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The folate status of pregnant women in the Republic of Ireland; the current position

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ISBN: 978-1-905767-77-9

Publication date: December 2017

Foreword

This piece of work was commissioned by ***safe***food to provide an up-to-date picture of the folate status of women in the Republic of Ireland who are in the first trimester, or 3-month period, of pregnancy. The data presented will inform policy and practice relating to folic acid.

This report takes the form of an executive summary. Details of the study are reported in full elsewhere (1-5).

Contents

List of tables

List of abreviations

BMI	body mass index
DFE	dietary folate equivalent
FFQ	food frequency questionnaire
IQR	interquartile range
LMP	last menstrual period
nmol/L	nanomoles per litre
NTD	neural tube defect
pmol/L	picomoles per litre
RBC	red blood cell
RDA	recommended daily allowance
ROI	Republic of Ireland
SD	standard deviation
µg	microgram
UK	United Kingdom
WHO	World Health Organization

Acknowledgements

*safe*food would like to acknowledge:

- Professor Michael Turner of the UCD Centre for Human Reproduction at the Coombe Women and Infants University Hospital, principal contractor for this research project
- Professor Jayne Woodside, Queen's University Belfast, who led the team in Belfast
- Shona Cawley, Research Fellow, who worked on this project
- Those who collaborated on the project: Dr Dan McCartney, Dublin Institute of Technology; Professor Anne Molloy, Trinity College Dublin; Dr Mary Rose Sweeney, Dublin City University; Dr Alyson Hunter, Royal Jubilee Maternity Hospital, Belfast; Professor Richard Layte, Trinity College Dublin; and Dr Bob McDonnell, Health Service Executive
- The women who particpated in this study at the Coombe Women and Infants University Hospital, Dublin.

1 Introduction

Neural tube defects (NTDs) arise due to incomplete closure of the neural tube within a month of conception (6). The "neural tube" is the embryonic structure that eventually forms the brain and spinal column. The 2 most common NTDs are:

- Anencephaly, a condition in which most of the brain, or cerebrum, and skull do not develop, and is incompatible with life – babies are usually stillborn or die shortly after birth
- Spina bifida, a condition in which the foetal spinal column does not close properly, resulting in damage to the nerves and subsequent paralysis of the legs at minimum.

Other NTDs include:

- Encephalocoele, a condition in which part of the brain protrudes out through a defect in the skull
- Hydrocephalus (once known as "water on the brain"), a condition in which cerebrospinal fluid accumulates in the brain.

Spina bifida and encephalocoele both have an increased perinatal and infant mortality, or death rate. ("Perinatal" means a number of weeks before and after birth.). Although 80% of infants with spina bifida survive, the condition is associated with varying degrees of physical disability.

The United Kingdom (UK) and Ireland have had to date a higher rate of NTDs than other European countries (7). A recent (2015) study has also shown that the incidence rates of NTDs in the Republic of Ireland (ROI) have increased from 0.92 per 1,000 births in 2009 to 1.17 per 1,000 births in 2011 (8). Furthermore, in the ROI, the majority of babies with spina bifida are live-born, and so the burden of illness is heavy for the individuals and their families. In economic terms, the direct (healthcare) and indirect (societal) costs are also high for the individual affected and for the health services (9).

Since the early 1990s it has been known that folic acid supplementation – adding synthetic folic acid to the diet in the form of a pill – 12 weeks before and during the early stages of pregnancy can reduce the risk of the fetus developing NTDs by 70% (10, 11). Additional folic acid is needed to support the effective closure of the neural tube, which happens at approximately 21 to 28 days after conception. All women who may become pregnant are therefore advised to take a daily supplement of 400 micrograms (µg) of folic acid prior to conception and until the twelfth week of pregnancy (12).

International data shows that not all women comply with the current guidelines for folic acid supplementation (13-15). One of the key barriers is that many pregnancies are unplanned. Previous

studies in the ROI have shown that between 19% and 44% of women start taking folic acid before pregnancy (16-19). The number of women who take folic acid at any time during their pregnancy is much higher, between 84% and 96%, but this is often after the critical period for neural tube closure (17-19).

