# **RESEARCH ARTICLE**

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# Paternal characteristics associated with maternal periconceptional use of folic acid supplementation



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# Abstract

**Background:** Maternal predictors of folic acid (FA) supplementation use to reduce offspring risk of neural tube defects are well known, while paternal determinants for maternal FA use are less known. Such knowledge is important to increase women's compliance to recommended periconceptional FA use.

**Methods:** In a nation-wide study of 683,785 births registered in the Medical Birth Registry of Norway during 1999–2010, the associations between paternal characteristics (age, education, occupation, country of origin) and maternal FA use were estimated by relative risks (RR) with 95% confidence intervals (CI), using log-binomial regression.

**Results:** Maternal FA use before and during pregnancy (adequate FA use) was found in 16% of the births. The association between paternal age and adequate FA use was inversely U-shaped; adjusted RRs for adequate FA use were 0.35 (95% CI 0.28–0.43) and 0.72 (95% CI 0.71–0.74) for paternal age < 20 and ≥ 40 years, respectively, comparing age 30–34 years. Compulsory education (1–9 years) among fathers was compared to tertiary education; the RR was 0.69 (95% CI 0.68–0.71) for adequate FA use. The lower risk of adequate FA use for paternal compulsory education was present in all categories of maternal education. Occupation classes other than "Higher professionals" were associated with decreased risk of adequate FA use, compared with the reference "Lower professionals". RR for adequate FA use was 0.58 (95% CI 0.56–0.60) comparing fathers from "Low/middle-income countries" with fathers born in Norway.

**Conclusion:** Adequate FA use in the periconceptional period was lower when fathers were younger or older than 30–34 years, had shorter education, had manual or self-employed occupations, or originated from low/middle-income countries. Partners may contribute to increase women's use of periconceptional FA supplementation.

**Keywords:** Pregnancy, Supplement use, Folic acid, Norway

# Background

Folate is necessary in foetal development, and folic acid (FA) supplementation is widely acknowledged to reduce the risk of neural tube defects (NTDs) [1–5]. FA is the synthetic form of the B-vitamin folate, which is essential in the synthesis of DNA, methylation, and DNA repair

[6]. Start of FA supplementation prior to conceiving is important in order to reduce the risk of NTDs because the neural tube closes between 21 and 28 days after conception [7].

Randomized clinical trials and non-randomized intervention trials have demonstrated that periconceptional FA use reduces the risk of NTDs [1–3]. Recent studies have reported that FA is associated with protection against other neurodevelopmental disorders and some severe pregnancy complications [8–10]. The protective effect of FA on NTDs has led health authorities

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in several countries, including Norway, to recommend women to take FA supplements before pregnancy and in early pregnancy [11–13].

Many countries in Europe, including Norway, have performed information campaigns to increase the use of periconceptional FA supplementation among women planning pregnancy [14–16]. Presently there is no mandatory folic acid food fortification in Norway [17]. Official Norwegian guidelines from 1998, states that all women planning their pregnancy should use 0.4 mg FA daily from 1 month before pregnancy and throughout the first 2–3 months of pregnancy to reduce the risk of NTDs [12]. However, the proportion of preconception FA supplementation use in Norway is still too low [18] and by 2015 it was 33% [19].

Previous studies have identified maternal factors associated with inadequate FA in the periconceptional period, such as low maternal age, shorter education, single parenthood, unplanned pregnancy, lower parity, smoking, alcohol use, less physical activity, or originating from a foreign country [15, 16, 20–24].

Since couples tend to exhibit concordant health behaviour's for dietary intake, smoking, alcohol consumption, physical activity, and body mass index (BMI) [25–27], a woman's partner may contribute to her use of periconceptional FA supplements. In fact, in an early report from the Norwegian Mother and Child Cohort Study (MoBa), 2000–2003, counting 22,500 women, FA supplements were used more frequently among women with partners with a higher education [22]. However, the study did not assess other paternal factors or combined paternal and maternal factors as to identify women with inadequate FA use.

Taking advantage of the Medical Birth Registry of Norway that to our knowledge is the only national registry with information on periconceptional use of FA supplements [28], we updated parent information with data from national registries to investigate whether paternal factors (age, education, occupation, country of origin) was associated with mothers' intake of recommended FA in pregnancy.

# Methods

# **Data-sources**

Maternal FA use before and/or during pregnancy was collected from the Medical Birth Registry of Norway (MBRN) [28]. Paternal and maternal demographic data came from the National Registry (NR). Information on paternal and maternal occupation originated from the Norwegian Labour and Welfare Administration (NAV), and we retrieved paternal and maternal educational data from the Norwegian National Education Database (NUDB) [29].

