

Special Report: Special Report:

Prevention of Neural Tube Defects by Periconceptual Folic Acid Supplementation in Europe

(Updated version December 2009)

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Norway

Poland

Portugal

Slovenia

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Recommendations

- 1) European countries could prevent most neural tube defects in planned pregnancies by putting in place an official policy recommending periconceptional folic acid supplementation and taking steps to ensure that the population are aware of the benefits of supplementation and the importance of starting supplementation **before** conception.
- 2) European countries should review their policies regarding folic acid fortification and supplementation taking into account available information on benefits and hazards of both. They should pay special attention to results of studies done post mandatory fortification in countries that have introduced it.
- 3) As many pregnancies are unplanned, European countries could achieve more effective prevention of neural tube defects by additionally introducing fortification of a staple food with folic acid. The particular objectives of this policy would be preventing neural tube defects among women who do not plan their pregnancy, and reducing socio-economic inequalities in neural tube defect prevalence.
- 4) Health effects of supplementation and fortification should be monitored, and policies should be reviewed periodically in light of the findings.
- 5) The European population should be covered by high quality congenital malformation registers which collect information about affected pregnancies (livebirths, stillbirths and terminations for fetal abnormality). One important use for the information would be to assess the effect of folic acid supplementation and fortification on NTD rates as well as rates of other congenital malformations

Summary

Background

This Special Report 2009 reviews progress in developing and implementing public health policies to raise periconceptional folate status in European countries up to the end of 2007. Data on the prevalence of neural tube defects from 20 countries was analysed to determine the extent to which neural tube defects had been prevented. Our findings were disappointing and prompted us to make a number of recommendations including fortifying a staple food with folic acid. This recommendation is already under consideration by many governments.

Methods

The EUROCAT network has currently 43 population-based congenital anomaly registries in 20 European countries collaborating in the epidemiological surveillance of congenital anomalies. NTD cases (including livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis) were extracted from the EUROCAT Central Registry database for 1980-2007 and prevalence rates were calculated. In addition, representatives from 21 countries participating in or interested in joining EUROCAT provided information about policy, health education campaigns and surveys of folic acid supplement uptake in their country.

Results

By January 2005, 15 of the 20 countries contributing data to this report had introduced an official policy advising women to take periconceptional folic acid supplementation. Four countries (Austria, Belgium, Croatia, Germany) have no official government policy at the time of writing, although professional groups within them advise supplementation.

Half the countries have launched some type of health education campaign so that the information about the protective effect of folic acid can reach women directly rather than uniquely through health professionals

We found that the majority of women surveyed are still not taking folic acid supplements periconceptionally. Only in the Netherlands and Denmark is the periconceptional use of folic acid above 30%, the other countries not reaching 10%. Mandatory fortification of a staple food (usually flour) with folic acid has been

seriously considered in eight countries contributing to this report (Denmark, Germany, Ireland, Northern Netherlands, Norway, Poland, Switzerland, and the UK). As of November 2009 food fortification with folic acid had not been implemented in any European country although it is now widespread in North and South America and in several countries in the Middle East.

Despite all measures taken to date, the majority of women in all countries surveyed are not taking folic acid supplements prior to and for the first weeks after conception.

This study shows a declining trend for anencephaly in the years 1992-2007, but not for spina bifida. We focused on this time period because all the folic acid advice and campaigns started after 1992.

A significant decline in prevalence of NTD since 1992 was found in Ireland, but not in the UK. In Continental Europe (excluding Southern Europe), in spite of the significant decrease in NTD prevalence in Northern Netherlands, the decrease for all registries combined is slight and non-significant. In South Europe the decline in NTD prevalence since 1992 was significant.

While livebirth NTD prevalence has decreased considerably in countries without a folic acid supplementation policy due to the increase in prenatal diagnosis and subsequent termination of affected pregnancies, the total prevalence has not significantly decreased. Reduction of livebirth prevalence is still relying more on prenatal screening and termination than on primary prevention with folic acid supplementation. In order to distinguish between decreases in prevalence due to primary prevention and those due to prenatal screening, information on terminations of pregnancy is essential.

The existence of an expanded network of congenital anomaly registries in Europe, collecting data on affected livebirths, stillbirths and terminations of pregnancy, is vital to track progress towards the prevention of NTDs. Information on NTD prevalence should be supplemented where possible by surveys of uptake of periconceptual folic acid supplementation in the population, and by monitoring of serum levels of folic acid.

Conclusion

The potential for preventing NTDs by periconceptional folic acid supplementation is still far from being fulfilled in Europe. In order to achieve a reduction in NTD prevalence, new efforts are needed in all countries to implement a combined strategy to increase folate status by dietary means, increase uptake of folic acid supplements periconceptionally, and to increase availability and identification of fortified foods. Mandatory fortification could improve folate status of all women of childbearing age, substantially reduce NTD prevalence, and reduce socio-economic inequalities in NTD prevalence. Additional benefits such as reduced specific cancer occurrence and cognitive decline have also been reported, although these have not been supported by randomised controlled trials.

As countries change their policies and practices regarding prevention of NTD, continued monitoring of NTD prevalence is vitally important. This requires data from population based registers of congenital anomalies with high ascertainment of cases among livebirths, stillbirths and termination of pregnancy for fetal anomaly

Part I

Overview of Neural Tube Defects

1. Introduction

Across Europe, an estimated 4,500 pregnancies are affected by Neural Tube Defects (NTD) each year. Evidence of a possible association between *folic acid* and NTD has been described in the scientific literature for more than three decades (Scott, Weir, & Kirke 1995). Since the early 1980s a number of intervention trials examining the effects of periconceptional folic acid on the prevalence of NTD have been published, with the first unambiguous evidence of the effectiveness of periconceptional folic acid coming in 1991 on the publication of the results of the Medical Research Council (MRC 1991). On the basis of this trial, it has been estimated that improving folate status sufficiently would result in the prevention of 72% of all NTD.

This report is an updated version of the EUROCAT NTD Report by the same name published in 2005 and focuses on periconceptional folic acid policies and implementation strategies across Europe since 1991 and the reported prevalence rates of NTD until 2007. Contributions from EUROCAT (European Surveillance of Congenital Anomalies) members representing 21 countries (20 countries with new data) are included in the form of chapters describing policy and practice in their respective countries in relation to: periconceptional folic acid supplementation, dietary advice, food fortification and women's knowledge about the advice and compliance with recommendations. These are set within the context of laws relating to termination of pregnancy for fetal abnormality and of what is known about the proportion of pregnancies that are planned. The prevalence of NTD up to the end of 2007 is examined in relation to policies on folic acid supplementation across Europe. Furthermore, since 2005 a variable on folic acid intake has been added to the set of data all registries are sending to the Central registry. This report will show, for the first time, the periconceptional folic acid intake among women giving birth to malformed infants in several registries. The report will focus on NTD, as it is for this group of anomalies that the body of evidence for the protective effect of folic acid is strongest.

