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INTERNATIONAL FEDERATION
FOR SPINA BIFIDA AND HYDROCEPHALUS

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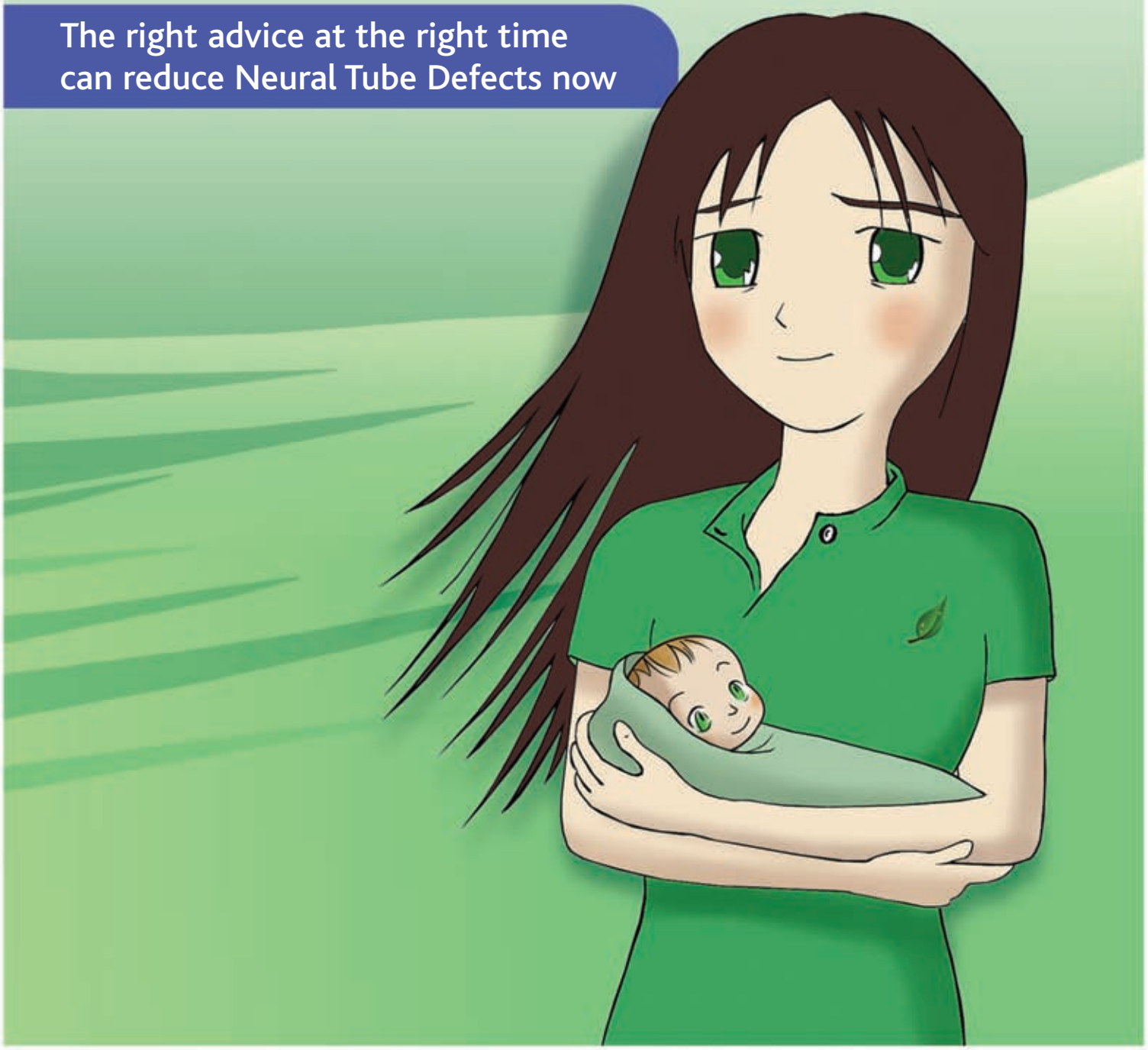
The right advice at the right time can reduce Neural Tube Defects now



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FOREWORD

The European Parliament at its best is here to represent the interests of European citizens and I believe that one of our responsibilities is to raise awareness about current and upcoming public health challenges. The prevention of diseases and disability, a better access to care and treatment, and the reduction of health inequalities across the EU are core principles which should lead EU action in the field of public health.

I am therefore concerned with the continuing high prevalence figures for Neural Tube Defects (NTDs) across the European Union. Indeed, NTDs are one of the few rare diseases recognised by the European Commission as frequently preventable. Up to 70% of cases could be prevented.

There is long standing scientific evidence about effective preventive measures for NTDs. Intake of adequate levels of folate by women of childbearing age is essential, in particular during preconception and early pregnancy. Yet our progress in preventing NTDs in the EU and by national governments in Europe remains disappointing.

Based on the shared conviction that most cases of NTDs are preventable - in particular with the right advice at the right time - the International Federation for Spina Bifida and Hydrocephalus (IF) and Bayer Schering Pharma Women's Healthcare (BSP), with the support of EUROCAT (the European Commission's network for epidemiologic surveillance of congenital anomalies), have joined forces to publish this report. The objective of the report is primarily to alert us to the state of play regarding NTDs in Europe. We can also hope, however, that it will initiate change.

I strongly welcome the work of IF, BSP and the support of EUROCAT and join them in their call to the European institutions to focus more closely on this issue. There is a need to take action to combat NTDs by making it an effective priority where rapid progress is necessary and possible. As a starting point NTD prevention should be specifically prioritised under the implementation of the EU's Recommendation on Rare Diseases for example, and included in the national action plans now being developed and implemented as a result of the Recommendation.

I hope all readers of this report will join us to help ensure that health inequalities do not start before birth.

Dr. Antonyia Parvanova,
Member of the European Parliament

INTRODUCTION

This report provides a policy and situation overview regarding Neural Tube Defects (NTDs) across a sample of EU member states (France, Germany, Italy, Poland, Spain, Sweden, the UK). NTDs are one of the most common but mostly preventable birth defects in Europe: although evidence indicates that up to 70% of NTDs can be avoided with primary prevention, progress towards the reduced occurrence of these birth defects remains disappointing, according to the European Surveillance Registry for Congenital Anomalies (EUROCAT)[1].

In the last few decades, tremendous progress has been made in the treatment and care of children and adults with Spina Bifida resulting from an NTD, mainly thanks to the interdisciplinary care system. Their lives are not always easy but are meaningful and good. However prenatal diagnoses mostly result in the physicians' advice to terminate the pregnancy when an unborn child with an NTD is detected. The psychological burden on parents of this difficult decision is significant. Therefore, all efforts should be focused on primary prevention, allowing the 'same child' to be born without a disability.

Against this reality, this report brings together in a succinct 'at a glance' format key facts about this important public health issue ranging from basic prevalence data about NTDs in Europe to an overview of government policies in this field. It reviews national efforts and highlights the potential for improving NTD prevention. It explores as well to what extent countries have enacted guidelines on folic acid supplements, launched education campaigns to raise awareness about the importance of folates in combating NTDs and to what extent women actually comply with guidelines in place.

It is hoped that it provides the starting point for a call to action, because the authors and partners strongly believe that Europe can and should do more to combat NTD incidence. At the very least they call for a renewed discussion and the development of best practice consensus to make meaningful progress.

Published jointly by IF, the International Federation for Spina Bifida & Hydrocephalus[2] and the Women's Healthcare Division of Bayer Schering Pharma AG[3], we would like to thank EUROCAT for the unstinting support and guidance, and particularly for the provision of comparable country-wide prevalence data and the review of the accurate use of EUROCAT data in this report.

METHODOLOGY & STRUCTURE

In addition to the information from EUROCAT's published reports on NTDs and folic acid policy in European countries, this report is based on research carried out by Burson-Marsteller Brussels[4] at the European Union level and in the following seven European countries: France, Germany, Italy, Poland, Spain, Sweden and the United Kingdom. Initial desk research was undertaken between May and August 2009, and followed by direct contact with national stakeholders to confirm our understanding of their position and seek their additional comments. EUROCAT reviewed the final report to ensure the accurate interpretation of their published data. It should be noted that all EUROCAT data on prevalence of NTDs was supplied by EUROCAT using the most recent numbers available; covering the period 1980-2002.

In the first phase, publicly available information was gathered on NTD prevalence, awareness of the issue, relevant national policies, guidelines and practices, through a range of sources including government, professional and patient association websites and published scientific literature.

In the second phase, interviews were carried out in each country with a selection of national stakeholders representing the different aspects of the debate, for example Spina Bifida patients' associations and organisations for gynaecologists and midwives. The information gathered during the interviews is incorporated in the country reports. A list of organisations participating in the interviews is provided in annex I.

In addition to individual sections summarising the status in each of these countries, the report provides an overview of the issue and conclusions at EU level. The country sections are all arranged in the same format for ease of reference and provide available data on NTD prevalence (provided by EUROCAT), abortion rates where available, folate levels in women of childbearing age, the national policy framework, national guidelines if they exist, education campaigns and the potential for (national) mandatory food fortification.

This report is not designed as a scientific report, but rather as a policy tool. It provides a description of the current policy environment with regard to the prevention

of NTDs, on the basis of the best available factual information and stakeholder opinions.

THE DATA SOURCE: EUROCAT 1980 – 2002

Established in 1979, EUROCAT now represents 43 registries in 20 countries accounting for 29% of the European birth population, equivalent to more than 1.5 million births per year.

EUROCAT's 2005 report[5] "NTD rates and survey of Folic Acid Policy and Practice in European Countries" provides the initial source of statistical data on NTDs. The report published data on NTDs for the period 1980 – 2002. The prevalence rates and percentages of terminated pregnancies set out in this report are based on the same time period but were specifically calculated by EUROCAT using the latest available figures, giving greater accuracy. In 2007, EUROCAT updated the survey on policies and practices and the country chapters reflect the content of this research.

There is variation country by country as to the number of registries contributing to EUROCAT. Furthermore there are differences in the percentage of births and regional variations covered for each country. To enable country by country comparison, the figures quoted in this report have been weighted. The authors of this report would like to thank Dr. Hermien de Walle, co-chair of the EUROCAT Folic Acid Working Group, for making this possible.

AN ADDITIONAL NOTE

The report's methodology has certain limitations. In the first place there may be developments in some countries which we have not identified or new initiatives that were launched after the research period closed. Moreover, as data are not complete for most countries, available information may be subject to different interpretations. Accordingly, the International Federation for Spina Bifida & Hydrocephalus and Bayer Schering Pharma AG would welcome feedback on this report. Please send any comments to the following e-mail address: NTDreport@ifglobal.org

THE FACTS ABOUT NEURAL TUBE DEFECTS

The neural tube (NT) is the precursor to the central nervous system in the developing embryo. An NTD is the failure of the neural tube to close during early foetal development. We now know that the neural tube should close completely within the first 28 days after conception.

