

# Predictors of preconceptional folic acid or multivitamin supplement use: a cross-sectional study of Danish pregnancy planners

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**Purpose:** Compliance with the Danish preconceptional folic acid (FA) recommendation – a daily supplement of 400 µg – is reported to be poor. Uncertainty remains, however, about the prevalence of compliers and health-related predictors of compliance in the preconceptional period.

**Methods:** We used self-reported baseline data from 5383 women, aged 18–40 years, enrolled in an Internet-based prospective cohort study of Danish pregnancy planners during 2007–2011. We estimated the prevalence proportions of FA or multivitamin (MV) use in relation to selected sociodemographic, lifestyle, reproductive, and medical characteristics. Multivariate binomial regression was used to obtain prevalence proportion differences with 95% confidence intervals for each level of study predictors, adjusted for all other predictors.

**Results:** Overall, 7.7% of women used FA supplements, 20.4% used MV supplements, 34.0% used both, 1.5% used other single vitamins or minerals, and 36.4% did not use any dietary supplements. The prevalence of FA or MV supplement use was higher among older women, women with higher education and income, and women with healthy lifestyle factors such as being a nonsmoker, nondrinker, physically active, maintaining a normal body mass index and having regular pap smears. Greater intercourse frequency and a history of spontaneous abortion were also positively associated with FA or MV supplement use. We found no clear association between use of FA or MV supplements and a diagnosis of hypertension, diabetes, thyroid disease, pelvic inflammatory disease, or chlamydia.

**Conclusion:** A large proportion of pregnancy planners do not use FA or MV supplements. Pregnancy planners with generally risky lifestyle behaviors are less likely to comply with the FA recommendation.

**Keywords:** pregnancy, preconceptional supplement use, vitamins, folic acid

## Introduction

In Denmark, women planning to conceive are advised to take a daily supplement of 400 µg folic acid (FA) until the 12th week of gestation to reduce the risk of neural tube defects (NTDs).<sup>1</sup> Starting FA supplementation before conception is an important component of effective prevention of NTDs, since the neural tube closes at gestational week 6, only a few weeks after the pregnancy may be recognized.<sup>2</sup> FA is primarily taken as single supplements or as a component of multivitamins (MVs) and other vitamin preparations made for pregnancy planners or pregnant women.

Despite campaigns promoting the FA recommendation in Denmark in 1999 and 2001, women in the preconceptional period appear to have neither adequate dietary intake of folate nor adequate supplementation from FA tablets or MV supplements.

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According to the National Survey of Dietary Habits from 2003 to 2008, only 5–10% of Danish women of fertile age have a sufficient intake of dietary folate.<sup>3</sup> The most recent data on periconceptional use of FA supplements in Denmark are from the Danish National Birth Cohort (DNBC). Between 2000 and 2002, the proportion of FA compliers among DNBC participants who planned their pregnancy increased from 14% to only 22%, and thus remained low even after the campaigns.<sup>4,5</sup> Several retrospective studies of pregnant women in other countries also reported poor compliance, with 12% of women in the UK,<sup>6</sup> 17% in Norway,<sup>7</sup> 23–30% in Australia<sup>8,9</sup> and 44% in the US<sup>10</sup> reporting FA supplement use in the preconception period. In addition, a prospective cohort study reported that only 6% of the women who became pregnant within 3 months of being interviewed in a general woman's survey in the UK followed the FA recommendation.<sup>11</sup>

In previous studies, young age, low education and income, smoking, overweight, and parity were reported to be predictors of noncompliance.<sup>5–8,10</sup> To date, no study has examined other health-related predictors of compliance during the preconceptional period, and we lack recent estimates of compliance with the FA recommendation reported from pregnancy planners during the preconceptional period. In the current study, we estimated the prevalence of FA and MV supplement use and identified sociodemographic, lifestyle, reproductive, and medical predictors of such use among Danish pregnancy planners.

