



An Roinn Sláinte
Department of Health



Folic Acid Supplementation

Report by the Department of Health Folic Acid Policy Committee, 2019.
gov.ie/health

Acknowledgements

The Department of Health would like to thank the members of the Committee for their contributions to the development of this report. In particular, we would like to thank the Committee Chair Professor Michael Turner, Director UCD Centre for Human Reproduction and National Lead for the Health Services Executive Clinical Programme in Obstetrics and Gynaecology, and Dr Helen McAvoy, Director of Policy, Institute of Public Health in Ireland. Special thanks are also due to all the Committee members and those who provided data and evidence to assist the Committee in making its recommendations, including the EUROCAT registry.

NOTE:

This report provided the recommendations for the *Clinical Practice Guidelines During Pregnancy*. These Guidelines issued jointly by the Institute of Obstetricians and Gynaecologists, the Royal College of Physicians of Ireland and the Directorate of Clinical Strategy and Programmes, Health Service Executive in November 2019.



Contents

Acknowledgements	1
Contents	3
Glossary of Terms	4
Summary.....	5
Context of the report.....	5
Committee conclusions on neural tube defects in Ireland	5
Committee conclusions on folate levels and supplement use:.....	6
1. Context.....	7
1.1 Report overview.....	8
1.2 Neural tube defects – an overview.....	9
1.3 The role of folate and folic acid in prevention of NTDs.....	9
1.4 Policy development on dietary folate, folic acid and NTDs in Ireland	10
1.4.1 Historical developments.....	10
1.4.2 Committee processes and the current policy landscape.....	12
1.5 Epidemiology of NTDs in Ireland.....	14
1.6 Sufficiency of folate levels to protect against NTDs in Ireland	17
1.7 Use of folic acid supplements in Ireland	17
2. Recommendations.....	19
2.1 Development of population guidelines for folate in pregnancy including at risk groups ...	20
2.2 Plan appropriate information campaigns for the general public and healthcare professionals	21
2.3 Consider the requirements for surveillance of NTDs and dietary folate intakes.....	21
2.4 Consider the requirements for food fortification with Folate	22
References.....	23
Appendix 1. Terms of Reference.....	28
Appendix 2. Membership of the FA Policy Committee	29
Appendix 3. National Dietary Surveys of Irish Adults (18-64yrs)	30
Appendix 4. Medication use – indications for higher dose folic acid use.....	31

Glossary of Terms

Congenital anomaly	Congenital anomalies are structural or functional anomalies that occur in the developing foetus
EUROCAT	European Network of Congenital Anomaly Registries
Folate	The generic name for the different forms of a water-soluble B vitamin found naturally in a variety of foods, but mainly in certain fruit and vegetables
FA	Folic Acid - the synthetic form of folate that is permitted to fortify food and is used in food supplements in the EU
FSAB	Food Safety Advisory Board – the previous statutory body with responsibility for food safety legislation. Functions transferred to FSAI in 1998.
FSAI	The Food Safety Authority of Ireland is a statutory body with national responsibility for co-ordinating the enforcement of food safety legislation in Ireland
NANS	National Adult Nutrition Survey
NSIFCS	North/South Ireland Food Consumption Survey
NTDs	Neural Tube Defects
Neural tube defects	Defined in the Irish data as one of the following – anencephaly, spina bifida or encephalocoeles
Pharmacokinetics	A term to describe the characteristic interactions of a substance (in this case FA) and the body in terms of its absorption, distribution, metabolism, and excretion
RCF	Red Cell Folate (folate in red blood cells)
Safefood	An all-island implementation body with a general remit to promote awareness and knowledge of food safety and nutrition issues on the island of Ireland.

Summary

Context of the report

- This report presents the findings of the Committee established to provide recommendations to the Minister for Health on the prevention of neural tube defects (NTDs) in Ireland.
- The Committee considers that there is considerable evidence in support of the introduction of mandatory fortification of foodstuffs with folic acid (FA). However, the Committee also recognises that this would be a significant undertaking in terms of resources and timing. In addition, the implications of Brexit would need to be worked through before any further consideration could be given to mandatory food fortification. With this in mind, other actions are needed to optimise both FA supplement use and dietary folate in the short-term.
- The Committee noted the importance of acting on evidence-informed approaches to reduce neural tube defects (NTD) in the context of policy commitments made within the *Healthy Ireland Framework* (2013-2025) and the *National Maternity Strategy* (2016-2026).
- This report should be considered in the context of the recommendations of statutory agencies, namely the Food Safety Authority of Ireland (2016) and SafeFood (2017) and also the *Clinical Practice Guidelines During Pregnancy*, (the Guidance issued jointly by the Institute of Obstetricians and Gynaecologists; the Royal College of Physicians of Ireland and the Directorate of Clinical Strategy and Programmes, Health Service Executive (2019)).
- This report provided the Folic Acid Supplementation recommendations for *Clinical Practice Guidelines During Pregnancy*.

Committee conclusions on neural tube defects in Ireland

- No significant progress has been made in reducing the incidence of NTDs in Ireland in the last decade.
- NTDs remain highly significant in Ireland in terms of pregnancy loss and infant death, lifelong disability and the wellbeing of parents and families.
- NTDs are consistently most likely to affect unplanned pregnancies, lower socio-economic families and women who have already had a baby previously with a NTD.
- Accurate and timely information on incidence of NTDs is critical to inform future measures.

Committee conclusions on folate levels and supplement use:

- Most women in Ireland have insufficient folate levels pre-pregnancy to protect their baby from developing a NTD.
- A healthy diet pre-pregnancy is important but not sufficient to protect against the occurrence of NTDs. The diet of most women in Ireland does not concur with Healthy Eating Guidelines and recommended levels of dietary folate, particularly among low income women.
- For most pregnancies in Ireland, there is inadequate use of FA supplements in terms of the duration of pre-pregnancy supplementation. This is particularly so among unplanned pregnancies. In general, less than half of women commence folic acid supplements before pregnancy and less than a quarter commence supplementation twelve weeks before conception.
- Recommendations on the timing, dose and duration of supplement use vary considerably between countries.
- Promotion campaigns on FA supplement use have played an important, but ultimately limited, role. Awareness has increased but this has not led to long-term sustained behaviour change in supplement use.
- Voluntary fortification of foods is significant in determining folate levels and the incidence of neural tube defects at population level.
- There have been significant changes in voluntary fortification of foods in Ireland in recent years. These changes relate to levels of fortification, range of food types within and between brands and emergence of low-cost supermarkets.

Committee recommendations:

The Committee has crafted its recommendations according to the terms of reference of the group. The recommendations are presented in detail in Part 4 of this report.

1. Context

1.1 Report overview

A Committee on Folic Acid was established by the Department of Health in 2016. The terms of reference of the Committee are presented in Appendix 1 with Committee membership listed in Appendix 2.

This report represents the recommendations of the Committee, as relevant to the following three elements of the Terms of Reference:

- 1. Development of population guidelines for folate in pregnancy including at risk groups**
- 2. Plan appropriate information campaigns for the general public and healthcare professionals**
- 3. Consider the requirements for surveillance of NTDs and dietary folate intakes**

The recommendations contained in this report will be provided to the Minister of Health to advise him on the best course of action in respect of preventing NTDs in Ireland through policy measures on FA supplements and naturally occurring dietary folate.

- 4. Consider the requirements for food fortification with folate.**

This term of reference which relates to food fortification was discussed by the Committee and there is considerable evidence in support of the introduction of mandatory fortification of foodstuffs with folic acid.

The Committee recognised that this option is dependent on a range of issues including food consumption patterns and preferences, supply chain issues, and the implications of Brexit, as well as the significant undertaking in terms of resources and timing involved. These issues would need to be worked through before any further consideration could be given to mandatory food fortification. With this in mind, other actions are needed to optimise both FA supplement use and dietary folate in the short-term.

Issues relating to the remaining terms of reference (i.e. research requirements and European and global developments) are covered throughout the report.

