Patterns and predictors of folic acid supplement use among pregnant women: the Norwegian Mother and Child Cohort Study[1–3]

Roy M Nilsen, Stein E Vollset, Håkon K Gjessing, Per Magnus, Helle M Meltzer, Margaretha Haugen, and Per M Ueland

ABSTRACT

Background: Patterns and predictors of maternal folic acid supplement use have not been examined in large prospective studies of pregnant women.

Objective: We examined the patterns and predictors of maternal folic acid supplement use from 2 mo before pregnancy through the eighth month of pregnancy.

Design: Data from 22 500 women in the Norwegian Mother and Child Cohort Study with deliveries recorded in 2000–2003 were analyzed.

Results: Folic acid supplement use increased from 11.8% at 2 mo before pregnancy to 46.9% at gestational month 3, but decreased to 26.0% at gestational month 8. Of 16 116 women (71.6%) who had taken folic acid supplements at some time before or during pregnancy, 72.4% had started use after becoming pregnant. Ten percent of the women had used supplements regularly from 1 mo before pregnancy throughout the first trimester. These women more frequently reported higher maternal and paternal education, planned pregnancies, infertility treatments, or chronic diseases. They were also more likely to be older, married, and nonsmokers and to have higher income and lower parity.

Conclusions: Most women started folic acid supplementation too late with respect to the prevention of neural tube defects. More effective intervention programs to improve periconceptional intakes of folic acid are needed and should consider both demographic and socioeconomic factors. *Am J Clin Nutr* 2006;84:1134–41.

KEY WORDS Predictors, pregnancy, folic acid, supplements, neural tube defects, cohort study

INTRODUCTION

Several studies, including randomized trials and observational studies, have shown that maternal intake of folic acid (FA) supplements before and early in pregnancy reduces the risk of neural tube defects (NTDs) in infants (1–5). In light of these reports, health authorities in numerous countries recommend periconceptional FA use to fertile women (6). In Norway, official guidelines from 1998 state that all women who may become pregnant should take a daily FA supplement of 0.4 mg from 1 mo before pregnancy throughout the first 2–3 mo of pregnancy to reduce the risk of NTDs (7). Mandatory food fortification with FA to increase intake, as done in the United States and other countries, has not yet been introduced in Norway or in any other European country (6).

Despite recommendations and information campaigns on FA supplementation before and early in pregnancy, the overall periconceptional use of this vitamin is still low in Norway (7, 8). Also, dietary folate intake has been shown to be low (9), which further underscores the need for a more effective promotion of FA use among fertile women. One way to achieve this is to incorporate information on patterns and predictors of FA supplement use among pregnant women in intervention programs designed for FA promotion.

Previous studies on FA awareness and use among fertile women have mainly focused on the time period around neural tube closure and not beyond the first 3 mo of pregnancy (7, 8, 10–15). Exploring the use of FA supplements beyond the first 3 mo is also of relevance, because FA use during pregnancy could have a beneficial effect on other adverse birth outcomes besides NTDs (16). In the present study, we used data from a large pregnancy cohort in Norway and examined patterns and predictors of FA supplement use from 2 mo before pregnancy through the eighth month of pregnancy.

SUBJECTS AND METHODS

Study population

This study drew on resources from the Norwegian Mother and Child Cohort Study (MoBa), which is an ongoing, long-term prospective cohort study that aims to include 100 000 pregnant women and their infants by the end of 2007 (17). The cohort was established in Western Norway in 1999 and has gradually expanded to a national level. During the period 1999–2005, >60 000 pregnant women had been enrolled, and this cohort formed the basis of the current report. Informed consent was

[1] From the Section for Epidemiology and Medical Statistics, Department of Public Health and Primary Health Care (RMN, SEV, and HKG), and the LOCUS for Homocysteine and Related Vitamins and the Section for Pharmacology, Institute of Medicine (PMU), University of Bergen, Bergen, Norway; the Medical Birth Registry, Norwegian Institute of Public Health, Bergen, Norway (SEV); and the Divisions of Epidemiology (HKG and PM) and Environmental Health (HMM and MH), Norwegian Institute of Public Health, Oslo, Norway.

[2] Supported by the Norwegian Research Council.

[3] Reprints not available. Address correspondence to RM Nilsen, Department of Public Health and Primary Health Care, University of Bergen, Kalfarveien 31, N–5018 Bergen, Norway. E-mail: roy.nilsen@uib.no.

