

RESEARCH TENDER CALL



TENDER INFORMATION DOCUMENT

Project Reference No.: 02-2015

Project Title: Folate status in pregnant women: current situation on the island of Ireland?

1. Objective/Knowledge Gap

Neural Tube Defects (NTDs) are one of a few largely preventable congenital defects, achieved through adequate folic acid intake. No recent data exists on the folic acid status of women in early pregnancy on the island of Ireland. The current project will provide an up-to date picture of folate status among women during the first trimester of pregnancy on the island of Ireland to inform future policy and practice around folic acid.

Aim

To provide an up-to date picture of folate status among women during the first trimester of pregnancy on the island of Ireland to inform future policy and practice around folic acid.

Objectives

1. To measure folate status using a robust biological marker in a representative sample of pregnant women in the Republic of Ireland (ROI) and Northern Ireland (NI) in the first trimester of pregnancy.
2. To identify the relationship between folate (and B12) status and BMI (and waist circumference if available) in the sample in this group.
3. To examine the reported compliance with folic acid supplementation recommendations for pregnancy among this group of women and compare to previous surveys to assess trends over time.

2. Background

Ireland and UK have among the highest prevalence rates of NTDs in Europe. Although the official rates are around 1 per 1000 births it is well recognised they are an underestimation of the true numbers of pregnancies affected (1, 2). Affected pregnancies may end in miscarriage and some women may choose to terminate the pregnancy in another jurisdiction. These cases aren't recorded in official figures.

A recent Irish surveillance study (2009-2011) which included the east, south and southeast regions, accounting for 62% of births nationally, reported a prevalence rate of 1.04 per 1000 births (1). Within this study, the Dublin area did show a slightly lower rate of 0.76 per 1000 births compared to other regions. An overall rise year on year was found in overall NTD rates. In Northern Ireland (NI) regional statistics for congenital abnormalities in recent years shows annual rates of between 0.6 to 1.3 per 1000 registered births affected by spina bifida, Anencephalus or Hydrocephalus (2). Over half the babies born with an NTD survive the first few days of life and of these approximately 85% live beyond a year (3). Many of these children will experience lifelong severe or moderate disability.

The overwhelming evidence that folic acid is effective at preventing NTD has resulted in many countries, including ROI and UK, recommending that women of childbearing age take a 400 µg daily folic acid supplement for 12 weeks pre conception until the end of the first trimester (4). More recently the advice has been extended to all women of childbearing age who are sexually active in Ireland to account for the fact that 50% pregnancies are unplanned.

Many countries including Ireland and UK introduced campaigns to increase knowledge of the folic acid recommendations among women and health professionals. However, they have largely been ineffective at reducing the prevalence rates. A large multi-centre European study examining 13 million birth records from 9 EU countries, found that no detectable impact on NTD incidence could be found between 1998 and 2008 with the introduction of policies and campaigns across Europe for women to take folic acid supplements (5). Compliance with supplement usage is low across Europe and elsewhere (6-10). In ROI and NI, a number of surveys between 1998 and 2002 show that less than a quarter of women take folic acid as prescribed.

There is limited folate status data on the island of Ireland in the last decade, particularly among women in early pregnancy. Measured red cell folate is a reliable biomarker of folate status. In NI a sample of nearly 300 pregnant women between 2005-6 results showed only 19% women started folic acid before pregnancy and found lower red cell folate in women who didn't take folic acid supplements prior to

conception. (10). The Food Safety Authority of Ireland have commissioned blood sampling from women of all ages, children and men during 2005-7 and in 2010-12 (11, 12). The later surveillance activity hasn't looked specifically at folate around the time of conception and during early pregnancy.

Mandatory fortification of flours or breads is a public health strategy in some countries, including the US and Canada, and the result has been a fall in the prevalence rates of NTDs in the population. This has been considered in Ireland and UK but concerns about (a) widespread unregulated voluntary fortification of many foodstuffs may put some subgroups at risk of high folic acid intakes (specifically men and older individuals) and (b) the potential of high intakes of folic acid in promoting pre-existing cancer (12-14).