The remaining sections will cover

- Descriptive information on NTDs and their impact on population health
- The current state of the evidence for the role of folate/FA in prevention of NTDs
- Policy developments on dietary folate, FA and NTDs in Ireland to date
- Processes undertaken by the Committee in reaching their conclusions and recommendations
- Assessment of the epidemiology of NTDs in Ireland
- Assessment of the sufficiency of folate levels pre-pregnancy in Ireland
- Assessment of FA supplement use pre-pregnancy in Ireland

1.2 Neural tube defects – an overview

Neural tube defects (NTDs) are major congenital anomalies that have a profound impact on families and the health services. NTDs threaten the survival of both the foetus and infant. People living with NTDs face significant challenges in terms of impacts on health and disability, social inclusion and quality of life (Yi, 2011; O’Connell, 2014). In population health terms, NTDs are highly significant as contributors to Ireland’s national stillbirth, perinatal and infant mortality rates as well as childhood and adult disability (Manning, 2015, Healthcare Pricing Office, 2016).

Parent experiences of pregnancy, childbirth and parenting can be profoundly affected when a neural tube defect occurs in their offspring. Pregnancy loss and stillbirth, as well as loss of the infant in the early weeks of life, are life-changing experiences for mothers and fathers (Sjogren, 2017). Families of children with life-long disability and illness related to neural tube defects are significantly impacted emotionally, practically and financially (Governey, 2014; International Federation for Spina Bifida and Hydrocephalus, 2016). The lifetime cost to the health service of meeting the needs of a child with spina bifida has been estimated nationally at €500,000 (Yunni, 2011).

NTDs are the most common major malformation of the central nervous system in the developing foetus. They arise at an early stage of pregnancy between 21 and 28 days after conception, with the cranial (head) closure preceding the caudal. These defects occur at a time when many women do not yet realise they are pregnant, as they have not yet experienced a missed menstrual period.

There are several forms of NTD including anencephaly, encephalocele, hydraencephaly, iniencephaly and spina bifida, as well as rarer forms.

Spina bifida, the most common form of NTD, is a condition in which there is incomplete closure of the spinal cord and vertebral column.

Anencephaly occurs when the head end of the neural tube fails to close, resulting in an absence of a significant portion of the brain and skull. Infants born with this condition are either stillborn or are usually born blind, deaf and unconscious. Infants usually die shortly after birth. Encephalocele is a defect where a sac-like portion of the brain is outside the skull. Hydranencephaly is a condition in which the two halves of the brain are missing and instead filled with sacs of cerebrospinal fluid. Iniencephaly is a rare NTD that results in extreme bending of the head to the spine.

1.3 The role of folate and folic acid in prevention of NTDs

It is now known that the majority of NTDs can be prevented through consumption of FA via oral supplements and through fortification of the food supply. Two landmark studies in the early 1990s estimated the effectiveness of pre-natal and early antenatal supplementation in preventing neural tube defects. These studies examined primary prevention as well as prevention of re-occurrence in women who had already conceived an infant with a NTD. Several studies also compared the level of protection offered by non-, partial or full compliance with pre-natal supplementation and at different doses of FA. These included studies in the context of planned pregnancies (Czeizel & Dudas, 1992) and observational studies on recurrence which provided a primer for subsequent randomised controlled trials (Smithells, 1981; Smithells, 1983; Mulinare, 1988; Medical Research Council, 1991).

A number of recent reviews reinforce the role of folate in the prevention of NTDs and in supporting the development of the foetus in utero, as well as in supporting maternal health during pregnancy and lactation (Molloy, 2008; Burke, 2009; Boilson, 2012; Lassi, 2013; World Health Organization, 2015; McDonnell, 2018). In addition, the importance of sufficient folate both before and during pregnancy in preventing maternal anaemia is becoming increasingly apparent (O'Malley, 2018) with co-existent iron deficiency an additional consideration (Molloy, 2014).

1.4 Policy development on dietary folate, folic acid and NTDs in Ireland

1.4.1 Historical developments

Findings from the studies referred to above led to the development of national guidelines. Following from guidelines issued in the USA (CDC, 1992), the Department of Health UK issued guidelines in the early 1990s (Department of Health-UK, 1992). These guidelines recommended that women planning to get pregnant should take 400 micrograms ($\mu\text{g}/\text{mcg}$) of FA orally each day prior to conception.

A summary of the main milestones in the development of policy positions on the prevention of NTDs in Ireland is provided below.

1993

A leaflet produced by the Department of Health aimed to raise awareness of three ways to increase FA consumption: folate rich foods, FA fortified foods and FA supplements. It recommended a combination of these three approaches. It recommended that all women likely to become pregnant should take 400mcg prior to conception and during the first 12 weeks of pregnancy.

1996

The Health Education Authority recommended that women trying to conceive should take 400mcg prior to conception and during the first 12 weeks of pregnancy.

1997

The Food Safety Advisory Board (FSAB) issued a report to the then Minister of Health recommending that the Minister should examine fortification (Food Safety Advisory Board, 1997). The FSAB recommended that all women of childbearing age should be advised to take 400mcg from at least four weeks before conception until the end of the twelfth week of pregnancy. Shortly after this, the functions of the FSAB were transferred to the Food Safety Authority of Ireland (FSAI).

2005

The FSAI convened a committee to examine policy options and a public consultation was held.

2006

FSAI published the *Report of the National Committee on Folic Acid Fortification* (FSAI, 2006). The FSAI recommended that all women of childbearing age who are sexually active are advised to take 400mcg until the twelfth week of pregnancy. The report also recommended that a policy of mandatory FA fortification be adopted.

2008

The Implementation Group produced its report. This report recommended deferral of mandatory fortification on the basis of (a) a baseline pre-fortification study for the years 2005-06 reporting a lower incidence of NCDs compared to previous years; (b) perceived inadequate data on safety concerns, with specific mention of cancer risk and (c) some evidence of improved folate status which was attributed to widespread consumption of foods voluntarily fortified with FA and the use of supplements (FSAI, 2008).

2016

The FSAI Scientific Committee produced a report: *Update Report on Folic Acid and the Prevention of Birth Defects in Ireland* (FSAI, 2016). This presented two options in terms of policy responses to enhance prevention of NTDs in Ireland. This report made several recommendations including that:

- Guidance should be provided to food manufacturers for voluntary food fortification with FA to support the effectiveness of the chosen national policy
- Advice to all women of childbearing age capable of becoming pregnant to take an additional 400mcg FA daily as a food supplement. This should be actively promoted, and its effectiveness monitored
- A comprehensive nationwide register of pregnancies affected by congenital birth defects including NTDs, underpinned by specific legislation, needs to be introduced in Ireland. In addition, a national retrospective study on the incidence of NTDs in Ireland since 2012, should be undertaken
- There should be on-going monitoring, informed by international best practice, of dietary intake and blood levels of folate, including FA in the food supply, total folate intake and corresponding blood folate status for the target group (women of childbearing age) in addition to other population sub-groups
- The policy should be reviewed on a regular basis to assess its effectiveness and safety.

The FSAI report presented two options for action in relation to fortification.

- **Option 1:** Mandatory fortification together with voluntary fortification and advice on supplementation. Mandatory fortification of bread or flour with folic acid. This should be accompanied by advice to all women of childbearing age who are capable of becoming pregnant to take an additional 400 µg folic acid daily as a food supplement. Voluntary fortification of foods with folic acid would continue. Mandatory fortification of flour or bread with folic acid would require legislation. Compared to the other option, this option has stronger evidence to support its effectiveness in further reducing the rate of NTD-affected pregnancies from the current rate
- **Option 2:** Voluntary fortification together with advice on supplementation. Continuation of current policy to advise all women of childbearing age who are capable of becoming pregnant to take an additional 400 µg folic acid daily as a food supplement. Voluntary fortification of foods with folic acid would continue. Compared to the other option, this option has weaker evidence to support its possible effectiveness in further reducing rates of NTD-affected pregnancies from the current rate.

In 2017 following a comprehensive review of the scientific evidence, a new recommendation in relation to FA supplements was published (United States Preventive Services Task Force, 2017). This recommended that:

“All women who are planning or capable of pregnancy should take 400 to 800mcg FA daily. The critical period for supplementation starts at least one month before conception and continues through the first two to three months of pregnancy.”

1.4.2 Committee processes and the current policy landscape

The Committee considered carefully

- (a) the policy changes occurring in the context of health promotion, maternity and infant health and nutrition in Ireland and their relevance to the issue of NTD prevention
- (b) the diverse range of relevant evidence on the prevention of NTDs.

