Original article Reproductive Health 160

# Supplement use pre-conceptually and in the first trimester of pregnancy in Birmingham, UK

Marwa Khattabi, Kate Jolly

School of Health & Population Sciences Professor Kate Jolly, PhD, MRCGP, University of Birmingham, Birmingham, UK

Correspondence to Dr. Marwa Khattabi, MRCGP, MSc, MBBCH, Coventry and Warwickshire Partnership NHS Trust, UK. e-mail: marwakhatt@gmail.com

Received: 7 September 2021 Revised: 10 October 2021 Accepted: 20 October 2021 Published: 31 December 2021

Journal of The Arab Society for Medical

Research 2021, 16:160-166

#### Background/aim

Sufficient levels of vitamins in the periconceptual period are important for embryonic and fetal development. It is well known that periconceptual folic acid supplementation prevents neural tube defects; however, evidence suggests that periconceptual supplement uptake is suboptimal. The aim of the study was to investigate the uptake of periconceptual supplements in women. The secondary aims were to characterize preconceptual supplement users by age, parity, level of education, ethnicity, first language, and presence of chronic health problems and to identify types of supplements used.

#### Patients and methods

This was a descriptive cross-sectional survey. A total of 180 women aged 16 years or older in their first trimester of pregnancy attending for their dating scan in Birmingham, UK. Percentages and 95% confidence intervals (CIs) of periconceptual supplement users were calculated. Statistical tests were carried out to examine the association of age, ethnicity, first language, parity, level of education, and presence of chronic health problems with preconceptual supplement use. Information about types of supplements used was also gathered.

#### Results

Supplements were taken preconceptually by 39.0% (95% CI: 32.1-46.2) of participants. However, 11.5% started using supplements in the first trimester of pregnancy, and 89 (49.4%, 95% CI: 42.2 to 56.7) participants had not used any supplements. Disparities in the use of preconceptual supplements were seen across a range of characteristics, although none of the differences were statistically significant.

#### Conclusion

Despite recommendations, periconceptual supplement uptake remains suboptimal. Strategies to improve supplement uptake might include active participation from primary health care professionals targeting all women of reproductive age, education campaigns, and population-based food folic acid fortification.

#### Keywords:

before pregnancy, neural tube defects, preconceptual, the first trimester

J Arab Soc Med Res 16:160-166 © 2021 Journal of The Arab Society for Medical Research 1687-4293

#### Introduction

Maternal and fetal adverse effects can result from micronutrient deficiency aggravated by pregnancy, such as maternal anemia [1]. Periconceptual folic acid supplements can prevent neural tube defects [2].

The effect of a nutritional deficiency or excess on the course and outcome of pregnancy varies according to the timing of its occurrence; therefore, good maternal nutrition and adequate use of supplements in the preconception period and in the first trimester of pregnancy are exceptionally important as numerous pregnancy complications start during this period [3]. In the UK, folic acid and vitamin D are both recommended for use by pregnant women [4].

Evidence suggests folic acid has a role in cell multiplication and cell differentiation, and maternal folate requirements increase during periods of rapid cellular growth and division. The lack of the essential folic acid can lead to impaired DNA synthesis and failure to methylate cellular lipids, proteins, and DNA [5]. Therefore, pregnant women with folate deficiency are at a higher risk of maternal and fetal complications.

Direct exposure of the skin to sunlight is the main source of vitamin D. Vitamin D deficiency is more common in people with dark skin. It is estimated that ~15% of all adults in the UK are vitamin D deficient [6]. Furthermore, people who are housebound, pregnant, or breastfeeding especially young women,

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or people who cover their skin for religious motives, are considered high-risk groups for vitamin D deficiency [7].

Adverse outcomes have been linked with maternal vitamin D deficiency, including preeclampsia and gestational diabetes [8]. Furthermore, Javaid et al. [9] argued that the bone mineral mass in a group of children at the age of 9 years was significantly linked to their maternal vitamin D level during pregnancy. In the UK, there is a concern over increasing numbers of infants and children with vitamin D deficiency and rickets [10].

The UK and most European countries recommend all women planning a pregnancy take daily folic acid supplements from at least 1 month before conception and throughout the first 12 weeks of pregnancy. The WHO and National Institution for Health and Care Excellence recommending a daily dose of 400 µg [11]; however, in certain circumstances, such as women taking antiepileptic medications, a dose of 5 mg/day is recommended [12].

