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Determinants of folic acid use in early pregnancy in a multi-ethnic urban population in The Netherlands: The Generation R study

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ABSTRACT

Objective. Recommendations on folic acid use to prevent neural tube defects have been launched in several countries. Adequate folic acid use seems to be low. This study assesses the prevalence of folic acid use and identifies its determinants.

Methods. The study was embedded in the Generation R Study Rotterdam, the Netherlands, a population-based prospective cohort study between 2002 and 2006. Complete information of 6940 women was available. Information on folic acid use and potential determinants was obtained by questionnaires and physical examination.

Results. Of all women 37% adequately used folic acid during the preconception period. Most important risk factors for inadequate use were unplanned pregnancy (OR 9.5, CI 7.2–12.4, $p<0.001$), low educational level (OR 2.5, CI 1.8–3.6, $p<0.001$) and non-western ethnicity, (OR 3.5, CI 2.9–4.3, $p<0.001$). After stratification for ethnicity, unplanned pregnancy remained the most important risk factor for inadequate use. Other risk factors for inadequate use were younger age, single marital status, smoking, multiparity (all $p<0.001$) and alcohol use ($p<0.05$). In contrast, previous spontaneous abortion decreased the risk of inadequate folic acid use ($p<0.001$).

Conclusion. Adequate preconception folic acid supplementation is still too low. Implementation of preconception programs and other public health strategies are strongly needed.

Introduction

From the early nineties recommendations have been launched that women planning pregnancy should use a folic acid supplement of 0.4 mg/day from at least 1 month before until 3 months after conception. (Centers for Disease Control, 1992) These recommendations were largely based on two randomized trials showing that folic acid supplementation reduces the risk of neural tube defects (NTDs) by 72% and 100%. (Czeizel and Dudas, 1992; MRC Vitamin Study Research Group, 1991).

Although folate is an essential micronutrient for cellular growth, the underlying mechanisms by which folate prevents NTDs are not clear. (Ashworth and Antipatis, 2001) However, it is known that pregnant women with folate deficiency are at increased risk for reproductive complications including NTDs. (Lumley et al., 2000) Despite campaigns to promote folic acid intake and evidence that this B vitamin also has beneficial effects against other reproductive failures, the number of women who take folic acid supplements in the recommended period remains low. (Meijer and de Walle, 2005) A strategy to improve intake is mandatory food fortification, which has not yet been introduced in any European country. (Botto et al., 2006; Health Council of the Netherlands, 2000; Meijer and de Walle, 2005; World Health Organization, 1998) Therefore, currently the most effective strategy in Europe, is to use a daily folic acid supplement.

The Dutch mass media campaign in 1995 together with continuing media attention in the following years to promote intake, resulted in an increase from approximately 19% to 36% adequate folic acid use in the Netherlands. In particular, adequate folic acid supplementation appeared to be insufficient in low educated women. (de Walle et al., 2002) It has furthermore been suggested that language proficiency is an important determinant for folic acid knowledge and, subsequently, folic acid intake. (van Eijsden et al., 2006) In order to develop more

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targeted strategies to improve adequate preconception folic acid use in the future, knowledge about other sociodemographic and lifestyle determinants might be important.

Methods

This study was embedded in the Generation R Study Rotterdam, the Netherlands, a population-based prospective cohort study from pregnancy onwards. The study was designed to identify determinants of growth and development from fetal life until young adulthood. (Jaddoe et al., 2007; Jaddoe et al., 2006) In total 8880 women enrolled in the study between 2002 and 2006. (Jaddoe et al., 2006) The Medical Ethics Committee of the Erasmus Medical Center approved the study protocol.