The Committee noted that the overall policy landscape has changed significantly in recent years. The Committee have given careful consideration to the fit of its recommendations with the wider Irish policy landscape relevant to health promotion, maternal and infant/child health and disability and food policy.

In particular, the *Healthy Ireland Framework* has brought a new focus on the importance of health promotion and the need for cross-Government and cross-sectoral co-operation to prevent ill-health. The Healthy Ireland Framework has enshrined the principles of prevention and early intervention within all policies, with a particular emphasis on the early years (Department of an Taoiseach, 2013). Revised Healthy Eating Guidelines, including a clear FA supplementation message, were issued in December 2016 (Department of Health, 2016).



The Government is working on scoping national nutrition policy actions.

In addition, the Government has published Ireland's first national maternity strategy. This strategy aims to ensure that parents are supported before, during and after pregnancy to allow them to give their child the best start in life. The Committee recognises the particular importance of prevention of neural tube defects in this context and the considerable importance placed on the issue by stakeholders responding to the public consultation on the strategy (Kielthy, 2016).



An emphasis on prevention and health promotion is reflected in *Creating a Better Future Together - National Maternity Strategy 2016-2025* (Department of Health, 2016) which proposes that a health and wellbeing approach underpins all maternity policy and service delivery.

The strategy commits to better pre-conceptual planning, as well as support for health behaviour change and 'making every contact count' in women's engagement with health services (HSE, 2006; HSE 2012; HSE, 2017). Providing additional supports to vulnerable and disadvantaged women is also emphasised. The Committee notes the importance of optimal prevention of neural tube defects in the context of these strategic priorities.

In addition, the Committee noted that reducing the incidence of NTDs across the island of Ireland and Great Britain is a shared concern. There are broadly similar rates of NTDs in Northern Ireland and shared communities, communication channels and food supply (Hunter, 2017).

The Committee has examined in detail all relevant data on trends in NTDs in Ireland (McDonnell, 2014; McDonnell, 2018).

In addition, the Committee has reviewed an extensive range of evidence sources relevant to the risk of neural tube defects to babies born in Ireland, in particular two reports produced by statutory bodies with roles in respect of food policy. These reports are the *Update Report on Folic Acid and the Prevention of Birth Defects in Ireland* (FSAI, 2016) and *The Folate Status of Pregnant Women in the Republic of Ireland* (SafeFood 2017).

This Committee has taken into account the insights from the FSAI scientific committee report (2016) as well as other insights from a variety of international evidence and data and the expertise of committee members, in coming to its recommendations to the Minister for Health.

This evidence included national data on:

- Dietary patterns of women and dietary folate in Ireland and factors affecting bioavailability of folate (McNulty, 1987; IUNA, 2001; McKillop 2002, McNulty 2004; McNulty, 2010; Caudill 2010; Simpson, 2010; Rossi 2011; EFSA NDA panel, 2014; McCartney, 2014; Layte 2014; Mullaney, 2014; Kelly et al 2015; Hoffman 2015; FSAI, 2016; Mullaney, 2016; SafeFood, 2017). A summary of the methodology used in the national survey data assessed in this context is presented in Appendix 3.
- Sufficiency of protective levels of red cell folate in pregnant women in Ireland (Sweeney, 2007; Obeid, 2014; Crider, 2014; Hopkins 2015; World Health Organization, 2015; FSAI, 2016; SafeFood, 2017)

- Supplement use including the knowledge, attitudes and behaviours of women in Ireland and the impact of awareness campaigns (de Walle, 2008; Delany, 2011; McNulty, 2011; McGowan 2012, Lindsey 2012; Layte 2014; O'Higgins, 2014; McKeating, 2015; Cawley, 2015; Cawley, 2016; Kennedy, 2016; FSAI, 2016; Safefood, 2017; McDonnell, 2018)
- An updated analysis of the folate status of women in Ireland commissioned to inform the committee (Safefood, 2017)
- Voluntary fortification of foods in Ireland's retail environment (Hoey, 2007; FSAI, 2008; Flynn, 2008; Anderson, 2010; FSAI, 2016; McDonnell, 2014; Kielthy, 2015; Flynn, 2015; Kelly, 2015)
- Pregnancy planning and advice in Ireland and unplanned pregnancies (McGee, 2008; McBride, 2012).

In addition, the Committee also reviewed international evidence on:

- Guidelines, and their underlying evidence, on supplement use internationally in terms of primary prevention and higher risk pregnancies (Gomes, 2015; Cawley, 2016; Viswanathan, 2017)

The effects of fortification of food in other jurisdictions (Atta 2016; Burton, 2016; Morris, 2015; Kancherla, 2017).

The Committee conclusions are presented in the Summary and detailed in the sections below.

1.5 Epidemiology of NTDs in Ireland

The incidence of NTDs in Ireland remains high by European standards (EUROCAT, 2010; EUROCAT, 2014; McDonnell, 2014; McDonnell, 2018).

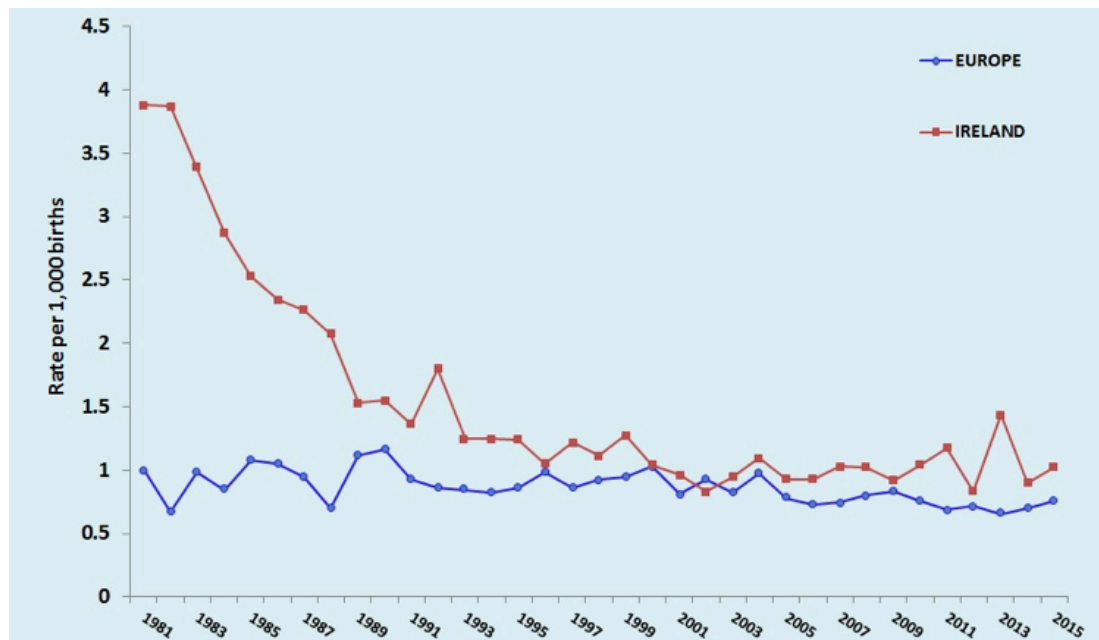
In Ireland the incidence rose from 0.92 per 1000 births in 2009 to 1.17/1000 in 2011. The increase was characterised principally by an increase in spina bifida cases. In Ireland in the period 2009-11, a total of 236 cases of neural tube defects were identified (McDonnell, 2014). Updated figures have been produced for the period 2012-2015. A rate of 1.05 per 1000 births has been recorded for that period. This rate is broadly similar to that recorded ten years previously. There have been fluctuations in the rate over the period, most notably a small but significant peak in 2013.

Between 2012 and 2015, of 274,732 live and stillbirths, there were 121 cases of anencephaly, 136 cases of spina bifida and 31 cases of encephalocele. Around half of all known NTDs in the period were spina bifida.

Figure 1 presents data on the incidence of NTDs over a 34-year period from 1981 to 2015.