Red blood cell (RBC) folate is an objective marker, or "biomarker", of folate status. (A "biomarker" is a naturally occurring process or substance that can be identified.) The World Health Organization (WHO) recommend that RBC folate concentrations should be above 906 nanomoles per litre (nmol/L) in women of reproductive age to achieve the greatest reduction in NTDs (20). Table 1 outlines the threshold levels used to assess the adequacy of a woman's folate status.

This report presents data on the folic acid status of women in the ROI at the point of their first antenatal visit, and relates this data to WHO recommendations.

Table 1: Folate status and related measures and thresholds

Measure	What this biomarker reflects	Threshold
Red blood cell folate concentration	Red blood cell folate concentrations are a useful indicator of folate status over the last 3 months.	➢ For deficiency: Less than 10 nmol/L (21) ➢ For prevention of NTDs in women of reproductive age: greater than 906 nmol/L (20)
Serum folate	Serum folate is considered an indicator of recent folate intake.	➢ For deficiency: Less than 10 nmol/L (21) ➢ For prevention of NTDs: No threshold is recommended (20)
Plasma vitamin B12	Vitamin B12 is required for folate metabolism. Low levels have been associated with a higher risk of NTDs.	➢ For deficiency: Less than 150 picomoles per litre (pmol/L) (21)

2 Aims and objectives

This research was commissioned to determine the folate status of pregnant women in the ROI and to

- Relate this data to WHO guidance
- Explore the relationship between folate status and maternal adiposity (excess fat)
- Assess folic acid supplementation practices and determine compliance with folic acid supplementation recommendations in the ROI.

3 Methods

A cohort observational study was carried out in the Coombe Women and Infants Hospital in Dublin between January and September 2014. The "cohort" in this case is the group of women being studied.

Recruitment

The study included women attending their first antenatal visit to the hospital, before they were 18 weeks pregnant.

The study excluded

- Women with a prior neural tube defect history
- Women with multiple pregnancy (twins and so on)
- Women who were unable to give written informed consent.

Study assessments

The study was fully explained to women and they were asked to:

- Provide consent to the use of routinely collected data on their clinical and sociodemographic status.
- Have their height and weight measured.
- Provide a blood sample.
- Complete a questionnaire on their pre-conceptual and post-conceptual dietary supplement use (taking around 20 minutes).
- Complete a 4-day diet history with a research dietitian, to capture dietary intake. Participants were also asked to complete a food frequency questionnaire (FFQ) to get information on brands and frequency of consuming foods that have been "fortified" with folic acid – folic acid has been added to the food.

Folate status measures

Folate status measures (RBC folate, serum folate and plasma vitamin B12) in blood were conducted using established microbiological assays (methods of quantification or measurement) in Trinity College Dublin (22).

Demographic and lifestyle data

This data was extracted from the existing hospital databases and from an additional demographic and lifestyle questionnaire, designed by the study team, the "Lifestyle Before and During Pregnancy" questionnaire. ("Demographics" describes the characteristics of a population, for example age, weight, smoker status, or any other information that may be of interest.) The questionnaire included questions on pre-conception planning and folic acid use, and health behaviour. In addition, data was collected on age, parity (meaning whether a woman has given birth before – "multipara" – or not – "nullipara"), marital status, smoking history, highest level of education reached, income, number of years living in the ROI and country of birth.

Information on socioeconomic status was derived using questions from the Central Statistics Office's *Survey on Income and Living Conditions 2013* (23). Relative income poverty was calculated by comparing equivalised household income against the 60% median income threshold (a household is considered to be in poverty if its equivalised income falls below the 60% median threshold). ("Equivalisation" is a way of calculating a representative income for household.) The detailed algorithmic methods used for the calculation of these indicators are published by the European Commission (24).

Height and weight

Height and weight was used to calculate body mass index (BMI): weight in kilograms (kg) divided by height in metres (m) squared (that is, the number multiplied by itself). Body mass index figures were classified by the WHO criteria (25) (Table 2).