NTDs result in malformations of the spine, skull and brain, leading to Spina Bifida, Anencephaly, and Encephalocele. In 95% of cases these congenital malformations occur with no previous family history. Anencephaly and Spina Bifida account for up to 95% of all NTDs with equal prevalence[6].

In Spina Bifida, which means 'split spine', the bones do not close round the spinal cord so the nerves become damaged as they can bulge out of the unborn baby's back. The level of disability depends both on where on the spine this occurs and the amount of affected nerve tissue involved. Paralysis of legs, loss of bowel and bladder control, Hydrocephalus ("water on the brain") and learning disabilities are often associated with Spina Bifida. 80% to 90% of infants born with Spina Bifida survive, with varying degrees of disability. Spina Bifida cannot be cured, although medical interventions mean that many people with Spina Bifida now live into old age and have a good quality of life. However, long-term care is often necessary.

More than 85% of children with Spina Bifida also have Hydrocephalus. This is an effect of Spina Bifida not an NTD in itself; it is an accumulation of cerebro-spinal fluid which arises from an imbalance in the production and drainage of that fluid, causing raised pressure inside the brain. In babies and young children, the skull bones are not fixed and the pressure causes the head to increase in size. Hydrocephalus needs surgical intervention; otherwise it can lead to blindness, brain damage or even death.

In Anencephaly, which is always a fatal condition, the brain fails to develop completely or is entirely absent. Pregnancies affected by Anencephaly often result naturally in miscarriages, stillbirths or death very soon after birth.

Encephalocele refers to a sack which is formed when the bones of the skull fail to develop. It may contain only cerebro-spinal fluid or part of the brain may also be present in the sac, resulting in brain damage.

Across Europe, the NTD total birth prevalence rate is 9.0 per 10,000 births, and the live birth prevalence rate is 4.17 per 10,000. Although prenatal screening and associated terminations mean that NTDs affect only a small percentage of the total number of births across the EU, up to 70% of NTDs are preventable through

adequate folate levels. These can be achieved through an easily accessible and economic means: folic acid supplements. Compared to the low cost of a solution, managing the consequences of an NTD carries a very high economic cost for health service resources, not to mention the great distress associated with terminations of pregnancy and perinatal losses.

THE CRUCIAL ROLE OF FOLATES IN THE PREVENTION OF NTDS

It is not yet fully understood why neural tubes fail to develop properly, but it is recognised that insufficient levels of folate during the critical period of pre-conception and early pregnancy are one of the primary causes in addition to genetic and environmental factors. Folate, also known as vitamin B9 or in the synthetic form folic acid, is essential for the production and maintenance of new cells in the body. It is therefore especially important during periods of rapid cell division and growth such as the first stage of pregnancy, when the neural tube is forming.

Recognition of the link between folic acid and NTDs has been found in scientific literature for five decades[7]. The first unambiguous evidence of the effectiveness of periconceptional folic acid came with the publication of the results of the Medical Research Council (MRC) Vitamin Study (MRC Vitamin Study Research Group in 1991). On the basis of this trial, current estimates show that sufficient folate levels would prevent up to 72% of all NTDs. (There is increasing evidence to suggest that folic acid may also protect against other congenital anomalies.[8])

Evidence also suggests that younger women and women from disadvantaged backgrounds are at particular risk of an NTD-affected birth due to poor diet, lack of awareness and the greater likelihood of unplanned pregnancies.

THE PUBLIC POLICY RESPONSE TO INCREASING FOLATE AWARENESS AND CONSUMPTION

While there is widespread agreement on the importance of folates for the prevention of NTDs, there has been less agreement among policymakers and stakeholders on the best way to raise folate consumption among women of childbearing age.

Increasing the intake of natural folate

Folate is found in a variety of foods, including cruciferous vegetables such as cabbage, cauliflower and broccoli. Official advice on nutrition for women who are trying to conceive usually advises them to increase their consumption of these folate-rich foods. However, the average woman's intake of such foods is usually insufficient to achieve the folate status necessary to reduce the risk of an NTD during pregnancy.

Folic acid supplements

Many national governments and health agencies now advise women to ensure a daily intake of 0.4 milligrams (mg) - also written as 400 micrograms (mcg) - folic acid prior to conception and into their pregnancy in order to reduce the risk of NTD-affected pregnancies. A dose ten times higher is recommended for women who have had a previous pregnancy affected by an NTD.

Education campaigns

The small number of women who take folic acid supplements at the right time may indicate that few women are aware of their benefits and the proper timing for intake before conception and during the first weeks of pregnancy. In response to this challenge, health education campaigns have been launched in some countries to ensure that key messages around folic acid supplementation reach women directly as well as through health professionals.

Food fortification – voluntary or mandatory?

Voluntary food fortification of some foods, usually breakfast cereals, with vitamins and minerals including folic acid is now common across Europe and has contributed towards raising folic acid levels.

A key benefit of mandatory fortification would be to raise folic acid levels among the whole population. This would help reduce NTDs among women who do not plan their pregnancy, and reduce socioeconomic inequalities in the incidence of NTDs. Fortification of flour with folic acid is now widespread in North and South America and in much of the Middle East, and countries with this policy have seen a decline in NTD rates.

However, in Europe no country has yet moved to compulsory fortification due to concerns about possible health risks related to raising the folic acid intake of the entire population. There are concerns that folic acid (supplements or fortification) may mask anaemia in older people caused by B12 deficiency, may increase the likelihood of conceiving twins (though this theory has been debunked), and may promote the progression of existing premalignant/preneoplastic and neoplastic lesions.

Against this background, a number of European countries are reviewing information on the benefits and hazards of folic acid fortification for the population as a whole.

FRANCE

Total birth prevalence NTD	7.63 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	1.93 per 10.000 (source: EUROCAT)
Total birth rate	13 per 1,000 population (one of highest in EU) 835 000 births a year (source: Eurostat 2008)
Termination of pregnancy	68.5% of the pregnancies were terminated because of prenatal diagnosis of an NTD (source: EUROCAT)
Unplanned pregnancies	No information available
Government recommendations	Yes, issued August 2000 by *Direction Générale de la Santé*
Professional recommendations	No
Recommendation: Amount of folic acid supplements	0.4mg dose per day; 5mg per day for women taking an anti-epileptic medication or with a previous NTD-affected pregnancy
Recommendation: Timing of folic acid supplementation	From 4 weeks before conception to 8 weeks after conception
Compliance with recommendations	About 30% to 50% of women of childbearing age have suboptimal folic acid levels
Food fortification policy	Voluntary
Education initiatives	Yes (by French Spina Bifida Association)
Next steps	2009 creation of a Working Group on rare diseases, including participation of the *Centre de Référence du Spina Bifida*

COMMENTARY

Since August 2000 government guidelines issued by France's *Direction Générale de la Santé* (DGS, General Directorate for Health) have urged folic acid supplements for women of childbearing age, and the French Spina Bifida Association has tried to raise awareness about the risks of low folate levels. However, compliance with the recommendations remains low.

"Fighting against Neural Tube Defects is like shouting in the middle of the desert. We always seem to be alone.

Pregnancy does not last 9 but 12 months, with 3 months of planning."

Hubert Journel - KOL

NTD PREVALENCE

The total birth prevalence rate of NTDs in France is 7.63 per 10,000 births, with a live birth prevalence rate of 1.93 per 10,000.

According to the national Food Safety Agency there are an estimated 800 NTD-affected births per year. A majority of women follow the advice of their physician to interrupt their pregnancy when their foetus is diagnosed with an NTD.

France has one of the highest birth rates in Europe at 13 births per 1,000 inhabitants representing nearly 800,000 births per year, according to Eurostat data.

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The French health authorities and a number of key French organisations have been active in addressing the need to improve folate levels in women of childbearing age, in order to reduce the incidence of NTDs. In 2001, the government published recommendations for the promotion of a diet rich in folates targeted at women of childbearing age, together with the medical prescription of folic acid supplements to women wishing to have a baby. The official recommendation is a daily dose of 0.4mg of folic acid from 4 weeks before conception to 8 weeks after conception. Women with a previous NTD pregnancy and women taking anti-epileptic medication are recommended a daily dose of 5mg.[9]

In 2001 as well, the French Federation of Spina Bifida Associations (FFASB) published a fact sheet on the prevention of NTDs where it states that folic acid intake prevents the development of Spina Bifida and Anencephaly and may also be useful for the prevention of orofacial and cardiovascular defects[10]. The FFASB recommends the intake of folic acid of 0.4-0.8 mg/per day for women with no medical history of NTDs and 4mg/per day for women with a previous history of NTDs.

More recently, the second *Programme national nutrition santé*[11] (PNNS2 – National programme on healthy nutrition) covering the period 2006 to 2010 is designed in part to improve folate intake by women of childbearing age so as to reduce the incidence of NTDs. This programme includes a fact sheet on folate[12] which

recommends an intake of folic acid supplements from 4 weeks before conception, but only one month after the baby is conceived, possibly in recognition that the neural tube closes within the first 28 days of conception. The plan also stipulates the implementation of a systematic prescription of adequate doses of folic acid supplements to women "consulting a doctor for the purpose of conceiving a child;" it also identifies the need to train healthcare professionals and develop and disseminate adequate communications tools. A contraception strategy has been put in place by the French health authorities to reduce the number of unplanned pregnancies.

TERMINATIONS

Abortion was legalised in France in 1975, and from 1982 up to 80% of the cost is now reimbursed for women living in poverty or under-aged women. Although the law authorises abortions up to 12 weeks into a pregnancy, there is no limit if there is a strong probability that the expected child will suffer from a severe disability or incurable illness (or if the pregnancy endangers the mother's health[13].)

According to EUROCAT, in the period 1980-2002, 68.5% of the pregnancies recorded were terminated because of prenatal diagnosis of an NTD.

UNPLANNED PREGNANCIES

No information is available. Although, studies[14] estimate that 50% of unplanned pregnancies are aborted.

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

According to the *Agence Française de Sécurité Sanitaire des Aliments*[15] (AFSSA, French Food Safety Agency) roughly 30% of women of childbearing age in France suffer from suboptimal folic acid levels, and some estimates show a 50% figure. An estimated 800 newborns suffer from NTDs each year[16].

FOOD FORTIFICATION POLICY

There is no mandatory food fortification policy in place in France. Some fortified breakfast cereals are available. In 2003, it was suggested that a five-year pilot project on flour fortification in vitamins B9 and B12 should be put in place but there is still no consensus on the benefits of food fortification with B vitamins. In 2007 the *Institut Danone* reported that international studies showing a possible link between folic acid intake and cancer (colorectal and breast cancers) have prevented France from putting in place a mass folic acid fortification programme[17].

