

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



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

ISBN: 978-1-905767-76-2

Publication date: December 2017

Foreword

This report provides an up-to-date analysis of the folate status of women presenting for antenatal care in Belfast, Northern Ireland. The data presented will inform policy and practice relating to folic acid.

Contents

Acknowledgements.....	3
1 Introduction	4
2 Aims and objectives	6
3 Methods.....	7
Study design	7
Data analysis	12
4 Results.....	14
Sample profiles.....	14
Response rates	15
Biomarker status.....	16
Dietary folate.....	19
Supplementation practices	20
5 Key findings.....	23
What was the folate status of the women?.....	23
Was there any difference in the blood folate levels of the women depending on their weight (maternal adiposity) or other characteristics?.....	23
Did the women follow the recommendation to take folic acid supplements before becoming pregnant?.....	23
What about the amount of folate that the women got from their diets?.....	24
6 Recommendations	25
Surveillance policy	25
Supplementation policy	25
Food fortification policy	25

	Communications.....	25
7	References.....	26

List of tables

Table 1: Folate status and related measures and thresholds	5
Table 2: Classification of adult underweight, overweight and obesity by body mass index (BMI).....	12
Table 3: Characteristics of the Iodine in Pregnancy Study population (n = 241)	14
Table 4: Characteristics of the Folate Study population (n = 56, 2 withdrawals).....	15
Table 5: Maternal plasma folate (nmol/L) measured at the first antenatal visit (n = 239).....	16
Table 6: Maternal red blood cell folate (nmol/L) measured at the first antenatal visit.....	17
Table 7: Maternal plasma B12 (pmol/L) measured at the first antenatal visit (n = 238)	17
Table 8: Relationship between folate status and maternal characteristics.....	18
Table 9: Maternal total dietary folate intake in early pregnancy (n = 103)	19
Table 10: Breakdown of maternal dietary folate (µg) (n = 103)	20
Table 11: Maternal dietary vitamin B12 intake in early pregnancy (n = 103)	20
Table 12: Folic acid supplementation practices of women presenting for antenatal care (n = 60)	21

List of abbreviations

ANOVA	analysis of variance
BMI	body mass index
FFQ	food frequency questionnaire
IQR	interquartile range
LMP	last menstrual period
NI	Northern Ireland
nmol/L	nanomoles per litre
NTD	neural tube defect
pmol/L	picomoles per litre
RBC	red blood cell
ROI	Republic of Ireland
SD	standard deviation
µg	microgram
UK	United Kingdom
WHO	World Health Organization

Acknowledgements

safefood would like to acknowledge:

- Professor Jayne Woodside, Queen's University Belfast, who led the team in Belfast
- Professor Michael Turner of the UCD Centre for Human Reproduction at the Coombe Women and Infants University Hospital, principal contractor for this research project
- Dr Paul McMullan and Dr Virginia Allen-Walker, who undertook recruitment and data collection 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 participated in this study at Royal Jubilee Maternity Hospital, Belfast.

1 Introduction

Neural tube defects (NTDs) arise due to incomplete closure of the neural tube within a month of conception (1). 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:

- Encephalocele, 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 encephalocele 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 (2). The most recent (2015) incidence rates of NTDs in Northern Ireland are 0.2 and 0.3 per 1,000 total registered births for hydrocephalus and spina bifida, respectively (3). For those babies with spina bifida who are live-born, the burden of illness is heavy for the individuals and their families. In economic terms, the direct healthcare and indirect, or societal, costs are also high for the individual affected and for the health services (4).

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 foetus developing NTDs (5, 6). 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 (7, 8).

International data shows that not all women comply with the current guidelines for folic acid supplementation (9–11). One of the key barriers is that many pregnancies are unplanned. Data last collected in Northern Ireland (NI) among nearly 300 pregnant women between 2005 and 2006 showed that only 19% of women started taking folic acid supplements before pregnancy, and found lower red blood cell (RBC) folate in women who did not take folic acid supplements before conception (12).