Table 2: Classification of adult underweight, overweight and obesity according to Body Mass Index

Body mass index (BMI)	Classification
Less than 18.5 kg/m²	Underweight
18.5 to 24.9 kg/m²	Healthy weight
25.0 to 29.9 kg/m²	Overweight
30.0 to 34.9 kg/m²	Class I obesity
35.0 to 39.9 kg/m²	Class II obesity
40.0 or greater kg/m²	Class III obesity

Folic acid supplement use

A detailed questionnaire was completed by participants, under the supervision of a research dietitian, to collect information on folic acid supplementation. The questionnaire included questions about the use of folic acid both before and after conception, as well as data on the dose and brand name of folic acid used and compliance with folic acid supplement use guidelines.

Dietary intake data

The data on dietary sources for folic acid collected in the diet history was combined with the data from the FFQ and entered into the "Nutritics" (University Edition) nutrient analysis software programme. This application converts reported food intakes in grams into nutrient intakes. The food composition tables used in Nutritics are derived from *McCance & Widdowson's Composition of Foods, Seventh Summary Edition* (26).

For this study, the Nutritics software has been customised to contain detailed brand information for all breads, spreads, other fortified foods and supplements on the Irish market. This is to comprehensively capture accurate total folate and vitamin B12 intakes and include contributions from voluntarily fortified (there is no mandatory fortification programme in ROI) products such as breakfast cereal, bread and fat spreads and supplements. These customised updates of the Nutritics software have been informed by a contemporary analysis of folate and vitamin B12 fortified foods and supplements available in the ROI (27). These data were extracted from Nutritics:

- Total dietary folate intake (µg)
- Natural folate intake (µg)
- Intake from fortified foods (µg).

The dietary intake values excluded intake from folic acid supplements.

Statistical analyses

Mean, or average, values and standard deviation (SD) – how far values range from the average – are reported, except where data was not normally distributed. In such cases, the median and interquartile ranges (IQR) are reported. (This means the value at the mid-point of a range is reported – for example, data for the fiftieth-highest folate level out of 100 tests taken – and also at one-quarter and three-quarters of the range, for example data for the twenty-fifth and seventy-fifth highest folate levels out of 100 tests taken). Appropriate statistical tests were applied to the data and these tests are detailed in section 4 (Results).

4 Results

Participant characteristics

The profile of the cohort of women who agreed to be interviewed for the study (number, or "n", = 502) (Table 3) was similar to those of the broader hospital population and the national obstetric population (mothers-to-be) in terms of their major sociodemographic and other indicators – for example, age, socioeconomic status and weight (28, 29).

Table 3: Characteristics of the study population (n = 502)

Characteristic	Value
Mean age in years (SD)	30.6 (5.5)
Median weight in kg (IQR)	67.5 (17.40)
Median body mass index (IQR)	24.7(5.9)
Proportion of women that are obese	19.3% (n=97)
Proportion of women nulliparas	42.6% (n=214)
Median gestation at first visit (IQR)] **(data for n = 437)**	12.1 weeks (1.6)
Proportion of women who planned their pregnancy	62.7% (n=315)
Proportion of women married	49.2% (n=247)
Proportion of women are current smokers	12.9% (n=65)
Proportion of women with third level education: diploma or higher **(data for n = 452)**	60.1% (n=272)
Proportion of women in consistent poverty **(data for n = 308)**	4.2% (n=13)
Proportion of women with a history of infertility **(data for n = 501)**	14.8% (n=74)
Proportion of women living in Dublin	63.5% (n=319)
Proportion of women born in Ireland	74.3% (n=373)

Folate status

The plasma folate, RBC folate and plasma B12 status of the women sampled is presented in Table 4, Table 5 and Table 6, respectively.