The latest official report to summarise the arguments for and against food fortification was published in 2008. Entitled "Folic acid and prevention of neural tube closure defects: The question is not yet solved", the report concluded that it would be best to increase awareness of current national recommendations on folic acid intake among women of childbearing age, rather than implement a mandatory food fortification policy[18].

"Prevention is better than cure."

Association nationale du spina bifida et handicaps associés **(ASBH - National Association of Spina Bifida and Related Handicaps)**

HEALTH EDUCATION INITIATIVES

Education campaigns are run by the French Spina Bifida Association. For example, in 2004 they published an information leaflet on folic acid, to be distributed all over the country and placed in waiting rooms of physicians, family planning centres, pharmacies, etc[19]. Advice to women on healthy nutrition during pregnancy has generally been disseminated via TV and newspapers, and health information websites such as *Doctissimo*.

"Motherhood is sometimes unplanned but can always be prepared: if you can become a mother take oral folic acid supplements."

Centre de Référence Spina Bifida **(Spina Bifida Reference Center)**

NEXT STEPS

Stakeholders interviewed for this survey "regret the low level of compliance with the existing guidelines, pointing out that doctors do not always advise women properly". They believe that improving this record should be a major priority.

The debate over food fortification is still underway in France, and as a contribution to the debate the *Centre de référence du Spina Bifida*[20] (Reference Centre for Spina Bifida) has scheduled an event in 2010 on the subject, particularly the question of flour fortification. Meanwhile the 2009 formation by the Ministry of Health of a Working Group on rare diseases,[21] which includes participation by the Centre among other stakeholders, may bring some answers.

GERMANY

Total birth prevalence NTD	13 per 10,000 (source: EUROCAT 1987-2002)
Live birth prevalence NTD	5.34 per 10,000 (source: EUROCAT 1987-2002)
Total birth rate	8.2 children per 1,000 residents in 2008, making it the lowest of all 27 EU nations with 675,200 births (source: Eurostat 2008)
Termination of pregnancy	52.2% of the pregnancies were terminated because of prenatal diagnosis of an NTD (source: EUROCAT 1987-2002)
Unplanned pregnancies	31 - 50%
Government recommendations	No
Professional recommendations	Yes
Recommendation: Amount of folic acid supplements	Daily intake of 0.4mg for all women 4 mg for women with a previous NTD-affected pregnancy
Recommendation: Timing of folic acid supplementation	At least 4 weeks preceding pregnancy and during the first 3 months of pregnancy
Compliance with recommendations	86% of women do not reach recommended levels of folate
Food fortification policy	Voluntary
Education initiatives	None
Next Steps	None planned

COMMENTARY

The beneficial link between folate levels and the prevention of NTDs is well understood in Germany. Groups of experts and government officials have publicly debated this issue over the last ten years. However, the data on this issue are limited as there is no nation-wide monitoring system for birth defects or their causes. Furthermore, no clear government policy has yet been established to prevent NTDs in Germany.

Two German registries contribute to EUROCAT, which is the most comprehensive source of data on NTDs in Europe. These two registries were set up by the Länders of Rhineland-Palatinate and Saxony-Anhalt. The first covers the 3 major maternity hospitals for the district of Mainz representing around 3,300 births per year; the second covers residents of the entire Länder with around 17,000 births per year. Since 2006, the German Nutrition Society has been calling for the government to establish a national register of birth defects and to conduct regular national nutrition surveys.

NTD PREVALENCE

According to EUROCAT data for the period 1987-2002, the total NTD prevalence rate is 13 per 10,000 births, with a live birth prevalence of 5.34 per 10,000 births.

A report in 2006 by the German Nutrition Society estimated that NTDs occur in 1 to 2 per 1,000 births, corresponding to 700 to 1,400 newborns every year (calculated based on birth rates in 2004). According to the report, around 60% of cases are Spina Bifida, of which the majority are disabled for life and a suggested 40% die by the age of 2 years old. 35 – 45% of cases are reported to be Anencephaly, which is fatal[22].

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The health system in Germany is highly decentralised with responsibilities split between the regional and central governments. The prevention of NTDs does not figure in current policy, although preventative health figures highly on the health policy agenda and there is a current focus on healthy lifestyles that includes reference to unbalanced nutrition. Indeed, although the Federal Ministry of Food, Agriculture and Consumer Protection stressed to the Bundesrat in 2007 that one of "its primary goals is to reduce NTDs and thus it is focusing on improvement of folate intake in women of childbearing age", to date there is no government endorsed national guidance on reduction of NTD incidence through folic acid supplementation.

In place of government recommendations the German Nutrition Society[23] has been making recommendations since 1995. They recommend that women who are planning a pregnancy should take 400 mcg of folic acid daily, in the form of supplements, for at least the four weeks preceding the pregnancy and during the first three months of pregnancy. Women who have previously had an NTD-affected pregnancy are advised to take ten times the amount or 4 mg of folic acid, per day, over the same time period.

Other professional organisations make the same recommendation, including the German Society of Obstetrics and Gynaecology, the German Society of Human Genetics, the German Society of Paediatrics and Adolescent Medicine and the German Society of Neuropaediatrics.

TERMINATIONS

Under German law abortion is legal if the pregnancy implies a serious threat to the pregnant woman's physical or mental health, or if the foetus is affected by malformations. The 2008 federal termination statistics show that of the total 114,484 abortions, 2,989 were undertaken on the basis of a medical indication. The German Federal Institute for Risk Assessment estimates that approximately 500 pregnancies are terminated every year following the diagnosis of an NTD.

Data from EUROCAT show that 52.2% of the pregnancies recorded were terminated because of prenatal diagnosis of an NTD.

UNPLANNED PREGNANCIES

Studies of women who had recently given birth indicate that between 31% and 44% of pregnancies were not planned[24]. In assessing the supply of folic acid to the German population, the Federal Institute for Risk Assessment estimated that 40 – 50% of pregnancies are unplanned[25].

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

Despite recommendations from professional organisations, studies have shown that only very few women take folic acid supplements at the proper time and in the proper quantity needed to prevent NTDs. The 2nd German National Nutritional Survey[26] revealed that 86% of women did not reach the recommended levels of folic acid. Earlier studies found that 80.6% of women had an average folic acid intake of less than 150mcg, where 400mcg is the daily level recommended to prevent NTDs. In 2006, two leading German experts in this field concluded that there are no effective NTD prevention programmes in place in Germany[27].

FOOD FORTIFICATION POLICY

There is no mandatory food fortification policy in Germany. Folic acid is legally classified as a supplementary food with a recommended daily dose of 0.2mg; half the amount recommended in order to prevent NTDs.

For several years the NTD prevention debate in Germany has focused on whether or not food fortification is a suitable method for reducing NTD incidence. In 2002 the *Arbeitskreis Folsäure & Gesundheit*[28] (Folic Acid and Health Working Group) was formed and is composed of representatives from the professional medical societies, scientific institutions and parents' organisations. The German Federal Ministry for Health (BMG) and the Federal Ministry of Food, Agriculture and Consumer protection (BMELV), the German Nutrition Society (DGE) as well as the Federal Institute for Risk Assessment (BfR) send their observers to meetings of this group.

In late 2003 the Working Group called for mandatory fortification to prevent NTDs in its "Consensus paper on the medical importance of dietary supplementation with folic acid"[29]. In 2005, the Federal Institute for Risk Assessment concluded that any fortification policy would need to be accompanied by information campaigns and additional folic acid supplements for women wishing to have children. Furthermore it concluded that fortification of different foods would have to be restricted in order to avoid excessive intake by the rest of the population. A year later, the German Nutrition Society concluded that the fortification of flour with folic acid was the best strategy for improving the folate levels of the population. They recommended the supplementation of flour with 0.15mg folic acid for every 100g of flour[30].

"I believe we need a more sustained information campaign so that women of childbearing age are always aware of the importance of folic acid in the prevention of NTDs. TV spots are particularly important to reach all women."

Arbeitsgemeinschaft Spina Bifida und Hydrocephalus e.V.
(ASBH, Association for Spina Bifida and Hydrocephalus)

HEALTH EDUCATION INITIATIVES

There are currently no official health education initiatives.

In 2006, the Bundesrat called on the federal government to run a targeted information campaign, explaining the risks of suboptimal folic acid levels, especially for pregnant women, and the principles of a balanced diet. The responsible ministry responded that large information campaigns need to have a very clear message to be successful and that the issues of folic acid are very complex and the message needs to be targeted. They stated that any successful campaign would need to involve doctors, doctors associations, family advice centres and health funds.

The Federal Centre for Health Education[31] develops sexual education concepts and disseminates information and education material on sex education and family planning[32]. This includes advice on folate intake.

NEXT STEPS

The German Ministry of Food, Agriculture and Consumer Protection has recently set up a working group to evaluate current information campaigns and discuss whether it is still possible to further reduce the incidence of NTDs in Germany. No decisions have yet been taken by the group.

ITALY

Total birth prevalence NTD	6.10 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	3.26 per 10,000 (source: EUROCAT)
Total birth rate	9.6 births per 1,000 inhabitants 576,659 newborns in 2008 (source: Eurostat 2008)
Termination of pregnancy	45.6% of the pregnancies were terminated because of prenatal diagnosis of an NTD (source: EUROCAT)
Unplanned pregnancies	Around 40%
Government recommendations	Yes
Professional recommendations	Yes, Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects
Recommendation: Amount of folic acid supplements	Daily intake of 0.4mg for all women who may become pregnant Daily intake of 4-5mg for women at higher risk of having infants with NTDs
Recommendation: Timing of folic acid supplementation	3-4 weeks prior to and during the first three months of pregnancy
Compliance with recommendations	No consistent data across the country available, estimated to be low
Food fortification policy	Voluntary
Education initiatives	Yes. Ministry of Health, Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects, National Research Institute for Food and Nutrition, National Centre for Disease Prevention and Control, regional governments
Next Steps	None planned. Follow up of the work of the Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects

COMMENTARY

There is broad consensus in Italy about the importance of daily folic acid supplements before and during pregnancy in order to prevent NTDs. Nevertheless, general awareness and compliance among women, in particular regarding the intake recommendation before pregnancy, is still low. Patient, professional organisations and public authorities agree that continued educational efforts are needed.

NTD PREVALENCE

In Italy, six regional registries collect data on birth defects as part of EUROCAT. The total prevalence rate is 6.10 per 10,000 births, with a live birth prevalence of 3.26 per 10,000. These numbers are also reflected in the March of Dimes 2006 global birth defects report[33].

In 2008 there were 576,659 newborns[34] with the Eurostat recorded birth-rate at 9.6 births per 1,000 inhabitants.

The National Healthcare Action Plan 2006-2008 estimated that 30% of infant deaths during the first year of life were caused by premature birth and congenital malformations[35]. This is, potentially, a more serious problem for Italy than some other European countries as the birth-rate is lower than the overall morbidity rate of the population.