Red blood cell 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 greater than 906 nanomoles per litre (nmol/L) in women of reproductive age to achieve a reduction in NTDs (13). Table 1 outlines the threshold levels used to assess the adequacy of a woman’s folate status.

This research was commissioned by **safefood** to provide an up-to-date picture of folate status among women in early pregnancy in NI and to relate 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.	<ul style="list-style-type: none"> ➤ For deficiency: less than 10 nmol/L (14) ➤ For prevention of NTDs in women of reproductive age: greater than 906 nmol/L (13)
Serum folate	Serum folate is considered an indicator of recent folate intake.	<ul style="list-style-type: none"> ➤ For deficiency: Less than 10 nmol/L (14) ➤ For prevention of NTDs: No threshold is recommended (13)
Plasma vitamin B12	Vitamin B12 is required for folate metabolism. Low levels have been associated with a higher risk of NTDs.	<ul style="list-style-type: none"> ➤ For deficiency: Less than 150 picomoles per litre (pmol/L) (14)

2 Aims and objectives

This project was commissioned to determine the folate status of pregnant women in NI 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 Northern Ireland.

3 Methods

Study design

The data presented in this report were collected from 2 separate studies relating to nutritional status in pregnancy, and therefore the methodology for each are presented separately. Many of the methodologies were common to both studies. Both were observational cohort study designs. The “cohort” in this case is the group of women being studied

The first study, “Iodine Status and Thyroid Function in Pregnancy and the Postnatal Period in Women and Their Babies Living in Northern Ireland” (called the “Iodine in Pregnancy Study” in this report), was funded by the Endocrinology Trust Fund within the Royal Victoria Hospital, Belfast. The study aimed to establish the association between iodine status during pregnancy and both maternal and child health. This included collection of dietary assessment data, blood samples and demographic lifestyle questionnaires. (“Demographics” describes the characteristics of a population, for example age, weight, smoker status, or any other information that may be of interest.)

Given the target study population and methods of data collection (as outlined below), the study was amended to include outcome measures regarding folate status in pregnant women, once funding was confirmed and ethical approval for these changes given. Data collection for this study was undertaken between July 2014 and December 2015.

The second study, “Folate Status in Pregnant Women: Current Situation on the Island of Ireland” (called the “Folate in Pregnancy Study” in this report), was developed as part of the wider all-island **safe food**-funded study assessing folate status, folate intake and folic acid supplement use in Northern Ireland. The study aimed to recruit additional participants to enhance data collected as part of the Iodine in Pregnancy Study. Data collection for this study was undertaken between November 2016 and January 2017.

Data collection methods for the 2 studies were considered to be comparable, therefore methods of data analysis and results for the 2 cohorts are presented together.

Iodine in Pregnancy Study

Study outcomes

The overall aim of this study (15) was to establish the association between iodine status in pregnancy and both maternal and child health outcomes.

- **Primary trial endpoint** (which measures or observes the outcomes that will answer the main question posed by the study):
 - Median urinary iodine level at each trimester, or 3-month period, and the postpartum period (or postnatal period – a number of weeks after birth).
- **Secondary endpoints** (other measurements or observations that were not the target of the study initially):
 - Iodine knowledge
 - Relationship of thyroid hormone and urinary iodine levels in participants and their child
 - Relationship between maternal and child iodine levels
 - Average iodine-containing foods consumption.

Recruitment

A total of 241 women were recruited at their maternity “booking appointment” (often the first check-up a woman receives, scheduled at around 12 weeks gestation, or pregnancy) at the Royal Jubilee Maternity Hospital in Belfast. Advertisements and referrals from the direct care team were used to recruit women to the study.

The study included women attending a maternity booking appointment.

The study excluded:

- Women under 18 years old
- Women with known thyroid disease
- Women taking thyroid medication.