Table 4: Maternal plasma folate (nmol/L) measured at the first antenatal visit (n = 502)

Measurement descriptor	Maternal plasma folate levels
Median (IQ range) nmol/L	34.7 (18.1)
Range nmol/L	3.0-780.1
Proportion of women deficient in plasma folate, at less than 10 nmol/L[1]	3.6% (n = 18)

[1] (21)

Table 5: Maternal red blood cell folate (nmol/L) measured at the first antenatal visit (n = 502)

Measurement descriptor	Maternal red blood cell folate
Mean (SD) nmol/L	1137.7 (443.4)
Range nmol/L	262.0-3217.0
Proportion of women deficient in red blood cell folate, at less than 340 nmol/L [1]	1% (n = 5)
Proportion of women not meeting WHO guideline for prevention of NTDs, at less than 906 nmol/L [2]	33% (n = 167)

[1](20, 21) [2](20, 21)

Table 6: Maternal plasma vitamin B12 (pmol/L) measured at the first antenatal visit (n = 502)

Measurement descriptor	Maternal plasma B12 levels
Mean (SD) nmol/L	205 (111)
Range	57.0-724.0
Proportion of women deficient in plasma B12, at less than 150 pmol/L[1]	19.5% (n = 98)

[1] (20, 21)

It is clear that 33% of the women were not meeting the WHO guideline for red blood cell folate to prevent NTDs. It is also apparent that 3.6% and 19.5% of the women were deficient in plasma folate and plasma Vitamin B12, respectively.

Folate status in relation to body mass index

Table 7 shows the median serum folate and vitamin B12 measurements and the mean RBC folate levels analysed by BMI category. There was no difference in mean folate or B12 measure of women in the "overweight" or "class I obesity" categories when compared with women in the "healthy weight" BMI category. However, women with a BMI above 34.9 kg/m^2 (those with "class II obesity" and "class III obesity") had significantly lower serum folate ($p = 0.04$) and significantly lower plasma B12 ($p = 0.01$) values than women with a healthy weight BMI.

Table 7: Mean and standard deviation (SD) maternal red blood cell folate, median and interquartile range (IQR) serum folate and median and interquartile range (IQR) plasma vitamin B12 levels by body mass index category (n = 496)[a]

Body mass index category[a]	Red blood cell folate (nmol/l) Mean (SD)	Number of women (n)	p	Serum folate (nmol/l) Median (IQR)	Number of women (n)	p	Plasma B12 (pmol/l) Median (IQR)	Number of women (n)	p
Healthy weight[b]	1,139.8 (413.5)	263		36.2 (16.3)	263		208.0 (125.0)	262	
Overweight	1,103.8 (468.7)	136	0.94	32.6 (16.8)	136	0.17	201.0 (108.0)	136	0.20
Class I obesity	1,165.8 (443.3)	60	0.99	33.9 (18.6)	60	0.13	211.0 (100.0)	60	0.30
Class II-III obesity	1,213.3 (531.5)	37	0.88	29.8 (21.6)	37	0.04	181.0 (108.0)	37	0.01
Overall	1,138.5 (441.8)	496	-	34.7 (17.9)	496	-	205.0 (111.0)	496	-

[a] Body mass index of less than 18.5 = underweight; 18.5 to 24.9 = healthy weight; 25.0 to 29.9 = overweight; 30.0 to 34.9 = Class I obesity; 35.0 to 39.9 = Class II obesity; above 40 = Class III obesity. Underweight women were excluded (n = 6).

[b] The "healthy weight" category (BMI of 18.5 to 24.9) is used for all comparisons. "One-way" analysis of variance, or "ANOVA" (which tests for significant differences in the averages of at least 2 unrelated categories of data), was used to assess differences in mean RBC folate between the groups. Kruskall-Wallis and Mann-Whitney U tests were used to assess differences in median serum folate and median plasma B12 between the groups.

Folic acid supplementation practices

Detail on the timing of when women started folic acid supplementation is presented in Table 8. While 98.2% (n = 493) of 502 women reported that they took folic acid after they became pregnant, only 24.9% (n = 109) took it for more than 12 weeks pre-conceptionally.

On univariate analysis (which looks at just 1 variable), the strongest predictors of whether a woman will take folic acid pre-conception were

- Higher maternal age
- Higher education and income
- Being married
- Being nulliparous
- Not smoking
- Receiving infertility treatment
- Planned pregnancy.

