from Boston, Philadelphia, and Toronto, reported that 40% of women took FA supplements daily during the 3 months before pregnancy and during the first trimester.<sup>16</sup> These results compare well with our finding that 31% of women reported taking FA supplements before conception. Participants in our study were similar to all women giving birth in the United States in the year 2000 with regard to parity, age, and trimester of first prenatal care visit, and they were somewhat more likely to be non-Hispanic white (65% versus 58%) and to have more than 12 years of education (61% versus 46%).<sup>25</sup>

Most women do not meet the recommended levels for FA intake by consuming foods,<sup>9,10</sup> and FA-containing supplements remain an important vehicle for meeting recommendations. Most women in this study took FA supplements that contained various additional micronutrients, which may further improve the likelihood of a healthy pregnancy outcome.

Some of the factors that characterized women who did not take FA supplements during the periconceptional period are also associated with increased neural tube defect risk (eg, low education, Hispanic race-ethnicity, and Spanish language preference).<sup>26,27</sup> Recent improvements in FA supplement intake seem to be smallest among some of these most vulnerable groups, reiterating the need for interventions that focus on certain subgroups of the population.<sup>28</sup>

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**Table I**

Distribution of intake of FA-containing supplements during the 3 months before conception through the time of delivery\*

Category of supplement use	Percent (number)
Took no supplements	2.7 (68)
Took only non-FA-containing supplements	1.5 (39)
Took FA-containing supplements	95.8 (2411)
Total	100 (2518)
Among FA-containing supplement users, months before or after conception when supplement intake began	
During the 3 months before conception or earlier	31.3 (789)
First month after conception	21.3 (535)
Second month after conception	23.6 (594)
Third month after conception	11.3 (285)
Fourth month after conception	4.9 (122)
Fifth month after conception	1.9 (48)
Sixth month after conception	0.8 (20)
Seventh month after conception	0.4 (11)
Eighth month after conception	0.2 (6)
Ninth or 10th month after conception	< 0.1 (1)
Total	95.8 (2411)

\* Among 2,518 women with estimated dates of delivery from October, 1997 to December, 2000.



**Table II**  
Distribution of when intake of folic acid-containing supplements began, by maternal characteristics

Maternal Characteristics	Periconceptional intake, %* (n = 1070)	Early pregnancy intake, %* (n = 667)	Late pregnancy intake, %* (n = 150)	No intake, %* (n = 61)	Total (n = 1948)
Race-ethnicity					
Non-Hispanic white	66	28	4	2	1259
Non-Hispanic black	39	43	14	4	236
Hispanic	30	47	16	7	383
Other	46	39	11	4	70
Interview language					
English	56	34	7	3	1868
Spanish	19	46	30	5	80
Education					
Less than high school	26	46	22	7	261
High school	42	44	10	5	510
1-3 years of college	56	35	6	3	552
4 or more years of college	77	21	2	1	625
Age, yr					
13-19	25	51	18	6	225
20-24	38	46	12	4	381
25-34	63	30	5	2	1058
35 or more	71	21	5	3	284
Number of previous live births					
0	53	37	8	2	817
1	59	31	8	3	667
2 or more	53	34	8	5	464
Miscarriage					
None	52	37	8	3	1522
Any	66	25	6	3	426
Fertility treatments <sup>†</sup>					
No	53	36	8	3	1849
Yes	88	9	2	1	99
Vomiting in first trimester					
At least once per day	45	40	9	5	436
Less than once per day	54	37	8	1	397
Never	59	31	7	3	1115
Cigarette smoking <sup>‡</sup>					
None	57	32	8	3	1558
Any	46	42	7	5	390
Alcohol intake <sup>‡</sup>					
None	49	38	9	4	963
Any	61	31	7	2	985
Recreational drug intake <sup>‡</sup>					
None	56	33	8	3	1846
Any	34	51	9	6	102
First prenatal care visit					
First trimester	60	35	3	3	1685
Second trimester	25	32	40	3	225
Third trimester or none	26	8	42	24	38
Pregnancy awareness					
First trimester	56	35	6	3	1885
Second trimester or later	13	16	62	10	63
Daily servings of ready-to-eat breakfast cereal					
Less than 0.43	55	32	8	5	480
0.43 to < 0.86	59	33	7	1	472
0.86 to less than 1.14	54	36	7	3	499

Maternal Characteristics	Periconceptional intake, %* (n = 1070)	Early pregnancy intake, %* (n = 667)	Late pregnancy intake, %* (n = 150)	No intake, %* (n = 61)	Total (n = 1948)
1, 14 or more	52	36	9	3	497
State of residence					
Arkansas	57	35	6	2	233
California	39	45	13	4	256
Georgia	58	31	9	2	243
Iowa	63	31	5	1	248
Massachusetts	70	24	2	4	244
New Jersey	62	29	4	5	256
New York	53	36	9	2	222
Texas	38	42	15	5	246

\* Periconceptional intake: intake began during the 3 months before conception or the first month after conception; early pregnancy intake: intake began during the second or third month after conception; Late intake: intake began during, the fourth month or Later; no intake during the 3 months before conception through the time of delivery; only women with continuous intake (ie, intake was continued until delivery) were included in the analysis.

† A positive response to any of the following 3 questions served as a marker of maternal subfertility: "Did you have any surgical procedures ... [to help you become pregnant]?" ; "in the 2 months before you became pregnant with [baby's name], did you take any medications to help you become pregnant?"; or "did you have any other procedures to help you become pregnant. ...?"

‡ Any exposure during the during the 3 months before conception through the time of delivery.