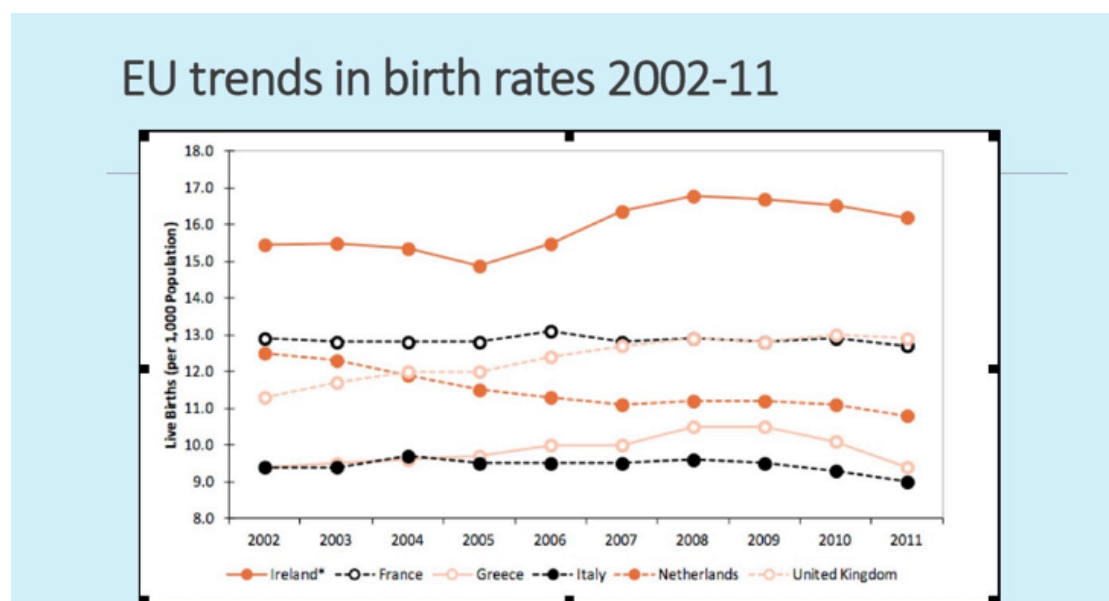
Figure 2 presents data on the incidence of liveborn babies with NTDs in Ireland compared with some other European member states. In some other European countries, the rate is lower as different clinical practices for the diagnosis and management of NTDs are in place.

Figure 1. Incidence of NTDs in the Republic of Ireland (1981-2015)



Source: McDonnell et al(2015) and McDonnell et al (2018)

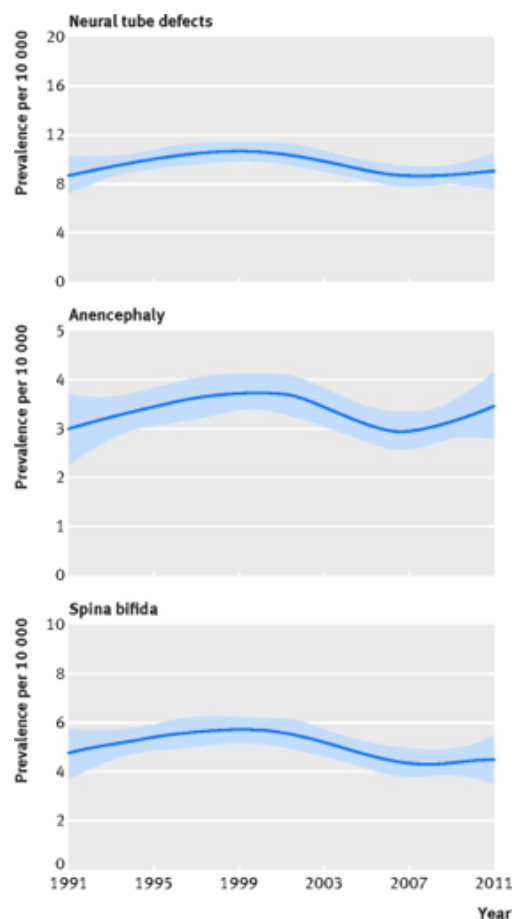
Figure 2. Live births of babies with NTDs in selected European member states (2002 -11)



Source: 'Population and Social Conditions', Eurostat. Figure modified from ESRI Perinatal Statistics Report, 2011.

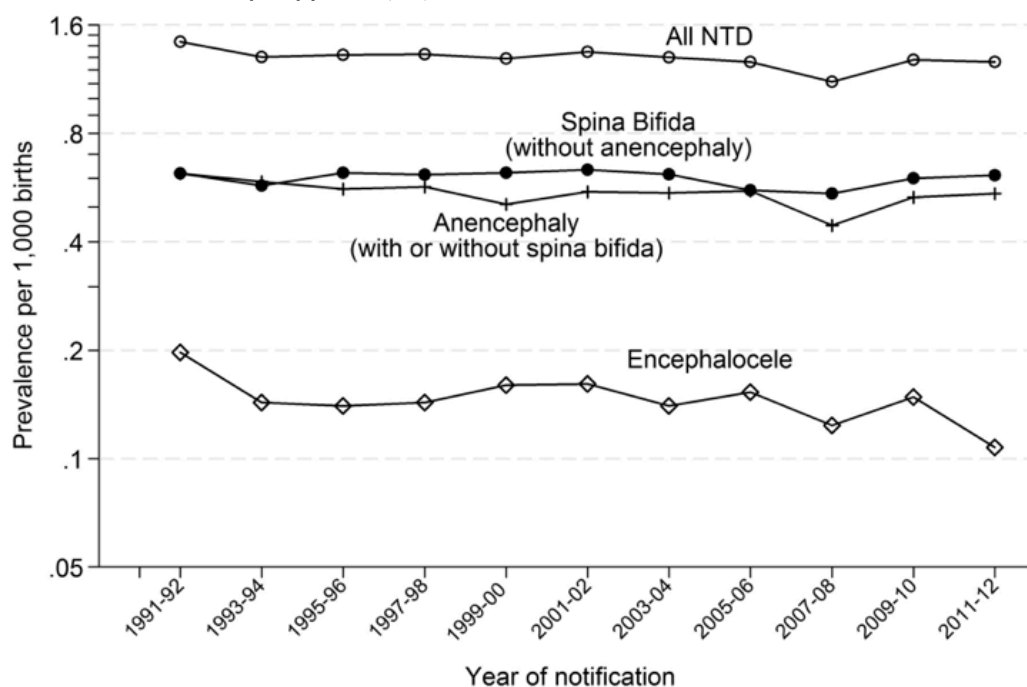
Other studies on the occurrence of NTDs are in line with the experience in Ireland up to 2011. An analysis of 12.5 million births in Europe between 1991 and 2011 found that the overall prevalence of NTDs was largely unchanged over that time period in European countries without mandatory fortification (Khoshnood, 2015 – see Figure 3), with similar findings in the UK (Morris, 2015 – see Figure 4).

Figure 3. Trends in total prevalence of non-chromosomal neural tube defects in Europe, 1991-2011: restrictive cubic spline estimates of pooled data in EUROCAT registries



(Source: Khoshnood, 2015)

Figure 4. Prevalence of NTD pregnancies (live births, late fetal losses after 20 weeks' gestation and terminations with an NTD) from 1991 to 2012 in two yearly periods (UK)



Source: (Morris, 2016)

1.6 Sufficiency of folate levels to protect against NTDs in Ireland

The majority of young women in Ireland remain inadequately protected against NTDs, due to both low folate intakes and absent or insufficient pre-conceptual supplement use (Safefood, 2017). Only 2.6% of women in Ireland presenting for antenatal care are achieving adequate dietary folate (Safefood, 2017). Promotion of a healthy diet pre-pregnancy and during early pregnancy is important, but dietary measures alone offer insufficient protection from NTDs (Molloy, 2008; Obeid, 2014; Hopkins 2015; Kelly et al, 2015).

Changes have occurred in the level and range of products voluntarily fortified with FA in Ireland. Studies indicate that overall, levels of voluntary fortification have declined. There has been considerable volatility in voluntary fortification practices within staple foods in Ireland (Kielthy, 2015; Kelly, 2015). There have been changes in

- The level of FA added to foods
- The range of food types fortified (bread, cereals, spreads, milks etc)
- Fortification practices both within and between brands
- The retail market – in particular the emergence of low-cost supermarkets with varying fortification practices linked to price differentials.

Reductions in the voluntary fortification of certain foodstuffs in the Irish retail market, coupled with changes in food purchase behaviours are possible contributory factors to the failure of NTD rates to fall (Kelly, 2015).