MBRN is a population-based registry containing information on all births in Norway since 1967 [28]. The registry holds demographic information on the mother and the father, the mother's health before and during pregnancy, including chronic diseases, information on in vitro fertilization (IVF), complications during pregnancy and delivery as well as information on the infant, including birth defects and other perinatal problems. Midwives and physicians attending the deliveries register the data. Since 1967, there has been mandatory reporting of all live and stillbirths from the 16 gestational week to MBRN.

NR contains demographic information on all residents in Norway since 1960, including the date of birth, country of origin, and the dates of immigration, emigration, or death [30]. NR assigns a unique personal identification number to all individuals born or immigrated to Norway, enabling accurate record linkages.

NAV was established in 2006 after governmental reorganization of the Directorate of Labour in Norway (founded in 1945), and has registered information on occupation, health status, and social benefits of all individuals with residence in Norway since 1992. The Norwegian occupational code system is based on the International Standard Classification of Occupations (ISCO), revised version from 1988 [31].

Since 1970, NUDB holds information on all individuals' education history from primary school up to doctoral studies in one database [32]. The classification is based on the Norwegian Standard Classification of Education.

# Maternal FA supplement use

We constructed a binary variable for intake of FA supplement use (0.4 mg/day) (regardless of concomitant multivitamin use) registered in the MBRN since December 1998 onwards; adequate FA use (recommended FA supplementation before and during pregnancy), and inadequate FA use (FA supplementation only before pregnancy, or only during pregnancy, or no record of FA use).

MBRN also registers multivitamin use, but our investigation focused on periconceptional FA use as such intake was according to official guidelines.

# Paternal characteristics

We used the following paternal variables in our analyses of adequate FA supplementation; paternal age (< 20, 20–24, 25–29, 30–34, 35–39, 40+ years); education (Compulsory (1–9 years), Intermediate (10–12 years), Tertiary (13–19 years)); occupation according to the class scheme of Erikson, Goldthorpe, and Portocarero (I Higher professionals, II Lower professionals, IIIa Higher routine, IV

Other self-employed workers, V Technicians, VI Skilled, VII Semiskilled and unskilled, VIIb Agricultural, Unclassified) (EGP) [33]; and country of origin according to the classification by World Health Organization, Health statistics and information systems, Estimates for 2000–2012 (Norway, High income countries, Low/middle-income countries) [34].

#### Covariates

We used directed acyclic graphs (DAGs) and subject-matter knowledge to select a minimally sufficient adjustment set of variables that identify the unconfounded association of paternal characteristics on adequate maternal FA supplementation use [35–37].

The potential confounders of the paternal characteristics and maternal FA use relationship included year of childbirth (continuous), paternal age (< 20, 20–24, 25–29, 30–34, 35–39, 40+ years), education (Compulsory, Intermediate, Tertiary), or country of origin (Norway, High-income countries, Low/middle-income countries).

Furthermore, we included maternal age (< 20, 20–24, 25–29, 30–34, 35–39, 40+ years), maternal education (Compulsory, Intermediate, Tertiary), and maternal country of origin (Norway, High-income countries, Low/middle-income countries) as possible confounders of the associations between paternal age, education, or country of origin, and maternal adequate FA use.

Maternal smoking was not included in the final models because smoking was not considered a confounder of the association of paternal characteristics on maternal FA supplementation use [38].

# Study population

During 1999–2010, 716,021 births were registered in MBRN. We excluded births (induced abortions) without information on FA or multivitamin supplementation use (2519) and births without maternal identification number (4091). For multiple births, we included data for the first birth and excluded 12,927 next born individuals. Among the remaining 696,484 births, we excluded 12,699 births without paternal identification number, leaving 683,785 live births and stillbirths for analyses.

# Statistical analysis

Associations between paternal characteristics (age, education, occupation, country of origin) and maternal FA use were estimated as relative risks (RRs) with 95% confidence intervals (CIs) by log-binomial regression, using the log-link function in Stata version 15 [39]. The 95% CIs were based on robust variance estimation with the sandwich estimator to correct for the intra-individual correlation in women with more than one pregnancy during the study period [40]. Births with missing data on covariates were excluded from the analyses. *P*-values for

overall difference between the categories of paternal characteristics were calculated using likelihood ratio tests. We evaluated and tested the potential effect modification of the association between paternal education and maternal FA use by stratification and likelihood ratio test.

## Results

Our study included 683,785 births during 1999-2010. Table 1 presents the characteristics of the parents. The median ages of the fathers and mothers at childbirth were 33 and 30 years, respectively. For about 41% of the births, the mothers were primiparous, and about 2% of the births were conceived after in vitro fertilization majority of the births (IVF). The Norwegian-born parents (84% of the fathers and 83% of the mothers). For about 34% of the births, the fathers had tertiary education, and for about 19% of the births, the fathers had compulsory education only. The paternal educational level varied by his country of origin. Fathers originating from low/middle-income countries generally had lower educational level compared to fathers originating from Norway and other high-income countries (not shown). Occupation classified as "Lower professionals," accounted for 22% of all the births. For about 14% of the births, the women smoked daily at the start of pregnancy, about 3% smoked intermittently, and 67% did not smoke. Nearly 17% of the smoking data were missing.