Pregnant women were asked by questionnaire at enrolment (median 14.3 weeks of gestation; 90% range 10.9–23.9 weeks) whether they had used folic acid supplementation (0.4–0.5 mg) and when intake was started. Based on Dutch recommendations, folic acid use was classified into two categories: 1) adequate use, defined as preconception start of folic acid supplementation; and 2) inadequate use, defined as no use of folic acid at all, or supplementation started from pregnancy recognition onwards. (Voedingsraad/Gezondheidsraad, 1992; Voedingsraad/Gezondheidsraad, 1993) In addition, we performed some additional analyses after categorization of the cohort into three groups (adequate use, subadequate use, no use), because folic acid supplementation from pregnancy recognition onwards (subadequate use) might still be beneficial (Shaw et al., 1995).

Information on possible determinants (sociodemographic factors, life style habits, obstetrical history) was obtained from questionnaires.

Sociodemographic factors included information on age, marital status, educational level and ethnicity. Ethnic background was derived from the country of birth of the woman herself and her parents. The different ethnic categories were Dutch, Moroccan, Turkish, Antillean and Surinamese. Women with other ethnic backgrounds than these were grouped as 'other-western' (European, North American, Oceanean, Japanese, Indonesian) or 'other non-western' (African, Asian, South- and Central American) (Statistics Netherlands, 2004a).

Educational level was assessed by the highest completed education and classified into three categories: 1) primary education; 2) secondary education; and 3) university or college (Statistics Netherlands, 2004b).

Life style habits included body mass index (BMI; in kg/m^2; calculated from length and weight measured at enrolment), smoking and alcohol consumption. Obstetrical history included information on parity, pregnancy planning, fertility treatment, previous spontaneous abortion or stillbirth. Pregnancy planning was defined as a confirmatory answer to the question "was the present pregnancy planned?"

First, we assessed the prevalence of folic acid use for the whole cohort. Second, to identify groups at risk and to examine differences in characteristics between adequate and inadequate users, we performed univariate logistic regression analyses. Next, multivariate logistic regression models were used to control for potential confounders, namely age, education, marital status, ethnicity, BMI, smoking or alcohol consumption, parity, pregnancy planning and previous spontaneous abortion (all factors associated with P values <0.1 were included into this multivariate model). Finally, to examine risk factors related to specific ethnic categories, similar analyses were used in strata of the largest ethnic groups. The size of the effect estimates is given in odds ratios (ORs) with 95% confidence intervals (CI). Statistical analyses were performed using Statistical Package of Social Sciences version 15.0 for Windows (SPSS Inc, Chicago, IL, USA).

Results

The response rate of the questionnaire on general characteristics and folic acid supplementation was 78%. Baseline characteristics are shown in Table 1. Thirty-seven percent of these 6940 women started folic acid supplement use preconceptionally (adequate), 35% from pregnancy recognition onwards (subadequate), and 28% did not use folic acid at all (total of 63% inadequate use).

Women who used inadequate folic acid were younger, more often single and lower educated (Table 2). All non-Dutch groups had increased risks for inadequate folic acid use. Smoking during pregnancy was strongly associated with inadequate folic acid use (OR 2.3, 95%CI 1.8–3.0). After controlling for potential confounders alcohol consumption during pregnancy became a risk factor for inadequate folic