Public awareness campaigns have been valuable in increasing knowledge and awareness of supplements. However, such campaigns are only effective in the short-term and there has been no sustained campaign on an annual basis, prior to 2015. There is some evidence that increases in knowledge and awareness may not be translating into behaviour change in both the short and long term.

1.7 Use of folic acid supplements in Ireland

The Safefood study concluded that less than half of women commenced folic acid supplementation pre-pregnancy, and that less than a quarter commenced supplementation 12 weeks prior to conception (Safefood, 2017). Of the women who commenced folic acid supplements four to eight weeks pre-conception, 78.4% achieved the optimal red blood cell folate level for NTD risk reduction at their first booking visit. By comparison, among women who commenced four to eight weeks after conception, around half achieved this red blood cell folate level.

No information was available on pre-pregnancy and antenatal FA supplement use in 47.5% of case files relating to infants with known NTDs. Where data on use of supplements was available, 13.7% reported that they had taken FA pre-pregnancy (McDonnell, 2014). Similarly, other research in Ireland found that the use of FA supplements was inadequate for most women (Delany, 2009; McNulty et al, 2011; Cawley, 2015; McKeating, 2015; Layte 2014; McGowan 2012, Lyndsey 2012). While awareness of the need to take FA supplements as part of pregnancy planning is reasonably high, there was limited understanding on the reasons for doing so and the need to take those supplements well in advance of trying for a baby.

Promoting early use of FA supplements is identified as a policy priority within the Maternity Strategy (Department of Health, 2016). However, there is little international consensus on the optimal supplement dose and duration for both normal risk and high-risk women. Dosages of between 400 and 800mcg have been proposed, with some evidence of greater protection associated with higher dosages. Similarly, longer periods of pre-conceptual supplementation for up to 3 months have been associated with higher protection than shorter periods (Viswanathan, 2017).

There are no studies in Ireland which provide estimates relating to the proportion of women seeking or receiving advice in terms of planning a pregnancy. Irish studies estimated that around 10% of people under 45 did not use contraception at their most recent sexual intercourse even though they did not want to conceive (Rundle, 2004; Layte et al, 2006). More recent estimates suggest that the proportion of pregnancies that are unplanned has changed little over time (McBride, 2010). Over three quarters of women who did not take folic acid pre-pregnancy stated that they did not expect to get pregnant and 35% did not know that they needed to take folic acid pre-pregnancy (SafeFood, 2017).

Nearly all pregnancies are detected using a home pregnancy testing kit. As pregnancy tests are becoming more sensitive, pregnancy can now be detected earlier than previously, even in advance of a missed menstrual period. This can bring new opportunities to provide high-level supplementation in very early pregnancy that may offer some protection, albeit far from the ideal level of protection offered by pre-conceptual supplementation (Amitai, 2015). In addition, some international evidence has shown some reduction in risk associated with high level supplementation if initiated shortly after the last missed menstrual period, but again far from the ideal level of protection offered by pre-conceptual supplementation (Berry, 2015).

In 2015, SafeFood launched a digital and publicity campaign aimed at increasing awareness of the importance of FA supplements and consumption levels. The second phase was launched in 2016 and ran for four weeks. It targeted women of childbearing age who are sexually active and could become pregnant, including those using contraception. Evaluation of the campaign found that knowledge of the need to take FA supplements increased from 27.5% to 60% among women who could get pregnant. There were also improvements in the knowledge that FA supplements could reduce the risk of spina bifida. There was an increase from 13% to 17% in women reporting that they routinely took supplements though they were not planning a pregnancy.

2. Recommendations

Based on the Committee's review of the evidence and our assessment of current policy and services, the Committee presents its recommendations below. The recommendations are structured according to the terms of reference of the group provided by the Department of Health.

2.1 Development of population guidelines for folate in pregnancy including at risk groups

The following text should be accepted as standard guidelines for the prevention of NTDs in Ireland -

1. All women who may possibly become pregnant within the next three months, whether intentionally or not, are advised to take oral Folic Acid (FA) 400 micrograms daily to prevent Neural Tube Defects (NTDs)
2. Women who intend to become pregnant are advised to start FA at least 6 weeks before they start trying to conceive so that their folate levels are optimised before closure of the neural tube
3. Women who are at increased risk of a pregnancy complicated by a NTD should arrange to see their doctor, because they may need a prescription-only higher dose of FA 5.0mg daily. Women who are prescribed 5.0 mg before pregnancy should continue on the same dose for the first trimester
4. After the first trimester and during breastfeeding, all women are advised to take oral Folic Acid 400 micrograms to meet the World Health Organization's recommended daily intake for pregnancy and breastfeeding. This promotes fetal and neonatal development as well as reducing the risk of anaemia in the mother.
5. Women who are considered at increased risk include women who:
 - (a) experienced a previous pregnancy complicated by a NTD
 - (b) have pregestational Type 1 or 2 diabetes mellitus
 - (c) have a first degree relative diagnosed with a NTD
 - (d) are on certain medications (as listed in Appendix 4)
 - (e) have moderate or severe obesity (BMI > 34.9 kg/m²).
6. All women should follow the National Healthy Eating Guidelines, but they should be aware that increasing their dietary intake of folate alone is unlikely, in the absence of mandatory food fortification or FA supplementation, to achieve optimal maternal folate levels.

The Healthy Eating Guidelines should be reviewed regularly to consider

- (a) the optimum dosage of supplementation
- (b) the optimum duration of supplementation prior to conception, during pregnancy and during lactation
- (c) identification of high-risk groups whose risk is demonstrated to be modifiable by use of FA supplementation at higher dose.

Opportunities for joint North/South communication on FA messages should be considered.

The HSE should be encouraged to support women who plan to become pregnant, through effective health promotion and brief intervention at the clinical interface to optimise their diet, achieve a healthy weight, quit smoking and abstain from alcohol in advance of trying to conceive, in line with the Making Every Contact Count approach (HSE, 2017)

The implementation of actions within national policy relating to the general health and wellbeing of women of childbearing age, particularly in regard to healthy eating and nutrition policy actions, should be prioritised.

2.2 Plan appropriate information campaigns for the general public and healthcare professionals

Link the recommendations to a comprehensive communications strategy in order to increase uptake through enhanced awareness, understanding and supported behaviour change.

Design a strategy with a focus on knowledge translation to the general public, especially women of child-bearing age, and all health care professionals, in particular those most likely to have clinical contact with women of child-bearing age.

Deliver consistent and ongoing communication through sustainable investment in a broad communication strategy, rather than one-off campaigns.

Retain a population-wide focus to the awareness programme, while also investing in the development of a social marketing focus on women living in socially disadvantaged circumstances, women at risk of unplanned pregnancy and multigravida.

Design, implement and evaluate evidence-informed approaches to brief intervention approaches in clinical practice, co-ordinated with the Making Every Contact Count model being developed by the HSE.

Enhance integration of FA supplement advice as a healthcare quality indicator within the performance of relevant programmes being operated by the Health and Wellbeing Division, Primary Care, Obstetrics and Gynaecology and Sexual Health services.

Increase the availability and uptake of the Healthy Eating Guidelines to healthcare professionals in Ireland working with women planning a pregnancy.

2.3 Consider the requirements for surveillance of NTDs and dietary folate intakes

Review the results of the national audit of NTDs for 2012-15 so that future supplementation or fortification interventions can be measured against the pre-intervention baseline data.

Designate the EUROCAT registry as a Health Information Resource prescribed by the Minister for Health under the Health Information and Patient Safety Bill.

Invest in the expansion and development of the Irish EUROCAT registry to ensure national coverage to provide population level surveillance on an ongoing basis and allow for meaningful comparison with other European member states and the UK. Integrate with the Maternal and Newborn Clinical Management System information system.

Agree a core set of indicators relevant to NTDs in Ireland and integrate these into a national surveillance programme on an ongoing basis. These indicators should include valid indicators of risk (dietary folate, supplement use); activities (promotion, brief intervention) and outcomes (NTDs).

Monitor the levels of red cell folate and Vitamin B12 at population level on an ongoing basis to provide clear estimates of levels of protection within the Irish population.