For about 16% of all births in the study population, the mothers were assigned to the category adequate FA supplementation users. However, during 1999 through 2010, the proportion of adequate FA supplementation use increased from 4% at the start of the study period (1999) to 26% in 2010.

Table 2 presents crude and adjusted RRs for adequate maternal periconceptional FA use by paternal variables (determinants). Adjusted analyses showed an inverse "U-shaped" relationship between paternal age and adequate maternal FA supplement use where the smallest RRs were found for paternal age below 20 years (RR 0.35 (95% CI 0.28-0.43)), 20-24 years (RR 0.68 (95% CI 0.66–0.71)), and 40 years and above (RR 0.72 (95% CI 0.71-0.74)) compared to paternal age 30-34 years. Paternal compulsory education was associated with reduced risk of adequate FA use (RR 0.69 (95% CI 0.68-0.71)) compared to paternal tertiary education. All paternal occupation classes were associated with reduced risk of adequate FA use except for "I Higher professionals", when compared to "II Lower professionals", in particular "VII Semiskilled and unskilled" (RR 0.75 (95% CI 0.73-0.76)), and "VIIb Agricultural" (RR 0.73 (95% CI 0.69-0.78)).

**Table 1** Paternal and maternal characteristics in 683,785 births in Norway. 1999–2010

	Births			
	Fathers	%	Mothers	%
Number of births	683,785	100.0	683,785	100.0
Age				
< 20	4401	0.6	15,464	2.3
20–24	48,448	7.1	100,016	14.6
25–29	162,671	23.8	223,480	32.7
30–34	235,401	34.4	228,203	33.4
35–39	151,540	22.2	99,727	14.6
40+	81,324	11.9	16,895	2.5
Education				
Compulsory education (1–9 years)	130,953	19.2	125,479	18.4
Intermediate (10–12 years)	302,384	44.2	230,320	33.7
Tertiary education (13–19 years)	229,818	33.6	298,036	43.6
Missing data	20,630	3.0	29,950	4.4
Occupational class <sup>a</sup>				
l Higher professionals	86,635	12.7	50,650	7.4
II Lower professionals	152,781	22.3	122,804	18.0
Illa Higher routine	77,540	11.3	197,174	28.8
IIIb Lower routine	40,070	0,070 5.9		16.8
IV Other self-employed workers	358	0.1	119	0.0
V Technicians	5550	0.8	1492	0.2
VI Skilled	108,755	15.9	15,961	2.3
VII Semiskilled and unskilled	111,584	16.3	73,994	10.8
VIIb Agricultural	7663	1.1	2720	0.4
Unclassified	52,824	7.7	51,264	7.5
Missing data	40,025	5.9	52,812	7.7
Country of origin <sup>b</sup>				
Norway	574,602	84.0	567,241	83.0
High income countries	33,487	4.9	30,920	4.5
Low/middle-income countries	75,497	11.0	85,597	12.5
Missing data	199	0.0	27	0.0
Marital status				
Unmarried			37,057	5.4
Married/Partnership			634,283	92.8
Divorced			3417	0.5
Missing data			9028	1.3
In vitro fertilization (IVF)				
No			669,024	97.8
Yes			14,761	2.2
Birth order				
1			280,178	41.0
2			244,532	35.8
			159,075	

**Table 1** Paternal and maternal characteristics in 683,785 births in Norway. 1999–2010 (Continued)

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Maternal chronic disease <sup>c</sup>		
No	623,817	91.2
Yes	59,968	8.8
Maternal smoking before pregnancy		
Non-smoker	456,797	66.8
Intermittent	18,518	2.7
Daily	93,662	13.7
Missing data	114,808	16.8
Maternal folic acid use in pregnancy		
No use	371,820	54.4
Only before	8930	1.3
Only during	192,169	28.1
Before and during	110,866	16.2

<sup>a</sup>Categorized according to the class scheme of Erikson, Goldthorpe and Portocarero (EGP) [33]

<sup>b</sup>Categorized according to the classification by World Health Organization, Health statistics and information systems, Estimates for 2000–2012 [34] <sup>c</sup>Asthma, hypertension, kidney disease, chronic urinary infection, rheumatoid arthritis, heart disease, epilepsy, diabetes mellitus (type I or II), and thyroid disease

Mothers whose children's father originated from low/middle-income countries had also a reduced risk of adequate FA use (RR 0.58 (95% CI 0.56–0.60)) compared to fathers originating from Norway.