Correlates of intake of FA-containing supplements during early or Late pregnancy, relative to intake during the periconceptional period: results from multinomial logistic regression

Table III

Maternal Characteristics	Adjusted odds ratio (95% CI)*		
	Early pregnancy intake <sup>†</sup> (n = 667)	Late pregnancy intake <sup>†</sup> (n = 150)	No intake <sup>†</sup> (n = 61)
Race-ethnicity			
Non-Hispanic white	Reference	Reference	Reference
Non-Hispanic black	2.3 (1.6-3.4)	4.9 (2.3-10.4)	2.0 (0.8-5.4)
Hispanic	2.0 (1.4-2.9)	2.8 (1.3-5.8)	4.8 (2.0-11.5)
Other	2.0 (1.1-3.5)	5.0 (1.7-14.9)	3.6 (0.9-15.0)
Interview language			
English	Reference	Reference	Reference
Spanish	2.0 (1.0-4.0)	7.2 (2.7-18.8)	2.2 (0.6-8.6)
Education			
Less than high school	2.2 (1.4-3.4)	7.9 (2.9-21.6)	4.6 (1.2-17.9)
High school	2.1 (1.5-3.0)	4.5 (1.9-11.0)	3.9 (1.2-13.0)
1-3 years of college	1.7 (1.2-2.3)	3.4 (1.5-8.0)	4.1 (1.3-13.3)
4 or more years of college	Reference	Reference	Reference
Age, yr			
13-19	2.5 (1.4-4.2)	2.3 (0.8-6.5)	2.9 (0.8-10.8)
20-24	1.9 (1.2-2.9)	1.4 (0.6-3.4)	1.4 (0.5-4.0)
25-34	1.3 (0.9-1.8)	0.9 (0.4-1.9)	0.8 (0.3-1.9)
35 or more	Reference	Reference	Reference
Number of previous live births			
0	Reference	Reference	Reference
1	0.8 (0.6-1.1)	1.2 (0.7-2.0)	1.5 (0.7-3.2)
2 or more	1.0 (0.7-1.4)	1.0 (0.5-2.0)	3.1 (1.3-7.0)
Miscarriage			
None	Reference	Reference	Reference
Any	0.7 (0.5-0.9)	0.9 (0.5-1.6)	0.9 (0.5-1.9)
Fertility treatments <sup>†</sup>			
No	Reference	Reference	Reference
Yes	0.2 (0.1-0.5)	0.2 (0.04-1.4)	0.4 (0.1-3.8)
Vomiting in first trimester			
At least once per day	1.2 (0.9-1.6)	1.5 (0.9-2.6)	1.7 (0.9-3.1)
Less than once per day	1.2 (0.9-1.6)	1.0 (0.6-1.9)	0.3 (0.1-1.0)
Never	Reference	Reference	Reference
Cigarette smoking <sup>†</sup>			
None	Reference	Reference	Reference
Any	1.4 (1.1-1.9)	0.9 (0.5-1.7)	2.4 (1.2-4.8)
Alcohol intake <sup>†</sup>			
None	Reference	Reference	Reference
Any	0.9 (0.7-1.1)	1.9 (1.1-3.1)	0.6 (0.3-1.1)
Recreational drug intake <sup>†</sup>			
None	Reference	Reference	Reference
Any	1.4 (0.9-2.3)	0.5 (0.2-1.6)	1.8 (0.6-5.2)
First prenatal care visit			
First trimester	Reference	Reference	Reference
Second trimester	1.7 (1.2-2.5)	24.9 (14.7-42.4)	1.5 (0.6-4.0)
Third trimester or none	0.3 (0.1-1.3)	11.8 (3.8-36.3)	8.9 (2.6-30.2)
Pregnancy awareness			
First trimester	Reference	Reference	Reference
Second trimester or later	1.3 (0.5-3.4)	9.3 (3.4-25.2)	6.5 (1.7-24.8)
Daily servings of ready-to-eat breakfast cereal			

Maternal Characteristics	Adjusted odds ratio (95% CI) <sup>*</sup>		
	Early pregnancy intake <sup>†</sup> (n = 667)	Late pregnancy intake <sup>†</sup> (n = 150)	No intake <sup>†</sup> (n = 61)
Less than 0.43	1.0 (0.8-1.4)	1.3 (0.7-2.5)	2.1 (1.0-4.2)
0.43 to < 0.86	1.2 (0.9-1.6)	1.1 (0.6-2.1)	0.4 (0.1-1.2)
0.86 to less than 1.14	1.4 (1.0-1.8)	1.1 (0.6-2.2)	1.1 (0.5-2.4)
1.14 or more	Reference	Reference	Reference
State of residence			
Arkansas	0.7 (0.5-1.2)	0.5 (0.2-1.2)	0.9 (0.2-3.4)
California	1.1 (0.7-1.7)	0.9 (0.4-1.9)	0.7 (0.2-1.9)
Georgia	0.6 (0.4-1.0)	0.6 (0.2-1.4)	0.8 (0.2-2.9)
Iowa	0.9 (0.6-1.5)	1.0 (0.4-2.5)	0.7 (0.2-3.3)
Massachusetts	0.7 (0.4-1.1)	0.3 (0.1-1.1)	2.5 (0.8-7.7)
New Jersey	0.7 (0.5-1.1)	0.5 (0.2-1.3)	1.9 (0.7-5.2)
New York	1.2 (0.8-1.9)	1.5 (0.6-3.5)	1.6 (0.4-5.5)
Texas	Reference	Reference	Reference

<sup>\*</sup> The reference group for each OR is women who began FA supplement intake during the periconceptual period (n = 1070). Each OR is adjusted for all other variables in the table and reflects risk of beginning FA supplement intake during the specified time period or having no intake, relative to beginning intake during the periconceptual period. Only women with continuous intake (ie, intake was continued until delivery) were included in the analysis.

<sup>†</sup> See Table II for variable definitions.