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

Health policies in Italy have been regionalised since 2001. The national government is responsible for setting up the strategic lines for policy, while the regions adopt and execute differing implementing measures. Women's health has not been a traditional focus of the healthcare policy agenda in Italy.

In 2004, experts, medical practitioners, patients and public authorities responsible for monitoring birth defects gathered together as the Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects, under the auspices of Italy's *Istituto Superiore di Sanità* (ISS, Italian High Institute of Health)[36]. The Network's activities range from education and awareness campaigns to monitoring of congenital anomalies and research on the use of folic acid supplements.

The Network and the government, recommend that all women of childbearing age who might become pregnant take a minimum supplement at least 0.4mg of folic acid on a daily basis from one month prior to conception and during the first trimester of the pregnancy. For women at higher risk of having infants with NTDs, the daily intakes should be increased up to 4-5mg. A daily consumption higher than usual (e.g. 0.35mg) is also

recommended during the breastfeeding period. Folic acid supplements are fully reimbursed by the state[37,38]. Some ongoing studies are analysing the benefits of recommending increased daily intakes of 0.5mg.

TERMINATIONS

In Italy abortion can be induced until 24 weeks of gestation in public hospitals when there is a congenital anomaly or malformation of the foetus which could seriously affect the woman's psychological or physical health. As a result of continued efforts to prevent unplanned pregnancies, the number of abortions has steadily declined over the past twenty years, having decreased from 17 per 1,000 in 1982 to 9.4 per 1,000 in 2006[39].

According to EUROCAT 45.6% of the pregnancies recorded were terminated because of prenatal diagnosis of an NTD. However it should be noted that one of the five Italian registries does not provide data on termination of pregnancy.

UNPLANNED PREGNANCIES

Various studies suggest that around 60% of pregnancies in Italy are planned[40,41,42].

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

Available data on women's compliance with the recommendations on supplementary folic acid intake are only gathered in some regions and hospitals. The Network estimates that although there is a slight trend in favour of folic acid supplements, few patients and primary care professionals are aware of the correct dosage and timing, in particular during the preconceptional period. Socio-economic and geographical factors play a significant role in explaining the differences in folic acid levels amongst women.

FOOD FORTIFICATION POLICY

There is no official food fortification policy in Italy. Fortification is voluntary, but there is a public debate on the potential benefits of compulsory fortification. Nevertheless, the current expert recommendations are that mandatory fortification seems inappropriate as national NTD-prevalence is not very high[43].

HEALTH EDUCATION INITIATIVES

The Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects has developed general information and awareness campaigns as well as specific educational programmes about the need for folic acid supplements to prevent NTDs. The campaigns are particularly targeted at the younger population and healthcare professionals. The Ministry of Health, the National Centre for Disease Prevention and Control, the National Research Institute for Food and Nutrition, the regional governments and patient organisations also have awareness programmes, under the overall coordination of the Network. Despite these, the level of folic acid intake is still insufficient, and there is a general consensus on the need for continued efforts to raise general awareness of the need for women of childbearing age to supplement their diet with folic acid to prevent NTDs, this need is greatest amongst lower socio-economic groups.

Official data from 2008 reveal that 13.2% of women are still unaware that foetal anomalies can be detected during the pregnancy[44]. In 2008, only 86.6% of women sought prenatal screening to detect the possible occurrence of an NTD.

"Folate supplementation, when done in the right dosage (0.4 - 0.8mg for women without risk and 4 - 5mg for women at higher risk), brings nothing but nutritional and health benefits, specially for childbearing aged women."

Associazione Ginecologi Extra Ospedalieri
(Association of Gynaecologists of Non Hospital Staff)

NEXT STEPS

There are no particular policy measures planned by the government at this stage regarding NTD prevention. The National Healthcare Action Plan 2009 – 2011 is expected to be launched shortly. The Italian Network for the promotion of Folic Acid for the Prevention of Congenital Defects will continue its activities on education, research and monitoring of NTDs.

POLAND

Total birth prevalence NTD	8.61 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	7.58 per 10,000 (source: EUROCAT)
Total birth rate	10.9 per 1,000 (2008) 414,000 live births (source: Eurostat 2008)
Termination of pregnancy	Not permitted. No information available
Unplanned pregnancies	No official information available, planned pregnancies are estimated to be low (10-20%)
Government recommendations	Yes, National Food and Nutrition Institute
Professional recommendations	Yes, Institute of Mother and Child
Recommendation: Amount of folic acid supplements	Daily intake of 0.4mg for all women of childbearing age
Recommendation: Timing of folic acid supplementation	Prior to and during the first weeks of pregnancy
Compliance with recommendations	Data from 2005: 70% take folic acid supplements during the pregnancy. Only 10.6% take folic acid before conception
Food fortification policy	Voluntary
Education initiatives	Yes, Polish Registry of Congenital Malformations and the Institute of Mother and Child
Next Steps	Implementation of the National Plan for diagnosis and treatment of NTDs 2009-2013, focus on education measures and access to screening and early diagnosis

COMMENTARY

Poland has the highest rate of NTD-related deaths in Europe. Since 1997, the government has run educational campaigns targeted at healthcare professionals and women of childbearing age. The government's National Health Programme recognises that it is still necessary to improve general awareness and education about the need to take folic acid supplements to prevent NTDs and, more generally to improve both access to and quality of women's and infants healthcare services.

"Women that live in rural areas are not taking folic acid supplements compared to women in urban areas. Therefore, not all women in Poland have adequate folate before they become pregnant."

Polski Rejestr Wrodzonych Wad Rozwojowych
(PRCM - Polish Registry of Congenital Malformations)

NTD PREVALENCE

The Polish Statistics Department recorded a total number of births of 414,000 in 2008, which corresponds to a birth rate of 10.9%[45]. According to EUROCAT the total NTD prevalence rate is 8.61 per 10,000 births, with a live birth prevalence rate of 7.58 per 10,000. This is the highest live birth prevalence rate compared to the live birth prevalence rate of the other countries examined, in this report.

Data from the Polish Registry of Congenital Malformations reveal that NTDs occur in 1.15 to 2.0 infants per 1,000 newborns, equivalent to between 350 and 700 newborns per year[46]. The mortality rate for infants with NTDs is very high: 34% of infants born with NTDs die, the highest rate in Europe. Most of the cases occur in the Eastern part of the country. It is also significant that 95% of NTD cases occur in women without prior history of NTDs in the family[47].

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The Ministry of Health drives the development and implementation of the health agenda in Poland[48]. Since 2004, the regions have also been involved in the implementation of healthcare policies. In 2009 the government approved a reform aimed at improving the Polish public health system and patient access to healthcare, which appeared to be undermined by poor funding[49].

Women's health has traditionally not been among the main health priorities of the government. Experts and patients have highlighted the need to improve reproductive health counselling and services. The National Health Programme 2007-2015 aims at improving women's access to screening and early diagnosis services during pregnancy[50].

In 2008, the government announced plans to create a committee responsible for developing health standards on infant health and related issues[51]. More recently, the National Plan for diagnosis and treatment of NTDs 2009-2013, published by the Ministry of Health, recognised the need to improve women and newborn's health as well as health education to prevent NTDs[52].

The government recommends that all women of childbearing age take a 0.4 mg daily supplementation of folic acid prior to and during the first weeks of pregnancy. A diet rich in folic acid is also recommended by health professionals.

TERMINATIONS

Abortion is illegal in Poland except in cases where the pregnancy constitutes a risk to the life or health of the pregnant mother or in cases where medical evidence indicates a high probability of severe and irreversible disability in the foetus[53] or an incurable or terminal illness; or if the pregnancy results from a crime. Despite these rules, patient associations have denounced persistent obstacles to access abortion in the above mentioned circumstances, which can be evidenced by the fact that in a country with almost 10 million women of reproductive age, there were only 124 recorded abortions undertaken in 2001.

There is no available data about the number of terminations linked to NTDs.

UNPLANNED PREGNANCIES

There are no reliable data available on the percentage of pregnancies that are unplanned in Poland. They are however estimated to be very high due to poor counselling services on family planning and reproductive health. The National Sanitary Inspectorate suggests that 50% of pregnancies in Poland are unplanned[54].

The EUROCAT 2005 report estimates that only 10% - 20% of pregnancies are planned, indicating that up to 90% are unplanned.

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

Data from the Polish Registry of Congenital Malformations in 2005 suggest that 70% of women took folic acid during their pregnancy, while only 10.6% did it before conception. This represents an increase compared to data from 2003, when 64% of women were found to take folic acid supplements during the pregnancy and 5.5% prior to becoming pregnant. Women living in rural areas and/or with lower education do not follow the recommendations for supplementary folic acid intakes[55].

FOOD FORTIFICATION POLICY

There is no compulsory food fortification policy in Poland. An expert group set up by the Ministry of Health in 2006 recommended fortifying selected types of flour with folic acid as well as promoting folic acid supplements for women of childbearing age by targeted educational measures[56]. The government and the National Food and Nutrition Institute recommend 0.4mg supplementary folic acid intakes daily to all women before and during pregnancy[57]. In recent years experts have discussed increasing the recommended daily intake up to 0.8 mg as well as extending the recommended timing to include the entire nine months of pregnancy. A diet rich in folic acid is currently also recommended.

"It is recommended that folic acid is not only used by women during pregnancy, but by all women who may get pregnant."

Instytut Matki i Dziecka **(Institute of Mother and Child)**

HEALTH EDUCATION INITIATIVES

From 1997 to 2007, the government's NTDs Primary Prevention Programme ran a campaign directed at healthcare professionals, women of childbearing age and the young population, aimed at disseminating information about the need to take folic acid supplements before and during the pregnancy in order to prevent NTDs[58]. The 2009-2013 National Plan for diagnosis and treatment of NTDs stressed the need to strengthen health education initiatives with this aim.

NEXT STEPS

The National Plan for diagnosis and treatment of NTDs 2009-2013 is being implemented. Over the next two years, the implementing measures are expected to focus on the improvement of access to screening and early diagnosis services. Educational and awareness raising campaigns are also expected to be reinforced.

Since 2008, the Government has been considering plans to create a special committee with the involvement of medical experts, which would be responsible for developing medical guidelines and protocols on healthcare during the pregnancy and the delivery.

The financial constraints on the Polish health system may undermine effective implementation of the above mentioned plans.