Table 3 presents crude and adjusted RRs with 95% CIs of adequate FA use by maternal and paternal education. Adjusted analyses showed that adequate FA use was less likely in births were fathers had compulsory education, regardless of maternal education. The association of paternal compulsory education and recommended FA use was weakened by increasing level of maternal education. However, even when the mother had tertiary education, the association of compulsory paternal education on adequate maternal FA use was significant (RR 0.75 (95% CI 0.73–0.77)), compared to fathers with tertiary education.

# **Discussion**

The present population-based study (683,785 births during 1999–2010) showed that recommended maternal FA use was low among fathers who were young or older at their children's birth, had achieved shorter education, held a manually or self-employed occupation, or originated from low/middle-income countries. Even among mothers who had achieved higher education, recommended periconceptional maternal FA use was low among less educated fathers.

Several studies have investigated the association between maternal socio-demographic, reproductive, and medical characteristics and adherence to recommended intake of periconceptional FA. A common feature among mothers is that young age, low educational level, low

**Table 2** Relative risks (RRs) with 95% confidence intervals (95% Cls) of adequate maternal periconceptional folic acid supplement use (before and during pregnancy) by paternal characteristics, in 683,785 births, Norway, 1999–2010

	Folic acid supplementation use		Unadjusted		Adjusted for paternal factors <sup>a b</sup>		Further adjusted for maternal factors <sup>a c</sup>	
Characteristics	Yes	No	RR*	95% CI	RR*	95% CI	RR*	95% CI
Paternal age (years)								
< 20	86	4315	0.11	0.09-0.13	0.10	0.08-0.13	0.35	0.28-0.43
20-24	3325	45,123	0.37	0.36-0.39	0.37	0.36-0.38	0.68	0.66-0.71
25–29	22,886	139,785	0.76	0.75-0.78	0.77	0.76-0.79	0.94	0.93-0.96
30–34	43,348	192,053	1.00	Reference	1.00	Reference	1.00	Reference
35–39	28,488	123,052	1.02	1.01-1.03	0.97	0.96-0.99	0.90	0.89-0.91
40+	12,733	68,591	0.85	0.83-0.87	0.80	0.78-0.81	0.72	0.71-0.74
Paternal education								
Compulsory (1–10 years)	11,694	119,259	0.40	0.39-0.40	0.52	0.51-0.53	0.69	0.68-0.71
Intermediate (11–13 years)	45,411	256,973	0.67	0.66-0.67	0.75	0.74-0.76	0.87	0.85-0.88
Tertiary (14–20 years)	51,894	177,924	1.00	Reference	1.00	Reference	1.00	Reference
Missing data	1867	18,763						
Paternal occupational class <sup>d</sup>								
I Higher professionals	19,957	66,678	1.05	1.04-1.07	1.05	1.03-1.06		
II Lower professionals	33,366	119,415	1.00	Reference	1.00	Reference		
Illa Higher routine	12,292	65,248	0.73	0.71-0.74	0.89	0.88-0.91		
IIIb Lower routine	5352	34,718	0.61	0.59-0.63	0.85	0.83-0.87		
IV Other self-employed workers	60	298	0.77	0.61-0.97	0.83	0.65-1.05		
V Technicians	836	4714	0.69	0.65-0.74	0.89	0.84-0.95		
VI Skilled	15,174	93,581	0.64	0.63-0.65	0.84	0.83-0.86		
VII Semiskilled and unskilled	11,643	99,941	0.48	0.47-0.49	0.75	0.73-0.76		
VIIb Agricultural	908	6755	0.54	0.51-0.58	0.73	0.69-0.78		
Unclassified	7575	45,249	0.66	0.64-0.67	0.96	0.94-0.99		
Missing data	3703	36,322						
Paternal country of origin <sup>e</sup>								
Norway	99,339	475,263	1.00	Reference	1.00	Reference	1.00	Reference
High income countries	6535	26,952	1.13	1.10-1.16	1.06	1.04-1.09	1.06	1.03-1.08
Low-middle-income countries	4975	70,522	0.38	0.37-0.39	0.35	0.34-0.36	0.58	0.56-0.60
Missing data	17	182						

<sup>&</sup>lt;sup>a</sup>All RRs for adequate folic acid supplementation adjusted for year of childbirth (continuous)

socioeconomic status, unplanned pregnancy, higher parity, smoking, single marital status, and non-western birthplace is the most important determinants for inadequate FA supplementation use [20–23]. Furthermore, maternal chronic diseases and IVF were positively associated with adequate periconceptional FA supplementation use [22, 38].