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TABLE 1
Characteristics of 22 500 participants in the Norwegian Mother and Child Cohort Study, 2000–2003

	No. of subjects[1]	Percentage
	n	%
Year of delivery		
2000	1075	4.8 ± 0.14[2]
2001	3361	14.9 ± 0.24
2002	7287	32.4 ± 0.31
2003	10 777	47.9 ± 0.33
Maternal age at delivery		
<25 y	2727	12.1 ± 0.22
25–34 y	16 292	72.4 ± 0.30
>34 y	3481	15.5 ± 0.24
Marital status		
Single or other	764	3.4 ± 0.12
Living together	9942	44.2 ± 0.33
Married	11 720	52.1 ± 0.33
Maternal income[3]		
<200 000 NOK	8636	38.4 ± 0.32
200 000–300 000 NOK	8831	39.2 ± 0.33
>300 000 NOK	4404	19.6 ± 0.26
Maternal education		
Primary school	761	3.4 ± 0.12
Secondary school	8601	38.2 ± 0.32
University or college	12 595	56.0 ± 0.33
Other[4]	444	2.0 ± 0.09
Paternal education		
Primary school	1277	5.7 ± 0.15
Secondary school	10 201	45.3 ± 0.33
University or college	9493	42.2 ± 0.33
Other[4]	780	3.5 ± 0.12
Prepregnancy BMI		
<25 kg/m^2	15 623	69.4 ± 0.31
25–29.9 kg/m^2	4776	21.2 ± 0.27
>29.9 kg/m^2	2101	9.3 ± 0.19
Previous no. of deliveries		
0	9290	41.3 ± 0.33
1	8159	36.3 ± 0.32
2	3924	17.4 ± 0.25
>2	1127	5.0 ± 0.15
Pregnancy planning		
No	4671	20.8 ± 0.27
Yes	17 491	77.7 ± 0.28
In vitro fertilization		
No report	21 221	94.3 ± 0.15
Yes	470	2.1 ± 0.10
Ovarian stimulation		
No report	21 164	94.1 ± 0.16
Yes	527	2.3 ± 0.10
Smoking in pregnancy		
No report	19 202	85.3 ± 0.24
Yes	3020	13.4 ± 0.23
Previous no. of stillbirths[5]		
0	12 549	95.0 ± 0.19
1	585	4.4 ± 0.18
>1	76	0.6 ± 0.07
Maternal chronic diseases		
No report	17 092	76.0 ± 0.28
Any report	5408	24.0 ± 0.28
Asthma	912	4.1 ± 0.13
Rheumatoid arthritis	45	0.2 ± 0.03
Epilepsy	142	0.6 ± 0.05
Diabetes (type 1 or 2)	98	0.4 ± 0.04
Urinary tract infection	633	2.8 ± 0.11
Chronic renal disease	53	0.2 ± 0.03
Hypertension	95	0.4 ± 0.04
Heart disease	95	0.4 ± 0.04
Other diseases	2448	10.9 ± 0.21
>1 disease	887	3.9 ± 0.13

[1] Because of missing data, not all numbers total the number of participants (n = 22 500).
[2] % ±SEM (all such values).
[3] NOK, Norwegian Kroner.
[4] Undefined category.
[5] Excludes 9290 women with no previous deliveries.

obtained from each participant before the study, and the study was approved by the Regional Committee for Medical Research Ethics and by the Norwegian Data Inspectorate.

In brief, pregnant women were recruited to the study through a postal invitation after they had signed up for the routine ultrasound examination at their local hospital (around 17–18 wk of gestation). At the ultrasound examination, participating women and their partners were also asked to donate biological specimens. After delivery, a blood sample was collected from the umbilical cord and a second blood sample was taken from the mother. In addition, the mother received 3 questionnaires during her pregnancy and the father received 1. The parents were further asked to respond to 4 additional questionnaires during the infants' early childhood (0–7 y). The cohort was linked to the Medical Birth Registry of Norway (18) to include registered outcomes.

The present study included 23 201 pregnancies and comprised women who returned both the baseline and a second follow-up questionnaire during pregnancy (≈18 and 30 wk of gestation, respectively) and who delivered in 2000–2003. We excluded 172 pregnancies on which we did not have supplement intake data and 529 pregnancies of women who participated more than once (ie, only the first pregnancy was included), leaving a total of 22 500 women for analyses.