The UK Chief Medical Officers and National Institution for Health and Care Excellence advise that all pregnant and breastfeeding mothers should be offered 10 µg of vitamin D daily, which can be accessed through the 'Healthy Start Vitamin Scheme' [13,14].

The primary aim of this study was to investigate the uptake of evidence-based periconceptual supplementation in women by estimating the prevalence of supplement use preconceptually, and in the first trimester, whereas the secondary aim characterize preconceptual supplements by age, ethnicity, first language, parity, level of education, and presence of chronic health problems, to explore the types of supplements that women use preconceptually and during the first trimester of pregnancy and to investigate the sources women used to gain information periconceptual supplements.

# Patients and methods

## **Patients**

This was a descriptive cross-sectional survey. Women aged 16 years or older who came for a dating pregnancy scan before 14 weeks of pregnancy at Birmingham Women's Hospital (United Kingdom) during the study period while the researcher was onsite were all invited to take part. Women with severe learning disability and women attending a scan for potential fetal loss (i.e. not a dating scan) were excluded from the study to minimize selection bias.

## Study design

All potentially eligible women were approached directly by the researcher; they were given information about the study. The anonymous questionnaire and patient information sheet were handed out to the participants and collected on the same day. For women with mild learning difficulties, or who did not speak English, family members and interpreters, where available, helped the participants read the patient information sheet and the questionnaire as it did not cover sensitive issues. The purpose of the study was explained, and it was explained to the participants that completing the questionnaire implied consent. The questionnaire included 11 questions about supplement use before pregnancy and during the first trimester and participant characteristics such as age, first language, level of education, presence of medical conditions, and whether this was their first pregnancy as well as types of supplements used. The completed questionnaires were collected by the researcher from two collection boxes clearly labeled and placed for the participants to drop the completed questionnaires.

# Sample size

A total of 201 women presenting for their dating antenatal scan at Birmingham Women's Hospital were approached by the researcher and handed a patient information sheet and the study questionnaire. Overall, 180 participants returned the completed questionnaires, with a response rate of 90%. With a sample size of 180 women, if the percentage of women taking folate supplements was 85%, a 95% confidence interval (CI) for this estimate would range from 79.1 to 89.5%; if preconception vitamin D use was 10%, a 95% CI was from 6.4 to 15.3%; and if the first trimester use of vitamin D was 50%, the 95% CI was 42.8-57.2.

## Ethical approval

The collected data were kept anonymous; there were no  $\,$ patient-identifiable data. An approval from the NHS ethical committee was obtained (reference: 14/NE/ 0141), and local research governance approvals were obtained before starting.

# Analysis and statistical procedures

Data collected were analyzed using STATA (12) software (Stata 13 Licensed software: Stata/IC 13. USA, 4905 Lakeway Drive, Texas 77845, Serial number: 301306229897) to produce descriptive statistics. The descriptive data were characterized using percentages with 95% CIs. Where appropriate,

the  $\chi^2$  test was used to compare the use of different supplements by categorically grouped characteristics such as parity, ethnicity, first language, and level of education. Multiple logistic regression was used to identify characteristics that may be associated with the use of supplements. All variables (age, ethnicity, first language, pregnancy order, level of education, and chronic health issues) were entered into the model simultaneously.

#### Results

A total of 201 women presenting for their dating antenatal scan at Birmingham Hospital Women's hospital were approached by the researcher and handed a patient information sheet and the study questionnaire. Overall, 180 participants returned the completed questionnaires, with a response rate of 90%. The basic characteristics of the total sample are summarized in Table 1.

## Prevalence of supplement use

A total of 70 (39%, 95% CI: 32.1-46.2%) women used supplements preconceptually. Furthermore,