In Denmark, a cross-sectional study consisting of 22,000 pregnant women (primiparious and multiparous) showed that only 14% of the women used FA as recommended and compliance was positively associated with being primiparous, older than 25 years and non-smoker [21]. Similarly, for about 16% of the births in our study, the mothers had followed the

<sup>&</sup>lt;sup>b</sup>RRs by paternal age, no other adjustment for paternal factors; RRs by paternal education adjusted for paternal age (< 20, 20–24, 25–29, 30–34, 35–39, 40+), paternal country of origin (Norway, high-income countries, low/middle-income countries); RRs by paternal occupation adjusted for paternal age, fathers country of origin, fathers education (compulsory, intermediate, tertiary); and RR by paternal origin of country, no other adjustment for paternal factors

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dCategorized according to the class scheme of Erikson, Goldthorpe and Portocarero (EGP) [33]

eCategorized according to the classification by World Health Organization, Health statistics and information systems, Estimates for 2000–2012 [34]

<sup>\*</sup>p-value for difference between categories of paternal characteristics was < 0.001 using likelihood ratio test

**Table 3** Relative risks (RRs) with 95% confidence intervals (95% CI) of adequate maternal periconceptional folic acid supplement use (before and during pregnancy) by combining maternal and paternal education in 683,785 pregnancies, Norway, 1999–2010

		Adequate folic acid use		Unadjusted		Adjusted <sup>a</sup>	
Maternal education	Paternal education	Yes	No	RR*	95% CI	RR*	95% CI
Compulsory education	Compulsory education	2557	48,326	0.46	0.43-0.50	0.53	0.50-0.57
	Intermediate education	4758	52,693	0.77	0.72-0.81	0.76	0.72-0.81
	Tertiary education	1292	10,651	1.00	Reference	1.00	Reference
	Missing information	208	4994				
Intermediate education	Compulsory education	5079	43,708	0.60	0.57-0.62	0.66	0.64-0.68
	Intermediate education	18,055	116,378	0.77	0.75-0.79	0.81	0.79-0.83
	Tertiary education	7477	35,269	1.00	Reference	1.00	Reference
	Missing information	426	3928				
Tertiary education	Compulsory education	3805	17,985	0.70	0.67-0.72	0.75	0.73-0.77
	Intermediate education	22,150	80,373	0.86	0.85-0.87	0.88	0.87-0.89
	Tertiary education	42,541	126,896	1.00	Reference	1.00	Reference
	Missing information	747	3539				
Missing data (maternal education)		28,179	1771				

<sup>&</sup>lt;sup>a</sup>Adjusted for paternal age (< 20, 20–24, 25–29, 30–34, 35–39, 40+), year of childbirth (1999–2010 (continuous)), paternal country of origin (Norway, high income countries, low/middle income countries), stratified by maternal education

national guidelines of FA use in the study period (1999–2010).

In Norway, a publication from the Norwegian Mother and Child Cohort Study (MoBa), comprising 27% of the births registered in MBRN during 2000–2003, showed similar results to ours [22]. They found a positive association between paternal education and recommended periconceptional FA use. In pregnancies with fathers having university or college education the adjusted relative risk (RR) of periconceptional maternal FA use was 1.4 (95% CI 1.1–1.8) compared to pregnancies with fathers with primary education. However, the association was weaker than for maternal education. When paternal *tertiary* education was compared to paternal *compulsory* education (reference) in our analyses, we found a similar result for adjusted RR of 1.45 (95% CI 1.42–1.48).

Couples who live together share the same environment, social network, financial resources, and to some extent, the same health risk; beneficial or negative to health outcomes depending on the health behaviour of the spouses [25, 27]. Furthermore, a Dutch study of 40,000 individuals aged 25–74 years showed that women seems more affected by their partner's educational level than men are with regard to healthy behaviour [41].

In accordance with our findings, a cross-sectional household survey conducted in Pakistan (comprising 6266 women), showed that maternal intake of iron and FA supplements was positively associated with the educational status of the mothers' husband [42].

The association of ethnic background and maternal periconceptional FA use have been studied in Norway

and other European countries (Netherlands, Belgium, Ireland and the United Kingdom) [23, 43–46]. These studies show that supplement use is less common among most ethnic minority groups than among the comparison groups. We have similar findings in our study, showing a lower risk of adequate maternal FA use among fathers originating from low/middle-income countries.

The strengths of our study included use of comprehensive data from population-based registries in Norway that assures generalizability of our results, and registration of individual-level information on periconceptional FA intake for all births in Norway since 1999 (except for terminated pregnancies).