Folic acid supplement use

The study participants were asked whether they had used any vitamin or mineral supplements. Users were also asked to report in detail which vitamins and minerals were taken and when and how often they were taken. By using both baseline and follow-up questionnaires, we gathered information about use at 4-wk intervals, ranging from 2 mo before pregnancy through approximately the eighth month after the first day of the last menstruation (ie, gestational month 8). A woman was defined as an FA user if she reported use of supplements containing FA more than once per week for a registered 4-wk period. Periconceptional intake was defined as starting FA supplement use 1 mo before pregnancy and continuing use throughout the first 3 mo of pregnancy.

Other variables

Potential predictors of FA supplement use included maternal income, maternal and paternal education, maternal body mass index (BMI; in kg/m^2) before pregnancy, fertility treatments [in vitro fertilization (IVF) and ovarian stimulation], smoking, and pregnancy planning. From the Medical Birth Registry, we also abstracted data on additional potential predictors, such as year of delivery, maternal age at delivery, marital status, number of previous deliveries (parity), number of previous stillbirths (≥12 wk of gestation), and data on reported chronic maternal diseases. The women reported their education by checking 1 of 7 predefined categories (including an undefined category). On the basis of this information, education was grouped into 4 levels: primary school (0–9 y), secondary school (10–12 y), university and college (>12 y), and other education. Women who reported daily or occasional smoking during their pregnancy were defined as smokers. Planning of pregnancy was defined as an affirmative answer to the question "Was the present pregnancy planned?" Chronic diseases were classified by using ICD–10 disease codes (*International Classification of Diseases*, 10th revision). All variables were treated as categorical unless stated otherwise.

TABLE 2
Monthly prevalence of folic acid supplement use among 22 500 participants in the Norwegian Mother and Child Cohort Study, 2000–2003

Gestational month	Current use of folic acid supplements[1]		Any use of folic acid supplements[2]		Start of folic acid supplementation[3]	
	No. of subjects	Percentage	No. of subjects	Percentage	No. of subjects	Percentage[4]
	n	%	*n*	%	*n*	%
−2	2650	11.8 ± 0.22[5]	2650	11.8 ± 0.22	2650	16.4 ± 0.29
−1	3512	15.6 ± 0.24	4454	19.8 ± 0.27	1804	11.2 ± 0.25
1	5537	24.6 ± 0.29	7248	32.2 ± 0.31	2794	17.3 ± 0.30
2	9147	40.7 ± 0.33	11 236	49.9 ± 0.33	3988	24.7 ± 0.34
3	10 548	46.9 ± 0.33	13 372	59.4 ± 0.33	2136	13.3 ± 0.27
4	8999	40.0 ± 0.33	15 504	68.9 ± 0.31	2132	13.2 ± 0.27
5	7397	32.9 ± 0.31	15 703	69.8 ± 0.31	199	1.2 ± 0.09
6	6626	29.4 ± 0.30	15 902	70.7 ± 0.30	199	1.2 ± 0.09
7	6253	27.8 ± 0.30	16 047	71.3 ± 0.30	145	0.9 ± 0.07
8	5855	26.0 ± 0.29	16 116	71.6 ± 0.30	69	0.4 ± 0.05

[1] Current use in a given gestational month.
[2] Any use within a given gestational month (cumulative numbers).
[3] Start of supplementation in a given gestational month.
[4] Percentage of the total number of folic acid users (n = 16 116).
[5] % ± SEM (all such values).

Statistical analyses

All statistical analyses were performed with and without adjustment for maternal age, marital status, maternal education, parity, and year of delivery. Predictors of periconceptional intake of FA were studied by using log-binomial regression analyses (19). The size of the effect of the predictors was quantified by relative risk (RR), with 95% CIs. A test for linear trend or group difference in supplement use was performed by incorporating the predictor as a continuous variable or as a categorized variable, respectively. Patterns of FA supplement use were examined by calculating the monthly prevalence of use in the total population as well as within categories of selected variables. In the latter case, the prevalence was adjusted by using a direct standardization method (20). First, the total population of pregnant women was considered as a standard and was distributed into all possible combinations of the groups of the adjustment variables. For each combination, we estimated the relative frequency or weight (w) from the total population. Second, the prevalence (p) of FA supplement use was estimated for each combination of the groups of the adjustment variables and the main variable (ie, the variable of interest) by using a log-binomial regression model. Finally, the adjusted prevalence of use within a group of the main variable was defined as the weighted average of the respective prevalence p, weighted by w. To investigate a possible group and group-by-month effect on supplement use, we used an adjusted log-binomial regression model for repeated measurements. For maternal epilepsy, FA use was divided into 2 time categories (before and after gestational month 3) rather than month-categories because of small numbers. All P values $<$ 0.05 were considered statistically significant. All analyses were performed with SAS version 8.2 for WINDOWS (SAS Institute Inc, Cary, NC).