Table 1
Baseline maternal characteristics; the Generation R Study 2002–2006

	Number of subjects $n=6940$
Sociodemographic factors	
Folic acid supplement use	
Adequate folic acid use	2592 (37.3)
Inadequate folic acid use	4348 (62.7)
Age	
<20 years	276 (4.0)
20–29.9 years	2989 (43.1)
30–35 years	2633 (37.9)
>35 years	1042 (15.0)
Marital status	
Married or living together	5892 (84.9)
No partner	985 (14.2)
Missing	63 (0.9)
Educational level	
Primary school	766 (11.0)
Secondary school	3139 (45.2)
University or college	2891 (41.7)
Missing	144 (2.1)
Ethnicity	
Dutch	3457 (49.8)
Moroccan	443 (6.4)
Turkish	618 (8.9)
Suriname and Antilles	859 (12.4)
Western otherwise	826 (11.9)
Non-western otherwise	705 (10.1)
Missing	32 (0.5)
Life style habits	
BMI	
<25	4243 (61.1)
25–30	1803 (26.0)
>30	857 (12.4)
Missing	37 (0.5)
Smoking	
Yes, still	827 (11.8)
Until pregnancy recognition	821 (11.9)
No	5192 (74.9)
Missing	100 (1.4)
Alcohol	
Yes, still	1119 (16.1)
Until pregnancy recognition	1840 (26.5)
No	3919 (56.5)
Missing	62 (0.9)
Obstetrical history	
Parity	
Primipara	3938 (56.8)
Multipara	2993 (43.1)
Missing	9 (0.1)
Pregnancy planning	
Yes	4852 (69.9)
No	1894 (27.3)
Missing	194 (2.8)
Previous spontaneous abortion	
Yes	1305 (18.8)
No	2781 (40.1)
Missing	2854 (41.1)

$n=6940$, Rotterdam, the Netherlands. 2002–2006.
Data represent n (%).
90% range of moment of enrolment $t=10.9$–23.9 weeks (median 14.3 weeks of gestation).

Table 2
Determinants of inadequate folic acid use given in frequency and risks: the Generation R Study 2002–2006

	Folic acid supplement use		OR (CI 95%)	Adjusted OR (CI 95%)[$]
	Adequate use *n*=2592	Inadequate use *n*=4348		
Sociodemographic factors				
Age				
<20 years	19 (6.9)	257 (93.1)	12.9 (8.1–20.7)[*]	1.5 (0.7–3.2)
20–29.9 years	815 (27.3)	2174 (72.7)	2.6 (2.3–2.9)[*]	1.4 (1.2–1.7)[*]
30–35 years	1286 (48.8)	1347 (51.2)	1	1
>35 years	472 (45.3)	570 (54.7)	1.2 (1.0–1.3)	1.0 (0.8–1.2)
Mean (range)	31.6 (17.8–46.3)	28.8 (15.3–44.7)		
Marital status				
Married or living together	2477 (42)	3415 (58)	1	1
No partner	102 (10.4)	883 (89.6)	6.3 (5.1–7.8)[*]	2.0 (1.4–2.7)[*]
Missing	13 (20.6)	50 (79.4)		
Educational level				
Primary school	83 (10.8)	683 (89.2)	8.6 (6.8–11.0)[*]	2.5 (1.8–3.6)[*]
Secondary school	952 (30.3)	2187 (69.7)	2.4 (2.2–2.7)[*]	1.3 (1.1–1.6)[**]
University or college	1541 (53.3)	1350 (46.7)	1	1
Missing	16 (22)	128 (88)		
Ethnicity				
Dutch	1838 (53.2)	1619 (46.8)	1	1
Moroccan	55 (12.4)	388 (87.6)	7.9 (5.9–10.5)[*]	6.6 (4.4–10.0)[*]
Turkish	98 (15.9)	520 (84.1)	5.9 (4.7–7.4)[*]	3.8 (2.7–5.3)[*]
Suriname and Antilles	154 (17.9)	705 (82.1)	5.1 (4.3–6.2)[*]	2.6 (1.9–3.5)[*]
Western otherwise	326 (39.5)	500 (60.5)	1.7 (1.5–2.0)[*]	1.5 (1.2–2.0)[*]
Non-western otherwise	117 (16.6)	588 (83.4)	5.6 (4.6–6.9)[*]	3.6 (2.6–4.9)[*]
Missing	4 (12.5)	28 (87.5)		
Life style habits				
BMI				
<25	1691 (39.9)	2552 (60.1)	1	1
25–30	645 (35.8)	1158 (64.2)	1.2 (1.1–1.3)[**]	1.0 (0.8–1.2)
>30	241 (28.1)	616 (71.9)	1.7 (1.4–2.0)[*]	1.1 (0.9–1.5)
Missing	15 (40.5)	22 (59.5)		
Smoking				
Yes, still	161 (19.5)	666 (80.5)	2.9 (2.5–3.5)[*]	2.3 (1.8–3.0)[*]
Until pregnancy recognition	237 (28.9)	584 (71.1)	1.7 (1.5–2.1)[*]	1.6 (1.2–2.0)[**]
No	2165 (41.7)	3027 (58.3)	1	1
Missing	29 (29)	71 (71)		
Alcohol				
Yes, still	500 (44.7)	619 (55.3)	0.6 (0.5–0.7)[*]	1.5 (1.2–1.8)[*]
Until pregnancy recognition	771 (41.9)	1069 (58.1)	0.7 (0.6–0.8)[*]	1.3 (1.0–1.6)[**]
No	1306 (33.3)	2613 (66.7)	1	1
Missing	15 (24.2)	47 (75.8)		
Obstetrical history				
Parity				
Primipara	1576 (40)	2362 (60)	1	1
Multipara	1011 (33.8)	1982 (66.2)	1.3 (1.2–1.4)[*]	1.6 (1.3–1.9)[*]
Missing	5 (55.6)	4 (44.4)		
Pregnancy planning				
No	101 (5.3)	1793 (94.7)	17.7 (14.4–21.8)[*]	9.5 (7.2–12.4)[*]
Yes	2423 (49.9)	2429 (50.1)	1	1
Missing	68 (35.1)	126 (64.9)		
Previous spontaneous abortion				
Yes	561 (43)	744 (57)	0.6 (0.5–0.7)[*]	0.7 (0.7–0.8)[*]
No	882 (31.7)	1899 (68.3)	1	1
Missing	1149 (40.3)	1705 (59.7)		