Following permission from their midwife, women were approached at their booking appointment with written and verbal information about the study. After they had read the information, and had any questions answered by the researcher, interested women completed written informed consent at their appointment.

Data collection

Data collected at the booking appointment (usually between 6 and 13 weeks of pregnancy) was used for the purpose of this report:

- *Demographic questionnaire* – including age, postcode, smoking status and medication use
- *Dietary intake assessment* – a prospective 4-day food diary and iodine food frequency questionnaire (FFQ)
- *Anthropometric data* – weight measured using calibrated scales and height measured using a stadiometer (a vertical ruler with a sliding marker for head height)
- *Venous blood sample* – drawn from the antecubital vein, in the arm, and analysed for thyroid function.

The demographic and 4-day food history data collected at the booking visit were used to inform the data collection for the all-island folate study. One of the collected blood tubes was processed and stored for serum folate and RBC folate analyses using established microbiological assays (methods of quantification or measurement) in Trinity College Dublin (16).

Ethical approval was obtained to present participants at the booking visit with an additional demographic and lifestyle questionnaire, the “Lifestyle Before and During Pregnancy” questionnaire, designed by the study team. This included questions on pre-conception planning and folic acid use, and health behaviours, and provided more detailed data on folic acid use and further knowledge for the all-island study. This was posted to participants with a stamped addressed envelope for return, and the researcher contacted participants by phone to assist with completion and optimise the rate of return. This questionnaire was only posted to a sub-sample of 60 participants, because of the time it took for ethical permission to be granted for this amendment.

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

Folate in Pregnancy Study

Study outcomes

The outcome measures of the study were:

Primary endpoint:

- Red blood cell folate status

Secondary endpoints:

- Folic acid use pre-conception
- Plasma folate
- Other indicators of folate status (for example plasma vitamin B12)
- Folate intake from supplements, food and fortified foods.

Recruitment

A total of 58 women were recruited at their maternity booking appointment (around 12 weeks gestation) at the Royal Jubilee Maternity Hospital in Belfast.

The study included:

- Singleton (single baby) pregnancies
- Women attending a maternity booking appointment

The study excluded:

- Women under 18 years old
- Participants with known non-singleton pregnancies (twins, triplets and so on).

Following permission from their midwife, women were approached at their booking appointment with written and verbal information about the study. After they had read the information, and had any questions answered by the researcher, interested women completed written informed consent at their appointment.

Data collection

Following consent to participate in the study, the following study assessments were undertaken:

- *Demographic lifestyle questionnaire* – including age, postcode, smoking status, pre-conception planning, medication use and health behaviours. Participants were given the

Lifestyle Before and During Pregnancy questionnaire to take home and complete. A stamped addressed envelope was provided for return. The researcher gave an overview of the questionnaire, and contacted participants by phone to assist with completion and optimise the rate of return. Basic demographic details including age, gestation, body mass index (BMI), ethnicity, parity (meaning whether a woman has given birth before – “multipara” – or not – “nullipara”) and time of last folic acid supplement were recorded at the booking appointment.

- *Dietary intake assessment* – comprising a 4-day diet history, folic acid supplement use and folate FFQ. Participants were asked to complete a 4-day food diary and an FFQ at home, and return these to the study team in the stamped addressed envelope provided. The FFQ was developed to take into account the different food products and supplements available in NI and the Republic of Ireland (ROI), informed by a recent paper on “food fortification” (the addition of nutrients to food) (17). The Lifestyle Before and During Pregnancy questionnaire outlined above included questions on participants’ folic acid supplement use.
- *Anthropometric data* – weight and height were measured using calibrated scales and stadiometer, respectively. These were recorded routinely at the maternity booking appointment by midwives, and noted by the researcher. Height and weight was used to calculate BMI: weight (kilograms) divided by height (metres) squared (that is, the number multiplied by itself). Body mass index figures were classified by the WHO criteria (18) (Table 2). Figures recorded in early pregnancy (before 16 weeks of gestation) are likely to reflect pre-pregnancy BMIs, in line with current recommendations (19-22).
- *Venous blood sample* – Twelve millilitres (ml), drawn from the antecubital vein by the midwife or healthcare assistant, was collected as an additional sample, during routine blood sample collection at this antenatal appointment. Blood samples were separated and stored at -80°C for the various assays (for example, ascorbic acid stabilisation for RBC folate) according to protocols (methods) provided by Trinity College Dublin. To allow adjustment for recent intake of folic acid supplements or foods fortified with folic acid, the number of hours since participants’ most recent intake of food or supplements containing folate or folic acid was recorded where possible.