RESULTS

Characteristics of the study population

Descriptive characteristics of the 22 500 women included in this study are provided in **Table 1**. Mean (±SD) maternal age was 29.8 ± 4.6 y (range: 14-46 y). More than one-half of the participants were married, and 78% reported that they had planned their pregnancy. Fifty-six percent of the participants were in the highest educational group, whereas 3% were in the lowest group. More than 40% of the women were pregnant for the first time, 2% had conceived by IVF, and 13% had smoked during the pregnancy. Twenty-four percent reported that they had ≥1 chronic diseases.

Patterns of folic acid supplement use before and during pregnancy

The overall monthly prevalence of FA supplement use is presented in **Table 2**. The proportions of users increased from 11.8% at 2 mo before pregnancy to 46.9% at gestational month 3. The number of users declined after the third month of gestation, but 26.0% of the participants had still used FA supplements at gestational month 8. Overall, 71.6% of the study participants had taken FA supplements at some point before or during pregnancy (Table 2). Among the 16 116 users, 27.6% had initiated supplementation before the pregnancy, 55.3% during the first trimester of pregnancy, 16.6% during the second trimester, and 0.4% during the eighth month of gestation (Table 2). Of the 4454 women who had begun taking FA supplements before the pregnancy, 84.0% stopped taking them before the eighth month of gestation (data not shown).

Patterns of folic acid supplement use by selected characteristics

The adjusted monthly prevalence of FA supplement use by pregnancy planning, IVF, maternal epilepsy, parity, maternal education, and smoking during pregnancy is shown in **Figure 1**. Use of supplements during the preconceptional period was ≈2.5 times higher in women who had planned their pregnancy than in women who had not. Similarly, preconceptional use was approximately twice as high in women who had conceived by IVF as in women who had not. FA supplementation among women with epilepsy differed only slightly from that of other study participants before pregnancy or during the first trimester. Thereafter,