## Methods

### Design of the present study

The present study was a cross-sectional analysis of baseline data from an Internet-based prospective cohort study of Danish pregnancy planners – *Snart-Gravid* (Soon Pregnant). The study design has been described in detail elsewhere.<sup>12,13</sup> Briefly, the study was initiated in June 2007. Participants were enrolled via the study website, and data were collected by email and self-administered questionnaires. Recruitment was achieved by a pop-up advertisement placed on a well-known health-related website (<http://www.netdoktor.dk>) and two press releases. Before enrolment, potential participants entering the study website were required to read a consent form and fill in a screening questionnaire in order to confirm eligibility. Further, participants were required to provide a valid email address and their personal civil registry (CPR) number, which is a unique ten-digit personal identification number allowing linkage to a number of nationwide registries. Eligible women were invited to complete a baseline questionnaire and bimonthly follow-up

questionnaires for 12 months or until conception occurred, after which active follow-up ended. Participants were initially randomized to receive either a short- or a long-form baseline questionnaire. Completion rates and missing data were similar for both questionnaire versions.<sup>13</sup>

### Study population and study period

Eligible women were Danish residents aged 18–40 years, living in a stable relationship with a male partner, not using birth control, not receiving any type of fertility treatment, and attempting to conceive for no more than 12 months. From June 1, 2007 to August 3, 2011, 5918 women completed the screener and the baseline questionnaire. Of these, one woman did not provide a valid CPR number in the screener, one woman was excluded because she was already pregnant (14 weeks), and 533 women were excluded because they had been attempting to conceive for more than 12 months. In total, 5383 eligible women enrolled in the study during the 4-year study period.

### Data collection

Data on preconceptional use of FA and MV supplements and sociodemographic, lifestyle, reproductive, and medical variables were assessed at baseline.

### Assessment of FA and MV supplement use

In the baseline questionnaire, women were asked “Do you take vitamins on a regular basis – daily or almost every day?”, “How long have you been taking vitamins on a regular basis – less than one year, 1–5 years, more than 5 years, or don't know?”, and “Which of the following vitamins or minerals do you take on a regular basis – MVs, vitamin A, beta-carotene, vitamin B, vitamin C, vitamin D, vitamin E, FA, calcium, magnesium, selenium, or other?” Participants who reported “multivitamin” or wrote the name of an MV product were defined “MV users.” Similarly, participants who reported “folic acid” or wrote “folate” were defined “FA users.” “Users” were defined as women who used either FA supplements, MV supplements, or both. Women who used single-vitamin or mineral supplements other than FA and women who did not take any dietary supplements were defined “nonusers.” A total of 197 (3.7%) women did not answer the initial vitamin question and were also defined as nonusers.

### Assessment of potential predictors of FA or MV use

Participants reported weight, height, physical activity, and smoking history in the baseline questionnaire, allowing

the calculation of body mass index (BMI), total metabolic equivalents (METs), and pack-years of smoking. BMI was calculated by dividing weight (kg) with height squared ( $\text{m}^2$ ). METs were estimated by summing the METs from moderate and vigorous physical activity (hours per week multiplied by 3.5 and hours per week multiplied by 7.0, respectively).<sup>14</sup> Data on smoking were categorized as pack-years of ever-smoking where 1 pack-year was defined as smoking 20 cigarettes per day in 1 year.