On multivariate analysis (which looks at more than 1 variable), planned pregnancy and nulliparity were the most important predictors of preconceptional folic acid use (3).

Table 8: Folic acid supplementation practices (n = 502)

Measurement descriptor	Women supplementing with folic acid	
	Percentage (%)	Number (n)
Proportion of women taking folic acid post-conception		
Yes	98.2	(493)
No	1.8	(9)
Proportion of women taking folic acid pre-pregnancy		
Yes	42.8	(215)
No	57.2	(287)
Proportion of women taking folic acid 12 weeks or more pre-pregnancy		
Yes	24.9	(109)
No	75.1	(328)

The women used a wide range of folic acid only and multivitamin supplements (Table 9). Details on the brands and the retail price of the supplements taken are presented in Table 10.

Table 9: Format in which women took folic acid supplements (n = 431)

Format	Women supplementing with folic acid	
	Percentage (%)	Number (n)
Folic acid only	40.4	(174)
Multivitamin	46.4	(200)
High dose folic acid	6.7	(29)
Unknown, as purchased abroad	6.5	(28)

Table 10: Brand of folic acid supplements taken by women (n = 431)

Brand	Women using this brand Percentage (%) Number (n)	Multi-vitamin or folic acid only	Cost (€)	Quantity of tablets	Price per tablet (€)
Pregnacare Original	34.3 (148)	Multi-vitamin	6.5 to 9.7	30	0.22 to 0.32
Clonfolic	31.5 (136)	Folic acid only	3.8	30	0.13
Own brand folic acid only (Tesco/ Boots)	8.4 (36)	Folic acid only	0.5 to 3.0	90	0.01 to 0.03
Pregnacare Plus omega-3	5.8 (25)	Multi-vitamin	18.0 to 20.0	28	0.64 to 0.71
Seven Seas Pregnancy Plus	1.2 (5)	Multi-vitamin	6.0	28	0.21
Galfar FA	1.2 (5)	Multi-vitamin	3.1	28	0.11
Pregnacare Max	1.4 (6)	Multi-vitamin	26.0	56	0.46
Centrum Pregnancy Care	1.2 (5)	Multi-vitamin	6.7	30	0.22
Pharmaton Matruelle	0.7 (3)	Multi-vitamin	17.0	30	0.57
Berocca	0.5 (2)	Multi-vitamin	11.0	30	0.37
Kelkin Folic Acid	0.5 (2)	Folic acid only	3.2	60	0.05
Sanatogen New Mother	0.2 (1)	Multi-vitamin	14.5	40	0.36
Purchased abroad	6.5 (28)	Folic acid/ multi-vitamin	Unknown	Un-known	Unknown
Clonfolic (high dose)	6.7 (29)	Folic acid only	7.9	28	0.28

Knowledge about folic acid supplementation

The results presented here include data for an additional group of women who reported taking folic acid at any point during their pregnancy (n=564). Of these 564 women, 92.0% (n = 516) said that they were taking folic acid "for a healthy baby" when asked to select reasons from a range of possible answers. However, when questioned in an open-ended manner – "Why do you take folic acid?"– only 56.4% (n = 318) of the women who took folic acid during their pregnancy mentioned the importance of folic acid in "spinal or brain development" or in the prevention of "spinal or brain defects", "spina bifida" or "neural tube defects". Numerous other reasons were reported by women for taking folic acid, including "for baby's health and development", "because my doctor told me to", "for prevention of miscarriage", "for nutrients" and "for baby's bones" (Table 11).

Among those who did not supplement their diet with folic acid pre-conceptionally (n = 331), the main reason reported was that the woman did not expect to get pregnant (76.4%). Over one-third of women (35%) who did not supplement pre-conceptionally, however, reported that they did not know that they needed to take folic acid before becoming pregnant (Table 12).

For those who took folic acid both before and after conception, and for those who took folic acid only after becoming pregnant, the main sources of this advice were the family doctor, family members and friends.