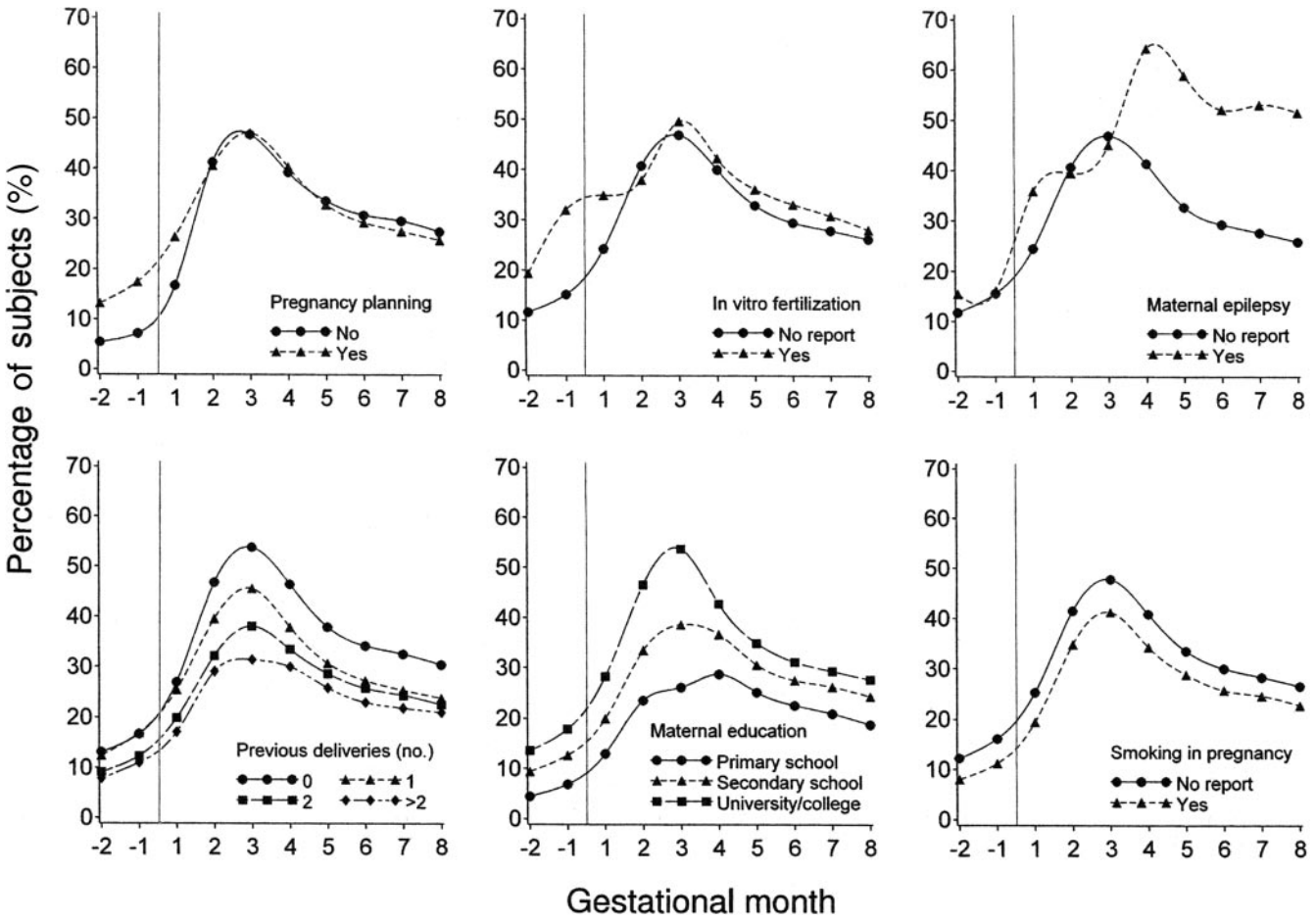

FIGURE 1. Monthly prevalence of folic acid supplement use among 22 500 participants in the Norwegian Mother and Child Cohort Study, 2000–2003, by pregnancy planning, in vitro fertilization, maternal epilepsy, number of previous deliveries, maternal education, and smoking during pregnancy. Prevalence was adjusted for maternal age, marital status, maternal education, number of previous deliveries, and year of delivery by using a direct standardization method. Curves were smoothed with spline interpolations. The vertical line refers to the first day of the last menstruation. A log-binomial regression model for repeated measurements showed significant group and group-by-month effects on supplement use for all variables in the figure (Wald test: all $P < 0.001$). Supplemental material for the figure is provided online (*see* Table 1 under "Supplemental data" in the current issue online at www.ajcn. org).

use increased and was almost twice as high in epileptic women. For other variables, use throughout pregnancy was higher in women with lower parity, in women with higher education, and in women who did not smoke.

Periconceptional folic acid supplement use

The crude prevalence of regular intake of FA supplements in the periconceptional period (ie, use more than once per week from 1 mo before pregnancy throughout the first 3 mo of pregnancy) by selected variables is presented in **Table 3**. The overall prevalence of periconceptional use of FA supplements in 2000–2003 was 10.2% ($n = 2303$). Of these women, 81.2% ($n = 1869$) had taken FA supplements daily, whereas 14.5% ($n = 334$) had taken them 4–6 times/wk and 2.4% ($n = 56$) had taken them <4 times/wk (data not shown). Of the 2303 periconceptional users, 15.8% ($n = 365$) had taken FA supplements alone, whereas 84.2% ($n = 1938$) had taken FA-containing vitamins or other supplements in addition to FA (data not shown). In Norway, the usual FA amount in prenatal FA tablets is 0.4 mg, whereas most FA-containing multivitamins contain 0.2–0.4 mg FA. Prescription high-dose FA contains 1 mg FA, and was used by ≈0.1% of FA users in the cohort (data not shown). Periconceptional use increased steadily from 6.8% in 2000 to 13.0% in 2003 (P for trend < 0.001). A significant increase (P for trend < 0.001) in FA supplement use was observed only in women who had planned their pregnancy (data not shown).