2. The Public Health Response to Evidence Concerning the Protective Effect of Folic Acid

2.1 Periconceptional Folic Acid Policies in European Countries

Table 1 summarises periconceptional folic acid supplementation policies around Europe. For more detail, the reader is advised to look at individual country chapters in Part II of this Report.

By January 2005, 15 of the 20 countries contributing data to this report had introduced an official policy advising women to take periconceptional folic acid supplementation. The first governments to formulate such a policy were in the Netherlands (1992), UK (1992) and Ireland (1993). Portugal recommends that health workers should educate women about the benefits of folic acid; Malta recommend raising folate status by dietary means only and four countries (Austria, Belgium, Croatia, Germany) have no official government policy at the time of writing, although professional groups within them advise supplementation.

The recommendation for periconceptional folic acid supplements in most countries is for a daily dose of 0.4 to 0.5 mg (except in Poland, where it is 1.0 mg, and Portugal, where no dose is specified). Higher doses, of 4 or 5 mg daily, are usually recommended for women who have had a previous pregnancy affected by an NTD. Some countries also have special recommendations for women on anticonvulsant therapy.

Half the countries have launched some type of health education campaign (Table1) so that the information about the protective effect of folic acid can reach women directly rather than uniquely through health professionals. This is particularly important as folic acid supplementation must start before conception and therefore before the consultation of health professionals during pregnancy. The details of these campaigns can be found in Part 2. There is little evidence as to how often health education campaigns need to be repeated for a sustained effect.

2.2 Uptake of Recommendations to Take Periconceptional Folic Acid Supplements

Surveys of the use of folic acid supplements periconceptionally in European countries are summarised in Table 1. Details are given in the individual country chapters in Part 2 of this report. Details of the methodology of each survey, where available, are given in Part 2, and figures shown in Table 1 should be interpreted in the light of these details.

Table 1: Current¹ Folic Acid Supplementation Policy in European Countries

Country	Periconceptional Folic Acid Policy ²			Year of study	% Women Using Folic Acid
	Status	Year current policy introduced	Health education campaign		
Austria	Unofficial	1998	No	1998	24% some part of advised period 10% for entire advised period
Belgium	Unofficial	-	Being prepared	2006	48% some part of advised period 24% for entire advised period
Croatia	Unofficial	-	Unofficial	2003	69% some part of advised period 20% for entire advised period
Denmark	Official	1997	1999 and 2001	2000-2	22% of women who planned pregnancies took supplements at correct time
Finland	Official	2004	Unofficial	2000	19% took FA before or in early pregnancy
France	Official	2000	2000 and 2004	?	30% some part of advised period 10% for entire advised period
Germany	Unofficial	1994	No	2000	4.3% for entire advised period
Hungary	Official	1996	Ongoing	2006	69% of pregnant women
Ireland	Official	1993	1993 and 2000/2001 with Ulster	2002	23% periconceptionally
Italy	Official	2004	2004 regional	2007	Depends very much on the region, range: 3-21%
Malta	Dietary	1994	No	2000	74% some part of advised period 15% for entire advised period
Netherlands	Official	1993	1995	2005	80% some part of advised period 51% for entire advised period
Norway	Official	1998	1998 (website)	2000	46% periconceptionally
Poland	Official	1997	Yes, but no date given	2005	70% some part of advised period 11% for entire advised period
Portugal	Official	1998	No	2005	24% for entire advised period

Slovenia	Official	1998	Unofficial	2007	88% some part of advised period 31% for entire advised period
Spain	Official	2001	2002	2007	71% some part of advised period 17% for entire advised period
Sweden	Official	1996	No	1997	8% some part of advised period
Switzerland	Official	1996	2008	2003	98% some part of advised period 37% for entire advised period
UK	Official	1992	1995	2002	45% periconceptionally
Ukraine	Official	2002	Unofficial		

¹ Policy as of December 2007

² Recommended dose is as supplements unless otherwise stated

In all countries other than Netherlands, only a minority of women were found to have taken folic acid supplements during the entire advised periconceptional period. The highest uptake in the studies was recorded in Netherlands, UK, Switzerland, Norway and Hungary with 30-51% periconceptional uptake. Since these are the results of specific studies, we added an extra variable to EDMP to assess folic acid intake for each woman. In 2.3 the results are shown.

It should be noted that the countries in which the highest uptake rates were found were those with official health education initiatives.

There is evidence that women of higher social status are more likely to know of the benefits of taking supplemental folic acid and to be aware of the correct timing (de Walle, van der Pal-de Bruin, & de Jong- van den Berg 1998; Sayers et al. 1997; US Department of Health and Human Services 1993), potentially leading to widening of socio-economic inequalities in NTD prevalence.

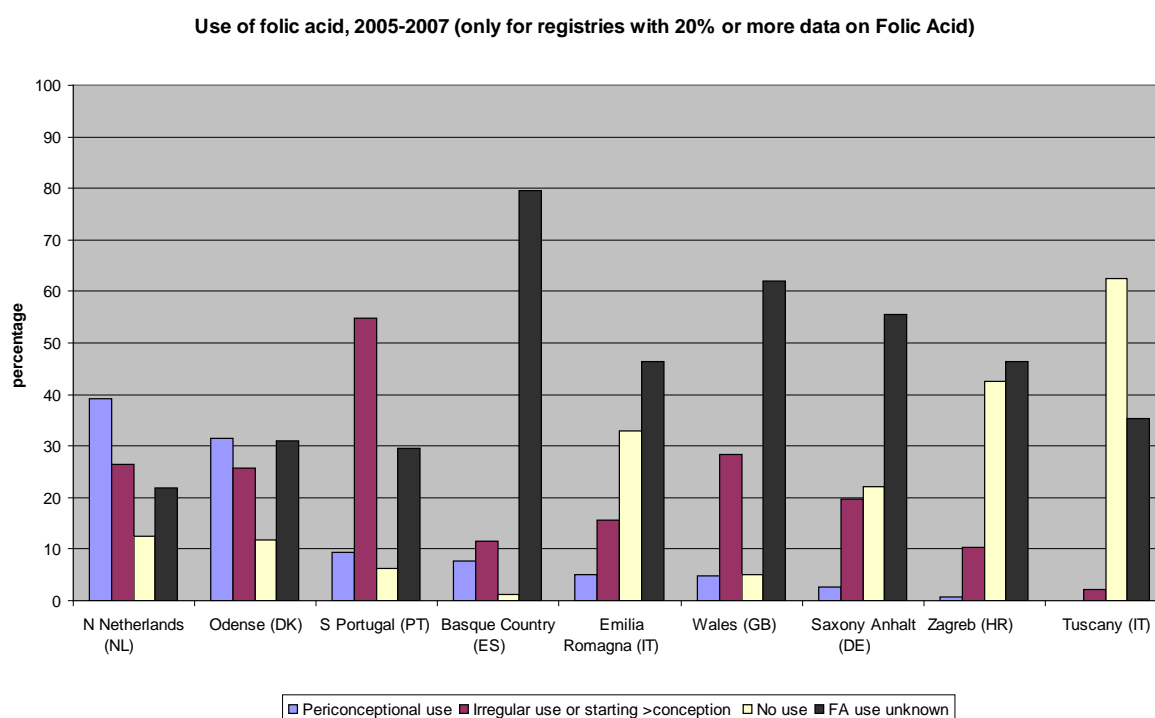
2.3 Monitoring of Intake of Folic Acid

Since 2005 EUROCAT has added an extra variable to the data entry programme of EUROCAT in order to have more information on the periconceptional intake of folic acid for individual cases. The results are shown in the graph hereunder. In general over the years 2005-2007 the following registries had some information on the use of folic acid periconceptionally: Denmark (Odense), Italy (Tuscany and Emilia Romagna), Ireland (Dublin and SE Ireland), Northern Netherlands, Switzerland (Vaud), Croatia (Zagreb), S

Portugal, Belgium (Antwerp), Spain (Basque country) and Germany (Saxony Anhalt).