To assess sociodemographic predictors of compliance among pregnancy planners, we examined the association between preconceptional FA or MV supplement use and the following variables: age (categorized as <25, 25–29, 30–34, and  $\geq 35$  years), schooling (primary and lower secondary school, high school, and other), vocational training (none, short [ $<3$  years], medium [3–4 years], and long [ $>4$  years]) and total monthly household income (<12,500, 12,500–24,999, 25,000–39,999, 40,000–64,999, and  $\geq 65,000$  DKK/month). We also examined lifestyle factors that could indicate intense efforts to conceive, such as intercourse frequency (categorized as <1, 1–3, and  $\geq 4$  times per week) and months attempting pregnancy at study entrance (0–1, 2–4, 5–6, and 7–12 months). Furthermore, compliance with other health recommendations, such as attending the national screening program for cervical cancer (pap smear) during the last 3 years (none vs one or more), smoking history (never smoked, <5, 5–9, and  $\geq 10$  pack-years), current alcohol intake (none, 1–3, 4–7, 8–14, and  $\geq 15$  drinks/week), BMI (<18.5, 18.5–24.9, 25–29.9, 30–34.9, and  $\geq 35$   $\text{kg}/\text{m}^2$ ), and engagement in physical activity (<10, 10–19, 20–39, and  $\geq 40$  METs/week), were also of interest. Finally, we studied the associations with previous spontaneous abortion (yes vs no), parity (nulliparous vs parous), and medical conditions that may increase health awareness in relation to pregnancy, which included hypertension (yes vs no), diabetes (yes vs no), thyroid disease (yes vs no), pelvic inflammatory disease (yes vs no), and infection with chlamydia (yes vs no).

## Data analysis

We estimated the prevalence proportion (PP) of FA or MV users in each level of study predictors. Multivariate binomial regression was used to obtain prevalence proportion differences (PPDs) with 95% confidence intervals (CIs) for each predictor level in relation to the reference group. The multivariate analyses for the PP and PPD for each study predictor were adjusted for all other covariates. Stata statistical software (version 11.2; College Station, Texas) was used for all analyses.

Missing values ranged between 0.1% (schooling) and 8.7% (total monthly household income). Because 1540 (28.6%) participants were initially randomized to receive the short-form baseline questionnaire, they did not receive the questions about hypertension, diabetes, thyroid disease, and pelvic inflammatory disease. For the analyses, we used multiple imputation methods to impute all missing values.<sup>15,16</sup>

## Results

Overall, 412 (7.7%) women used FA supplements exclusively, 1100 (20.4%) used MV supplements exclusively, and 1831 (34.0%) used both, yielding 62.1% users. A total of 82 (1.5%) used single vitamins or minerals other than FA, and 1958 (36.4%) did not use any dietary supplements, yielding 2040 (37.9%) nonusers of FA or MV supplements (Table 1). Among users, 57% had used supplements for less than 1 year.

Median age was 28 years for both users and nonusers. After mutual adjustment for covariates, higher age was associated with increased prevalence of FA or MV use (Table 2). Our data also indicate that women who finished high school were more likely to use FA or MVs compared with women with less schooling. Similarly, compared with women with a long vocational training ( $>4$  years), PPDs for having no vocational training and a short ( $<3$  years) vocational training were  $-5.7\%$  and  $-7.1\%$ , respectively, and compared with total monthly household of  $\geq 65,000$  DKK/month, PPD for <12,500 DKK/month was  $-8.7\%$ .

While intercourse frequency  $\geq 1$  times/week was associated with an increased prevalence of FA or MV use, there was no clear association between months attempting to conceive at study entrance and FA or MV use. Furthermore, women who had pap smears once or more during the last 3 years were more likely to use FA or MV supplements compared with women who did not have pap smears (PPD was  $-9.7\%$  for none versus one or more).

Smoking, alcohol use, and obesity ( $\text{BMI} \geq 30$   $\text{kg}/\text{m}^2$ ) were associated with a decreased prevalence of FA or MV use. Compared with women who never smoked, PPD for  $\geq 10$  pack-years of smoking was  $-11.3\%$ . Compared with

**Table 1** Dietary supplement use among 5383 pregnancy planners

	n	(%)
Users		
Folic acid exclusive	412	(7.7)
Multivitamins exclusive	1100	(20.4)
Folic acid and multivitamins	1831	(34.0)
Nonusers		
No use	1958	(36.4)
Other vitamins and minerals exclusive	82	(1.5)

**Table 2** Prevalence proportions (PPs), prevalence-proportion differences (PPDs) with 95% confidence intervals (CIs) of folic acid or multivitamin supplement use in relation to sociodemographic, lifestyle, reproductive, and medical characteristics, respectively in 5383 women