Periconceptional users and nonusers of folic acid supplements

Table 3 also presents crude and adjusted RRs for periconceptional FA use by selected variables. Univariate analyses showed that users were significantly more likely than nonusers to be older (≥25 y old), to be married or living together, to have higher incomes (≥200 000 NOK), to have lower BMIs (<25), and to have lower parity (<2 previous deliveries). Use was also significantly associated with higher maternal and paternal education, planned pregnancy, IVF, ovarian stimulation, and not smoking during pregnancy. After adjustment for maternal age, marital status, maternal education, parity, and year of delivery, the associations observed with the second level of maternal income, the second level of paternal education, and the highest BMI group were no longer significant. In general, women who had ≥1 chronic disease reported more use of FA supplements than did ostensibly healthy women (Table 3). Of several specific diseases

TABLE 3
Prevalence of and relative risks of periconceptional folic acid supplement use among 22 500 participants in the Norwegian Mother and Child Cohort Study, 2000–2003, by selected variables[1]

	Periconceptional folic acid supplement use[2]		Crude relative risk (95% CI)	Adjusted relative risk (95% CI)[3]
	No.	Percentage		
	n	%		
All	2303	10.2 ± 0.20[4]		
Year of delivery				
2000	73	6.8 ± 0.77	1	1
2001	235	7.0 ± 0.44	1.0 (0.8, 1.3)	1.0 (0.8, 1.3)
2002	595	8.2 ± 0.32	1.2 (1.0, 1.5)	1.2 (0.9, 1.5)
2003	1400	13.0 ± 0.32	1.9 (1.5, 2.4) [<0.001][5]	1.9 (1.5, 2.3) [<0.001]
Maternal age at delivery				
<25 y	152	5.6 ± 0.44	1	1
25–34 y	1760	10.8 ± 0.24	1.9 (1.7, 2.3)	1.4 (1.2, 1.6)
>34 y	391	11.2 ± 0.53	2.0 (1.7, 2.4) [<0.001]	1.6 (1.3, 2.0) [<0.001]
Marital status				
Single or other	29	3.8 ± 0.69	1	1
Living together	821	8.3 ± 0.28	2.2 (1.5, 3.1)	1.7 (1.2, 2.4)
Married	1450	12.4 ± 0.30	3.3 (2.3, 4.7) [<0.001]	2.4 (1.7, 3.5) [<0.001]
Maternal income[6]				
<200 000 NOK	655	7.6 ± 0.29	1	1
200 000–300 000 NOK	928	10.5 ± 0.33	1.4 (1.3, 1.5)	1.0 (0.9, 1.1)
>300 000 NOK	676	15.3 ± 0.54	2.0 (1.8, 2.2) [<0.001]	1.3 (1.2, 1.5) [<0.001]
Maternal education				
Primary school	12	1.6 ± 0.45	1	1
Secondary school	595	6.9 ± 0.27	4.4 (2.5, 7.7)	3.7 (2.1, 6.6)
University or college	1649	13.1 ± 0.30	8.3 (4.7, 14.6)	6.0 (3.4, 10.6)
Other[7]	38	8.6 ± 1.33	5.4 (2.9, 10.3) {<0.001}[5]	4.1 (2.2, 7.8) {<0.001}
Paternal education				
Primary school	69	5.4 ± 0.63	1	1
Secondary school	850	8.3 ± 0.27	1.5 (1.2, 2.0)	1.2 (0.9, 1.5)
University or college	1253	13.2 ± 0.35	2.4 (1.9, 3.1)	1.4 (1.1, 1.8)
Other[7]	75	9.6 ± 1.05	1.8 (1.3, 2.4) {<0.001}	1.2 (0.9, 1.7) {<0.001}
Prepregnancy BMI				
<25 kg/m^2	1672	10.7 ± 0.25	1	1
25–29.9 kg/m^2	442	9.3 ± 0.42	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)
>29.9 kg/m^2	189	9.0 ± 0.62	0.8 (0.7, 1.0) [<0.001]	0.9 (0.8, 1.1) [0.064]
Previous no. of deliveries				
0	1001	10.8 ± 0.32	1	1
1	891	10.9 ± 0.35	1.0 (0.9, 1.1)	0.9 (0.8, 1.0)
2	331	8.4 ± 0.44	0.8 (0.7, 0.9)	0.7 (0.6, 0.7)
>2	80	7.1 ± 0.77	0.7 (0.5, 0.8) [<0.001]	0.6 (0.5, 0.7) [<0.001]
Pregnancy planning				
No	184	3.9 ± 0.28	1	1
Yes	2083	11.9 ± 0.24	3.0 (2.6, 3.5) {<0.001}	2.4 (2.1, 2.8) {<0.001}
In vitro fertilization				
No report	2113	10.0 ± 0.21	1	1
Yes	117	24.9 ± 1.99	2.5 (2.1, 2.9) {<0.001}	2.0 (1.7, 2.3) {<0.001}
Ovarian stimulation				
No report	2146	10.1 ± 0.21	1	1
Yes	84	15.9 ± 1.59	1.6 (1.3, 1.9) {<0.001}	1.4 (1.1, 1.7) {0.003}
Smoking in pregnancy				
No report	2130	11.1 ± 0.23	1	1
Yes	150	5.0 ± 0.40	0.4 (0.4, 0.5) {<0.001}	0.6 (0.5, 0.7) {<0.001}
Previous no. of stillbirths[8]				
0	1239	9.9 ± 0.27	1	1
1	56	9.6 ± 1.22	1.0 (0.8, 1.3)	1.1 (0.9, 1.5)
>1	7	9.2 ± 3.32	0.9 (0.5, 1.9) [0.762]	1.4 (0.7, 3.0) [0.198]
Maternal chronic diseases				
No report	1642	9.6 ± 0.23	1	1
Any report	661	12.2 ± 0.45	1.3 (1.2, 1.4) {<0.001}	1.2 (1.1, 1.3) {<0.001}