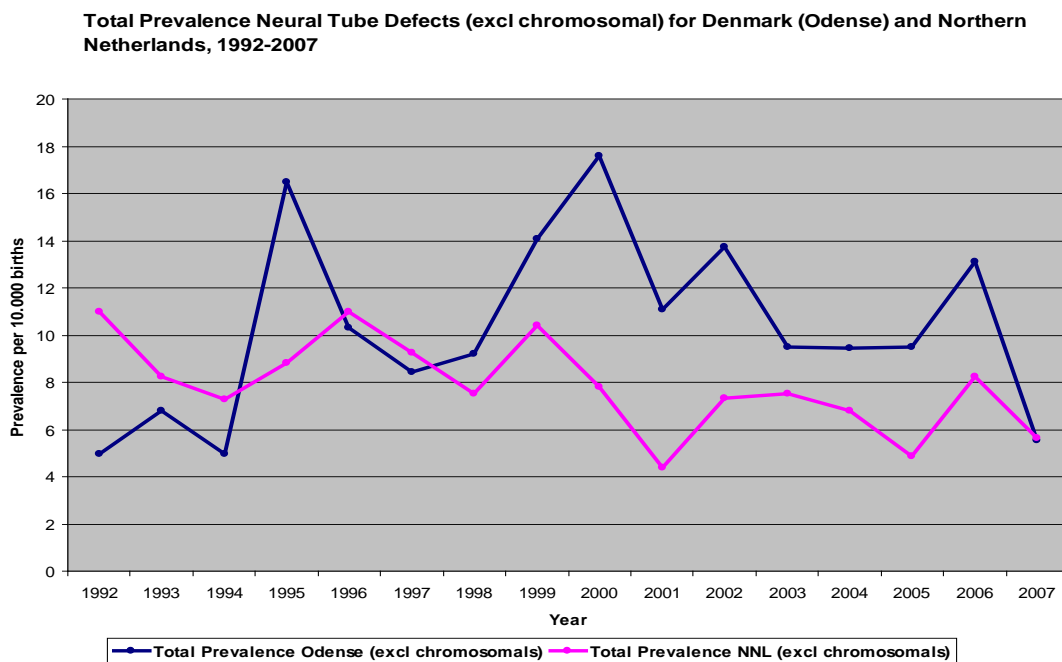
We restricted the figure (Figure 1) to include the 9 registries with information on folic acid for more than 20% of their cases (periconceptual use, some use or no use).

Figure 1: Use of folic acid, 2005-2007 (only for registries with 20% or more data on Folic Acid)



The figure shows that of the nine registries that have some information on uptake, the uptake is very disappointing. The Northern Netherlands and Odense (Denmark) have the highest percentage women taking folic acid in the periconceptual period, 4 weeks before conception till 8 weeks after. Figure 2 shows the NTD prevalence rates shown for these 2 countries. This is the prevalence excluding chromosomal anomalies because it is thought that folic acid has the potential to be protective for multifactorial malformations, not for chromosomal anomalies.

Figure 2: Total Prevalence Neural Tube Defects (Excl Chromosomal) for Denmark (Odense) and Northern Netherlands, 1992-2007



There is a significant decreasing trend in the Netherlands ($\chi^2=5.1$, $p=0.02$) but not in Denmark ($\chi^2=0.52$, $p=0.47$).

The 7 other registries reported less than 10% periconceptional use of folic acid, so the overall uptake is very low. In 2005-2007 there were in total 41,516 cases with congenital malformations in the database. For 5,628 (13.6%) folic acid information is known and the mothers of 969 (2.3%) cases took folic acid in the periconceptional period. These numbers are too small to do a reliable statistical analysis.

In the near future we will publish the results of a survey we did in all the registries about the amount of information GPs, hospitals and midwives are collecting routinely on folic acid intake before and during pregnancy.

2.4 Fortification of Food with Folic Acid

Mandatory fortification of a staple food (usually flour) with folic acid has been seriously considered in eight countries contributing to this report (Denmark, Germany, Ireland, Northern Netherlands, Norway, Poland, Switzerland, and the UK) and the case for it is still being reviewed. As of November 2009 food fortification with folic acid had not been implemented in any European country

although it is now widespread in North and South America and in several countries in the Middle East.

Food voluntarily fortified with folic acid (mainly breakfast cereals) is available in many European countries. In a study investigating the effects of consumption of folic acid-fortified bread compared with folic acid tablets, bread was found to be equally effective in increasing folate status as indicated by both increased red cell and serum folate concentrations (Armstrong NC. et al. 2001). However, it may be difficult for women to identify foods fortified with folic acid and to determine the amount in relation to their needs due to limitations/restrictions on food labelling.

3. NTD Prevalence Rates in Europe 1980-2007

NTD prevalence rates over time by country can be found in the Country Specific Chapters of Part 2. Registry descriptions can be found on our new website address: <http://eurocat.bio-medical.co.uk>. Most registries are population-based and register affected fetuses / babies in livebirths, stillbirths from 20 weeks gestation and terminations of pregnancy for fetal abnormality. Laws in each country regarding whether and until what gestational age termination of pregnancy for fetal abnormality is legal are summarised in Table 2.

Table 2: Laws Regulating Termination of Pregnancy for Fetal Abnormality

Country	Is it Legal?	Gestational Age Limit for Non-Lethal Serious Anomalies	Gestational Age Limit for Lethal Anomalies
Austria	Yes	No upper limit	No upper limit
Belgium	Yes	No upper limit	No upper limit
Croatia	Yes	No upper limit	No upper limit
Denmark	Yes	Before viability	No upper limit
Finland	Yes	24 weeks	24 weeks
France	Yes	No upper limit	No upper limit
Germany	Yes	No upper limit	No upper limit
Hungary	Yes	No upper limit	No upper limit
Ireland	No	Not legal	Not legal
Italy	Yes	Before viability	Before viability
Malta	No	Not legal	Not legal

Netherlands	Yes	24 weeks	No upper limit
Norway	Yes	18 weeks	No upper limit
Poland	Yes	<23	<23
Portugal	Yes	24 weeks	No upper limit
Slowenia	Yes	No upper limit	No upper limit
Spain	Yes	22 weeks	22 weeks
Sweden	Yes	22 weeks	22 weeks
Switzerland	Yes	24 weeks	24 weeks
UK ¹	Yes	No upper limit	No upper limit
Ukraine	Yes	22 weeks	22 weeks

Information as of April 2008

¹ Except Northern Ireland

3.1 Methods

Data for all cases of NTD were extracted from the EUROCAT Central Registry database 1980-2007.