2.4 Consider the requirements for food fortification with Folate

The Committee recognised that this option is dependent on a range of issues including food consumption patterns and preferences, supply chain issues, implications of Brexit, as well as the significant undertaking in terms of resources and timing involved. These issues would need to be worked through before any further consideration could be given to mandatory food fortification. With this in mind, other actions are needed to optimise both FA supplement use and dietary folate in the short-term.

References

- Amitai Y, Koren G. The FA Rescue Strategy: High-Dose FA Supplementation in Early Pregnancy. *JAMA Pediatr.* 2015 Dec 1; 169(12):1083-4
- Anderson, W.A. Slaughter, D. Laffey, C. Lardner, C. (2010) Reduction of folic acid during baking and implications for mandatory fortification of bread. *Journal of Food Science and Technology*, 45(6) p.p. 1104-1110
- Atta, C.A. Fiest, K.M. Frolkis, A.D. Jette, N. Pringsheim, T. St Germaine-Smith, C. Rajapakse, T. Kaplan, G.G. Metcalfe, A.(2015) Global Birth Prevalence of Spina Bifida by Folic Acid Fortification Status: A Systematic Review and Meta-Analysis. *The American Journal of Public Health*, 106(1). e. 24-34
- Berry RJ, Li Z, Erickson JD, et al. Prevention of neural-tube defects with FA in China. China-U.S. Collaborative Project for Neural Tube Defect Prevention. *N Engl J Med.* 1999; 341:1485-90
- Boilson, A. Staines, A. Kelleher, C.C. Daly, L. Shirley, I. Shrivastava, A. Bailey, S.W. Alverson, P.B. Ayling, J.E. McDermott, A.P. Scott, J.M. Sweeney, M.R. (2012) Unmetabolized FA prevalence is widespread in the older Irish population despite the lack of a mandatory fortification program. *The American Journal of Clinical Nutrition*, Vol 96. pp. 613-621
- Burke, B. Lyon Daniel, K. Latimer, A. Moran, K. Mulinare, J. Prue, C. Steen, J. Watkins, M. (2009) *Preventing Neural Tube Birth Defects: A Prevention Model and Resource Guide*. Atlanta: Centers of Disease Control and Prevention
- Burton, A. (2016) FA: time for Europe to mandate fortified flour? *The Lancet*. 15 pp. 1208-1209
- Caudill, M. A. (2010) Folate bioavailability: implications for establishing dietary recommendations and optimizing status. *Am J Clin Nutr.* , 91(5), 1455S–1460S. <http://doi.org/10.3945/ajcn.2010.28674E>
- Cawley, S. Mullaney, L. Kennedy, R. Farren, M. McCartney, D. and Turner, M.J. (2017) Duration of periconceptual folic acid supplementation in women booking for antenatal care. *Public Health Nutrition*. 2017 Feb; 20(2):371-379. doi: 10.1017/S1368980016002585.
- Cawley, S. Mullaney, L. McKeating, A. Farren, M. McCartney, D. Turner, M.J. (2016) A review of European guidelines on periconceptual FA supplementation. *European Journal of Clinical Nutrition*, 2016 Feb; 70(2):143-54. doi: 10.1038/ejcn.2015.131
- Cawley, S. Mullaney, L. McKeating, A. Farren, M. McCartney, D. Turner, M.J. (2016) Knowledge about FA supplementation in women presenting for antenatal care. *European Journal of Clinical Nutrition*. 2016 Nov;70(11):1285-1290. doi: 10.1038/ejcn.2016.104.
- Cawley, S. Mullaney, L. McKeating, A. Farren, M. McCartney, D. Turner, M.J. (2015) An analysis of folic acid supplementation in women presenting for antenatal care. *Journal of Public Health* 2016 Mar; 38(1):122-9. doi: 10.1093/pubmed/fdv019.
- Centers for Disease Control. (1992) Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. Atlanta: Centers for Disease Control.
- Crider, K.S. Devine, O. Hao, L. Dowling, N.F. Li, S. Molloy, A.M. Li, Z. Zhu, J. Berry, R.J. (2014) Population red blood cell folate concentrations for prevention of neural tube defects: Bayesian model. *BMJ* 2014 Jul 29;349:g4554. doi: 10.1136/bmj.g4554
- Czeizel, A. E. Dudas, I. (1992) Prevention of the first occurrence of neural-tube defects by periconceptual vitamin supplementation. *The New England Journal of Medicine*. 1992 Dec 24;327(26):1832-5.
- Delany, C. McDonnell, R. Robson, M. Corcoran, S. Fitzpatrick, C. De La Harpe, D. (2011) FA Supplement Use in the Prevention of Neural Tube Defects in 2009. *Ir Med J.* Jan; 104(1):12-5
- Department of an Taoiseach (2013). *Healthy Ireland – A Framework for Health and Wellbeing 2013-2015*.
- Department of Health (2015) *Creating a Better Future Together - National Maternity Strategy 2016 -2025*.
- Department of Health (2016) Healthy Eating Guidelines [online]. Available from: <https://www.hse.ie/eng/about/who/healthwellbeing/our-priority-programmes/heal/healthy-eating-guidelines/> [accessed on 8 May 2018]

- Department of Health (UK) (1992). Expert Advisory Group. FA and the prevention of neural tube defects. London: Department of Health
- deWalle, H.E.K. deJong-van den Berg, L.T.W. (2008) Ten years after the Dutch public health campaign on FA: the continuing challenge. *Eur J Clin Pharmacol.* 2008. 64. pp. 539-543
- EUROCAT Central Registry (2010) *EUROCAT Special Report: Prevalence of Neural Tube Defects in younger mothers in Europe 2000-2008*. Antrim: EUROCAT Central Registry
- EUROCAT Central Registry (2014) *EUROCAT Special Report: Geographic Inequalities in Public Health Indicators Related to Congenital Anomalies*. Antrim: EUROCAT Central Registry
- European Food Safety Authority. (2014) *Draft Scientific Opinion - Scientific Opinion on Dietary Reference Values for folate. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)*. Parma: European Food Safety Authority
- Flynn, M.A.T. (2015) Empowering people to be healthier: public health nutrition through the Ottawa Charter. *Cambridge University Press.* 2015. 74(3) pp.303-312
- Flynn, M.A.T. Anderson, W.A. Burke, S.J. Reilly, A. Public health nutrition FA food fortification: the Irish experience (2008). In: *The challenge of translating nutrition research into public health nutrition*. [online] Dublin. Available at: <https://www.cambridge.org/core/services/aop-cambridge-core/content/view/9CCCA96E65FD6D6F9391DD07727EEE81/S0029665108008720a.pdf/div-class-title-session-1-public-health-nutrition-folic-acid-food-fortification-the-irish-experience-div.pdf>
- Food Safety Advisory Board (1997). *The value of FA in the prevention of neural tube defects*. Dublin: Food Safety Advisory Board
- Food Safety Authority Ireland (2006) *Report of the National Committee on FA Food Fortification*. Dublin: Food Safety Authority Ireland
- Food Safety Authority Ireland (2008) *Report of the Implementation Group on FA Food Fortification to the Department of Health and Children*. Dublin: Food Safety Authority Ireland
- Food Safety Authority Ireland (2016) *Report of the Scientific Committee of the Food Safety Authority of Ireland. Update Report on FA and the Prevention of Birth Defects in Ireland*. Dublin: Food Safety Authority
- Gomes, S. Lopes, C. Pinto, E. (2015) Folate and FA in the periconceptional period: recommendations from official health organizations in thirty-six countries worldwide and WHO. *Public Health Nutrition* 2016 Jan;19(1):176-89. doi: 10.1017/S1368980015000555.
- Governey, S. Culligan, E. Leonard, J. O'Connell, J. Faulkner, A. (2014) *The Health and Therapy Needs of Children with Spina Bifida in Ireland*. Dublin: Temple Street Children's University Hospital.
- Health Service Executive (2006) Training Programme for Public Health Nurses and Doctors in Child Health Screening, Surveillance and Health Promotion. Unit 7 Food & Nutrition. Kildare: Health Service Executive
- Health Service Executive (2016). Making Every Contact Count: A Health Behaviour Change Framework and Implementation Plan for Health Professionals in the Irish Health Service. Health Service Executive. ISBN No 978-1-78602-038-3
- Healthcare Pricing Office, Health Service Executive. (2016) *Perinatal Statistics Report, 2014*. Dublin: Health Service Executive
- Hoey, L. McNulty, H. Askin, N. Dunne, A. Ward, M. Pentieva, K. Strain, J.J. Molloy, A.M. Flynn, C.A. Scott, J.M. (2007) Effect of a voluntary food fortification policy on folate, related B vitamin status, and homocysteine in healthy adults. *The American Journal of Clinical Nutrition.* 86. pp. 1405-1413
- Hoffman, R. Gerber, M. (2015) Food Processing and the Mediterranean Diet. *Nutrients.* Sep 17; 7(9):7925-64. doi: 10.3390/nu7095371
- Hopkins, S. M., Gibney, M. J., Nugent, A. P., McNulty, H, Molloy, A. M., Scott, J. M., Flynn, A., Strain, JJ, Ward, M, Walton, J. and McNulty, B. A. 2015. 'Impact of voluntary fortification and supplement use on dietary intakes and biomarker status of folate and vitamin B-12 in Irish adults'. *Am J Clin Nutr.* 2015 Jun;101(6):1163-72. doi: 10.3945/ajcn.115.107151.
- Hunter -personal communication. Also, Hunter (2017)- *The folate status of pregnant women in the Republic of Ireland; the current position*. Dublin: Safefood
- International Federation for Spina Bifida and Hydrocephalus (2016) *Right to Health: Reality of Persons with Spina Bifida and Hydrocephalus*. Brussels: International Federation for Spina Bifida and Hydrocephalus