Table 2: Classification of adult underweight, overweight and obesity by body mass index (BMI)

Body mass index (BMI)	Classification
Less than 18.5 kg/m ²	Underweight
18.5 to 24.9 kg/m ²	Healthy weight
25.0 to 29.9 kg/m ²	Overweight
30.0 to 34.9 kg/m ²	Class I obesity
35.0 to 39.9 kg/m ²	Class II obesity
40.0 or greater kg/m ²	Class III obesity

Data analysis

The data on dietary sources for folic acid collected in the diet history were 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* (23).

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 NI) 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 Ireland (17). These data were extracted from Nutritics:

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

The dietary intake values excluded intake from folic acid supplements.

Questionnaire data recording demographic and lifestyle details and folic acid supplementation usage were entered into “IBM SPSS Statistics Version 22.0” (a programme that analyses and predicts statistics). The data are presented using “descriptive statistics” – summaries that describe the basic features of the data. Folate status was compared between BMI categories and other lifestyle characteristics using either “one-way” analysis of variance, or “ANOVA”, (which tests for significant differences in the averages of at least 2 – and in this case 3 – unrelated categories of data); or “independent samples t-tests” (2 categories).

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 (IQR) ranges 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 the results section.

4 Results

Sample profiles

Iodine in Pregnancy Study

The profile of the study population (number, or “n”, = 241) (Table 3) was broadly representative of the NI obstetric population (mothers-to-be) in terms of their major sociodemographic and other indicators (24).

Table 3: Characteristics of the Iodine in Pregnancy Study population (n = 241)

Characteristic	Number of population (n)	Percentage of population (%)
Age		
Less than 30 years	106	44.0
30 years or older	135	56.0
Body mass index category		
Underweight	4	1.7
Healthy weight	110	45.6
Overweight	77	32.0
Obese	50	20.7
Parity		
Nullipara	114	47.3
Multipara	127	52.7
Pregnancy intention		
Planned pregnancy	189	78.4
Unplanned	52	21.6
Smoking		
Current smoker	25	10.4
Former smoker	2	0.8
Never smoked	214	88.8
Place of residence		
Belfast	133	55.4
Outside Belfast	107	44.6

Folate in Pregnancy Study

The profile of the cohort of women sampled for the folate study was broadly comparable, given the relatively small numbers, to those from the Iodine Study (Table 4).

Table 4: Characteristics of the Folate Study population (n = 56, 2 withdrawals)

Characteristic	Number of population (n)	Percentage of population (%)
Age (data for n = 50)		
Less than 30 years	14	28.0
30 years or older	36	72.0
Body mass index category (data for n = 55)		
Underweight	0	0.0
Normal	29	52.7
Overweight	9	16.4
Obese	17	30.9
Parity (data for n = 50)		
Nullipara	17	34.0
Multipara	33	66.0
Place of residence (data for n = 48)		
Belfast	26	54.2
Outside Belfast	22	45.8

Response rates

- The number of samples available for the biomarker study assessments in the Iodine in Pregnancy Study was:
 - Plasma folate (n = 239)
 - Red blood cell folate (n = 240)
 - Plasma vitamin B12 (n = 238).
- The response rate for the dietary history (4-day food diary) was:
 - n = 75 (31.1%) in the Iodine in Pregnancy Study
 - n = 28 (50%) in the Folate in Pregnancy Study

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

- n = 103 (34.5%) in total.
- The response rate for the Lifestyle Before and During Pregnancy questionnaire was:
 - n = 28 (46.6%) in the Iodine in Pregnancy Study
 - n = 32 (57.1%) in the Folate in Pregnancy Study
 - n = 60 (51.7%) in total.