Total *n*=6940, Rotterdam, the Netherlands. 2002–2006.
Data are in *n* (% within row) or odds ratio (95% confidence interval).
[$] Adjusted for age, marital status, educational level, ethnicity, BMI, smoking, alcohol consumption, parity, pregnancy planning and previous spontaneous abortion.
[*] $p<0.001$.
[**] $p<0.05$.

acid use (OR 1.5, 95%CI 1.2–1.8). BMI was not significantly associated with inadequate folic acid use after adjusting for potential confounders.

Pregnancy was planned in 70% of the women, of whom 2% became pregnant after fertility treatment (*n*=107/4852). Thirty percent of the women who became pregnant after fertility treatment did not start folic acid supplementation preconceptionally. Overall, unplanned pregnancy was the highest risk factor for inadequate folic acid use (OR 17.7, 95%CI 14.4–21.8). Multiparity was also positively associated with inadequate folic acid use (OR 1.6, 95%CI 1.3–1.9). A previous spontaneous abortion was associated with a decreased risk of inadequate folic acid use (OR 0.7, 95%CI 0.6–0.8).

The results of the analyses with the cohort categorized into three groups (adequate use, subadequate use, no use) showed same tendencies for all described risk estimates. Adequate and subadequate folic acid users were comparable with respect to demographic and pregnancy characteristics.

The largest ethnic groups were Dutch (*n*=3457), Moroccan (*n*=443), Turkish (*n*=618), Antillean and Surinamese (*n*=859), other-western (*n*=826), other non-western (*n*=705).

Overall, trends for ethnic specific risk factors for inadequate use were similar as those for the whole group. The largest and most significant effects were found for pregnancy planning, educational level, smoking and previous spontaneous abortion (Fig. 1.).

Unplanned pregnancy remained the highest risk factor for inadequate folic acid use and the largest effect was observed in the Dutch and Turkish population. For low educational level, the effect estimates were only significant in the Dutch and Turkish population. Risk estimates for smoking were significant for the Dutch, Turkish, 'other-western' and 'non-western' population. After stratification for ethnicity, previous spontaneous abortion still decreased the risk of inadequate folic acid use. However, these effect estimates were only significant among the Dutch and 'other-western' population.