Irish Universities Nutrition Alliance. *North/South Ireland Food Consumption Survey*. Dublin: Food Safety Promotion Board; 2001.

<http://www.iuna.net>

Kancherla, V. (2018). Countries with an immediate potential for primary prevention of spina bifida and anencephaly: Mandatory fortification of wheat flour with folic acid. *Birth Defects Research* 2018 Mar 13. doi: 10.1002/bdr2.1222.

Keilthy, P. McAvoy, H. Keating, T. (2015) *Consultation on the development of a National Maternity Strategy*. Dublin: Institute of Public Health in Ireland.

Kelly, F. Gibney, E.R. Boilson, A. Staines, A. Sweeney, M.R. (2015) FA levels in some food staples in Ireland are on the decline: implications for passive FA intakes?. *J Public Health (Oxf)*. 2016 Jun; 38(2):265-9. doi: 10.1093/pubmed/fdv025. Epub 2015 Mar 8

Kennedy, R.A.K. Mullaney, L. Reynolds, C.M.E. Cawley, S. McCartney, D.M.A. Turner, M.J. (2016) Preferences of women for web-based nutritional information in pregnancy. *Public Health Journal*, 2017 Feb;143:71-77. doi: 10.1016/j.puhe.2016.10.028.

Khoshnood, B. Loane, M. de Walle, H. Arriola, L. Addor, M.C. Barisic, I. Beres, J. Bianchi, F. Dias, C. Draper, E. Garne, E. Gatt, M. Haeusler, M. Klungsoyr, K. Latos-Bielenska, A. Lynch, C. McDonnell, B. Nelen, V. Neville, A.J. O'Mahony, M.T. Queisser-Luft, A. Rankin, J. Rissmann, A. Ritvanen, A. Rounding, C. Sipek, A. Tucker, D. Verellen-Dumoulin, C. Wellesley, D. Dolk, H. (2015) Long term trends in prevalence of neural tube defects in Europe: population based study. *BMJ*, 2015 Nov 24;351:h5949. doi: 10.1136/bmj.h5949.

Kielthy, S.E. Emerson, K.A. Ussher, G.D. Douglas, F.E. Lyons, O.C. Lardner, C.M. Flynn, M.A.T. (2015) *FA and the prevention of neural tube defects: exploring the Irish food supply from 2007 to 2014*. In: Proceedings of The Nutrition Society.

Lassi, Z.S. Salam, R.A. Haider, B.A. Bhutta, Z.A. (2013) *FA supplementation during pregnancy for maternal health and pregnancy outcomes (Review)*. London: The Cochrane Collaboration

Layte, R. McCrory, C. (2014) *Growing Up in Ireland Maternal Health Behaviours and Child Growth in Infancy: Analyses of the Infant Cohort of The Growing Up in Ireland Study* <https://www.esri.ie/pubs/BKMNEXT286.pdf>

Manning, E. Corcoran, P. Meaney, S. Greene, R.A. (2015) *Perinatal Mortality in Ireland Annual Report 2013*. Cork: National Perinatal Epidemiology Centre

McBride, O. Morgan, K. McGee, H. (2012) *Irish Contraception and Crisis Pregnancy Study 2010 (ICCP-2010) A Survey of the General Population*. Dublin: Crisis Pregnancy Programme

McCartney, DMA. Younger, KM. Walsh, J. O'Neill, M. Sheridan, C. Kearney, JM. (2013) Socio-economic differences in food group and nutrient intakes among young women in Ireland. *British Journal of Nutrition*. 2013 Dec 14;110(11):2084-97. doi: 10.1017/S0007114513001463.

McDonnell, R. Delany, V. O'Mahony, MT. Mullaney, C. Lee, B. Turner, MJ. (2014) Neural tube defects in the Republic of Ireland in 2009–11. *Journal of Public Health*. 2015 Mar;37(1):57-63. doi: 10.1093/pubmed/fdu016.

McDonnell, R. Delany, V. O'Mahony, M.T. Lynch, C. McKeating, A. (2018) An Audit of Neural Tube Defects in the Republic Of Ireland for 2012-2015. *Irish Medical Journal* 111(3)

McGee, H. Rundle, K. Donnelly, C. Layte, R. (2008). The Irish Study of Sexual Health and Relationships – Subreport 2. Sexual Health Challenges and Related Service Provision. Report developed for the Crisis Pregnancy Agency and the Department of Health and Children

McGowan, C.A. McAuliffe, F.M. (2012) Maternal nutrient intakes and levels of energy underreporting during early pregnancy. *Eur J Clin Nutr*, 66:906-913. doi: 10.1038/ejcn.2012.15

McKeating, A. Farren, M. Cawley, S. Daly, N. McCartney, D. Turner, M.J. (2015) Maternal FA supplementation trends 2009 – 2013. *Acta Obstet Gynecol Scand* 2015; 94: 727–733. doi: 10.1111/aogs.12656

McKeating, A. Maguire, P.J. Daly, N. Farren, M. McMahon, L. Turner, M.J. (2015) Trends in maternal obesity in a large university hospital 2009–2013. *Acta Obstetrica et Gynecologica Scandinavica*. Sep; 94(9):969-75. doi: 10.1111/aogs.12685. Epub 2015 Jun 23

McKillop, D.J. Pentieva, K. Daly, D. McPartlin, J.M. Hughes, J. Strain, J.J. Scott, J.M. McNulty, H. (2002) The effect of different cooking methods on folate retention in various food that are amongst the major contributors to folate intake in the UK diet. *Br. J. Nutr.* 2002;88:681-8. doi:10.1079/BJN2002733