Table 1 Summary of basic characteristics of the total sample

Variables	Full sample (N=180)		
	n (%)	95% CI	
Age (years)			
≤19	12 (6.7)	3.9-11.3	
20–30	82 (45.6)	38.5-52.9	
31–40	75 (41.7)	34.7-49.0	
Over 40	11 (6.1)	3.5-10.6	
Ethnicity			
White	72 (40)	33.1-47.3	
Mixed/multiple ethnic groups	11 (6.1)	3.5-10.6	
Black	23 (12.8)	8.7-18.5	
Asian/Asian British	60 (33.3)	26.9-40.5	
Other	13 (7.2)	4.3-12.1	
Not stated	1 (0.6)	0.1-3.1	
1st pregnancy			
No	111 (61.7)	54.4-68.5	
Yes	69 (38.3)	31.5-45.6	
First language			
English	124 (68.9)	61.8–75.2	
Other	56 (31.1)	24.8-38.21	
Health problems			
No	157 (87.2)	81.6–91.3	
Yes	23 (12.8)	8.7–18.5	
Level of educationa			
No qualification	22 (12.2)	8.2-17.8	
GCSE	49 (27.2)	21.2-34.2	
A level	25 (13.9)	9.6–19.7	
University degree	67 (37.2)	30.5-44.5	
Postgraduate degree	11 (6.1)	3.5-10.6	
Other	4 (2.2)	8.7–5.6	
Not stated	1(0.6)	0.1-3.1	

<sup>&</sup>lt;sup>a</sup>One hundred seventy nine participants responded to this question.

participants reported that they did supplements either preconceptually or in early pregnancy (49.4%, 95% CI: 42.2-56.7). Table 2 summarizes commencement of supplement use in the first trimester of pregnancy.

### Characteristics of preconceptual supplement users

Only two (16.7%) of women aged less than 20 years took preconceptual supplements, compared with 40.5% of women aged 20 years or more. Only 27.3% of women with no educational qualifications took preconceptual supplements, compared with 40.8% with any educational qualification; these differences were not statistically significant. A similar proportion of the white and the nonwhite ethnic groups used preconceptual supplements (37.5 and 40.0% respectively), as did similar proportions of women with English as a first language or not.

Table 3 summarizes the characteristics of preconception supplement users and those who did not use supplements.

### Characteristics of women who did not use supplements

A total of 10 (83.3%) women who were 19 years or younger did not use preconceptual supplements compared with 59.5% who were 20 years or older.

Overall, 93 (59.5%) women who had GCSE or higher did not use supplements compared with 72.7% of those who had no qualifications. Furthermore, ~62% of women from a white ethnicity did not take preconceptual supplements, which was similar to the percentage in other ethnic backgrounds (60%).

Table 3 summarizes the characteristics of women who did not use preconceptual supplements.

Table 2 Frequency of supplementation preconception and first trimester of pregnancy

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Supplement status	N=110 [n (%)] <sup>a</sup>	95% CI
Started supplements preconceptually	70 (39)	32.1–46.2
Started with positive pregnancy test	2 (1.1)	0.3-4.1
Started after first appointment with GP/ midwife	11 (6.1)	3.5–10.6
Started supplements at other times (not specified)	4 (2.2)	0.9–5.6
Cannot remember when supplements were started	4 (2.2)	0.9–5.6
No supplements used at all	89 (49.4)	42.2-56.7

<sup>&</sup>lt;sup>a</sup>This is the percentage from the whole sample of 180 participants. 95% CI=95% confidence interval.

Table 3 Characteristics of users and nonusers of preconceptual supplements

Variables	Preconceptual supplement users ( $N=70$ ) $[n \ (\%)]^a$	Women who did not use preconceptual supplements ( $N=110$ ) $[n \ (\%)]^{b}$	<i>P</i> value
Age			
19 years or	2 (16.7)	10 (83.3)	0.10
younger			
20+	68 (40.5)	100 (59.5)	
Educationc			
GCSE and higher	64 (40.8)	93 (59.2)	0.225
No qualification	6 (27.3)	16 (72.7)	
Ethnicityc			
White	27 (37.5)	45 (62.5)	0.811
Other ethnic	43 (40.0)	64 (60.0)	
groups			
First language			
English	48 (38.7)	76 (61.3)	0.973
Other	22 (39.3)	34 (60.7)	
Pregnancy order			
First pregnancy	31 (44.9)	38 (55.1)	0.206
Not first	39 (35.1)	72 (64.9)	
pregnancy			
Health problems			
Yes	13 (56.5)	10 (43.5)	0.067
No	57 (36.3)	100 (63.7)	

<sup>&</sup>lt;sup>a</sup>The percentage of supplement users in that variable. <sup>b</sup>The percentage of nonsupplement users in that variable. <sup>c</sup>One missing data.