Total prevalence rates were calculated as the number of affected livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis divided by the total number of births (live and still) in the registry population. Livebirth prevalence rates were calculated as the number of affected livebirths divided by the total number of livebirths in the registry population.

Prevalence rates are given for anencephalus, spina bifida and all NTD combined. Cases with both anencephalus and spina bifida were classified as having anencephalus.

The χ^2 for trend was used to test if prevalence was significantly decreasing or increasing in time. Logistic regression was used in which the year of birth was taken as independent variable for decreasing or increasing prevalence. The test was done only for the **total prevalence** and **total prevalence without chromosomal anomalies** whenever appropriate. We did not test livebirth prevalence as the influence of prenatal testing and termination of pregnancy is becoming more important every year. Livebirth prevalence is not a reliable measure for discussing the role of folic acid prevention.

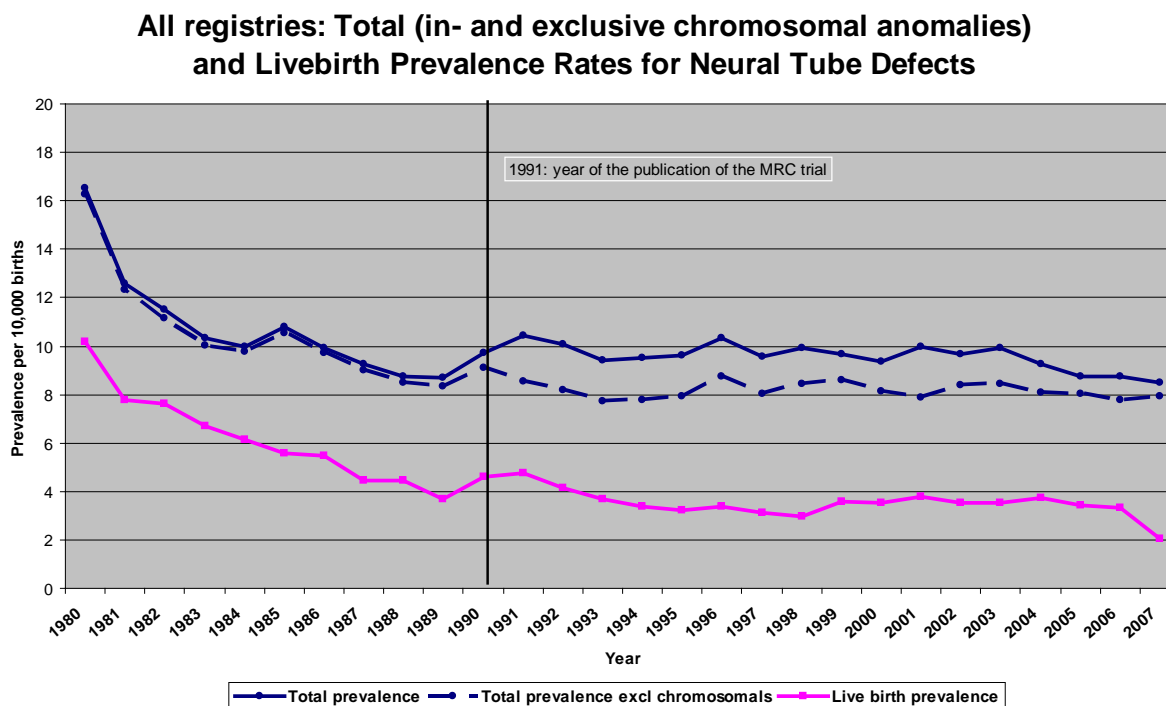
Further details of methods can be found in the original EUROCAT special report (2003) on the Prevention of Neural Tube Defects by Periconceptional

Folic Acid Supplementation in Europe on this website:
<http://www.eurocat.ulster.ac.uk/pubdata/Folic-Acid.html>.

3.2 Results

Figure 3 shows a significantly decreasing prevalence of NTD from 1980 and onwards. In the beginning of the nineties it became clear from the MRC study (1991) and Czeizel's Hungarian study (Czeizel 1993) that folic acid had a preventive effect on NTDs. That was the impetus for launching campaigns in several European countries. An effect of folic acid is therefore to be expected from 1992 onwards and not before. As the main focus in this report is the effect of periconceptional folic acid we tested the prevalence for significance from 1992 onwards.

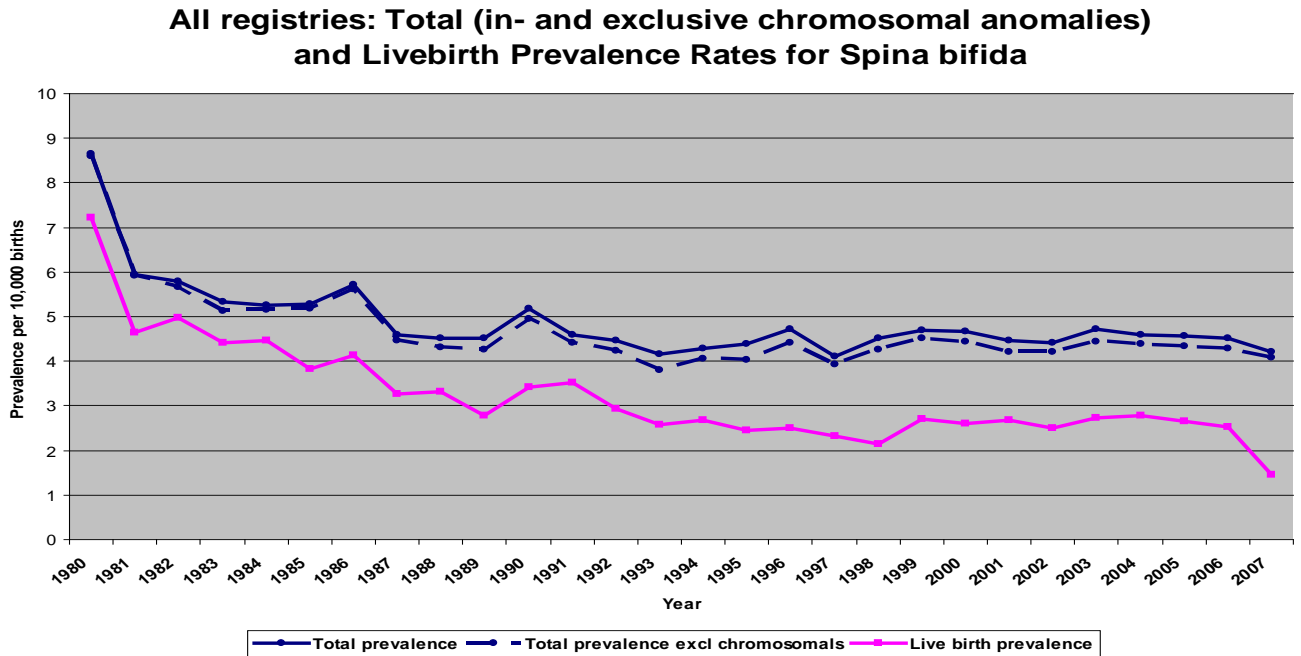
Figure 3: All Registries: Total (In- and Exclusive Chromosomal Anomalies) and Livebirth Prevalence Rates for Neural Tube Defects