Characteristics	Nonusers	Users	Unadjusted	Adjusted <sup>a</sup>		
	n (2040)	n (3343)	PP (%)	PP (%)	PPD (%)	95% CI
<b>Sociodemographic factors</b>						
Age, years						
<25	461	507	52.4	58.8	-5.2	-11.6, 1.1
25-29	882	1515	63.2	62.5	-1.6	-6.7, 3.5
30-34	518	1037	66.7	66.7	2.7	-2.3, 7.6
≥35	179	284	61.3	64.1	Ref	0
Schooling						
Primary/lower secondary school	387	405	51.1	56.6	-5.9	-10.0, -1.8
High school	1386	2612	65.3	62.5	Ref	0
Other	267	326	55.0	56.4	-6.1	-10.5, -1.8
Vocational training						
None	345	379	52.4	57.4	-5.7	-11.2, -0.2
Short (<3 years)	716	906	55.9	56.0	-7.1	-11.2, -3.0
Medium (3-4 years)	622	1,252	66.8	62.5	-0.6	-4.3, 3.0
Long (>4 years)	357	806	69.3	63.1	Ref	0
Household income, DKK/month						
<12,500	64	64	50.0	51.8	-8.7	-19.8, 2.2
12,500-24,999	280	370	56.9	61.8	1.2	-4.8, 7.3
25,000-39,999	552	805	59.3	61.8	1.2	-3.5, 5.8
40,000-64,999	854	1572	64.8	62.5	1.9	-3.5, 5.8
≥65,000	290	532	64.7	60.6	Ref	0
<b>Lifestyle factors</b>						
Intercourse frequency, times/week						
<1	392	495	55.8	54.7	-5.9	-10.3, -1.5
1-3	1236	2217	64.2	62.5	1.8	-1.5, 5.1
≥4	412	631	60.5	60.7	Ref	0
Attempting pregnancy, months						
0-1	868	1457	62.7	62.5	Ref	0
2-4	569	994	63.6	65.0	2.5	-0.5, 5.5
5-6	252	372	59.6	61.3	-1.1	-5.4, 3.2
7-12	351	520	59.7	61.3	-1.1	-4.9, 2.6
Pap smears <sup>b</sup> , last 3 years						
None	545	556	50.5	62.5	-9.7	-13.2, -6.2
≥1	1495	2787	65.1	72.2	Ref	0
Smoking status, pack-years						
Never smoked	1052	2097	66.6	62.5	Ref	0
<5	526	726	58.0	58.1	-4.3	-7.6, -1.1
5-9	280	327	53.9	53.1	-9.4	-14.3, -4.7
≥10	182	193	51.5	51.2	-11.3	-16.8, -5.8
Alcohol intake, drinks/week						
None	601	1097	64.6	67.0	Ref	0
1-3	795	1404	63.9	62.5	-4.5	-7.5, -1.5
4-7	466	602	56.4	55.4	-11.6	-15.4, -7.8
8-14	130	204	61.1	60.3	-6.7	-12.4, -1.0
≥15	48	36	42.9	48.6	-18.4	-29.1, -7.6
BMI, kg/m <sup>2</sup>						
<18.5	91	128	58.5	65.2	-2.7	-9.4, 4.0
18.5-24.9	1219	2,192	64.3	62.5	Ref	0
25-29.9	424	651	60.6	63.4	-1.8	-5.1, 1.5
30-34.9	185	239	56.4	60.1	-5.1	-10.1, -0.1
≥35	121	133	52.4	58.1	-7.1	-13.4, -0.8

(Continued)