Our study had some limitations. Maternal FA intake could have been misclassified; in the beginning of the study period, FA users were underreported to the MBRN [47]. Our results may therefore be somewhat weaker than the true associations. Furthermore, we could not adjust for pregnancy planning, maternal physical activity or maternal use of alcohol [16, 18, 20–24], as these potential confounders/covariates were not available in our dataset. However, a recent longitudinal study during 2014 on men's pregnancy planning comprising about 800 participants in Sweden, showed that 81% of the pregnancies were planned and the level of paternal education was positively associated with pregnancy planning [48]. Moreover, data from 22,500 mothers in the MoBa study with deliveries recorded in 2000-2003 showed that 78% of the mothers had planned their pregnancy [22]. However, MoBA is not entirely representative of the

<sup>\*</sup>p values for interaction between maternal and paternal education were calculated by likelihood-ratio tests (unadjusted p value < 0.001; adjusted p value < 0.001)

total pregnant population in Norway, since the participants are somewhat better educated, slightly older at delivery, and with a lower percentage of smokers than the overall pregnant population.

Information about fathers was not available in 12,699 births (2% of all births in the study population) and were excluded from the study population. They represent births with fathers unreported by the pregnant woman or fathers without identification number from the NR. Among the excluded births (missing father information), 10% of the mothers had adequate periconceptional FA supplementation (16% in the study population) with an RR of 0.63 (95% CI 0.60–0.66) for adequate maternal FA use comparing births with unregisterd fathers with births having registered fathers.

Adjusting for maternal confounders (maternal age, education, or country of origin) in our analysis reduced the strength of the associations between paternal determinants (age, education or country of origin) and adequate maternal periconceptional FA use. This suggest that paternal factors are important, but targeting maternal demographic and socioeconomic conditions and other factors related to low use is still important. However, our findings have implications for public health practice. Recent research on men's birth intentions has shown that 63% of pregnancies were intended (wanted) by the father [49]. Further, our study demonstrates the importance of the partner's impact on maternal reproductive health and family planning through shared decision-making.

# **Conclusions**

In conclusion, our study supports the importance of father's prenatal role in their children's health. In order to improve maternal periconceptional FA supplementation use, information and knowledge about the importance of FA's preventive potential needs to be directed to both men and women. Furthermore, our findings show that women having partners originating from low/middle-income countries, partners at age < 30 and > 34 years, having compulsory education only, and having occupations other than "higher professional", compared to "lower professionals", are particularly susceptible to low periconceptional FA use. Therefore, campaigns for improved FA supplementation use should focus particularly on these groups.

## Abbreviations

BMI: Body mass index; DAGs: Directed acyclic graphs; IVF: In vitro fertilization; MBRN: Medical Birth Registry of Norway; MoBa: Norwegian Mother and Child Cohort Study; NAV: Norwegian Labour and Welfare Administration; NTDs: Neural tube defects; NUDB: Norwegian National Education Database

## Acknowledgements

The Norwegian Cancer Society, Western Norway Regional Health Authority, and the University of Bergen are acknowledged.

#### Funding

The Norwegian Cancer Society, Western Norway Regional Health Authority, project number 911629 to Dr. Nina Øyen, and the University of Bergen supported this study. The study sponsors had no role in the design, analysis, interpretation of data, or writing of this manuscript.

#### Availability of data and materials

Principal investigator, prof. Nina Øyen, sought and obtained all permissions to access data from the Medical Birth Registry of Norway (MBRN), the National Registry (NR), the Norwegian Labour and Welfare Administration, and the Norwegian National Education Database (NUDB). The datasets analysed during the current study are not freely available due to national regulations.

## Authors' contributions

JHM conceived the study, performed all analyses, and led the writing. NØ and TB conceived the study and participated in manuscript preparation and writing. RMN participated in the analyses and writing. TF participated in the statistical analyses. ST participated in manuscript preparation. All authors helped to conceptualize ideas, interpret findings, and review drafts of the manuscript. All authors read and approved the final manuscript. No conflicts of interest are declared.

#### Ethics approval and consent to participate

The study was approved by the Regional Committee for Medical and Health Research Ethics of Western Norway (REK ref. number 2010/3310).

#### Competing interests

The authors declare that they have no competing interests.

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# Received: 4 February 2017 Accepted: 15 May 2018 Published online: 30 May 2018

## References

- MRC. Prevention of neural tube defects: results of the Medical Research Council vitamin study. MRC vitamin study research group. Lancet. 1991; 338(8760):131–7.
- Czeizel AE, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. N Engl J Med. 1992;327(26): 1832–5
- Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong LY, Gindler J, et al. Prevention of neural-tube defects with folic acid in China. China-U.S. collaborative project for neural tube defect prevention. N Engl J Med. 1999;341(20):1485–90.
- Scientific Advisory Committee on Nutrition. Folate and Disease Prevention. TSO (The Stationery Office), vol. 2006. London: Scientific Advisory Committee on Nutrition.
- De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database Syst Rev. 2015;12:CD007950.
- Wagner C. Biochemical role of folate in cellular metabolism (reprinted from folate and health disease, pgs 23-42, 1995). Clin Res Regul Aff. 2001;18(3): 161–80
- Sadler TWTW, Langman J. Langman's medical embryology, 11th ed. / T.W. Sadler; original illustrations by Jill Leland; computer illustrations by Susan L. Sadler-Redmond; scanning electron micrographs by Kathy Tosney; ultrasound images by Nancy Chescheir and Hytham Imseis. United States: Philadelphia: Wolters Kluwer Lippincott Williams & Wilkins; 2010.