- McNulty, B. Pentieva, K. Marshall, B. Ward, M. Molloy, A.M. Scott, J.M. McNulty, H. (2011) Women's compliance with current FA recommendations and achievement of optimal vitamin status for preventing neural tube defects. *Human Reproduction*. , 26 (6). pp. 1530-1536. doi: 10.1093/humrep/der078
- McNulty, H. McPartlin, J.M. Weir, D.G. Scott, J.M. (1987) Folate catabolism in normal subjects. *Hum Nutr. Appl. Nutr.* , 41, 338-341
- McNulty, H. Pentieva, K. (2004) Folate bioavailability. *Proc. Nutr. Soc.* Nov; 63(4):529-36. PMID:15831124
- McNulty, H. Pentieva, K. (2010) Folate bioavailability. In: *Folate in Health and Disease*, 2nd edn. Ed Bailey, L.B. CRC Press, Boca Raton, FL, USA, 25-47.
- Medical Research Council Vitamin Study Research Group (1991). Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet*, 1991;338:131-7
- Molloy, A.M. Einri, C.N. Jain, D. Laird, E. Fan, R. Wang, Y. Scott, J.M. Shane, B. Brody, L.C. Kirke, P.N. Mills, J.L. (2014) Is low iron status a risk factor for neural tube defects? *Birth Defects Res A Clin Mol Teratol*; 2014 Feb;100(2):100-6. doi: 10.1002/bdra.23223.
- Molloy, A.M. Kirke, P.N. Brody, L.C. Scott, J.M. Mills, J.L. Effects of folate and vitamin B12 deficiencies during pregnancy on fetal, infant, and child development. *Food and Nutrition Bulletin*; 2008, 29(2) pp.101-111
- Morris, J.K. Rankin, J. Draper, E.S. Kurinczuk, J.J. Springett, A. Tucker, D. Wellesley, D. Wreyford, B. Wald, N.J. (2015) Prevention of neural tube defects in the UK: a missed opportunity. *Arch Dis Child* 2016 Jul;101(7):604-7. doi: 10.1136/archdischild-2015-309226.
- Mulinare, J. Cordero, J.F. Erickson, J.D. Berry, R.J. (1988) Periconceptional use of multivitamins and the occurrence of neural tube defects. *JAMA*; 260:3141-5
- Mullaney, L. Cawley, S. Kennedy, R. O'Higgins, AC, McCartney, D. and Turner, M.J. (2016) Maternal nutrient intakes from food and drinks consumed in early pregnancy in Ireland. *Journal of Public Health* 2017 Dec 1;39(4):754-762. doi: 10.1093/pubmed/fdw106.
- Mullaney, L. O'Higgins, AC. Cawley, S. Doolan, A. McCartney, D. and Turner, M.J. (2014) An estimation of periconceptual under-reporting of dietary intake. *Journal of Public Health*; Oct 2014. pp1-9.
- O'Higgins, A. Murphy, O.C. Egan, A. Mullaney, L. Sheehan, S. Turner, M.J. (2014) The Use of Digital Media by Women Using the Maternity Services in a Developed Country *Ir Med J* 2014;107(10):313-315
- O'Malley, EG. Cawley, S. Kennedy, RK. Reynolds, CME. Molloy, A. and Turner, MJ (2018) Maternal anaemia and folate intake in early pregnancy. *Journal of Public Health* Jan 31. doi: 10.1093/pubmed/fdy013
- Obeid, R. Koletzko, B. Pietrzik, K. 2014. 'Critical evaluation of lowering the recommended dietary intake of folate'. *Clin Nutr*; Apr 33(2):252-9. doi: 10.1016/j.clnu.2013.12.013. Epub 2014 Jan 14
- Rossi, M. Amaretti, A. Raimondi, S. (2011) Folate production by probiotic bacteria. *Nutrients*. 2011 Jan; 3(1):118-34. doi: 10.3390/nu3010118. Epub 2011 Jan 18
- Rundle K, Leigh C, McGee H, Layte R. Irish Contraception and Crisis Pregnancy (ICCP) Study: A Survey of the General Population. Dublin, Crisis Pregnancy Agency, 2004
- Safefood (2017) The folate status of pregnant women in Ireland; the current position.
- Simpson, J.L. Bailey, L.B. Pietrzik, K. Shane, B. Holzgreve, W. (2010) Micronutrients and women of reproductive potential: required dietary intake and consequences of dietary deficiency or excess. Part I – Folate, Vitamin B12, Vitamin B6. *The Journal of Maternal-Fetal & Neonatal Medicine* 2010 Dec;23(12):1323-43. doi: 10.3109/14767051003678234.
- Sjögren, K. (2017) Higher mortality among mothers of children with birth defects. *Science Nordic*. <http://sciencenordic.com/higher-mortality-among-mothers-children-birth-defects> on 13 February 2017
- Smithells, R.W. Nevin, N.C. Seller, M.J. et al. (1983) Further experience of vitamin supplementation for the prevention of neural tube defect recurrences. *Lancet* May 7;1(8332):1027-31
- Smithells, R.W. Sheppard, S. Schorah, C.J. Seller, M.J. Nevin, N.C. Harris, R. Read, A.P. Fielding, D.W. (1981) Apparent prevention of neural tube defects by periconceptional vitamin supplementation. *Archives of Disease in Childhood*. 1981. 59. pp. 911-918

Sweeney, M.R. McPartlin, J. Scott, J. (2007) FA fortification and public health: Report on threshold doses above which unmetabolised FA appear in serum. *BMC Public Health*, 2007 Mar 22;7:41.

US Preventive Service Task Force (2017) FA Supplementation for the Prevention of Neural Tube Defects. *JAMA*, Jan 10;317(2):183-189. doi: 10.1001/jama.2016.19438.

Viswanathan, M. Treiman, K.A. Kish-Doto, J. Middleton, J.C. Coker-Schwimmer, E.J.L. Nicholson, W.K. (2017) FA Supplementation for the Prevention of Neural Tube Defects - An Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 317(2) pp. 190-203

World Health Organization (2015) *Guideline: Optimal serum and red blood cell folate concentrations in women of reproductive age for prevention of neural tube defects*. Geneva: World Health Organization

Yi, Y. Lindemann, M. Colligs, A. Snowball, C. (2011) Economic burden of neural tube defects and impact of prevention with FA: a literature review. *European Journal of Pediatrics*, 170(11). pp. 1391-1400

Yunni, Y. Lindemann, M. Colligs, A. Snowball, C. (2011) Economic burden of neural tube defects and impact of prevention with FA: a literature review. *Eur J Pediatr*, 170 pp. 1391-1400

Terms of Reference

To develop a Folate Policy which will include the following elements:

- Development of population guidelines for folate in pregnancy including at risk groups
- Plan appropriate information campaigns for the general public and healthcare professionals
- Consider the requirements for food fortification with Folate
- Consider the requirements for surveillance of NTDs and dietary folate intakes
- Consider research requirements
- To take account of EU, WHO and other relevant international developments

The Committee will be inclusive of FSAI, Safefood, HSE, ICGP, Institute of Obstetricians and Gynecologists and representatives of Department of Health.

In conducting its work the Committee will take account of the ongoing developments as outlined above, consider short, medium and long term measures and prioritise actions to ensure adequate folate intakes in at risk groups.

The Chair of the Committee shall be determined by the DOH.

The Committee may seek expert advice on issues as deemed necessary.

Membership of the FA Policy Committee

NAME	DESCRIPTOR	ORGANISATION
Prof Michael Turner	Director	UCD Centre for Human Reproduction
	National Lead for the Health Services Executive Clinical Programme in Obstetrics and Gynaecology	Health Service Executive
Dr John Devlin	Ex- Deputy Chief Medical Officer	Department of Health
Ursula O'Dwyer	Health Promotion Policy Advisor	Department of Health
Audrey Hagerty	Ex-Principal Officer, Food Unit	Department of Health
Tommy Wilson	Food Unit	Department of Health
Sinead Curran	Dietitian Manager	Irish Nutrition and Dietetic Institute
Dr Clíodhna Foley-Nolan	Ex-Director Human Health and Nutrition	Safefood
Prof Anne Molloy	Associate Professor in School of Medicine	Trinity College Dublin
Dr Mary Flynn	Chief Specialist Public Health Nutrition	Food Safety Authority of Ireland
Sarah O'Brien	Lead- Healthy Eating Active Living	HSE
Dr Una Fallon	Consultant in Public Health Medicine	HSE Midlands
Dr Helen McAvoy	Director of Policy	Institute of Public Health in Ireland
Dr Mary T. O'Mahony	Specialist in Public Health Medicine	HSE
	Lead on EUROCAT registry	EUROCAT

National Dietary Surveys of Irish Adults (18-64yrs)

National Adult Nutrition Survey (NANS) (2008-2010)

- 4-day semi-weighed food diary
- Nutrient intake estimated using UK food composition tables updated with Irish data
- Anthropometry (measured)
- RCF measured

North South of Ireland Food Consumption Survey (NSIFCS) (1997-1999)

- 7-day estimated food diary
- Nutrient intake estimated using UK food composition tables updated with Irish data
- Anthropometry (measured)

Irish National Nutrition Survey (INNS) (1988-1989)

- 7-day diet history
- Anthropometry (measured)

Medication use – indications for higher dose folic acid use

Chloramphenicol

Methotrexate

Metformin

Sulfasalazine

Phenobarbital

Phenytoin

Primidone

Triamterene

Barbiturates