As for the other four risk estimates comprising age, marital status, alcohol use and multiparity, similar trends were found after stratification for ethnicity. However, most risk estimates were no longer significant. Younger age (20–30 years) was only significantly associated with inadequate folic acid use in the Dutch population (OR 1.4, 95%CI 1.1–1.9). Single marital status remained only significant for the Dutch and 'other-western' population (OR 2.1, 95%CI 1.2–3.7, and OR 3.2, 95%CI 1.2–8.6). The same effect was found for multiparity in the Dutch and Turkish population (OR 1.7, 95%CI 1.3–2.2, and OR 2.1, 95%CI 1.1–4.2). Finally, if a woman consumed alcohol during pregnancy the risk of inadequate use of folic acid was significant in the Dutch population (OR 1.7, 95%CI 1.3–2.2) and, with a decreased risk, in the Moroccan population (OR 0.04, 95%CI 0.002–0.7).

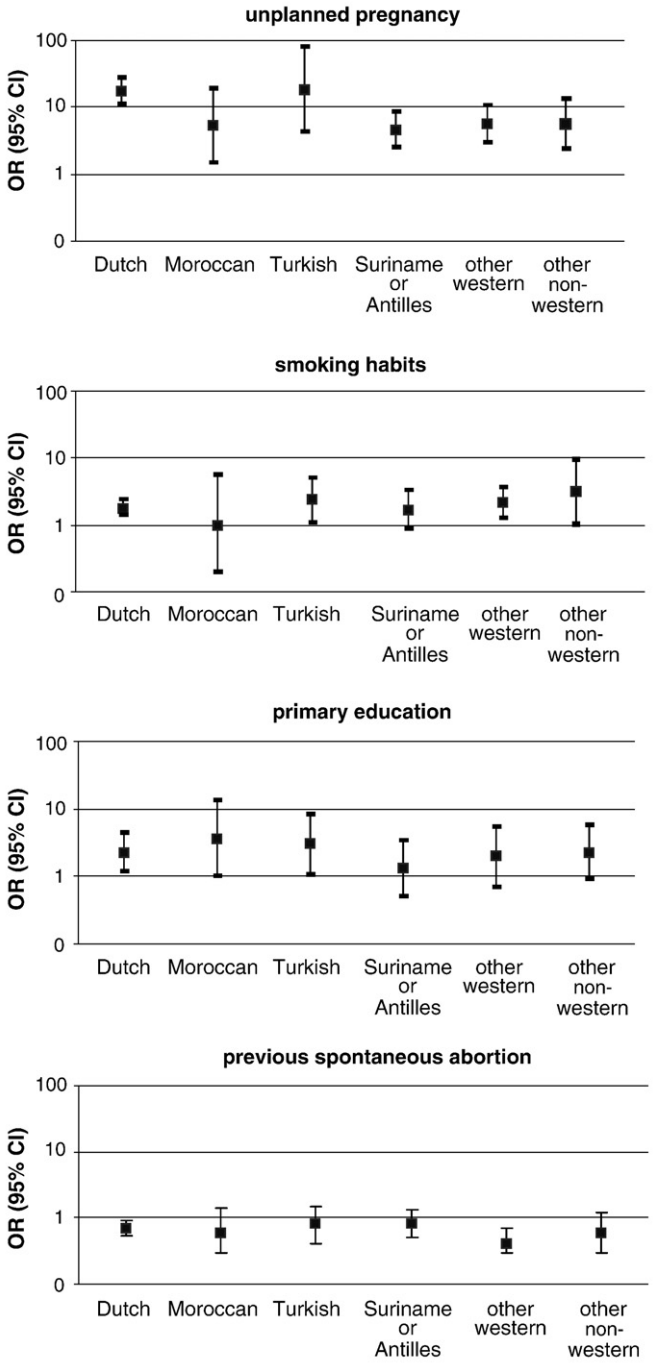

Fig. 1. Ethnic specific risk factors for inadequate folic acid: the Generation R Study 2002–2006. Four main determinants of inadequate folic acid use stratified for ethnicity and adjusted for age, marital status, educational level, BMI, smoking, alcohol consumption, parity, pregnancy planning and previous spontaneous abortion. Rotterdam, the Netherlands. 2002–2006.