SPAIN

Total birth prevalence NTD	6.81 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	4.27 per 10,000 (source: EUROCAT)
Total birth rate	11.4 per 1,000 inhabitants 519,000 newborns in 2008 (source: Eurostat 2008)
Termination of pregnancy	24.4% of the pregnancies were terminated because of prenatal diagnosis of an NTD (source: EUROCAT)
Unplanned pregnancies	No reliable data available, estimated 12.1% of women aged between 14 and 29 in 2008, compared to 9.9% in 2004
Government recommendations	Yes
Professional recommendations	Yes, Spanish Society of Gynaecology and Obstetrics (SEGO), Spanish Society of Family and Community Medicine (SEMFYC), Spanish Society of General Practitioners (SEMG)
Recommendation: Amount of folic acid supplements	Daily intake of 0.4mg for all women and 4mg for women at high risk of having infants with NTDs due to previous NTD-affected pregnancy.
Recommendation: Timing of folic acid supplementation	1-2 months prior to and during the first 3 months of pregnancy 2 months prior to conception for women at risk of having an infant with NTDs
Compliance with recommendations	The majority of pregnant women take folic acid supplements (71%), but only 10-20% take it before conception
Food fortification policy	Voluntary
Education initiatives	Ministry of Health and some regions
Next Steps	Adoption of a framework strategy on sexual and reproductive health and education and related legislation

COMMENTARY

Health authorities, experts and healthcare professionals agree that most NTDs can be prevented through folic acid supplements prior to and during the first stages of pregnancy. Health Ministry guidelines on the prevention of birth defects recognise that there is a broad scientific consensus on the benefits of supplementary folic acid intakes in the fight to prevent birth defects and in particular NTDs.

While the majority of women are thought to know that they should take these supplements during their pregnancy, only a minority are aware of the importance of supplementary intakes before conception and in the early weeks of gestation in order to prevent NTDs.

NTD PREVALENCE

In 2008 the birth rate for Spain was 11.4 per 1,000 inhabitants[59]. This represents about 1.38 children per woman, according to 2007 figures[60]. According to EUROCAT data, the total NTD prevalence rate in Spain is 6.81 per 10,000 births, with a live birth prevalence rate of 4.27 per 10,000. The government estimates that there are 320 - 400 newborns with an NTD per year[61].

NTD prevalence has decreased in Spain over the last 20 years. However, scientific studies suggest that this is due to improved prenatal diagnosis of NTDs and consequent pregnancy terminations, rather than the implementation of primary prevention measures (folic acid supplements) which have had limited impact[62].

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The health system in Spain is completely decentralised. The central government, in cooperation with the regional governments, sets up the basic priorities and policy framework strategies, which are further developed and implemented at the regional level according to local needs and their own policy priorities. The areas that have been addressed in this manner include pregnant women and healthcare programmes for newborns[63].

Women and infants' health has traditionally been a priority for the Spanish government. There is an emerging focus on prevention, including promotion of healthy lifestyles, sexual health and education, for which the government is planning to adopt a framework strategy.

The health authorities believe that there is clear scientific evidence that folic acid intake before and during conception can reduce the risk of NTDs by 40% in the case of Anencephaly and by 45% in the case of Spina Bifida[64]. Government guidelines, from 1998 updated in 2001, therefore recommend that women planning a pregnancy or at risk of becoming pregnant take a daily supplement of 0.4 mg of folic acid from 1-2 months prior

to the pregnancy until the third month of pregnancy. Women with one or more risk factors of having an infant with an NTD should take a 4mg daily supplement of folic acid from 2 months prior until the third month of pregnancy. A healthy diet, rich in folic acid is recommended as well. These recommendations are regularly reviewed by the government in cooperation with experts and healthcare professional organisations[65,66].

TERMINATIONS

Abortion is currently allowed in Spain up to 22 weeks after conception in the case of suspected physical or physiological defects of the foetus; serious risk of the physical or physiological health of the pregnant mother; or when the pregnancy was the consequence of a rape. At the time of writing this report, the government had proposed legislation which would have fully reimbursed abortions in these circumstances until the 14th week.

Official data reveal that abortions in Spain increased by 91.5% between 1998 and 2007 when a total of 112.138 abortions were reported. The highest abortion rate was among women from under 20 up to 29 years of age. Data from 2008 estimated that half (49.5%) of the unplanned pregnancies in Spain that year ended with an abortion, which represents a significant increase compared to 2000 (31%)[67,68].

A total of 2.91% of reported abortions were linked to foetal health problems.

According to EUROCAT data, 24.4% of the pregnancies recorded were terminated because of prenatal diagnosis of an NTD; although it should be noted that one of the four registries contributing to EUROCAT at the time did not record termination numbers.

UNPLANNED PREGNANCIES

There are no reliable data available on the percentage of pregnancies that are unplanned.

Official data from 2008 suggest that 12.1% of pregnancies in women aged between 14 and 29 were unplanned, which represents an increase by 2.2% compared to 2004[69].

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

Data from the 2006 Health Ministry guidelines on the prevention of birth defects reveal that the majority of pregnant women take folic acid during their pregnancy, but only 10-20% of women take folic acid before conception. While representing improved compliance, these data nevertheless confirm the need to increase awareness about the importance of taking folic acid supplements prior to pregnancy.

"Folic acid intake is a priority public health issue in Spain, where there is still no official position from the Government. There is also a need to guide the folic acid "market", both with regards to food fortification and vitamin supplements, because it currently does not meet the needs of the population."

Sociedad Española de Nutrición **(SEN - Spanish Nutrition Association) /**
Fundación Española de la Nutrición **(FEN - Spanish Nutrition Foundation)**

FOOD FORTIFICATION POLICY

Spain does not have mandatory rules on food fortification.

HEALTH EDUCATION INITIATIVES

In 2001[70], when the government updated its recommendations on folic acid supplements, it also acknowledged the need to improve dissemination of information by the health authorities and professionals. In Spain, primary healthcare professionals are responsible for providing women with the relevant information. A professional study from 2002 also highlighted the need for public authorities and medical practitioners to implement intensive awareness raising campaigns about the need for folic acid supplements prior to conception in order to prevent NTDs[71]. The Ministry of Health updated its guidelines on the prevention of births defects in 2006[72]. Some regions implement educational programmes on this topic.

Healthcare professional organisations also inform medical practitioners and the general public about the folic acid recommendations[73,74].

NEXT STEPS

The Spanish government is expected to adopt a framework strategy on sexual and reproductive health. The strategy, which will be reviewed every five years, seeks primarily to reduce the number of unplanned pregnancies. It will also include educational measures on general reproductive health focused on targeting the younger population. Unfortunately, no particular measures on the prevention of NTDs are planned at this time.

SWEDEN

Total birth prevalence NTD	No EUROCAT data available
Live birth prevalence NTD	No EUROCAT data available
Total birth rate	11.9 per 1,000 inhabitants 109,000 newborns (source: Eurostat 2008)
Termination of pregnancy	No EUROCAT data available
Unplanned pregnancies	Unplanned pregnancies are estimated to be high (50-75%)
Government recommendations	Yes, National Food Administration and National Board of Health and Welfare
Professional recommendations	No
Recommendation: Amount of folic acid supplements	Daily intake of 0.4mg for all women aged between 18-45 year olds Daily intake of 4-5 mg for women at risk
Recommendation: Timing of folic acid supplementation	One month prior to and first three months after conception
Compliance with recommendations	No information available
Food fortification policy	Voluntary
Education initiatives	Yes, National Food Administration and National Board of Health and Welfare
Next Steps	Implementation of targeted educational and information campaigns by the National Food Administration and National Board of Health and Welfare

COMMENTARY

In order to reduce NTDs and the number of abortions linked to unplanned pregnancies in Sweden, the national government aims to strengthen education campaigns to encourage all women aged between 18 and 45 year olds to take daily supplements of folic aid.

"NTDs are the second most common foetal damage following congenital heart disease. For RBU members who represent the spina bifida-group it goes without saying that we are wholeheartidly in favour of a daily extra intake of folic acid, minimum one month before conception and three months into pregnancy. We are also in favour of mandatory flour fortification."

Riksförbundet för Rörelsehindrade Barn och Ungdomar
(RBU, National Association for Disabled Children and Youths)

NTD PREVALENCE

Government data from the 2009 annual health state report, based on NTD figures from 2003 – 2006, indicates that 20 – 25 children are born with Spina Bifida each year. It states that the number of pregnancies affected by Spina Bifida is judged to have stayed at around the same level since the early 1970's. In 2007 the Swedish registry of birth defects recorded a total NTD birth prevalence rate of 10 per 10,000; there were 102 reported cases of NTD. Of these the majority of pregnancies were terminated following detection via ultrasound. The National Food Administration believes that the prevalence in the last few years has averaged at 12 – 15 children born with Spina Bifida each year.

In 2008 the birth rate in Sweden was 11.9 births per 1,000 inhabitants[75].

There is no available EUROCAT data on only NTDs for Sweden, for the period covered by this report. Available data in the EUROCAT 2005 report does not distinguish between NTDs and NTDs excluding chromosomal anomalies.

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

Women and newborn's health rank relatively low on the health policy agenda, as Sweden has one of the best neonatal care systems in the world[76]. Over the last few years the Ministry of Health has focused on prevention of unplanned pregnancies in order to reduce abortions[77].

To prevent NTDs the government recommends that all women of childbearing age take a 0.4mg daily supplementation of folic acid from one month before conception and during the first months of pregnancy, except for women with a diet highly rich in folic acid such as vegetarians. A diet rich in folic acid is recommended during the whole pregnancy.

Higher daily folic acid intakes of 4-5mg are recommended to women who have already had an infant with an NTD, or have an increased need for folic acid due to a concurrent disease or medication.

TERMINATIONS

Induced abortion is legal up to 18 weeks of gestation on request of the pregnant woman. An ethical committee at the National Board of Health and Welfare may allow induced abortion until the 22nd gestational week on the basis of particular medical and social circumstances.

Estimates suggest that each year 80 abortions are carried out on foetuses with Spina Bifida.

UNPLANNED PREGNANCIES

There are no official data about the percentage of unplanned pregnancies in Sweden. Estimates indicate that the rate could be similar to that in Norway; where between 50-75% of pregnancies are unplanned[78]. The Swedish government is currently addressing how to reduce the number of unplanned pregnancies across the country.

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

There are no reliable data available about the percentage of women who take folic acid supplements before and during pregnancy in order to prevent NTDs. Sources suggested that no more than 25% of women in Sweden respect the folic acid recommendations and that there are wide variations in compliance corresponding to women's level of education.

FOOD FORTIFICATION POLICY

Food fortification is currently voluntary in Sweden. Compulsory food fortification for the whole population was assessed as inappropriate in the absence of sufficient scientific evidence about its potential link to increased risk of cancer[79,80]. Recently, some experts have however called on the National Board of Health and Welfare to reconsider mandatory flour fortification as a means of reducing NTD incidence.

HEALTH EDUCATION INITIATIVES

The National Food Administration and the National Board of Health and Welfare are developing information and education campaigns aimed at encouraging women to take supplements of folic acid in order to prevent NTDs.