The total prevalence for NTDs for all registries included in this report is significantly decreasing from 1992 onwards. Over the years 1992-2007 χ^2 for trend =10.9, $p=0.001$. For the non-chromosomal NTDs χ^2 for trend =9.3,

p=0.002. The figures below show whether this is due to spina bifida, anencephaly or both.

Figure 4: All Registries: Total (In- and Exclusive Chromosomal Anomalies) and Livebirth Prevalence Rates for Spina Bifida



In figure 4 for the years 1992-2007 the χ^2 for trend =1.1, p=0.29, the odds ratio (OR) for year of birth is 0.997 (95% CI:.991-1.003), therefore no significant decrease in trend for spina bifida over the years 1992-2007. For the non-chromosomal spina bifida χ^2 for trend =.31, p=0.58.

Figure 5: All Registries: Total (In- and Exclusive Chromosomal anomalies) and Livebirth Prevalence Rates for Anencephaly

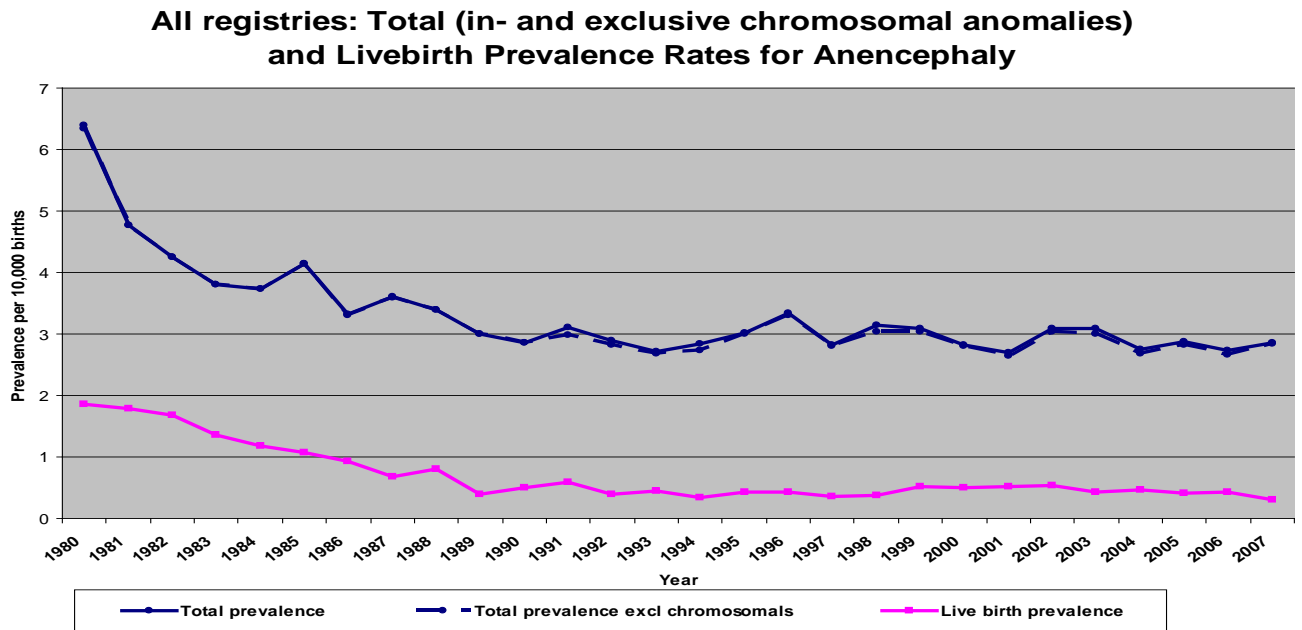
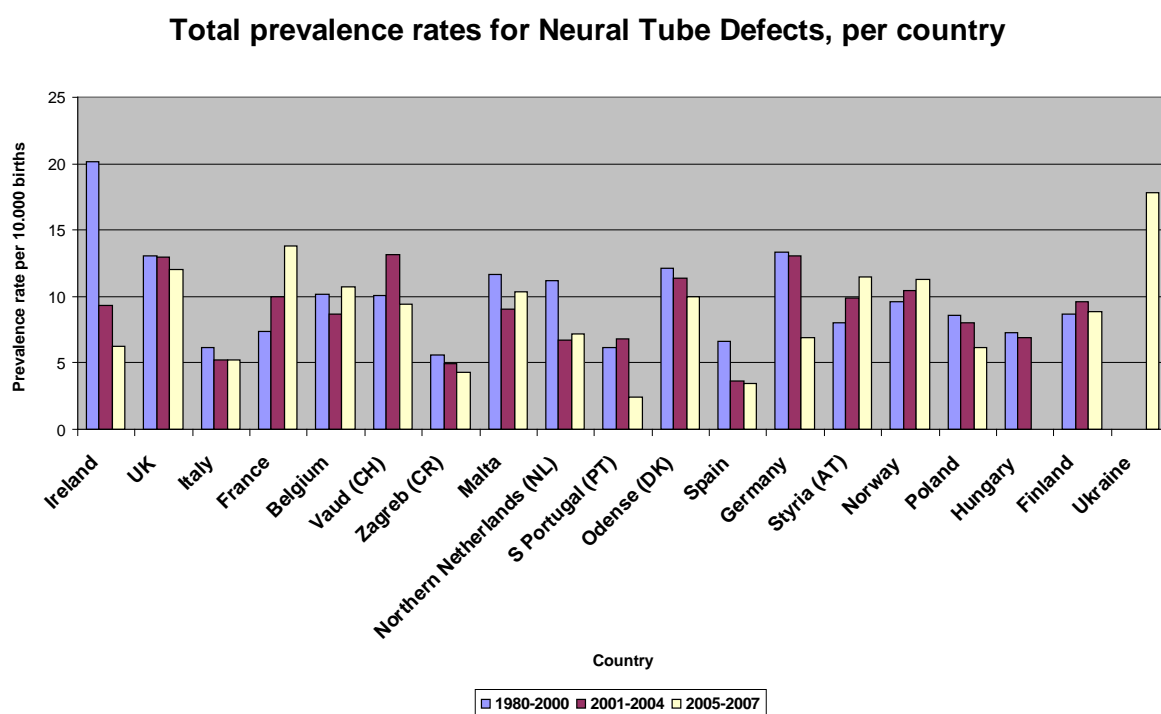


Figure 5 shows a significantly (slightly) decreasing trend for anencephaly over the years 1992-2007, χ^2 for trend =6.4, $p=0.012$, the odds ratio (OR) for year of birth is 0.991 (95% CI:.984-.998). For the non-chromosomal anencephaly χ^2 for trend =6.9, $p=0.009$. This decrease might be real but can also be caused by the fact that anencephaly is diagnosed earlier in pregnancy in recent years and therefore less notified to the registries.