- Suren P, Roth C, Bresnahan M, Haugen M, Hornig M, Hirtz D, Lie KK, Lipkin WI, Magnus P, Reichborn-Kjennerud T, et al. Association between maternal use of folic acid supplements and risk of autism spectrum disorders in children. JAMA. 2013;309(6):570–7.
- Roth C, Magnus P, Schjolberg S, Stoltenberg C, Suren P, McKeague IW, Davey Smith G, Reichborn-Kjennerud T, Susser E. Folic acid supplements in pregnancy and severe language delay in children. JAMA. 2011;306(14): 1566–73.
- Nilsen RM, Vollset SE, Rasmussen SA, Ueland PM, Daltveit AK. Folic acid and multivitamin supplement use and risk of placental abruption: a populationbased registry study. Am J Epidemiol. 2008;167(7):867–74.
- Centers for disease control. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR. 1992;41(RR-14):1–7.
- National Council on Nutrition and Physical Activity. Recommendations and means to increase folate intake among women in fertile age [Anbefalinger og virkemidler for økt folatinntak blant kvinner i fertil alder]. Report no 1/ 1998. Oslo: National Council on Nutrition and Physical Activity [Statens Ernæringsråd]; 1998.
- Nordic Nutrition Recommendations 2012. In: Integrating nutrition and physical activity. Edited by 2014 NCoM. 5th ed. Copenhagen; 2014. http:// dx.doi.org/10.6027/Nord2014-002.
- Lumley J, Watson L, Watson M, Bower C. Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. Cochrane Database Syst Rev. 2001;(3):CD001056. https://doi.org/10.1002/ 14651858.CD001056.
- Daltveit AK, Vollset SE, Lande B, Oien H. Changes in knowledge and attitudes of folate, and use of dietary supplements among women of reproductive age in Norway 1998-2000. Scand J Public Health. 2004;32(4): 264–71
- Bower C, Miller M, Payne J, Serna P. Promotion of folate for the prevention of neural tube defects: who benefits? Paediatr Perinat Epidemiol. 2005;19(6): 435–444
- Ministry of Health and Care Services. [National action plan for a better diet (2017–2021)] Nasjonal handlingsplan for bedre kosthold (2017–2021). In: Edited by omsorgsdepartementet MoHaCSH-o: Departementenes sikkerhets- og serviceorganisasjon; 2017. p. 57.
- Nilsen RM, Mastroiacovo P, Gunnes N, Alsaker ER, Bjorke-Monsen AL, Eussen SJ, Haugen M, Johannessen A, Meltzer HM, Stoltenberg C, et al. Folic acid supplementation and interpregnancy interval. Paediatr Perinat Epidemiol. 2014;28(3):270–4.
- Medical birth registry and abortion registry statistical database [Medisinsk fødselsregister og abortregisteret - statistikkbanker] [http://statistikk.fhi.no/mfr/]. Accessed 23 May 2018.
- Cueto HT, Riis AH, Hatch EE, Wise LA, Rothman KJ, Mikkelsen EM. Predictors
  of preconceptional folic acid or multivitamin supplement use: a crosssectional study of Danish pregnancy planners. Clin Epidemiol. 2012;4:259–65.
- Knudsen VK, Orozova-Bekkevold I, Rasmussen LB, Mikkelsen TB, Michaelsen KF, Olsen SF. Low compliance with recommendations on folic acid use in relation to pregnancy: is there a need for fortification? Public Health Nutr. 2004;7(7):843–50.
- Nilsen RM, Vollset SE, Gjessing HK, Magnus P, Meltzer HM, Haugen M, Ueland PM. Patterns and predictors of folic acid supplement use among pregnant women: the Norwegian mother and child cohort study. Am J Clin Nutr. 2006;84(5):1134–41.
- 23. Timmermans S, Jaddoe VW, Mackenbach JP, Hofman A, Steegers-Theunissen RP, Steegers EA. Determinants of folic acid use in early pregnancy in a multi-ethnic urban population in the Netherlands: the generation R study. Prev Med. 2008;47(4):427–32.
- Braekke K, Staff AC. Periconceptional use of folic acid supplements in Oslo. Acta Obstet Gynecol Scand. 2003;82(7):620–7.
- Jackson SE, Steptoe A, Wardle J. The influence of partner's behavior on health behavior change: the English longitudinal study of ageing. JAMA Intern Med. 2015;175(3):385–92.
- Desrosiers A, Thompson A, Divney A, Magriples U, Kershaw T. Romantic partner influences on prenatal and postnatal substance use in young couples. J Public Health (Oxf). 2016;38(2):300–7.
- Cornelius T, Desrosiers A, Kershaw T. Spread of health behaviors in young couples: how relationship power shapes relational influence. Soc Sci Med. 2016;165:46–55.