Table 4 Results of multiple logistic regressions for preconceptual supplement intake

	Variables	Odds ratioa	95% CI of ORb	P value
Age	Base (≥20 years)	1		
	≤19 years	0.24	0.05-1.25	0.09
Ethnicity	Base (other)	1		
	White	1.02	0.95-0.50	0.95
Education	At least GCSE	1		
	No qualification	0.60	0.20-1.77	0.36
1st pregnancy	Base (no)	1		
	Yes	1.74	0.90-3.34	0.11
Language	Base (English)	1		
	Other	1.14	0.52-2.51	0.74
Health problems	Base (no)	1		
	Yes	2.33	0.94-5.75	0.07

Constant=0.502. aAdjusted for age, ethnicity, education, pregnancy order, first language, and chronic health problems. 95% CI of OR: 95% confidence intervals for odds ratios.

## Adjusted analyses (multivariable logistic regressions)

A multivariate logistic regression was performed to measure the association between maternal factors and preconceptual supplement use. Variables examined were, age, ethnicity, pregnancy order, chronic health problems, English as a first language, and level of education. The results are summarized in Table 4.

The adjusted odds ratio (OR) of taking preconceptual supplements in women with known chronic health problems was 2.3 times higher than the odds in a healthy woman (OR=2.33, P=0.067). The results also show that the OR of taking preconceptual

supplements in women with no qualifications was 40% less than the odds in women with a GCSE or higher, but the differences between preconceptual supplement use in those who had a qualification and those who did not have one was not statistically significant.

Furthermore, the OR for women aged 19 years or younger for taking preconceptual supplements was around 75% less than the odds of supplement use in women aged 20 years or older (OR=0.24, P=0.09). The logistic regression analysis demonstrated that maternal age, ethnicity, first language, pregnancy

Table 5 Types of supplements used

Supplement used	n (%)	95% CI
Folic acid only	99 (40.2)	34.3–46.4
Vitamin D only	17 (6.9)	4.36-10.8
Healthy start	24 (9.7)	6.7-14.1
Other pregnancy supplements (pharmacy/supermarket brands)	70 (28.5)	27.4-39.0
Supplements for the general population	7 (2.9)	1.4-5.8
Other supplements <sup>a</sup>	29 (11.8)	4.7–11.3
Total <sup>b</sup>	246 (100)	

Other supplements: <sup>a</sup>either supplements not listed in the questionnaire or participants were unable to identify supplements used. <sup>b</sup>This is the total number of selected choices, not total number of participants.

order, presence of health problems, and level of education did not have a statistically significant effect on preconceptual supplement use in this sample.

# Type of supplements used

Participants were asked to select which supplements they used at some point during the periconceptual period. They were asked to tick all relevant choices; therefore, it is not necessary that the participants were on all of the selected supplements at one time, or at the time of completing the questionnaire. A total of 99 (40%) participants reported using folic acid alone, whereas 17 (7%) reported using vitamin D only. Table 5 summarizes the types of supplements that women used.

# **Discussion**

This study aimed to find the prevalence of supplement use preconceptually and during the first trimester of pregnancy and to identify the demographic features of preconceptual supplement users and types of supplements used. The results from this study suggested that 39% of women participating in the study were using preconceptual supplements; however, only 11.6% started using supplements after becoming pregnant, and 49.4% reported not using any periconceptual supplements. Folic acid alone was the commonly used supplement by women (40%), whereas ~10% reported using healthy start vitamins. Overall, 29% reported using over-the-counter pregnancy supplements (supermarket or pharmacy branded supplements), and 7% reported using vitamin D supplements alone. There were no significant differences in the prevalence of preconceptual supplement use by ethnicity and speaking English as a first language, but younger women, women with fewer educational qualifications, second or subsequent pregnancies, and women without long-term health problems were less likely to take supplements, although not statistically significantly different.

The questionnaire provided information on whether the participants took folic acid alone, vitamin D, or branded supplements; however, there was no information on the supplement doses. These results add to the pre-existing knowledge on periconceptual supplements use and suggests that the prevalence of periconception folic acid use in Birmingham is suboptimal.

The study results are consistent with previous research publications in the UK and Europe, where studies report that despite efforts to increase the general uptake rate, the rate are low [15]. The prevalence of preconceptual folic acid use in European women is 30.1% and around 29% in Middle Eastern and African women [16]. However, in Zambia, 27.2% of women reported taking folic acid supplements during the first trimester [17], and similarly, this was less than 30% in Ghana [18].