Results from both cohorts for the dietary history and lifestyle questionnaire are presented together from here on.

Biomarker status

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

Table 6 and Table 7, respectively.

Table 5: Maternal plasma folate (nmol/L) measured at the first antenatal visit (n = 239)

Measurement descriptor	Maternal plasma folate levels
Median (IQR) nmol/L	35.7 (18.1)
Mean (SD) nmol/L	39.1 (29.8)
Range nmol/L	2.7 to 264.5
Proportion of women deficient in plasma folate, at less than 10 nmol/L ¹	2.5% (n = 6)

(14)

Table 6: Maternal red blood cell folate (nmol/L) measured at the first antenatal visit

Measurement descriptor	Maternal red blood cell folate levels
Mean (SD) nmol/L	868.7 (407.2)
Median (IQR) nmol/L	783.0 (507.3)
Range nmol/L	160.0 to 2,326.0
Proportion of women deficient in RBC folate, at less than 340 nmol/L ¹	5.0% (n = 12)
Proportion of women not meeting WHO guideline for prevention of NTDs, at less than 905 nmol/L ²	62.1% (n = 149)

¹ (13, 14)

Table 7: Maternal plasma B12 (pmol/L) measured at the first antenatal visit (n = 238)

Measurement descriptor	Maternal plasma B12 levels
Mean (SD) pmol/L	234.5 (117.4)
Median (IQR) pmol/L	208.0 (111.3)
Range pmol/L	53.0 to 990.0
Proportion of women deficient in plasma B12, at less than 150 pmol/L ¹	19.3% (n = 46)

¹ (13, 14)

Table 8 demonstrates the biomarker data according to a number of characteristics, including BMI. Biomarkers did not differ significantly according to BMI status or place of residence. Plasma and RBC folate were significantly higher in those aged 30 and over and in those who did not smoke; and all biomarkers were significantly higher in those who had planned their pregnancy.

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

Table 8: Relationship between folate status and maternal characteristics

	Number (n)	Plasma folate (nmol/L) Median (IQR)	(p)	Red blood cell folate (nmol/L) Mean (SD)	(p)	Plasma B12 (pmol/L) Median (IQR)	(p)
Age			.008		<.001		.078
Less than 30 years	106	33.5 (22.5, 41.5)		746.2 (323.7)		193.0 (161.0, 261.0)	
30 years or older	134	38.2 (27.5, 46.1)		965.6 (440.3)		213.0 (168.0, 288.5)	
Body mass index category			.824		Reference category		.079
Underweight/Normal	113	34.0 (24.7, 44.5)		830.6 (387.9)		218.0 (170.0, 287.5)	
Overweight	77	38.1 (26.6, 43.1)		906.7 (399.8)	.417	210.5 (167.3, 288.3)	
Obese	50	35.8 (24.8, 42.6)		896.1 (458.9)	.611	182.0 (149.5, 249.5)	
Pregnancy intention			<.001		<.001		.017
Planned	188	37.9 (26.8, 45.4)		921.1 (422.1)		211.5 (168.0, 289.5)	
Unplanned	52	28.3 (17.2, 36.2)		679.4 (277.9)		183.5 (148.3, 238.0)	
Smoking			.002		<.001		.052
Current	24	25.6 (15.7, 36.2)		637.4 (241.4)		180.5 (121.7, 228.7)	
Former or never	216	36.6 (26.3, 44.4)		894.4 (414.1)		209.5 (167.0, 281.0)	
Place of residence			.329		.232		.967
Belfast	133	34.8 (24.7, 42.4)		840.4 (409.2)		210.0 (165.3, 273.5)	
Outside Belfast	107	36.8 (26.3, 45.6)		903.7 (403.8)		203.5 (165.5, 301.7)	