Table 11: Knowledge and attitudes related to folic acid and neural tube defects*

Advice source for those who took folic acid during pregnancy[a]	Percentage (%)	Women receiving advice Number (n)
	9.4	(53 out of 563)
Midwife	5.3	(30 out of 563)
Nurse	63.1	(355 out of 563)
Family doctor	3.6	(20 out of 563)
Obstetrician	25.6	(144 out of 563)
Family members or friends	11.7	(66 out of 563)
Internet	6.2	(35 out of 563)
Magazines	3.9	(22 out of 563)
Radio or television	5.0	(28 out of 563)
Other		
Source of advice for those who took folic acid before pregnancy[a]		
Midwife	7.6	(19 out of 251)
Nurse	6.8	(17 out of 251)
Obstetrician	4.8	(12 out of 251)
Family doctor	55.0	(138 out of 251)
Family members or friends	33.5	(84 out of 251)
Magazines	7.6	(19 out of 251)
Internet	17.5	(44 out of 251)
Radio	5.2	(13 out of 251)
Other	6.0	(15 out of 251)
"Why do you take folic acid?"[b]		
I don't usually eat the right foods	20.4	(114 out of 560)
Prevents heart disease	4.3	(24 out of 560)
Good for health	41.4	(232 out of 560)
For a healthy baby	92.0	(516 out of 560)
Family and friends say it is good	37.0	(207 out of 560)
Doctor and nurse say it is good	3.6	(300 out of 560)
"Why did you not take folic acid before becoming pregnant?"		
Did not expect to get pregnant	76.4	(253 out of 331)
Did not think I needed to take it	35.0	(116 out of 331)
Vitamins are too expensive	0.0	(0 out of 331)
Vitamins gave me side effects	0.6	(2 out of 331)

* Data presented in this table published in (3)

[a] Data missing for n = 1.

[b] Data missing for n = 4. Respondents were asked to select reasons from a range of possible answers.

Table 12: Knowledge about reasons for taking folic acid among women who supplemented with folic acid during pregnancy (n = 564)*

Reason stated for taking folic acid supplements[a]	Women supplementing with folic acid	
	Percentage (%)	Number (n)
To prevent spina bifida	34.2	(193)
It is important for baby's health	14.4	(81)
To prevent neural tube defects	8.9	(50)
It is important for baby's development	6.9	(39)
It is important for pregnancy	6.7	(38)
To support spine development	6.0	(34)
Don't know	5.5	(31)
Because the doctor told me to	3.4	(19)
To prevent spine defects	3.2	(18)
To support brain development	2.7	(15)
To prevent brain defects	1.4	(8)
To enhance nutrient intake	1.2	(7)
Because I was planning the pregnancy	1.2	(7)
To support bones or bone development	1.1	(6)
Because I have epilepsy	0.9	(5)
To prevent miscarriage	0.7	(4)
To prevent cleft palate	0.5	(3)
To prevent osteoporosis	0.2	(1)
To prevent cystic fibrosis	0.4	(2)
To prevent Down's syndrome	0.4	(2)
To improve energy levels	0.2	(1)

* * Data presented in this table published in (3)
[a] Responses to an open-ended question

Women living in poverty or who had lived in the ROI for less than 5 years had the lowest level of knowledge around the use of folic acid to prevent NTDs (3).

Relationship between length of supplementation and folate status

Women who started to take folic acid supplements more than 4 weeks before their last menstrual period (LMP) were more likely to have an optimal RBC folate level than those who started when their pregnancy test showed a positive response (Table 13). It should be noted that only 39.5% of women who started folic acid 8 weeks or more after their LMP had an optimal RBC folate level even though the pregnancy blood was not taken until a median of 12 weeks gestation.