Data is emerging that other dietary factors may modify the role that folate has in NTD risk. Evidence on the role of overweight and obesity in increasing NTD risk is growing (15-19). In the US population where mandatory folic acid food fortification is in place, maternal obesity was found to be the greatest attributable fraction of risk (10%) for spina bifida compared to low dietary folate intake accounting for less than 5% (16). Evidence also indicates that it may be that overweight and obesity doesn't simply have a dilution effect on folic acid intake but in obesity there is differential uptake of folate by different cell types in the body (20, 21). Folate metabolism is also dependent on levels of other B vitamins and data on the island found that obese women have a lower B12 vitamin status (22), indicating a role for vitamin B12 in NTD risk.

3. Approach

The research approach will employ quantitative methodology. **safe food** are open to suggestions on the detail of the approach. The approach chosen must view the aim from a population perspective rather than at a clinical level. Data on reported folic supplement use required in addition to Body Mass Index.

4. Technical Specification

- a) Explanation and justification of the proposed study methodology
- b) Data Handling and reporting
- c) Quality Assurance

(a) Explanation and justification of the proposed study methodology

A full justification and rationale for the proposed methodology and analytical approach will be required. Measured BMI and reported folic acid supplement use (ideally dose plus brand specific) must also be included. Specific polymorphisms and vitamin B12 status are known to or thought to interplay with folate status

and thus NTD risk. Applications may decide to include indicators of these later factors in their application but must provide cost options for their inclusion and exclusion.

The sample for testing must be representative of pregnant women across the island of Ireland and include multiple sampling locations.

(b) Data Handling and Reporting

1. An interim report (electronic and hardcopy) containing a summary of the findings to date will be submitted to **safefood** at six monthly intervals of the research.
2. The contractor is responsible for collating all results and a final report will be submitted to **safefood** on completion of the study.
3. All forms, documentation and electronic files must be retained by the contractor until further notice from **safefood** in case of issues arising after the completion of the research.

(c) Quality Assurance

1. Ethical approval will be an essential component to the approach where human interventions are involved.
2. Any laboratory analysis must be conducted by an accredited laboratory.
3. **safefood** will visit the contractors during the course of the survey to assess how the work is being carried out.

5. Proposed Activities/Deliverables

The proposed activities and deliverables will be dependent on the methodology proposed and will include:

- Submission on a 6 monthly basis of a summary report
- Submission of a final report to be submitted to **safefood** within the 18 month study period

6. Evaluation of Tenders

Tender bids will be evaluated according to the quality of proposals and applicants using the following criteria:

Quality of the proposal:

- ✓ Anticipated deliverables;
- ✓ Research method and facilities;
- ✓ Value for money;
- ✓ Potential for application;
- ✓ Work plan, including the overall timeframe.

Quality of Applicants:

- ✓ Experience in subject area;
- ✓ Quality Assurance and Quality Control.

7. *Duration of Project*

Estimated duration of the project: Maximum 12-18 months. A detailed timescale of research should be submitted by each applicant. Preference may be given to an application that can achieve the objectives in shorter timeframes.

8. *Scientific Aspects*

Potential applicants are encouraged to contact the Research Administration Office at **safefood** for further information about this research project.

9. *Tender Application Forms and Guidelines*

The Tender Application Form and associated Guidelines can be downloaded from www.safefood.eu. They can also be obtained by emailing research@safefood.eu, quoting the project reference number 02-2015. Alternatively please contact **safefood** as per the details below.