Figure 6 shows the total NTD prevalence for all countries in three time periods.

Figure 6: Total Prevalence Rates for Neural Tube Defects, Per Country



The decrease in prevalence is most significant in Ireland. In May 2006, The Food Safety Authority of Ireland (FSAI) and the Irish Department of Health & Children (DoHC) recommended fortification of all bread (with the exception of minor bread products) on a mandatory basis with folic acid at a level which provides 120 µg per 100g of bread as consumed. It is mentioned earlier that no EU country has mandatory food fortification with folic acid. However, this was not implemented, and in 2008, the FSAI recommended postponement of fortification, following preparatory studies by the implementation group which showed that the rate of NTD affected births had decreased further. In addition, there had also been a significant increase in folic acid intake in the Irish diet as a result of increased voluntary fortification by food producers in recent years. Furthermore, although termination of pregnancy is forbidden in Ireland, there is always the possibility of terminations abroad.

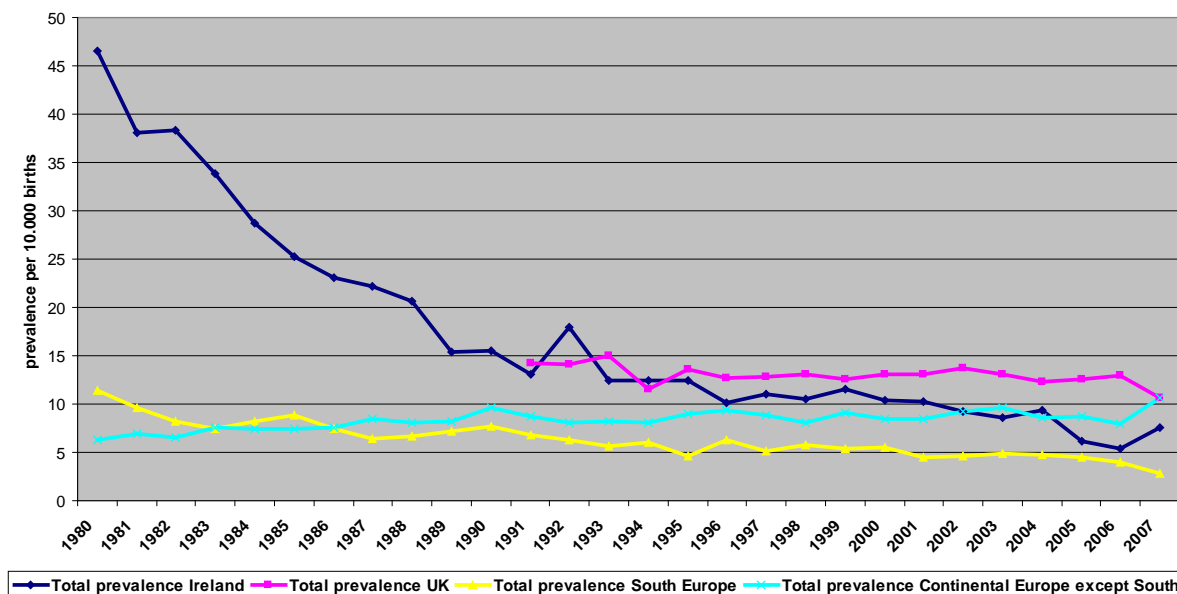
Another country worth mentioning is the UK. The UK, together with Ireland was the country with historical high rates for NTDs. In the recent period of 2005-2007 the prevalence is now of the same order as France, Belgium, Malta, Denmark, Austria and Norway.

The chapter on France in the second part of this report shows that it is especially the registry of Isle de la Reunion that has high prevalences over the years 2002 -2007. This registry is one of the overseas departments of France and is the outermost region of the European Union. It is located in the Indian Ocean, east of Madagascar. The population is different genetically and environmentally from Europe, so there is no reason to expect the prevalence to be similar to that of other French registries.

NTD prevalence has changed over time, so regions with a high prevalence in the past do not necessarily continue to have a high prevalence. Figure 7 shows how the prevalences are changing in different parts of Europe.

Figure 7: Total Prevalence for Neural Tube Defects for Several Regions in Europe

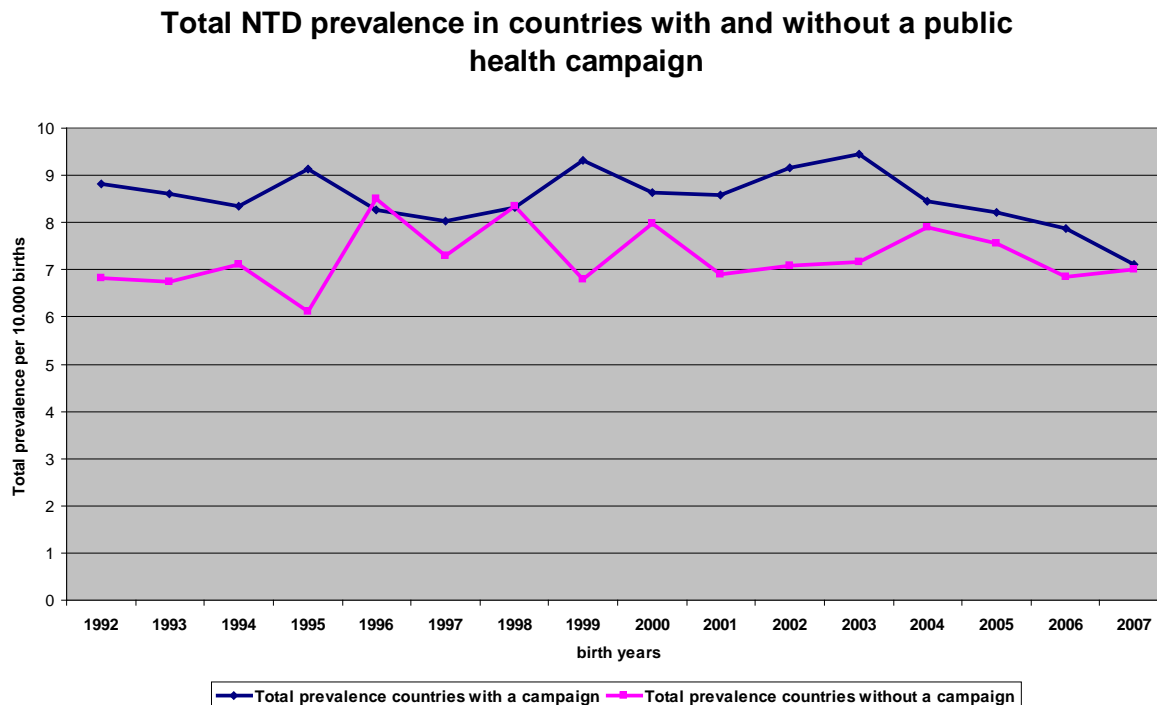
Total prevalence for Neural Tube Defects for several regions in Europe