(*Continued*)

TABLE 3 (*Continued*)

	Periconceptional folic acid supplement use[2]		Crude relative risk (95% CI)	Adjusted relative risk (95% CI)[3]
	No.	Percentage		
	n	%		
Asthma	101	11.1 ± 1.04	1.2 (1.0, 1.4)	1.2 (1.0, 1.5)
Rheumatoid arthritis	7	15.6 ± 5.41	1.6 (0.8, 3.2)	1.7 (0.9, 3.3)
Epilepsy	17	12.0 ± 2.73	1.2 (0.8, 2.0)	1.3 (0.9, 2.0)
Diabetes (type 1 or 2)	17	17.3 ± 3.82	1.8 (1.2, 2.8)	1.7 (1.1, 2.6)
Urinary tract infection	69	10.9 ± 1.24	1.1 (0.9, 1.4)	1.2 (0.9, 1.4)
Chronic renal disease	6	11.3 ± 4.35	1.2 (0.6, 2.5)	1.3 (0.6, 2.8)
Hypertension	10	10.5 ± 3.15	1.1 (0.6, 2.0)	1.2 (0.7, 2.1)
Heart disease	17	17.9 ± 3.93	1.9 (1.2, 2.9)	1.8 (1.2, 2.7)
Other diseases	291	11.9 ± 0.65	1.2 (1.1, 1.4)	1.1 (1.0, 1.3)
>1 disease	126	14.2 ± 1.17	1.5 (1.2, 1.7) {<0.001}	1.4 (1.2, 1.6) {<0.001}

[1] Relative risks were calculated by using log-binomial regression analyses.
[2] Regular use from 1 mo before pregnancy throughout the first 3 mo of pregnancy.
[3] Adjusted for maternal age, marital status, maternal education, number of previous deliveries, and year of delivery.
[4] % ± SEM (all such values).
[5] *P* value for linear trend (in square brackets) and group difference (in curly brackets) were calculated by using log-binomial regression analysis (chi-square test).
[6] NOK, Norwegian Kroner.
[7] Undefined category.
[8] Excludes 9290 women with no previous deliveries.

studied, only asthma, diabetes (type 1 or 2), and heart disease were significantly associated with use of FA supplements. Use was also more prevalent among women with other diseases (nonspecified group) and among those who reported >1 disease.

DISCUSSION

We found that 72% of the participating women in 2000–2003 had used supplements containing FA at some point before or during pregnancy but that only 10% had taken FA supplements regularly from 1 mo before pregnancy throughout the first 3 mo of pregnancy (ie, the periconceptional period). Women who had used FA supplements regularly during the periconceptional period were more likely to be older, to be married or living together, to be nonsmokers, to have higher incomes, to have higher education, to have lower parity, to have planned their pregnancy, and to have received fertility treatments.