One-way ANOVA used to test differences in mean RBC folate status between BMI groups. T-tests used to test for differences in mean RBC folate status between age groups, pregnancy intention, smoking status and place of residence. Plasma folate and plasma B12 were not normally distributed, therefore equivalent “non-parametric” tests, in which the data do not have to fit the expected distribution, were used to assess differences in these characteristics.

Dietary folate

The results from the analysis of the dietary histories are presented in Table 9, Table 10 and Table 11. The dietary analysis showed that only 2.9% of the women were meeting their folate requirements for pregnancy (Table 9). About three-quarters of the women who provided dietary data were meeting their vitamin B12 dietary requirements for pregnancy and lactation (milk production) (Table 11).

Table 9: Maternal total dietary folate intake in early pregnancy (n = 103)

Measurement descriptor	Maternal dietary folate intake levels
Total dietary folate μg	
Median (IQR)	234.6 (88.3)
Dietary folate equivalents μg	
Median (IQR)	248.0 (97.3)
Proportion of women achieving WHO recommended daily allowance for pregnancy, at least $600\mu\text{g}^1$ dietary folate equivalents	2.9% (n = 3)

¹ (25)

Table 10: Breakdown of maternal dietary folate (μg) (n = 103)

Folate measure	Dietary folate intake levels (μg)
Total dietary folate	
Median (IQR)	234.6 (88.3)
Natural folate	
Median (IQR)	185.6 (70.9)
Synthetic folate ¹	
Median (IQR)	81.0 (16.0)
Dietary folate equivalents	
Median (IQR)	248.0 (97.3)

¹Folate derived from fortified foods

Table 11: Maternal dietary vitamin B12 intake in early pregnancy (n = 103)

Measurement descriptor	Maternal dietary vitamin B12 intake levels
Dietary B12 μg	
Median (IQR))	4.0 (2.8)
Proportion of women achieving WHO recommended daily allowance for pregnancy, at least 2.6 μg ¹	76.7% (n = 79)

¹ (25)

Supplementation practices

The supplementation practices of the women surveyed using the Lifestyle Before and During Pregnancy questionnaire are presented in Table 12. The folic acid supplementation rate for the cohort of women sampled was 98% at the time of the first antenatal visit.

Table 12: Folic acid supplementation practices of women presenting for antenatal care (n = 60)

Measurement descriptor	Women supplementing with folic acid	
	Percentage (%)	Number (n)
Proportion of women taking folic acid during the pregnancy		
Yes	98.3	(59)
No	1.7	(1)
Proportion of women taking folic acid pre-conceptionally (n = 60)		
Yes	58.3	(35)
No	41.7	(25)
Proportion of women who started folic acid supplementation (n = 58) ^a		
➤ 12 weeks or more before last menstrual period (LMP)	31.0	(18)
➤ 8 to 12 weeks before LMP	17.2	(10)
➤ 4 to 8 weeks before LMP	10.3	(6)
➤ 0 to 4 weeks before LMP	1.7	(1)
➤ 0 to 4 weeks after LMP	3.4	(2)
➤ 4 to 8 weeks after LMP	32.8	(19)
➤ 8 weeks or more after LMP	3.4	(2)
Proportion of women taking folic acid 12 weeks or more pre-conceptionally (n = 58) ^a		
Yes	31.0	(18)
No	69.0	(40)
Time when women started taking folic acid supplementation pre-conceptionally (n = 35)		
Median weeks pre-pregnancy (IQR)	12.0 weeks (24.0)	
Time when women started taking folic acid supplementation post-conceptionally (n = 23)		
Median weeks after LMP (IQR)	4.0 weeks (1.0)	

^a Of the 60 women who completed the long, detailed folic acid supplementation questionnaire, only 58 reported the time at which they started taking folic acid.