In addition to this, in 2007, the National Food Administration planned to send an annual letter to all women aged between 18 and 45 years old, containing information about the need to take folic acid supplements to prevent NTDs such as Spina Bifida, alongside the free provision of folic acid supplements. However, this never materialised due to lack of funds. As a result there continues to be no targeted education measures in place to promote folic acid intake.

"According to a survey conducted by Livsmedelsverket in 2008, only 48 percent of Swedish women believe that folic acid intake for women of childbearing age is important. There is a clear need to increase the knowledge of the importance of having a diet with plenty of folate rich foods and taking supplements with folic acid at least one month before pregnancy, and at Livsmedelsverket we want to incorporate this into our long term communication goals."

***Livsmedelsverket* (The National Food Administration)**

NEXT STEPS

There is currently no further policy measure planned on the prevention of NTDs and/or folic acid supplements. The National Food Administration and the National Board of Health and Welfare are expected to develop and implement educational and information campaigns targeted at women and healthcare professionals.

"Despite all information efforts, no more than 25 percent of pregnant Swedish women take folic acid supplements. It is especially hard to convey the information to women with lower education."

***Socialstyrelsen* (The National Board of Health and Welfare)**

UNITED KINGDOM

Total birth prevalence NTD	15.83 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	2.24 per 10,000 (source: EUROCAT)
Total birth rate	12.9 per 1,000 inhabitants 794,000 newborns (source: Eurostat 2008)
Termination of pregnancy	78.25% of the pregnancies were terminated because of prenatal diagnosis of an NTD (source: EUROCAT)
Unplanned pregnancies	Estimated 40%
Government recommendations	Yes, Ministry of Health since 1992
Professional recommendations	Yes, Association for Spina Bifida & Hydrocephalus (ASBAH)
Recommendation: Amount of folic acid supplements	0.4 mg per day; 5 mg per day if previous NTD complication
Recommendation: Timing of folic acid supplementation	Before pregnancy and until 12 weeks afterwards
Compliance with recommendations	38% of women respected guidelines (1998)
Food fortification policy	Food Standards Agency recommendation voluntary
Education initiatives	Currently, no
Next Steps	With the FSA recommendation set to be reconfirmed, the question of mandatory food fortification is back on the agenda of the UK government.

COMMENTARY

The Department of Health (DoH) and the National Health Service (NHS) provide advice for women seeking to get pregnant, specifically outlining the importance of folates for the development of the baby. However, there is little outreach activity at present and it is acknowledged that women in groups that are most likely to suffer from low levels of folate continue to still be at risk. The relatively high rate of unplanned teenage pregnancies presents an additional challenge in this area. Compulsory food fortification with folic acid has been recommended by the Food Standards Agency (FSA) but was put on hold pending further scientific review.

"Although there is an increased awareness about the link between folate levels and the developments of NTDs in the UK, unfortunately a lot of women of childbearing age with their first pregnancy remain unaware of the importance of adequate folate levels"

Royal College of Midwives (RCM)

NTD PREVALENCE

The total prevalence rate of NTDs in the UK is 15.83 per 10,000 births, with a live birth prevalence rate of 2.24 per 10,000 births (according to EUROCAT data over the period 1991 – 2002).

The UK saw a sharp reduction in NTD prevalence after the introduction of periconceptional folic acid policies in the early 1990s. In 2007, in England and Wales there were 1.2/10,000 live male births and 1.4/10,000 live female births with an NTD[81]. In total in 2007 in England and Wales there were 52 live births, 19 stillbirths and 294 abortions coded as an NTD[82].

To put this prevalence rate in context it should be noted that the UK also has a high birth rate at 12.9 per 1,000 inhabitants, representing some 794,000 births each year, according to Eurostat.

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The NHS provides specific advice to women seeking information on food and nutrition prior to and during their pregnancy[83]. It recommends that women take folic acid to help in the development of the foetus[84]. This includes the Department of Health recommendations that women should take a daily supplement of 0.4mg of folic acid "while they are trying to conceive and should continue taking this dose for the first 12 weeks of pregnancy"[85]. Women who have previously had a baby with an NTD are advised to take a higher dose of folic acid, on advice from their doctor. Eating foods that are rich in folic acid is also recommended.

Food issues, nutrition and vitamins fall under the scope of the government's Food Standards Agency. In May 2007 the FSA Board agreed unanimously that 'mandatory fortification' with folic acid would be introduced

alongside controls on voluntary fortification and advice on the use of supplements.

TERMINATIONS

Abortion has been legal since 1967[86] in Great Britain. (The situation in Northern Ireland is ambiguous). The general law authorises abortions if two doctors agree to it, and that it takes place during the first 24 weeks of pregnancy. However, in the case of foetal abnormalities, there are no time limits on the termination of pregnancies[87].

EUROCAT data shows that, from 1991 – 2002, 78.25% of the pregnancies recorded were terminated because of prenatal diagnosis of an NTD.

UNPLANNED PREGNANCIES

Teenage pregnancies are a particular challenge for British healthcare and for the risk of NTDs. The UK has the highest rate of teenage pregnancies in Western Europe and in the developed world is second only to the United States.

An estimated 60% of total pregnancies are thought to be planned, indicating that 40% are unplanned.

FOLATE LEVELS IN WOMEN OF CHILDBEARING AGE

A number of studies undertaken in the UK have shown that while the majority of women know something about the protective effect of folic acid, fewer than half of them take it prior to conception. Uptake is lower among young women, smokers, those with less formal education, of lower social class, or from ethnic minorities[88].

According to the Scientific Advisory Committee on Nutrition (SACN) and the 2006 report[89] from its Folate Subgroup, although average daily folate intakes were above the recommended nutrient intake (RNI) in all age groups, there was some evidence of marginal folate status in young women and people aged 65 years and over. That report however also noted the clear evidence that increasing folate intake would reduce the number of NTD-affected pregnancies, and recommended that flour should be fortified with folic acid.

FOOD FORTIFICATION POLICY

Food fortification seems to be high on the political agenda in the UK. The FSA and key stakeholders including the Association for Spina Bifida and Hydrocephalus (ASBAH), Birth Defects Foundation (BDF Newlife) and the National Childbirth Trust all support an increase in folate intake by women. No binding rules have yet been introduced. Some foods, such as breakfast cereals and spreads, are already fortified with folic acid and other vitamins and minerals. In 2007, after an open consultation, the FSA Board agreed unanimously that 'mandatory fortification' with folic acid should be introduced, alongside controls on voluntary fortification and advice on the use of supplements. However, this recommendation was not implemented because the government's Scientific Advisory Committee on Nutrition was waiting to review the results of a number of ongoing trials looking at any potential negative effects of folic acid intake among all age groups[90].

After appraising scientific data on the potential negative effects of folic acid supplements, the SACN concluded[91] that the new evidence does not change their previous recommendation for the introduction of mandatory fortification with folic acid. In a letter of 9 October 2009[92] the FSA informed the UK's Chief Medical Officer of its intention to reconfirm its 2007 recommendation in support of mandatory food fortification.

"The best approach to reach the right levels of folate in women of childbearing age is a combined approach of food fortification and folic acid supplements. Food fortification in itself is not enough to increase folate levels in order to reduce NTDs."

Association for Spina Bifida and Hydrocephalus (ASBAH)

HEALTH EDUCATION INITIATIVES

The NHS "Healthy Start" initiative provides vouchers to low-income families to buy fresh fruit, fresh vegetables, milk and vitamins, including folic acid[93].

The FSA website "Eat well, be well"[94] provides advice on which foods to eat and which foods to avoid during pregnancy. It contains sections on the facts behind food issues, including folic acid fortification. With regard to folic acid, the FSA recommends that in order to reduce the risk of NTDs, women should ensure a "daily intake of 400 micrograms (mcg) of folic acid supplements from the time a woman stops using contraception until the twelfth week of pregnancy". It also recommends that women eat the following foods which contain folate (the natural form of folic acid): green vegetables and brown rice, fortified bread and breakfast cereals. If folic acid is taken as a supplement that contains other vitamins, it recommends making sure that 400mcg of folic acid is in the supplement and that it does not contain Vitamin A.

The last major awareness campaign about NTDs ran from 1995 to 1998 and was led by the now defunct Health Education Authority (HEA)[95]. The department of Health was expected to run an awareness campaign aimed at the hard to reach and high risk groups of women. However no evidence of this campaign was found during the research.

A number of patient organisations focus on raising awareness and support for those affected by Spina Bifida and other birth defects in the UK.

NEXT STEPS

The results of a trial into whether the intake of Inositol, another vitamin, will prevent NTDs are awaited. In February 2009, the Institute of Child Health in London and the Great Ormond Street Hospital announced that they were conducting clinical trials into the prevention of NTDs by Inositol (the PONTI study)[96]. The trials look into why folic acid intake in some women has no effect in preventing NTDs. Instead, it is conducting research into whether taking Inositol will help prevent NTDs which cannot be prevented by folic acid. The trials are conducted on women who have experienced a pregnancy involving an NTD and are planning a further pregnancy.

Stakeholders interviewed for this report believe that the government could do much more to promote awareness about the benefits of folic acid supplements because previous campaigns, notably by the FSA, have not reached all the potentially affected women.

The FSA has reconfirmed its recommendation to progress to mandatory food fortification, this issue has now moved into the political arena and is due to be discussed by the national Parliament.

EU OVERVIEW

Total birth prevalence NTD	9 per 10,000 (source: EUROCAT)
Live birth prevalence NTD	4.17 per 10,000 (source: EUROCAT)
Total birth rate	EU27 was 10.9 per 1,000 inhabitants 5.4 million children born in EU27 (source: Eurostat 2008)
Termination of pregnancy	48.2% of the pregnancies were terminated because of prenatal diagnosis of an NTD. Note, not all registries record terminations (source: EUROCAT)
Unplanned pregnancies	Varies widely, although in most European countries more than 50% are unplanned
Government recommendations	All countries covered by this report with the exception of Germany have government recommendations EU Communication on Rare Diseases recognises NTDs as preventable rare disease through folic acid supplements
Professional recommendations	All countries covered by this report with the exception of Sweden and France have professional recommendations. The European Association of Perinatal Medicine has issued recommendations urging women to take folic acid supplements before pregnancy
Recommendation: Amount of folic acid supplements	N/A
Recommendation: Timing of folic acid supplementation	N/A
Compliance with recommendations	EUROCAT reports low compliance
Food fortification policy	Voluntary. Safe upper limit of folic acid in food supplements and food set by EU wide legislation
Education initiatives	N/A
Next Steps	Spanish Presidency (January – June 2010) has identified correcting health inequalities as its health priority. National Rare Disease Action Plans to be developed by all 27 Member States

COMMENTARY

The European Union's role in the area of health is to encourage cooperation between the member states and if necessary, to support their actions, as set out in Article 168 of the Treaty on the Functioning of the European Union (more commonly known as the Lisbon Treaty, which entered into force on 1st December 2009)[97]. NTDs fall under the category of 'rare diseases' referring to diseases where there are a limited number of patients and scarcity of relevant knowledge and expertise exist, and where the European Commission, acting for the EU as a whole, can provide a high level of added-value. The existing definition of rare diseases in the EU was adopted by the Community action programme on rare diseases 1999-2003 as those diseases presenting a prevalence of not more than 5 per 10,000 persons in the European Union.