Discussion

In this multi-ethnic pregnancy cohort between 2002 and 2006, adequate preconception use of folic acid was as low as 37%. Thus, over the past years this percentage has not significantly changed. (de Walle et al., 2002) The most important factors for inadequate folic acid use appear to be unplanned pregnancy, low socioeconomic status (SES), and non-Dutch ethnicity. Other identified determinants are younger age, single marital status, multiparity, previous spontaneous abortion, smoking and alcohol consumption. Remarkably, this latter determinant only transformed into a risk factor for inadequate folic acid use after controlling for confounders. Since alcohol use, folic acid use and SES are highly correlated, this may explain this change in the effect estimate.

Pregnancy planning appeared to be the most important factor for inadequate folic acid use, even among the various ethnic groups, which is in accordance with previous studies (Morin et al., 2002a; Morin et al., 2002b; Nilsen et al., 2006).

In our cohort, 70% of the pregnancies were planned, which is lower than the 85% reported for the general Dutch population. (Delft M van and Ketting, 2002) A possible explanation is the large number of immigrants in our cohort and the lower rate of pregnancy planning of this particular group (60.6%). (Morin et al., 2002a; Morin et al., 2002b; van Eijsden et al., 2006) However, we are aware that the question pregnancy planning may be subject to confounding by social desirability (Morin et al., 2002a; Morin et al., 2002b). Remarkable is that 30% of the women who became pregnant after fertility treatment did not adequately use folic acid. This could be explained by a lack of information provided by the general practitioner or gynecologist, which emphasizes the need of postgraduate training, or calls for a change in information routines in the fertility clinics.

Folic acid use is extremely low among low educated women, independent of ethnicity. This finding is also in line with other adverse health behaviors, such as smoking and alcohol consumption during pregnancy in these women. (Nilsen et al., 2006; Strine et al., 2005) Since low educated women tend to plan their pregnancy less, this is not surprising. However, it could also be assumed that this target group is less conscious about general health (Morin et al., 2002a; Morin et al., 2002b).

In addition, awareness about folic acid is still low among low educated women. (de Walle et al., 2002) Apparently it is difficult to communicate not only the importance of folic acid use, but also the importance of a healthy lifestyle during pregnancy, towards low educated women. Adequate folic acid use was very low among pregnant non-Dutch women. Van Eijsden et al. (2006) reported that folic acid use was low in a multi-ethnic metropolitan pregnancy cohort in the Netherlands. Even though our study population is different from theirs because it comprises of different ethnic groups, the prevalence of inadequate folic acid use is comparable. It seems

that in the Moroccan population alcohol use was associated with adequate folic acid use. A possible explanation can be that Moroccans who drink have adapted to a more western lifestyle and therefore are more willing to take folic acid supplementation. Smoking and multiparity appear to be specific risk factors for inadequate folic acid use among the Dutch Turkish population, which is in accordance with the findings of Nilsen et al. (2006) Furthermore, the prevalence of smoking and multiple births is high in the Dutch Turkish population (Garssen et al., 2005; van Leest et al., 2002). It is remarkable that unplanned pregnancy was the only and also lowest specific risk factor significantly associated with inadequate use of folic acid among the Suriname and Antillean population. A possible explanation may be the reluctance in this population to use medication. Beliefs about the lack of efficacy of folic acid use may have contributed to inadequate folic acid use in these women as well (Moss and McDowell, 2005). Among the 'other non-western' population pregnancy planning and smoking were associated with inadequate folic acid use. However, the numbers in this group are too small to draw strong conclusions.