- Irgens LM. The medical birth registry of Norway. Epidemiological research and surveillance throughout 30 years. Acta Obstet Gynecol Scand. 2000; 79(6):435–9.
- Kinge JM, Steingrimsdottir OA, Moe JO, Skirbekk V, Naess O, Strand BH. Educational differences in life expectancy over five decades among the oldest old in Norway. Age Ageing. 2015;
- Hammer H. The central population registry in medical research. Tidsskr Nor Laegeforening, 2002;122(26):2550.
- STYRK-08: [Standard Classification of Occupations (STYRK-08)] Standard for yrkesklassifisering (STYRK-08). In: Notater. Oslo–Kongsvinger: Statistics Norway; 2011. ISSN 1891-5906. https://www.ssb.no/en/.
- 32. Vangen T: Nasjonal utdanningsdatabase NUDB. 2007.
- Erikson R, Goldthorpe JH. The constant flux: a study of class mobility in industrial societies: Oxford University Press, USA; 1992.
- Global Health Estimates 2015: Disease burden by Cause, Age, Sex, by Country and by Region, 2000-2015. Geneva: World Health Organization; 2016.
- 35. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. BMC Med Res Methodol. 2008;8(1):70.
- 36. Textor J, Hardt J, Knuppel S. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology. 2011;22(5):745.
- 37. Pearl J. An introduction to causal inference. Int J Biostat. 2010;6(2):Article 7.
- 38. Nilsen RM, Leoncini E, Gastaldi P, Allegri V, Agostino R, Faravelli F, Ferrazzoli F, Finale E, Ghirri P, Scarano G, et al. Prevalence and determinants of preconception folic acid use: an Italian multicenter survey. Ital J Pediatr. 2016;42(1):1–10.
- StataCorp. Stata Statistical Software: Release 15. College Station. TX: StataCorp LLC: 2017.
- Cameron AC, Miller DL. A Practitioner's guide to cluster-robust inference. J Hum Resour. 2015;50(2):317–73.
- 41. Monden CW, van Lenthe F, de Graaf ND, Kraaykamp G. Partner's and own education: does who you live with matter for self-assessed health, smoking and excessive alcohol consumption? Soc Sci Med. 2003;57(10):1901–12.
- Nisar YB, Dibley MJ, Mir AM. Factors associated with non-use of antenatal iron and folic acid supplements among Pakistani women: a cross sectional household survey. BMC Pregnancy Childbirth. 2014;14:305.
- 43. Kinnunen TI, Sletner L, Sommer C, Post MC, Jenum AK. Ethnic differences in folic acid supplement use in a population-based cohort of pregnant women in Norway. BMC Pregnancy Childbirth. 2017;17(1):143.
- Baraka MA, Steurbaut S, Leemans L, Foulon W, Laubach M, Coomans D, Jansen E, Dupont AG. Determinants of folic acid use in a multi-ethnic population of pregnant women: a cross-sectional study. J Perinat Med. 2011;39(6):685–92.
- 45. McGuire M, Cleary B, Sahm L, Murphy DJ. Prevalence and predictors of periconceptional folic acid uptake–prospective cohort study in an Irish urban obstetric population. Hum Reprod. 2010;25(2):535–43.
- Brough L, Rees GA, Crawford MA, Dorman EK. Social and ethnic differences in folic acid use preconception and during early pregnancy in the UK: effect on maternal folate status. J Hum Nutr Diet. 2009;22(2):100–7.
- Nilsen RM, Vollset SE, Gjessing HK, Skjaerven R, Melve KK, Schreuder P, Alsaker ER, Haug K, Daltveit AK, Magnus P. Self-selection and bias in a large prospective pregnancy cohort in Norway. Paediatr Perinat Epidemiol. 2009; 23(6):597–608.
- Bodin M, Kall L, Tyden T, Stern J, Drevin J, Larsson M. Exploring men's pregnancy-planning behaviour and fertility knowledge:a survey among fathers in Sweden. Ups J Med Sci. 2017;122(2):127–35.
- 49. Lindberg LD, Kost K. Exploring U.S. men's birth intentions. Matern Child Health J. 2014;18(3):625–33.