There are also some key organisations which are active in the area of birth defects at the European and international level. These include: the International Federation for Spina Bifida and Hydrocephalus (IF)[98], the European Organisation for Rare Diseases (EURORDIS)[99], and the Health and Environment Alliance (HEAL)[100].

NTD PREVALENCE

Data on prevalence of NTD-related births are difficult to compare given the variations in registries which contribute to EUROCAT country by country. EUROCAT covers 16 of the EU member states plus other European countries including Croatia, Norway, Switzerland and the Ukraine. The total birth prevalence rate of NTDs is 9 per 10,000 births. The live birth prevalence rate across Europe is 4.17 per 10,000 births.

Average of data collected 1980-2002 for all NTDs	All EUROCAT Registries
Total Prevalence	9
Live birth Prevalence	4.17
Cases	13,180
Live births	5,529 = 41.9%
Foetal deaths	1,292 = 9.8%
Termination of pregnancy because of prenatal diagnosis of NTD*	6,359 = 48.2%

*not all registries recorded terminations

POLICY FRAMEWORK & RECOMMENDATIONS ON FOLIC ACID SUPPLEMENTATION

The second EU public health action programme covering the period 2008-2013[101] includes calls for action on the prevention of rare diseases, nutrition and sexual health. In November 2008 the Commission issued its Communication on Rare Diseases: Europe's Challenges[102] in which it recognised NTDs as one of the few preventable rare diseases and cites the prevention of NTDs through the intake of folic acid supplements as an example of possible primary prevention. The Communication goes on to say that "Action in this field should be the topic for a debate at EU level led by the Commission aiming to determine for which rare diseases primary preventive measures may be successful."

"At EU level, we should make an offer to all pregnant women to have a scan for NTDs."

European Board College of Obstetrics and Gynaecology (EBCOG)

On 9 June 2009 the EU's Council of Ministers approved a Recommendation "on action in the field of rare diseases"[103] which endorses the communication and signals reinforced cooperation and an intensification of EU efforts to combat rare diseases. By approving the Recommendation, all 27 EU health ministers called for a more coherent strategy to deal with rare diseases covering common definitions and inventories, research, the creation of centres of expertise across Europe and the gathering of expertise at EU level.

In an earlier but slightly broader European initiative, EU and Norwegian health ministers in 2004 issued a "Common statement of representatives of national food safety agencies and institutions involved in nutrition"[104] which highlights salt, folic acid and obesity as three priority issues. The signatories recognised the importance of folic acid as a means to prevent NTDs, the fact that women of childbearing age with bad nutritional status are at higher risk and that it is difficult to achieve the recommended 400 micrograms of folic acid through diet.

"It should be mandatory for any doctor to discuss the topic of folic acid with women who want to get pregnant."

European Board College of Obstetrics and Gynaecology (EBCOG)

Governments in six of the seven countries covered by this report (France, Italy, Poland, Spain, Sweden, and UK) have issued recommendations to women of childbearing age to take a daily supplement of 0.4mg of folic acid. Many of these countries also have professional guidelines and official education initiatives to raise awareness about NTDs being a preventable condition.

The European Association of Perinatal Medicine (EAPM) advises women of childbearing age to take folic acid supplements before pregnancy; women with no prior history of NTDs should take 0.4mg while women with a prior history should take 4.0mg[105]. The EAPM has published instructions to doctors to provide advice on folic acid intake.

Outside the EU framework, WHO Europe is promoting policy and programmes to protect the health of mothers and newborn children[106]. These programmes address the importance of folic acid and vitamin B supplements in the context of the WHO guidelines on the feeding and nutrition of infants and young children[107].

COMPLIANCE WITH RECOMMENDATIONS

Only a minority of women actually follow existing recommendations and take folic acid supplements during the advised period. EUROCAT found that the countries with the highest uptake rates were those where education campaigns to raise awareness accompanied the recommendations.

DATA COLLECTION

Created in 1979, the European Surveillance on Congenital Anomalies (EUROCAT)[108] is a European Network of population-based registries for the epidemiologic surveillance of congenital anomalies. Funded under different Community Health Programmes, since 2004 EUROCAT has been funded through the Public Health Programme of the European Commission's DG SANCO[109]. The registries currently contributing to EUROCAT represent 29% of births in Europe.

TERMINATIONS

All EU member states except Ireland and Malta authorise abortions in the case of foetal abnormalities, although the situation in Northern Ireland is ambiguous[110]. The gestational limit for abortions in the case of 'non-lethal' foetal anomalies is 24 weeks, but several countries including France, Germany and the UK have no limit. In the case of 'lethal anomalies" many countries have no gestational limit.

48.2% of NTD-affected pregnancies recorded in Europe between 1980 and 2002 were terminated, however not all registries contributing to this data record terminations.

UNPLANNED PREGNANCIES

Only where pregnancies are planned, can government education campaigns and guidelines have their optimum impact. But as the table below shows, a significant percentage of pregnancies are unplanned in many countries such as in Ireland, Poland, Portugal and Switzerland; in Italy and Malta there are simply no figures. These statistics should help shape government policies so that currently non-targeted women do have access to necessary information about the benefits of folic acid.

Available data on the proportion of pregnancies which are thought to be planned varies widely between countries in the EU and in addition it is difficult to assess due to the differing definitions of "unplanned"; the reality is that many studies are undertaken amongst women who have recently given birth and so do not include those pregnancies which are terminated and are often based on estimates or very limited data. For example when EUROCAT examined the situation in 2005 (see table below), there was no reliable information available for 6 of the 15 countries looked at.

Overall for Europe, in most countries more than 50% of pregnancies are said to be unplanned. According to an analysis of 19 studies published in the International Journal of Obstetrics and Gynaecology, the number of unplanned pregnancies ranged from 10% to 78%[111].

Country	Proportion of pregnancies thought to be planned[112]
Austria	No information
Belgium	No information
Croatia	75% in one small study
Denmark	68% of ongoing pregnancies in one small study
Finland	37%-86% depending on definition of planned
France	No information
Germany	65-70% in a number of studies
Ireland	40-45 %
Italy	No information
Malta	No information
Netherlands	Estimated at 85%
Norway	Estimated at between 50 – 75%
Poland	Estimated at between 10 – 20%
Portugal	Thought to be low
Spain	No information
Sweden	Estimated at between 50 – 75%
Switzerland	Estimated to be very low
UK	Estimated at 60%

"There are many measures on a population and individual level that could now, or after more research, reduce the risk of congenital anomalies arising in the first place - ie, primary prevention. These interventions involve nutrition (eg, folic acid supplementation or fortification); prevention of maternal infection and disease (rubella vaccination, periconception care for women with epilepsy or diabetes, avoidance of teratogenic drugs); controlling of chemical exposures from occupational and environmental sources; and special action on pregnancy exposure for major health determinants such as smoking, alcohol, and obesity.The recent EU communication regarding European action on rare diseases emphasises the need for primary prevention in its true sense. Avoiding confusion in terminology will help us put this recommendation into practice."

Dolk, H. and on behalf of the EUROCAT Project Management Committee 2009, "What is the "primary" prevention of congenital anomalies?", Lancet, vol. 374, no. 9687, p. 378

FOOD FORTIFICATION POLICY

In recent years, the European Commission and its scientific bodies have encouraged debate among EU governments and scientific bodies over the benefits of taking folic acid supplements. While voluntary food fortification can be mandated at EU level, compulsory fortification measures can only be decided at national level. The EU Directive on food supplements[113] and the EU Regulation on voluntary food fortification[114] establish the maximum amounts of vitamins and minerals that may be added to food supplements and, respectively, to foods. There is no mandatory folic acid fortification in the EU Regulation due to the lack of consensus among the member states on the positive effects of staple food fortification in preventing NTDs.

"There is a clear link between family planning and pre-conceptional health promotion."

European Society of Contraception and Reproductive Health (ESC)

In 2008, the European Food Safety Agency (EFSA) established a Scientific Cooperation Working Group

"The reality of unplanned pregnancies and need for pre-conceptional folate intake points to the important link between contraceptive and pre-conceptional counselling to prevent birth defects."

European Society of Contraception and Reproductive Health (ESC)

(ESCO WG) on "Analysis of risks and benefits of fortification of food with folic acid"[115]. The Working Group was asked to review current practice in member states regarding the level of voluntary fortification of foods with folic acid, and consider new evidence regarding potential risks of high intakes of folic acid for all population groups. *(Note, in November 2009 the ESCO WG adopted its report[116] which concluded that "current data are insufficient to allow a full quantitative risk assessment of folic acid and that scientific developments within this area should be closely monitored").*

All the countries in this report have considered introducing mandatory fortification of a staple food (usually flour) with folic acid, but none have introduced such rules, most often due to continuing uncertainty around potential risks. Voluntary fortification (usually of breakfast cereals) is common.

"Policies in Europe should recognise the proven health benefits of folate levels in preventing NTDs. All women of childbearing age should have enough daily folate to prevent NTDs. Fortification of staple foods with folic acid is a good strategy to provide a base level of folate, however, women planning a pregnancy must take additional folic acid supplements to ensure they receive 400mcg per day."

International Federation for Spina Bifida and Hydrocephalus (IF)

NEXT STEPS

Although the European Union's role will now be mostly supportive of action at national level, the Council's 2009 Recommendation on Rare Diseases signals an intensification of EU efforts to combat diseases like NTDs. By 2013, the Commission must issue a report on implementation of the Recommendation.

In the meantime in line with the Commission's 2008 Communication on rare diseases the EU will set up an EU Advisory Committee on Rare Diseases (EUACRD) to aid in the implementation of the Communication; this Committee replaces the current EU Rare Diseases Task Force and should be set up by the end of 2009. (*Note, EUACRD was established by a Commission decision on 2 December 2009*). It also confirmed the organisation of a European Rare Diseases day in February every year; the first day took place in 2008, and the third is scheduled for 28 February 2010. The Communication also called for European conferences to raise the awareness of professionals and the general public about rare diseases, and on 13-15 May 2010, the 5th European Conference on Rare Diseases will take place in Krakow (Poland).

CONCLUSIONS

Despite the high level of collective understanding about NTDs and their cause, this report reveals that any significant progress to reduce their incidence is lacking. Since up to 70% of all NTDs are fully preventable, this situation is particularly tragic whether looked at from an emotional or medical viewpoint, or from that of individuals, and society as a whole, affected by this preventable condition.