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References

1. McDonnell R. Epidemiology of Neural Tube Defects in Ireland. National Meeting on Neural Tube Defects; George's Hall, Dublin Castle, Dublin 2013.
2. Department of Health Social Services and Public Safety. CMO Annual Report 2011-12. Belfast; Department of Health Social Services and Public Safety; 2013 [cited 2014 30/01/2014,]; Available from: <http://www.dhsspsni.gov.uk/cmo-annual-report-2011-12-tables.pdf>.
3. Food Safety Authority of Ireland. Mandatory Folic Acid Fortification of Bread Recommended. Dublin: Food Safety Authority of Ireland; 2006 [cited 2008 August 16]; Available from: http://www.fsai.ie/news/press/pr_06/pr20060718.asp.
4. EUROCAT. Survey of Folic Acid Policy and Practice in European Countries Northern Ireland University of Ulster 2007.
5. Botto LD, Lisi A, Robert-Gnansia E, Erickson JD, Vollset SE, Mastroiacovo P, et al. International retrospective cohort study of neural tube defects in relation to folic acid recommendations: are the recommendations working? *British Medical Journal* 2005;330(7491):571.
6. Stockley L, Lund V. Use of folic acid supplements, particularly by low-income and young women: a series of systematic reviews to inform public health policy in the UK. *Public Health Nutrition* 2008;11(8):807-21.
7. McGuire M, Cleary B, Sahm L, Murphy DJ. Prevalence and predictors of periconceptional folic acid uptake—prospective cohort study in an Irish urban obstetric population. *Human Reproduction*. 2010;25(2):535-43.
8. Walsh T, O'Broin S, Cooley S, Donnelly J, Collins C, McMillan H, et al. Maternal folate status and neural tube defects in Ireland: the need for a national food fortification program. *Irish Medical Journal* 2007;100(5):469-72.
9. Ward M, Hutton J, Donnell RM, Bachir N, Scallan E, O'Leary M, et al. Folic Acid Supplements to Prevent Neural Tube Defects: Trends in East of Ireland 1996-2002. *Irish Medical Journal* 2004;97(9):274-6.
10. McNulty B, Pentieva K, Marshall B, Ward M, Molloy AM, Scott JM, et al. Women's compliance with current folic acid recommendations and achievement of optimal vitamin status for preventing neural tube defects. *Human Reproduction*. 2011;26(6):1530-6.
11. Flynn MAT, Anderson WA, Burke SJ, Reilly A. Session 1: Public health nutrition Folic acid food fortification: the Irish experience. *Proceedings of the Nutrition Society*. 2008;67(04):381-9.
12. Food safety Authority of Ireland. FSAi advises against any further folic acid food fortification,. FSAI; 2013 [cited 2013 09/09/2013]; Available from: https://www.fsai.ie/news_centre/press_releases/folic_acid_food_fortification_09092013.html.
13. Food Standards Agency. Folic Acid Fortification, . 2007 [cited 2014 20/01/2014]; Available from: <http://food.gov.uk/scotland/scotnut/folicfortification/#.UvTbm1t5c>.
14. Scientific Advisory Committee on Nutrition. Folic acid and colorectal cancer risk: Review of recommendation for mandatory folic acid fortification,. 2009.
15. Carmichael SL, Rasmussen SA, Shaw GM. Prepregnancy obesity: A complex risk factor for selected birth defects. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2010;88(10):804-10.
16. Agopian AJ, Tinker SC, Lupo PJ, Canfield MA, Mitchell LE, and the National Birth Defects Prevention S. Proportion of neural tube defects attributable to known risk factors. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2013;97(1):42-6.
17. Gao L-J, Wang Z-P, Lu Q-B, Gong R, Sun X-H, Zhao Z-T. Maternal overweight and obesity and the risk of neural tube defects: A case-control study in China. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2013;97(3):161-5.
18. McMahon DM, Liu J, Zhang H, Torres ME, Best RG. Maternal obesity, folate intake, and neural tube defects in offspring. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2013;97(2):115-22.
19. Wang M, Wang Z-P, Gao L-J, Gong R, Sun X-H, Zhao Z-T. Maternal body mass index and the association between folic acid supplements and neural tube defects. *Acta Paediatrica*. 2013;102(9):908-13.

20. Tinker SC, Hamner HC, Berry RJ, Bailey LB, Pfeiffer CM. Does obesity modify the association of supplemental folic acid with folate status among nonpregnant women of childbearing age in the United States? *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2012;94(10):749-55.
21. da Silva VR, Hausman DB, Kauwell GPA, Sokolow A, Tackett RL, AU - Rathbun SL, et al. Obesity affects short-term folate pharmacokinetics in women of childbearing age,. *International Journal of Obesity*,. 2012;37:1608-10.
22. Kerr MA, Livingstone MBE, Bradbury I, Scott JM, Ward M, Nates CJ, et al. The relationship between body mass index and B vitamin status,. *Proceedings of the Nutrition Society*,. 2004;63(1a):52A.