The folic acid supplementation rate at recruitment was 98.4%. In 58.3% of cases the women started before pregnancy, whilst only 31.0% reported starting taking supplementation more than 12 weeks before LMP. Such a rate is higher than reported in other surveys (12) but this may be due to the questionnaires being returned by post rather than at the end of the first visit; it therefore may indicate response bias, through social desirability - a tendency of survey respondents to answer questions in a manner that will be viewed favourably by others - or due to an extended sample time period affecting the accuracy of the women's recall.

5 Key findings

What was the folate status of the women?

- Almost two-thirds of a sample of women in early pregnancy in Northern Ireland had red blood cell folate levels that were sub-optimal, that is, below the level needed for the prevention of NTDs. One in 20 of the women were found to be deficient.
- While there is no cut-off point for plasma folate for the prevention of NTDs, a small number (2.5%) of women were deficient in plasma folate.
- One in 5 women were deficient in vitamin B12, relative to the WHO guidance, and two-thirds had a measure that was sub-optimal. 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) or other characteristics?

- There was no difference in folate status according to BMI category.
- Plasma folate and RBC folate were significantly higher in those aged 30 and over and in those who did not smoke; and all biomarkers were significantly higher in those who had planned their pregnancy.

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

- Almost all women (98%) reported taking folic acid supplements at the time of the first antenatal appointment in the hospital.
- Almost half of women were not taking folic acid supplementation prior to pregnancy.

- Less than one-third (31%) of women had commenced folic acid supplementation more than 12 weeks before becoming pregnant as recommended.

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

- Only 2.9% of the women achieved the WHO recommended dietary allowance of folate for pregnancy of 600 µg per day.
- The majority of the dietary folate came from naturally occurring folate in food rather than from foods fortified with 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.

7 References

1. Watkins M L, Scanlon K S, Mulinare J and Khoury M J (1996). Is maternal obesity a risk factor for anencephaly and spina bifida? *Epidemiology*. 7(5):507–12.
2. Busby A, Abramsky L, Dolk H and Armstrong B (2005). Preventing neural tube defects in Europe: Population based study. *British Medical Journal*. 330(7491):574–5. Epub 2005/03/12.
3. Public Health Agency (PHA) (2016). *Director of Public Health Annual Report 2016*. Belfast: PHA.
4. Yi Y, Lindemann M, Colligs A and Snowball C (2011). Economic burden of neural tube defects and impact of prevention with folic acid: A literature review. *European Journal of Pediatrics*. 170(11):1391–400. Epub 2011/05/20.
5. Czeizel A E and Dudas I (1992). Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *New England Journal of Medicine*. 327(26):1832–5. Epub 1992/12/24.
6. Medical Research Council (MRC) Vitamin Study Research Group (1991). Prevention of neural tube defects: Results of the Medical Research Council Vitamin Study. *Lancet*. 338(8760):131–7. Epub 1991/07/20.
7. Expert Advisory Group, Department of Health (1992). *Folic Acid and the Prevention of Neural Tube Defects*. Dublin: Department of Health.
8. National Institute for Health and Care Excellence (NICE) (2008). *Maternal and Child Nutrition Public Health Guideline*. Manchester: NICE.
9. Brough L, Rees G A, Crawford M A and Dorman E K (2009). Social and ethnic differences in folic acid use preconception and during early pregnancy in the UK: Effect on maternal folate status. *Journal of Human Nutrition and Dietetics*. 22(2):100–7. Epub 2009/02/20.
10. Kim M H, Han J Y, Cho Y J, Ahn H K, Kim J O, Ryu H M, Kim M Y, Yang J H and Nava-Ocampo A A (2009). Factors associated with a positive intake of folic acid in the periconceptional period among Korean women. *Public Health Nutrition*. 12(4):468–71. Epub 2008/12/25.
11. Mannien J, de Jonge A, Cornel M C, Spelten E and Hutton E K (2014). Factors associated with not using folic acid supplements preconceptionally. *Public Health Nutrition*. 17(10):2344–50. Epub 2013/10/11.
12. McNulty B, Pentieva K, Marshall B, Ward M, Molloy A M, Scott J M and McNulty H (2011). Women's compliance with current folic acid recommendations and achievement of optimal vitamin status for preventing neural tube defects. *Human Reproduction*. 26(6):1530–6. Epub 2011/03/29.