Countries belonging to ‘South Europe’ are: Italy, Croatia, Portugal, Malta and Spain. ‘Continental Europe’ is represented by France, Belgium, Switzerland, Northern Netherlands, Denmark, Germany, Austria, Norway, Poland, Hungary, Ukraine and Finland. Regions or countries that show a statistically declining trend after 1992 are Ireland ($p < .001$) and Southern Europe ($p < .001$).

In the beginning of this report we showed in which countries public health campaigns about folic acid have taken place (Table 1). Figure 8 compares the NTD prevalence for countries that have had a campaign to encourage folic acid use with those that have not had a campaign. The countries that had a campaign (between 1992-2007) are: Ireland, UK, France, the Netherlands, Denmark, Spain, Norway, Poland and Hungary. There was no significant decline in prevalence in either group. This was tested for the whole period of 1992-2007. However, it is clear from the picture that the lines come together in recent years and that especially in countries with a public health campaign the decline from 2003 onwards is obvious. For example in 2007 there is a significant decline of 20% (OR=.80, 95% CI: .68-.95) in countries with a public health campaign. We also commented before (figure3) that the total prevalence for NTDs for all registries is significantly decreasing from 1992 onwards.

Figure 8: Total NTD Prevalence in Countries with and without a Public Health Campaign



3.3 Discussion

This study shows a declining trend for NTDs in the years 1992-2007, driven by the decline in anencephaly. We focused on this time period because all the folic acid advice and campaigns started after 1992.

In Ireland it is difficult to distinguish the effect of the folic acid supplementation policy on NTD prevalence rates from the decline in prevalence starting well before the implementation of national policy. It is possible that one explanation for this decline may be the increasing folate content of the Irish diet starting before the national policy. However, since 1992 the decline has continued, probably because of voluntarily fortified foods and better use of folic acid supplementation.

In the UK registries participating in this study there has been no decline since 1992.

In Continental Europe (excluding Southern Europe), in spite of the significant decrease in NTD prevalence rates in Northern Netherlands, the decrease for all registries combined is slight and non-significant.

In South Europe the decline in prevalence since 1992 was significant. The explanation for this could be increased consumption of folate rich / fortified food and /or use of periconceptional folic acid supplementation, but it is also known that increased socio-economic status decreases the risk for NTD.

While live birth NTD prevalence has decreased considerably in countries without a folic acid supplementation policy due to the increase in prenatal diagnosis and termination of affected pregnancies in these countries, the total prevalence has not significantly decreased. This emphasizes two points. Firstly, reduction of livebirth prevalence is still relying more on prenatal screening and termination than on primary prevention with folic acid supplementation. Secondly, in order to distinguish between decreases in prevalence due to primary prevention and those due to prenatal screening, information on terminations of pregnancy is essential.

The existence of an expanded network of congenital anomaly registries in Europe, collecting data on affected livebirths, stillbirths and terminations of pregnancy, is vital to track progress towards the prevention of NTDs. Information on NTD prevalence should be supplemented where possible by surveys of uptake of periconceptional folic acid supplementation in the population, and by monitoring of serum levels of folic acid.

This study showed that registries have only little or no information about whether the mother actually took folic acid periconceptionally. This is disappointing. Apparently the perceived need for monitoring this is low. Specific studies on this topic in contributing countries showed that only a minority of women took supplements during the entire advised period.

Overall in Europe, some progress has been made in the primary prevention of NTDs. This is especially true for anencephaly and for specific countries like the Netherlands and Ireland. Southern Europe decreased significantly while continental Europe only had a minor decrease in NTD prevalence. It is very difficult to estimate how many affected pregnancies in Europe are being prevented by use of folic acid. There is still room for improvement, especially since the percentage of unplanned pregnancies is still high. Therefore, folic acid fortification of staple foods might be an option to achieve significant prevention of NTDs.

Mandatory fortification with folic acid has been introduced in around 50 countries worldwide as a strategy to help women increase their folate levels. Reports from the US and Canada have shown an effective and significant decline in NTDs (De Wals et al. 2007; Godwin et al. 2008; Williams et al. 2005). Hesecker et al. reported that countries with mandatory folic acid fortification achieved a significant decrease in the prevalence of NTD. He concludes in his study that the degree of reduction in NTD prevalence in a population is related to the baseline NTD prevalence. This decline was independent of the amount of folic acid administered and reveals a „floor effect“ for folic acid preventable NTDs. Thus, not all cases of NTDs are preventable by increasing folate intake (Hesecker et al. 2009). At the moment, mandatory fortification of folic acid is not

implemented in Europe. Fortification of staple foods with folic acid would provide a more effective means of ensuring an adequate intake, especially for those groups of women who are unlikely to plan their pregnancies or to receive or respond to health promotion messages. Fortification together with supplementation is likely to be a more cost-effective option than supplementation only for preventing NTD, since a supplementation only policy requires a health education campaign more extensive and effective and possibly more frequent than those implemented so far.

In Europe there has been reluctance to proceed to mandatory food fortification which we believe stems from two factors:

- 1) Lack of recognition of the public health importance of neural tube defects, possibly because the great majority of NTD pregnancies are now terminated, rendering them invisible to all but the family affected.
- 2) The possibility of health risks related to raising the population folic acid status. (Cornel, de Smit, & den Berg 2005)

There has been concern regarding the potential risk of masking the symptoms of pernicious anaemia caused by vitamin B₁₂ deficiency. If undiagnosed, there is potential for irreversible neurological damage in those at high risk of this deficiency, namely the elderly. However, it is argued that B₁₂ deficiency can be diagnosed simply with or without the presence of anaemia (Bower & Wald 1995). Furthermore, the masking of pernicious anaemia, which has concerned people at a theoretical level, has not been observed in countries with mandatory fortification of flour with folic acid.

Evidence continues to mount about the beneficial effects of folic acid for the prevention of other congenital anomalies. The evidence regarding effects of folic acid on cancer is not conclusive. Although there is evidence that folic acid may be protective against the development of new cancers, there is concern at the possibility that it may promote the development of undiagnosed pre-malignant and malignant lesions. The European Food Safety Authority summary report wrote: "There are currently insufficient data to allow a full

quantitative risk assessment of folic acid and cancer or to determine whether there is a dose-response relationship or a threshold level of folic acid intake associated with potential colorectal cancer risk. The evidence regarding the effects of folic acid on cardiovascular disease is also inconclusive.