Table 13: Percentage of women who had optimal red blood cell folate levels at first antenatal visit, relative to when they started taking folic acid supplements and in relation to their last menstrual period (n = 437)

Time when women started taking folic acid supplements	Number of women in this group (n)	Proportion of women with red blood cell folate above 906nmol/L		p
		Percentage (%)	Number (n)	
12 weeks or more before LMP[a]	109	88.1	(96)	<0.001
8 to 12 weeks before LMP	27	92.6	(25)	<0.001
4 to 8 weeks before LMP	51	78.4	(40)	<0.001
0 to 4 weeks before LMP	5	80.0	(4)	Not analysed[a]
0 to 4 weeks after LMP	40	50.0	(20)	0.71
4 to 8 weeks after LMP	167	53.3	(89)	Ref.[b]
8 weeks or more after LMP	38	39.5	(15)	0.12

[a] Numbers too small for statistical analysis.

[b] Reference category used for all comparisons. Cross-tabulation used to assess differences in the percentage of people who achieve optimal RBC folate.

Women who started folic acid supplementation more than 4 weeks before their LMP had a higher serum and RBC folate than those women who started folic acid around the time of neural tube closure (at 3 to 4 weeks post-conception or 5 to 6 weeks since the woman's last menstrual period) (Table 14). The mean time of starting folic acid supplementation in pregnancy was 5.5 weeks (SD 2.1), which was most likely soon after the home pregnancy test showed positive.

Table 14: Maternal red blood cell and serum folate (nmol/l), relative to time when women started folic acid supplementation (n = 437)

Time when women started taking folic acid supplements	Red blood cell folate (nmol/L) Mean (SD)	Number of women (n)	p	Serum folate (nmol/L) Median (IQR)	Number of women (n)	p
12 weeks or more before last menstrual period (LMP)	1,431·1 (460·2)	109	<0·001	39·0 (14·9)	109	<0·001
8 to 12 weeks before LMP	1,463·4 (385·1)	27	<0·001	39·1 (16·7)	27	<0·001
4 to 8 weeks before LMP	1,199·7 (903·0)	51	0·03	31·0 (16·0)	51	0·04
0 to 4 weeks before LMP	1,075·4 (251·0)	5	0·99	36·1 (22·5)	5	0·12
0 to 4 weeks after LMP	966·9 (387·6)	40	0·99	28·1 (17·2)	40	0·23
4 to 8 weeks after LMP	998·4 (361·4)	167	Ref.[a]	31·0 (16·6)	167	Ref.[a]
8 weeks or more after LMP	884·7 (368·5)	38	0·67	20·2 (22·9)	38	0·30

[a] Reference category used for all comparisons. One-way ANOVA used to assess differences in mean RBC folate between groups. Kruskall-Wallis and Mann-Whitney U tests used to assess differences in median serum folate between groups.

Dietary folate

Table 15 shows the women's dietary intake data for folate. The median intake of total dietary folate and dietary folate equivalents for this group of women would meet basic non-pregnancy requirement for women (200 µg per day). However, the intake falls short of the 600 µg per day requirement in early pregnancy: only 2.6% of the women were meeting their folate dietary requirements for pregnancy.

Table 15: Maternal dietary folate intake (including fortified folic acid) per day (n = 392)

Measurement Descriptor	Maternal dietary intake levels
Total dietary folate µg Median (IQR)	235.2 (143.6)
Median percentage of dietary folate from natural folate[a]	81.7%
Median percentage of dietary folate from synthetic folate	10.9%
Natural folate µg Median (IQR)	190.7 (93.4) (Range 35.1 to 1,637.4)
Synthetic folate µg Median (IQR)	25.6 (79.3) (Range 0 to 800)
Dietary folate equivalents (DFE)[b] µg Median (IQR)	255.1 (185.2)
Proportion of women achieving WHO recommended daily allowance (RDA)[c] for pregnancy, at 600µg or more [c]	2.6% (n = 10)
Proportion of women achieving Food Safety Authority of Ireland RDA for pregnancy, at 500µg or more [d]	5.4% (n = 21)

[a] As median and interquartile ranges for dietary folate, natural folate and fortified folic acid are reported, the natural and fortified folates do not add to give the total median dietary folate.

[b] The quantity of DFEs occurring naturally in food equals the micrograms of folate as reported (1.0 DFE). The DFE provided by fortified foods is 1.7 times the µg of added folic acid (1.7 DFE) (30).

[c] (31).

[d] (32).