**Table 2** (Continued)

Characteristics	Nonusers	Users	Unadjusted	Adjusted <sup>a</sup>		
	n (2040)	n (3343)	PP (%)	PP (%)	PPD (%)	95% CI
Physical activity, METs/week						
<10	388	476	55.1	56.5	Ref	0
10–19	649	1080	62.5	62.0	5.5	1.5, 9.4
20–39	666	1230	64.9	62.5	5.9	2.0, 9.9
≥40	337	554	62.2	60.7	4.2	–0.5, 8.8
<b>Reproductive history</b>						
Previous spontaneous abortions (%)						
No	1848	2955	61.5	62.5	Ref	0
Yes	192	388	66.9	70.2	7.7	3.7, 11.8
Parous, ever had live birth						
No	1358	2234	62.2	54.2	Ref	0
≥1	682	1109	61.9	52.9	–1.2	–4.2, 1.9
<b>Medical history</b>						
Hypertension (%)						
No	1303	3116	62.1	62.5	Ref	0
Yes	137	227	62.4	63.4	1.1	–6.2, 8.4
Diabetes (%)						
No	2020	3300	62.0	54.2	Ref	0
Yes	20	43	68.3	59.7	13.8	–1.0, 28.6
Thyroid disease (%)						
No	1989	3263	62.1	62.5	Ref	0
Yes	51	80	61.1	59.4	–3.1	–15.4, 9.2
Pelvic inflammatory disease (%)						
No	1733	2905	62.6	62.5	Ref	0
Yes	307	438	58.8	60.8	–1.7	–5.9, 2.6
Chlamydia (%)						
No	1591	2661	62.6	54.2	Ref	0
Yes	449	682	60.3	54.0	0.1	–3.0, 3.3

**Note:** <sup>a</sup>Mutually adjusted for all other covariates. <sup>b</sup>National screening program for cervical cancer.

no alcohol intake PPD for ≥15 drinks/week was –18.4%. Compared with normal weight (BMI = 18.5–24.9 kg/m<sup>2</sup>), PPDs of FA or MV use for BMIs of 30–34.9 and ≥35 kg/m<sup>2</sup> were –5.1% and –7.1%, respectively. Furthermore, women who engaged in physical activity were more likely to use FA or MVs than sedentary women (<10 METs/week).

Among women who had a previous spontaneous abortion, the PPD of FA or MV use was 7.7% higher than women who did not report having a previous abortion. However, being multiparous was not associated with increased FA or MV use.

Finally, there was no clear association between being diagnosed with either hypertension, diabetes, thyroid disease, pelvic inflammatory disease, or infections with chlamydia and preconceptional FA or MV supplement use.

## Discussion

### Prevalence proportions

Our data indicate that 62% of the 5383 pregnancy planners in this study adhere to the Danish FA recommendation.

By interpreting “users” as compliers, we may overestimate the proportion of compliers following the FA recommendation. The questionnaire provided information on whether the women took an FA or MV supplement or not, but there was no information on the exact dose of FA ingested or the brand name of the FA or MV product. In addition, 20% of the women used MVs exclusively. Since MV supplements have no standard definitions,<sup>17–20</sup> it cannot be assumed that all MVs contained FA. However, most MVs on the Danish market contain 400 µg FA, especially those made for use during pregnancy.

No previous study has collected data on FA and MVs during the preconception period. The prevalence among pregnancy planners in our study is higher than the prevalence of preconception FA (12%–44%)<sup>5–10</sup> and MV use (11%)<sup>8</sup> reported by pregnant women in previous studies. However, these studies collected data during the second and third trimesters, which may decrease the recall of FA and MV use during the preconceptional period. In addition, the studies were relatively small, with 588 women attending an antenatal



clinic in Melbourne in gestational weeks 36–38,<sup>8</sup> 1541 women attending an antenatal ultrasound screening in gestational weeks 17–19 in Oslo,<sup>7</sup> and 327 pregnant women calling the California Teratogen Information Service in gestational week 13 in the US.<sup>10</sup> Consequently, prevalence estimates reported in these studies may have been imprecise.

The definition of compliance with the FA recommendation differs among studies. In the study by Forster et al,<sup>8</sup> 29% took prepregnancy FA supplements, but only 23% reported taking FA for at least 4 weeks before pregnancy. In the study by Braekke and Staff,<sup>7</sup> 17% of the women started the supplementation before the first day of the last menstruation. However, an additional 16% started FA supplementation at 0–4 weeks of gestation. Thus, 33% of the women started FA within 4 weeks of gestation. This proportion may be more comparable with our findings, since some “users” in our study may have been in gestational weeks 0–4 at baseline.