There are however many reasons for optimism, including broad recognition of the need to improve NTD prevention, a consensus with regard to both the causes and ways to prevent NTDs and the scope for major reductions in prevalence. But the sad fact remains: for over ten years professional bodies and many public authorities have acknowledged that folic acid supplements could reduce up to 70% of NTD cases but progress has been disappointing.

Experience indicates that education campaigns to raise awareness and support for existing recommendations have improved compliance, but EUROCAT reports that these campaigns simply have not had as much impact as hoped for or as needed. As a result, some countries have reviewed the question of mandatory food fortification, but no country in this survey has yet taken action. In fact to the best of our knowledge no country anywhere in Europe has introduced mandatory food fortification.

Today much of the discussions now underway to improve the combat against NTDs appear to focus on food policy and nutrition while health fora are not prioritising the condition. In our research, we found willingness and indeed eagerness among stakeholders for further discussion and further exchange of information, knowledge and experience. All this could be coordinated under the auspices of the EU Recommendation on Rare Diseases.

The facts confirmed by this report are well known:

- The majority of women in the countries surveyed are still not taking folic acid supplements prior to conception or during the first weeks of pregnancy.
- While there has been a decrease in the rate of live births with NTDs in recent years, this reflects improved prenatal screening and subsequent medical termination of pregnancies. It is not an indication of progress in NTD prevention.
- Although not fully reported in many countries, the abortion rate for NTD-related foetuses is as high as 78% in some countries. The psychological burden related to the termination of these pregnancies can not be underestimated.
- Awareness of the risk of an NTD-affected pregnancy remains low among all women prior to their first pregnancy. This is particularly true among women of lower socio-economic status.
- Significant numbers of pregnancies in Europe are not planned – in some countries this is more than 50%. This is a common cause of concern for many countries in Europe and is a vitally important factor in the incidence of NTDs. If a woman is not planning her pregnancy, then she does not plan to ensure she has adequate folate levels (through folic acid supplements, fortified foods or by any other means).
- NTDs are more common among younger women, and women of a lower socio-economic class with a lower level of formal education. Combined with the factors above, these women seem less likely to be responsive to education campaigns.

Against this background, some of the countries surveyed are considering the introduction of mandatory food fortification programmes to ensure that all women of childbearing age have adequate folate levels. But our analysis suggests that there is a need for a renewed focuss to eliminate NTDs in Europe.

OUR RECOMMENDATION: A RENEWED FOCUS

The neural tube should close within the first 28 days after conception. Folic acid supplements beyond this period may still be helpful for other reasons, but will not help reduce the incidence of NTDs. Even knowledgeable stakeholders do not always fully recognise the implications of this timing: many women may not know that they are pregnant before it is too late to increase their folate levels.

Most national guidance confirms that doctors advise women to take folic acid supplements at their first visit. But this is too late, if in some countries more than 50% of all pregnancies are unplanned, because these women have not been exposed to the necessary

health education material and visit the gynaecologist only after they have missed one menstrual period. At this point it is already too late for folic acid supplements to have any major impact on preventing NTDs. Preconception counselling should be actively promoted in all European countries.

Several countries do indeed advise folic acid supplements prior to conception and most governmental or official recommendations call for the intake of folic acid supplements by women planning a pregnancy. In the majority of countries, this guidance originates with the public body responsible for food policy and is not a priority in the public health arena. But these recommendations do not reach the women who have not either planned their pregnancy or discussed the matter with their doctor. Moreover, national guidance varies in this regard.

There is an essential need to provide the right advice, to the right women, at the right time. This means that all women of childbearing age should be advised of the critical importance of adequate folate levels to prevent up to 70% of NTDs.

There is already consensus in the surveyed countries and globally that adequate folate levels prior to conception prevent the majority of NTDs. There is also consensus that the appropriate level of folic acid supplements is 0.4mg for women of childbearing age, or ten times higher in the case of a prior NTD-affected pregnancy. The authors of this report believe that progress has been disappointing because advice, education and action are not linked closely enough to the at-risk groups or to current medical knowledge.

It is in fact essential that all women of childbearing age improve their folate levels prior to conception, due to the risk of unplanned pregnancy and the fact that the neural tube closes within 28 days after conception.

To achieve this extended reach, initiatives must now focus on promoting the preconception intake of folic acid supplements by women of childbearing age.

This could be achieved in many ways:

- Education in health and reproductive health lessons in schools. Young European women simply do not know about the link between folic acid and NTDs before their first pregnancy and this fact does not appear to be included in the curriculum for health and sex education in schools.
- Governments could send annual letters to women between 18 and 45 years of age, providing information about the need to have adequate folate levels prior to conception in order to help prevent NTDs such as Spina Bifida.
- Some countries report multiple abortions amongst at-risk women. Clinicians should be advised to add folate level counselling to patients in these circumstances.
- Gynaecologists, family planning specialists and other clinicians should be required to advise women about folate levels at every consulting opportunity.
- Nutritional advice remains important. A varied and balanced diet provides natural folate. However, on its own a healthy diet may not provide enough folate.

A FINAL NOTE ON DATA

The starting point for any credible policy, whether at national or European level, lies in consistent and comparable data. But lack of data – comparable or not – is a major weakness in the fight against NTDs. While EUROCAT data on NTD prevalence rates etc is reliable and comparable, the data on other vital aspects of NTD incidence is neither. This is particularly clear with unplanned pregnancies. In today's world of electronic data and digital communications, this is unacceptable. We urge the European Union and its member states to correct this situation.

CONCLUSION IN SUMMARY

Our report results suggest a consensus among EU member states on the need to reduce the NTD incidence and to end the reliance on abortions, and late termination of pregnancies, linked to this largely preventable birth defect. We applaud their efforts so far. However, we conclude that the right advice is NOT reaching the right women at the right time. **We therefore call for a new focus on improving folate levels in all women of childbearing age.** We believe that under the auspices of the Rare Diseases Recommendation and potentially through other policies, Europe could, and should, reinvigorate its efforts to eliminate preventable NTDs by giving the right advice, to the right women, at the right time.

ANNEXES

ANNEX I: ORGANISATIONS INTERVIEWED

EU

- International Federation for Spina Bifida and Hydrocepahlus (IF)
- European Surveillance of Congenital Anomalies (EUROCAT)
- European Midwives Association (EMA)
- European Board College of Obstetrics and Gynaecology (EBCOG)
- European Association of Perinatal Medicine (EAPM)
- European Society of Contraception and Reproductive Health (ESC)

FRANCE

- Centre de Référence Spina Bifida (Spina Bifida Reference Center)
- Association nationale du spina bifida et handicaps associés (ASBH - National Association of Spina Bifida and Related Handicaps)
- Hubert Journel, Key Opinion Leader (KOL)
- Collège national des gynécologues et obstrétitiens français (CNGOF - National College of French Gynaecologists and Obstetricians)

GERMANY

- Bundesinstitut für Risikobewertung (BfR - Federal Institute for Risk Assessment)
- Ludwig-Maximilians - University of Munich, Dr. von Hauner Children's Hospital, Div. Metabolic Diseases and Nutritional Medicine
- Arbeitsgemeinschaft Spina Bifida und Hydrocephalus e.v. (ASBH - Association for Spina Bifida and Hydrocephalus)
- Deutscher Hebammenverband (German Midwives Association)

ITALY

- Associazione Ginecologi Extra Ospedalieri (Association of Gynaecologists of Non Hospital Staff)
- Centro Documentazione sulla Salute Perinatale e Riproduttiva (SaPeRiDoc - Documentation Centre on Perinatal and Reproductive Health)
- Istituto Nazionale di Ricerca per gli alimenti e la Nutrizione (INRAN - National research institute for food and nutrition)

POLAND

- Instytut Matki i Dziecka (Institute of Mother and Child)
- Federacja na rzecz Kobiet i Planowania Rodziny (Polish Federation for Women and Family Planning)
- Polski Rejestr Wrodzonych Wad Rozwojowych (PRCM - Polish Registry of Congenital Malformations)

SPAIN

- Federación de Asociaciones de Matronas de España (FAME - Federation of Midwives Associations in Spain)
- Fundación Jiménez Díaz (Jiménez Días Foundation)
- Sociedad Española de Nutrición (SEN - Spanish Nutrition Association)/ Fundación Española de la Nutrición (FEN - Spanish Nutrition Foundation)

SWEDEN

- Livsmedelsverket (National Food Administration)
- Socialstyrelsen (National Board of Health and Welfare)
- Svensk Förening För Obstetrik & Gynekologi (SFOG - Swedish Society of Obstetrics and Gynaecology)
- Riksförbundet för Rörelsehindrade Barn och Ungdomar (RBU - National Association for Disabled Children and Youths)

UNITED KINGDOM

- Association for Spina Bifida and Hydrocephalus (ASBAH)
- University College London Institute of Child Health
- Royal College of Midwives (RCM)

ANNEX II: ABOUT THE PARTNERS

INTERNATIONAL FEDERATION
FOR SPINA BIFIDA AND HYDROCEPHALUS

INTERNATIONAL FEDERATION FOR SPINA BIFIDA & HYDROCEPHALUS

The International Federation for Spina Bifida and Hydrocephalus (IF) is the world-wide umbrella organisation (INGO) for Spina Bifida and Hydrocephalus organisations. It was created in 1979 by national organisations of people with these impairments and their parents. Today IF's membership consists of 38 regional and national umbrella organisations for Spina Bifida and Hydrocephalus; IF has intensive contact with regional and national organisations in over 50 countries, spread over five continents.

The mission of IF is to improve the quality of life of people with Spina Bifida and Hydrocephalus throughout the world and to decrease the prevalence of Spina Bifida and Hydrocephalus by primary prevention.

www.ifglobal.org

Bayer HealthCare

WOMEN'S HEALTHCARE DIVISION; BAYER SCHERING PHARMA AG

Building on almost 100 years of expertise, Bayer Schering Pharma is today a leading provider in women's healthcare. We focus on three key areas: contraception, menopause management and gynaecological therapies.

Bayer Schering Pharma is one of the ten largest specialty pharmaceutical companies in the world. We market our products in more than 100 countries, and in 2008 generated sales of over €10.7 billion.

Approx. 38,000 members of staff currently work for Bayer Schering Pharma worldwide – more than 5,600 in research and development alone. We aim to improve people's quality of life with our products. To achieve this, we concentrate on the research and development of innovative drugs and novel therapeutic approaches. At the same time, we are constantly improving established products. In this context, Bayer Schering Pharma uses experience it has gained from over a century in the business. We concentrate on four business units in which we make essential contributions to medical progress: Diagnostic imaging, General medicine, Speciality medicine and Women's Healthcare.

www.bayerscheringpharma.de

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