As far as we are aware, this represents the largest study ever conducted to examine patterns and predictors of FA supplementation among pregnant women. Other strengths of this study are the detailed information on vitamin and mineral supplement intake, analysis of a multitude of potential predictors of supplement use, and the prospective study design, in which data on exposures and supplement use are collected before delivery. However, the participants in our study may still not be completely representative of the general pregnant population. During the period 2000–2003, the participation rate was 43% and the cohort covered ≈12% of the total pregnant population in Norway (17). A comparison of educational information using national data for 2003 (21) indicated that women with the highest education level may have been overrepresented in the cohort (national: 31%; cohort: 56%). Furthermore, a demographic comparison with the use of data from the Medical Birth Registry of Norway in 2002 (22) showed that single women (cohort: 3.4%; registry: 6.9%) and those aged <25 y (cohort: 12.1%; registry: 17.1%) were underrepresented in the cohort, although the use of FA seemed to be similar (registry, preconceptional use: 9.0%; cohort, periconceptional use: 8.2%). Also, our study is limited by the self-report of supplements. Some women may have underreported or provided incorrect information on the type, timing, and frequency of supplement use.

Our results regarding differences in characteristics between periconceptional FA supplement users and nonusers agree with other reports (7, 8, 10–15, 23). In our study, maternal education and marital status were strong predictors of use. Women with the highest educational level had an RR of 6.0 of use compared with women with the lowest educational level, whereas married women had an RR of 2.4 of use relative to single women. Also, planned pregnancy and IVF, which is consistent with planned pregnancy, were strongly related to periconceptional use (adjusted RRs of 2.4 and 2.0, respectively). We also found that users of FA supplements more frequently reported chronic diseases (especially diabetes and heart disease) and higher paternal education. Although the association of paternal education with use was weaker than that of maternal education, it is conceivable that fathers might also influence the use of supplements and thus be an important factor in promoting periconceptional FA use.

Women who use antiepileptic medications appear to have a higher risk of having children with congenital malformations and are thus advised to take higher doses of FA supplements (24). We did not find an increased use of FA-containing supplements during the periconceptional period among women with epilepsy. However, the proportion of women who did use supplements after gestational month 3 was approximately twice as high among women with epilepsy as in women who did not have this disease. This could indicate that most epileptic women were not familiar with the special recommendations, but that they initiated supplement use after being informed at their first antenatal health examination, which usually

takes place during the third month of gestation. On the background of this finding and of previous reports (8), more efforts should be carried out for improving periconceptional intake by women with epilepsy in Norway.

Close to 80% of the women reported that they had planned their pregnancies. Still, only 16% of the study participants had taken FA supplements preconceptionally 1 mo before pregnancy. Even in the highly motivated group of women who had conceived by IVF, only 32% had taken supplements 1 mo before conceiving. We furthermore found that 25% of the supplement users in this study initiated use during the second month of gestation and that almost one-half of the study participants had taken FA supplements during the third month of gestation. This shows that many women use FA supplements in connection with their pregnancy, but that they start too late with respect to NTD prevention. Of 16 116 (72%) women who had taken FA at some time before or during their pregnancy, 17% had initiated use after the first trimester of pregnancy, which indicates that it might still be feasible through effective campaigns and promotions to raise the use of FA supplements during the earlier stages of pregnancy.

The results of this study are relevant not only to countries where food fortification with FA is under consideration (such as Norway), but also to countries (such as the United States, Canada, and Chile) where fortification has already been implemented to reduce NTDs. Although mandatory food fortification with FA has improved blood folate status in women of reproductive age (25–27), many fertile women do not receive the daily recommended level of 0.4 mg FA through their diets alone (28, 29). It is therefore important that fertile women maintain the use of FA supplements to meet the recommendations for NTD prevention (28, 29).

Some studies have indicated that the use of FA supplements throughout or during pregnancy may also have a beneficial effect on adverse pregnancy outcomes in addition to NTDs (30–32). If intake of FA could reduce the incidence of such outcomes, this would provide yet another reason for more effective interventional programs aimed at promoting the use of FA supplementation among women of reproductive age.

In conclusion, although most of the participating women in 2000–2003 took supplements containing FA at some point before or during pregnancy, the overall percentage of periconceptional FA use was low. Interventional programs designed to improve overall intake of FA supplements should focus on demographic and socioeconomic conditions and other factors that are related to low use. Also, women with clinical conditions that place them at increased risk of NTDs should be particularly targeted.

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RMN conceived the study, performed all analyses, and led the writing. SEV conceived the study and participated in the analyses and writing. HKG participated in the statistical analyses. PM, the principal investigator of the Norwegian Mother and Child Cohort Study, participated in the writing. HMM and MH were involved in the original study question and participated in the analyses. PMU was involved in the conception of the study and participated in manuscript preparation. All authors helped to conceptualize ideas, interpret findings, and review drafts of the manuscript. No conflicts of interest are declared.

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