Women with unplanned pregnancies are less likely to use FA supplements before pregnancy. In the studies by Forster et al<sup>8</sup> and Goldberg et al,<sup>10</sup> the prevalence of unplanned pregnancy was 19% and 36%, respectively. These studies estimated FA use among all pregnancies (planned and unplanned), making their results difficult to compare with ours. In the study by Braekke and Staff,<sup>7</sup> there was no information about unplanned pregnancies or contributions of FA from MV supplements, both increasing the possibility of underestimation of the proportions of FA users in this study.

In Denmark, the largest and most recent study of lifestyle factors in relation to compliance with the FA recommendation was conducted among 18,294 pregnant women (gestational weeks 10–12) enrolled in the DNBC during 2000–2002.<sup>5</sup> In this study, FA supplements were derived from single FA tablets, MV tablets, and vitamins made for pregnant or lactating women. Compliance was defined as taking 320 µg FA per day, from 4 weeks before the date of the last menstrual period until gestation week 6. A total of 76% of the pregnancies were planned, and the overall proportion of women who complied with the recommendation was only 16% among planners. During the 10-year time period to the present study, there may have been an increase in the awareness as well as more available information about prepregnant recommendations, which may partly explain the observed increase in the prevalence of compliers with the FA recommendation found in this study. In contrast to the DNBC, our data on supplement use and potential predictors were reported during the preconceptional period, and information was recorded prospectively, which increases the validity of the study. On the other hand,

Snart-Gravid study participants may be more health-conscious than the general population of pregnancy planners, possibly overestimating the prevalence of FA or MV use. Even so, it is unlikely that an overestimation of supplement use would meaningfully distort the associations between predictors and FA or MV use. In addition, differences in sociodemographic factors among Snart-Gravid study participants compared with the general population may also contribute to an overestimation of FA or MV use.

## Predictors of FA or MV use

Our study agrees with previous studies that found that maternal age,<sup>5,7,10</sup> education,<sup>5,6,10</sup> income,<sup>6,8</sup> smoking,<sup>5,8</sup> and BMI<sup>10</sup> were associated with preconception FA use. Although a history of childbirth may increase awareness of preconceptional FA use, previous studies found that a previous childbirth either decreased the likelihood of FA use in subsequent pregnancies or was not related to FA use.<sup>5,7,8</sup> We found only little association between parity and FA use in our study.

The positive associations between previous spontaneous abortion and intercourse frequency and FA or MV use found in our study have not been reported previously. These findings may indicate a relation between a high desire to conceive and increased knowledge about the preconceptional FA guidelines.

While lifestyle recommendations during pregnancy are widely available, less advice is available for women trying to conceive. In addition to the FA recommendation, Danish women planning a pregnancy are advised to avoid alcohol altogether.<sup>1</sup> A total of 32% reported no alcohol intake in our study, which was slightly more than the 12% reported from the DNBC previously.<sup>21</sup> In addition, we found the lowest proportion of FA or MV users among women with the highest alcohol intake. Together with the concern that excessive alcohol intake impedes the normal bioavailability and metabolism of folate,<sup>22</sup> these results underscore the need to target women at high risk of not following the FA recommendation, as well as those not following other preconceptional guidelines.

Being diagnosed with a chronic disease has previously been associated with increased dietary supplement use in general.<sup>23</sup> Pregnancy planners with a chronic illness might be more prone to use FA or MVs because of increased health awareness, but we found little association between a diagnosis of hypertension, diabetes, thyroid disease, pelvic inflammatory disease or infections with chlamydia and preconceptional use of FA or MVs.

## Conclusion

Our findings indicate that more than one-third of the pregnancy planners in this study do not follow the preconceptional FA recommendation. We found that pregnancy planners with other risky behaviors, such as smoking and alcohol use, obesity, and being physically inactive, are less likely to comply with the FA recommendation or use MVs.

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## Disclosure

The authors report no conflicts of interest in this work.

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