13. World Health Organization (WHO) (2015). *Guideline: Optimal Serum and Red Cell Folate Concentrations in Women of Reproductive Age for Prevention of Neural Tube Defects*. Geneva, Switzerland: WHO.
14. World Health Organization (WHO) (2008). *Conclusions of a WHO Technical Consultation on Folate and Vitamin B12 Deficiencies*. Geneva, Switzerland: WHO.
15. McMullan P, Hamill L, McCance D, Woodside J and Mullan K (2016). Iodine nutritional status among pregnant women and their offspring in Northern Ireland (NI). *Endocrine Abstracts*. 44 OC6.4.
16. Molloy A M and Scott J M (1997). Microbiological assay for serum, plasma, and red cell folate using cryopreserved, microtiter plate method. *Methods in Enzymology*. 281:43–53. Epub 1997/01/01.
17. Kelly F, Gibney E R, Boilson A, Staines A and Sweeney M R (2016). Folic acid levels in some food staples in Ireland are on the decline: Implications for passive folic acid intakes? *Journal of Public Health*. Epub 2015/03/11.
18. World Health Organization (WHO) (2006). "BMI Classification." *Global Database on Body Mass Index*. Geneva, Switzerland: WHO.
19. Centre for Maternal and Child Enquiries (CMACE) and Royal College of Obstetricians and Gynaecologists (RCOG) (2010) *Joint Guideline: Management of Women with Obesity in Pregnancy*. London: CMCAE/RCOG.
20. National Collaborating Centre for Women's and Children's Health (2008). *Antenatal Care: Routine Care for the Healthy Pregnant Woman*. London: Royal College of Obstetricians and Gynaecologists.
21. Scott-Pilai R, Spence D, Cardwell C R, Hunter A and Holmes V A (2013). The impact of body mass index on maternal and neonatal outcomes: A retrospective study in a UK obstetric population. *BJOG: An International Journal of Obstetrics and Gynaecology*. 120(8):932–9.
22. National Institute for Health and Care Excellence (NICE) (2010). *Weight management before during and after pregnancy*. Manchester: NICE.
23. Finglas P M, Roe M A, Pinchen H M, Berry R, Church S M, Dodhia S K, et al (2015). *McCance and Widdowson's The Composition of Foods, Seventh Summary Edition*. Cambridge: Royal Society of Chemistry.
24. Public Health Intelligence Unit (PHI) (2017). *Children's Health in Northern Ireland - A Statistical Profile of Births Using Data Drawn From the Northern Ireland Child Health System, Northern Ireland Maternity System and Northern Ireland Statistics and Research Agency*. Belfast: PHIU.
25. World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) (2004). *Vitamin and Mineral Requirements in Human Nutrition*. Bangkok, Thailand: WHO/FAO.

safefood:

7 Eastgate Avenue, Eastgate, Little Island, Co. Cork

7 Ascaill an Gheata Thoir, An tOiléan Beag, Co. Chorcaí

7 Aistyyett Avenue, Aistyyett, Wee Isle, Co. Cork

Tel: +353 (0)21 230 4100 ***Fax:*** +353 (0)21 230 4111

Email: info@safefood.eu ***Web:*** www.safefood.eu

www.safefood.eu
HELPLINE
NI 0800 085 1683
ROI 1850 40 4567