The sample was selected from women presenting for dating antenatal scan appointment Birmingham Women's Hospital; therefore, this would represent a broad sample of pregnant women including low-risk and high-risk pregnancies. Another strength is that we tried to minimize recall bias by limiting the target sample to those in their first trimester, as there would be a higher possibility of recall bias if women were approached at a later gestational period [19]. Furthermore, women were shown pictures of commonly used supplements to help them identify which supplements they were taking, to minimize recall bias [20].

On the contrary, data collection took place in a hospital setting; therefore, women may have wanted to give a socially acceptable response rather than the facts [21]. However, to minimize this possibility, the questionnaires were anonymous, and women were asked to place completed questionnaires in a special box or post them back. Furthermore, lack of

compliance information may have contributed to overestimating the actual supplement use [22] Although there is a chance of underreporting with self-completed consumption associated questionnaires, this inclines to be random, tending not to introduce false associations [23]. Another limitation is that the data were collected by one researcher; therefore, only women presenting during the times that the researcher was available on site were included. Furthermore, the sample size was relatively small; the limited sample size is only able to detect relatively large differences between groups, as women with characteristics were of limited numbers.

Primary health care professionals can have an important role in promoting supplement use in the periconception period by educating women and discussing periconceptual supplement use during new patient checks, contraceptive pill checks, cervical screening tests, and when they come to contact with women of reproductive age. Furthermore, special consideration should be given to cultural barriers, language barriers, and economic factors to improve the delivery of supplement information [24]. Some general practice surgeries have television screens playing health information in patient's waiting rooms, including information on periconceptual supplements, which can be a valuable approach in raising supplement awareness in all patients not only women of reproductive age. Furthermore, health visitors and community pharmacists can play a role in improving periconceptual supplement Initiatives including folic acid supplements and information leaflets in pregnancy test kits can be a valuable step in making supplements readily available to women in early stages of pregnancy [25]. Furthermore, community nurses may contribute to raising awareness by educating schoolgirls about the importance of preconceptual supplements and their effects on preventing neural tube defects. Public health awareness campaigns can shed some light on the beneficial effects of folic acid and may improve its use; however, their effects can be variable [26].

# Conclusion

Despite various initiatives to improve the prevalence of periconceptual supplement use, our results suggest that uptake remains suboptimal. Strategies to improve supplement uptake by active participation from primary health care professionals can be useful, especially when targeting all women of reproductive age rather than women planning a pregnancy. Furthermore, education campaigns, and populationbased food folic acid fortification might be considered, bearing in mind the possible masking effects of folic acid on vitamin B12 deficiency anemia, especially in the elderly.

#### **Acknowledgements**

Professor Kate Jolly is partly funded by the National Institute for Health Research (NIHR) Applied Health Research Collaboration West Midlands. The views expressed in this article are those of the authors and not necessarily those of the National Institute for Health Research (NIHR) or the Department of Health and Social Care.

Authors contribution: Dr Marwa Khattabi carried out all stages of the research study as part of an MSc dissertation. Professor Kate Jolly supervised the project and assisted with study design, ethical approval, and reviewing the final manuscript.

# Financial support and sponsorship

#### **Conflicts of interest**

There are no conflicts of interest.