The task to prevent NTDs by adequate folic acid intake is far from being fulfilled. Our data suggest that launching recommendations on folic acid use has not been enough to increase intake.

Ten years ago, the United States introduced mandatory fortification of grains with folic acid. Since then a significant decline was seen in the prevalence of NTDs. (Botto et al., 2006; U.S. Department of Health and Human Services FDA, 1996) In addition, it has been suggested that folic acid fortification might have other beneficial effects as well. (French et al., 2003; Thompson et al., 2001) In the Netherlands mandatory food fortification is again under review. In the past, one of the reasons against the introduction of mandatory folic acid fortification has been that it masks the diagnosis of megaloblastic anemia. Nowadays this is not an argument anymore, because vitamin B12 deficiency can easily be diagnosed (Health Council of the Netherlands, 2000). However, if mandatory food fortification is going to be introduced in the Netherlands, we emphasize the importance of surveillance programmes to monitor potential side effects (Smith et al., 2008).

We are aware that there is a gap between awareness and actual adequate folic acid intake, especially among lower educated women. (de Walle et al., 2002) Information and advice are the most important factors for adequate folic acid use. (Morin et al., 2002b) In the past, mass media contributed significantly to folic acid awareness. However, this was an incidental and anonymous activity which was not enough to change behavior in the major proportion of women. (Busby et al., 2005) We assume that "face-to-face" communication embedded in preconception counseling is more likely to be successful in actually changing life style behaviors, especially in immigrant women, because these women are often missed in providing information about the need of adequate folic acid use. (de Weerd et al., 2002; Kreps and Sparks, 2008; Morin et al., 2002a; Morin et al., 2002b) Therefore, all women planning to become pregnant should have access to preconception counselling, with special attention for language barriers and health literacy determined by cultural, religious and social issues (Health Council of the Netherlands, 2007; Kreps and Sparks, 2008; Sheldon, 2007).

Interestingly, there is an inverse relation between adequate folic acid use and adverse health behaviors such as smoking and alcohol consumption during pregnancy. For this reason, this study supports the further development and improvement of national public health strategies together with programs of preconception care.

This was a survey embedded in a large multi-ethnic cohort study in Rotterdam. The population in our study may not be a complete representative of the general Rotterdam population because of an overrepresentation of high educated women in our cohort. (Central Bureau of Research and Statistics Rotterdam, 2003) Moreover, extrapolation to the whole Dutch population seems inappropriate, since this was a multi-ethnic cohort from a metropolitan area. Information on folic acid use was retrospectively obtained by questionnaires in Dutch or English. Although a questionnaire is a valid method for retrospective information collection, misclassification or bias through language proficiency should always be considered. For this reason, women who did not speak Dutch or English were offered individual help in Arabic, French, Portuguese or Turkish by translated questionnaires and study staff speaking these languages. However, because response rates of these women were still lower, some underestimation of the effect estimates might have occurred (Jaddoe et al., 2007; Jaddoe et al., 2006).

Last, although we have specific information when supplementation was started, data on actual duration of folic acid use are lacking. However, it can be assumed that women taking preconception folic acid are likely to use folic acid supplementation throughout the entire advised period. Moreover, preconception intake of folic acid results in a maternal folate depot which lasts for several weeks.

Conclusions

Adequate preconception use of folic acid is still low. Unplanned pregnancy, low socioeconomic status and non-Dutch ethnicity are the main determinants of inadequate folic acid use. There is a relation between folic acid use and adverse lifestyle factors. To change not only awareness but also attitude towards adequate preconception folic acid use, a change in total lifestyle is necessary. Preconception health educational programmes should be developed and applied to improve the intake of folic acid.

Conflict of interest statement

There are no conflicts of interest.

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