5 Key findings

What was the folate status of the women?

- One-third of a sample of women in early pregnancy in the ROI had RBC folate measures that were lower than the amount recommended by the WHO to prevent NTDs. One per cent of the women were found to be deficient.
- While there is no cut-off point for plasma folate for the prevention of NTDs, 3.6% of women were deficient for plasma folate.
- Nineteen and a half per cent of the women were deficient in vitamin B12 relative to the WHO guidance. This is an important finding: vitamin B12 may be a factor contributing to low folate status, as it is required for folate metabolism.

Was there any difference in the blood folate levels of the women depending on their weight (maternal adiposity)?

- There was no difference in mean folate or B12 levels of women in the "overweight" or "class I obesity" BMI categories when compared with women in the "healthy weight" BMI category.
- Women in the "class II obesity" and "class III obesity" categories (those with a BMI above 34.9) had statistically significantly lower serum folate and lower plasma B12 levels than women with a healthy weight BMI.

Did the women follow the recommendation to take folic acid supplements before becoming pregnant?

- Ninety-eight per cent of the women reported that they took folic acid after they became pregnant.
- Only 24.9% of the women who took folic acid took it for more than 12 weeks before conception as recommended.
- Statistical analysis showed that the women who planned their pregnancy and the women for whom it was their first pregnancy were most likely to take folic acid before pregnancy.

What sort of supplements did the women use?

- Women reported taking both folic acid only supplements (40%) and multivitamins (46%).

Who advised the women to take folic acid supplements?

- The family doctor, family members and friends were the main sources of advice for those who women who took folic acid both pre-conceptionally and post-conceptionally and for those who took folic acid only after becoming pregnant.

Why did the women take folic acid supplements?

- Ninety-two per cent of the women who reported taking folic acid at any point during their pregnancy said that they were taking folic acid "for a healthy baby" when asked to select reasons from a range of possible answers.
- However, when questioned in an open-ended manner – "Why do you take folic acid?" – only 56.4% of the women who took folic acid during their pregnancy mentioned the importance of folic acid in "spinal or brain development" or in the prevention of "spinal or brain defects", "spina bifida" or "neural tube defects". Numerous other reasons were reported by women for taking folic acid, including "for baby's health and development", "because my doctor told me to", "for prevention of miscarriage", "for nutrients" and "for baby's bones".

Why did some women not take folic acid supplements?

- Among those who did not supplement their diet with folic acid before conception, the main reason reported was that the woman did not expect to get pregnant (76.4%).
- Over one-third of women (35%) who did not supplement pre-conceptionally reported that they did not know that they needed to take folic acid before becoming pregnant.

What was the relationship between taking supplements and blood folate levels?

- Women who started to take folic acid supplements more than 4 weeks before their LMP were more likely to have an optimal RBC folate then those who only started when their pregnancy test showed positive.

- Only 39.5% of women who started folic acid 8 weeks or more after their LMP had an optimal RBC folate.

What about the amount of folate that the women got from their diets?

- Only 2.6% of the women achieved the WHO RDA of folate for pregnancy of 600 μg per day.
- The majority of the women's dietary folate came from naturally occurring folate in food rather than from fortified folic acid.

6 Recommendations

Surveillance policy

- Folate and vitamin B12 measurements in pregnant women should be monitored regularly as a public health issue.
- Supplementation practices before conception should also be monitored on an ongoing basis.

Supplementation policy

- Supplementation policy needs to address the issue of unplanned pregnancy more clearly, to support women taking folic acid supplements before a pregnancy.

Food fortification policy

- The results from this study should be used to inform discussions on food fortification policy.

Communications

- Communications about folic acid requirements for pregnancy need to clearly acknowledge that it is not possible to achieve sufficient intakes of folate from a healthy diet to prevent NTDs.
- An ongoing public health campaign involving both the traditional communication channels and web-based media about the importance of folic acid supplementation is needed to inform the behaviour of women who may become pregnant whether intended or not.
- Primary care healthcare professionals should be supported to effectively communicate the folic acid message to the women in their care.

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