### References

- 1 Ramakrishnan J, Manjrekar R, Rivera J, Gonzáles-Cossío T, Martorell R. Micronutrients and pregnancy outcome: a review of the literature. Nutr Res 1999: 19:103-159.
- 2 Mulinare J. Epidemiologic associations of multivitamin supplementation and occurrence of neural tube defects. Ann N Y Acad Sci 1993;
- 3 Greenberg JA, Bell SJ, Guan Y, Yu YH. Folic acid supplementation and pregnancy: more than just neural tube defect prevention. Rev Obstet Gynecol 2011; 4:52-59.
- 4 National Institute for Health and Clinical Excellence. Maternal and child nutrition. NICE guidelines [PH11]. London: NICE; 2008.
- 5 Crider KS, Yang TP, Berry RJ, Bailey LB. Folate and DNA methylation: a review of molecular mechanisms and the evidence for folate's role. Adv Nutr 2012: 3:21-38.
- 6 Hoare J, Henderson L, Bates CJ, Prentice A, Birch M, Swan G, Farron M. National diet and nutrition survey: adults aged 19 to 64 years. Volume 5: summary report. London: TSO; 2004.
- 7 National Institute for Health and Clinical Excellence. Vitamin D: increasing supplement use among at-risk groups. London: NICE guidelines [PH56];
- 8 Hypponen E, Laara E, Reunanen A, Jarvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birthcohort study. Lancet 2001; 358:1500-1503.
- 9 Javaid M, Crozier S, Harvey NC, Gale CR, Dennison E, Boucher BJ, et al. Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years: a longitudinal study. Lancet 2006; 367:36-43.
- 10 Gordon CM, Feldman HA, Sinclair L, Williams AL, Kleinman PK, Perez-Rossello J, et al. Prevalence of vitamin D deficiency among healthy infants and toddlers. Arch Pediatr Adolesc Med 2008; 162:505-512.
- 11 National Institute for Health and Clinical Excellence, Maternal and child nutrition, 2014; NICE guidelines [PH11]. London: NICE; 2008.
- 12 National Institute for Health and Clinical Excellence. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. 2021; CG137. Available at: http://publications. nice.org.uk/the-epilepsies-the-diagnosis-and-management-of-

- 166
  - theepilepsies- in-adults-and-children-in-primary-and-cg137. [Accessed August 29, 2021].
- 13 National Institute for Health and Clinical Excellence. Pre conception-advice and management guidance, 2021. National Institute for Health and Care Excellence. Available at: http://www.nice.org.uk. [Accessed August 29, 2021].
- 14 Department of Health. Vitamin D advice on supplements for at risk groups, 2012. Available at: http://www.dh.gov.uk/health/2012/02/advicevitamin- d/. [Accessed December 1, 2014].
- 15 Department of Health. Vitamin D advice on supplements for at risk groups. 2012. Available at: [http://www.dh.gov.uk/health/2012/02/ advicevitamin- d/. [Accessed August 1, 2021].
- 16 Kinnunen TI, Sletner L, Sommer C, Martine C. Post4 and Anne Karen Jenum. BMC Pregnancy Childbirth 2017; 17:143.
- 17 Simuyemba MC, Bwembya PA, Chola M, Michelo C. A root cause analysis of sub-optimal uptake and compliance to iron and folic acid supplementation in pregnancy in 7 districts of Zambia. BMC Pregnancy Childbirth 2020; 20:20.
- 18 Mohammed BS, Kawawa AR, Wemakor A. Prevalence and determinants of uptake of folic acid in peri-conceptional period in a rural lower-middleincome country, Ghana. Basic Clin Pharmacol Toxicol 2020; 126:254–262.

- 19 Raphael K. Recall bias: a proposal for assessment and control. Int J Epidemiol 1987; 16:167–170.
- 20 Boslaugh S. Encyclopedia of epidemiology. Vols 1–2. 1st ed. Thousand Oaks, CA: SAGE publication Inc; 2007.
- 21 Grimm, Pamela. (2010). Social Desirability Bias. 10.1002/ 9781444316568.wiem02057
- 22 Cueto HT, Riis AH, Hatch EE, Wise LA, Rothman KJ, Mikkelsen EM. Predictors of preconceptional folic acid or multivitamin supplement use: a cross-sectional study of Danish pregnancy planners. Clin Epidemiol 2012; 4:259–265.
- 23 White MA, Masheb RM, Burke-Martindale C, Rothschild B, Grilo C. Accuracy of self-reported weight among bariatric surgery candidates: the influence of race and weight cycling. Obesity (Silver Spring) 2007; 15:2761–2768.
- 24 Ray JG, Singh G, Burrows RF. Evidence for suboptimal use of periconceptional folic acid supplements globally. BJOG 2004; 111:399–408.
- 25 Viswanathan M, Siega-Riz AM, Moos MK, Deierlein A, Mumford S, Knaack J, et al. Outcomes of maternal weight gain. Evid Rep Technol Assess (Full Rep) 2008; 168:1–223.
- 26 Watson MJ, Watson LF, Bell RJ. A randomized community intervention trial to increase awareness and knowledge of the role of periconceptional folate in women of childbearing age. Health Expect 1999; 12:255–265.