Observational studies suggested that high intakes of folic acid were associated with a lower risk of CVD but randomised trials have not confirmed these findings (ESCO 2009).

4. Conclusions

- The evidence that most NTD are preventable by increasing folate status before conception is very strong
- Government response to this evidence has been variable in Europe. Some countries have been slow to introduce policies while others very actively promote periconceptional folic acid supplementation
- The majority of women in countries surveyed are still not taking folic acid supplements periconceptionally
- Most countries have implemented some type of health education campaign designed to reach women before conception. However, there are still five countries that have had no campaigns at all. No difference was found in the decrease in NTD prevalence between countries with and without a campaign
- There is a decreasing trend of anencephaly over the years 1992-2007 which is significant but falls short of expectations; the prevalence of spina bifida is not declining
- There is an immense challenge facing those involved in public health and the care of prospective mothers to replace termination of pregnancy with primary prevention by folic acid as the chief method of reducing the number of infants affected by this very serious group of congenital anomalies
- In order to achieve a reduction in NTD prevalence, new efforts are needed in all countries to implement a combined strategy to:
 - increase folate status by dietary means
 - increase uptake of folic acid supplements periconceptionally
 - increase availability and identifiability of fortified foods

- The possibility of preventing the majority of NTD through mandatory fortification of a staple food has not yet been introduced by any of the countries surveyed. Mandatory fortification could improve folate status of all women of childbearing age, substantially reduce NTD prevalence, and reduce socio-economic inequalities in NTD prevalence. Suggestions for additional benefits such as reduced specific cancer occurrence and cognitive decline are also made. However, evidence for this is not supported by randomised controlled trials
- As countries change their policies and practices regarding prevention of NTD, continued monitoring of NTD prevalence is vitally important. This requires data from population based registers of congenital anomalies with high ascertainment of cases among livebirths, stillbirths and termination of pregnancy for fetal anomaly

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Report on Periconceptional Folic Acid Supplementation for Austria

Prof Andrea Berghold, Prof Martin Haeusler

Folic Acid Supplementation Policy

Austria has no official government recommendation for periconceptional folic acid supplementation. But in 1988 the Austrian Pediatric Society and the Austrian Society for Prenatal and Perinatal Medicine recommended periconceptional folic acid supplementation (0.4 mg per day) for all women wishing to become pregnant. Women who were already pregnant should start folic acid supplementation during the first four weeks of gestation and continue until the 8th week. For women with a high risk for recurrence of a neural tube defect, periconceptional folic acid supplementation with 4 mg per day was recommended.

Food Fortification Policy

Austria has no official food fortification policy but, as in many other countries, food companies voluntarily fortify some breakfast cereals, malted drinks and some other foods.

The Austrian government is discussing a proposal for mandated folic acid fortification of flour. This may be decided in 2008. Problems to be solved beforehand include the permission of the European Union and technical requirements of flour mills.

Health Education Initiatives

Austria has undertaken no official health education initiatives on the role of folic acid in reducing the risk for neural tube defects. No such initiatives are planned for the near future in.

Knowledge and Uptake of Folic Acid

A study carried out in St Pölten² looked at maternal knowledge and periconceptional folic acid supplementation among women delivered between 1.12.1997 and 31.3.1998. Women were interviewed with a standardized questionnaire. 238 women participated in the study and 234 questionnaires were analysed. 57 (24%) women used folic acid; however 33 out of 57 did not start use until after 12 weeks' gestation.

61 out of 161 (38%) who answered this question knew that folic acid prevented fetal neural tube defects.

Proportion of Pregnancies that are Planned

The proportion of pregnancies that are planned in Austria is unknown.

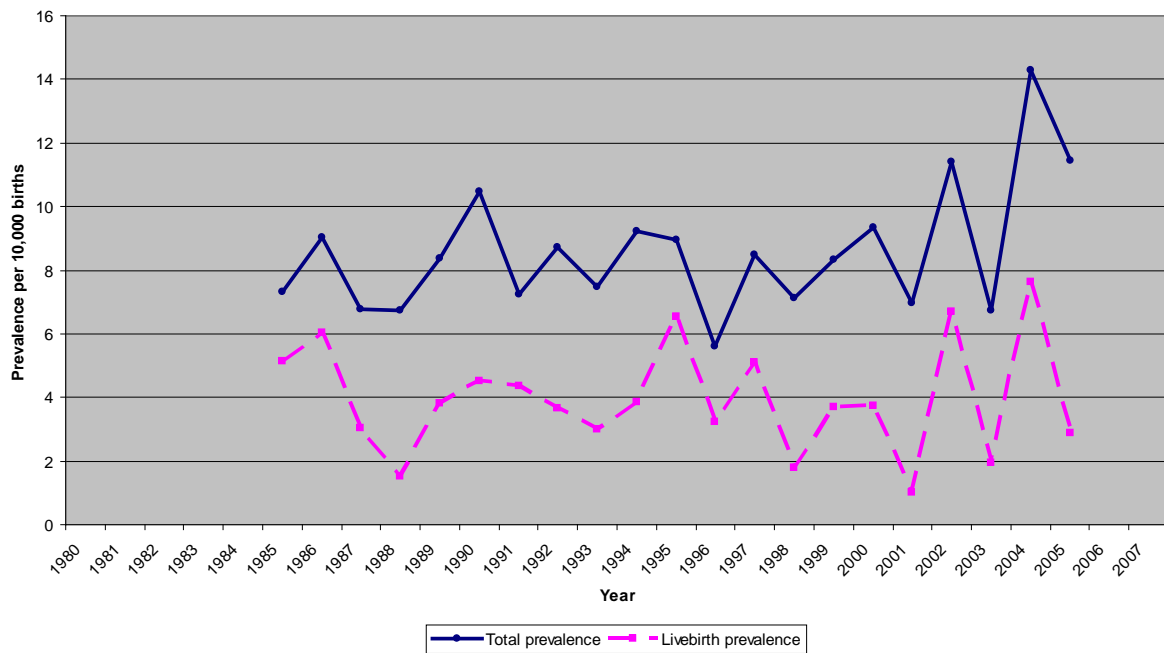
Laws Regarding Termination of Pregnancy (TOP)

“Termination of pregnancy is allowed irrespective of gestational age, if the pregnancy poses a serious threat to the pregnant woman’s physical or mental health, or if there is a serious possibility that the child will be mentally or physically handicapped”. However, in practice this is handled with caution to avoid the accusation of euthanasia. In the case of non-lethal malformations, MFM (maternal-fetal medicine) specialists in Austria agree to terminate pregnancies before viability (i.e. < 24 weeks gestational age). In rare cases of severe malformations diagnosed late they might agree to terminate pregnancies after viability after consulting an ethics committee. In the case of lethal malformations TOP is possible whenever the mother wishes. No medical doctor can be forced to perform TOP.

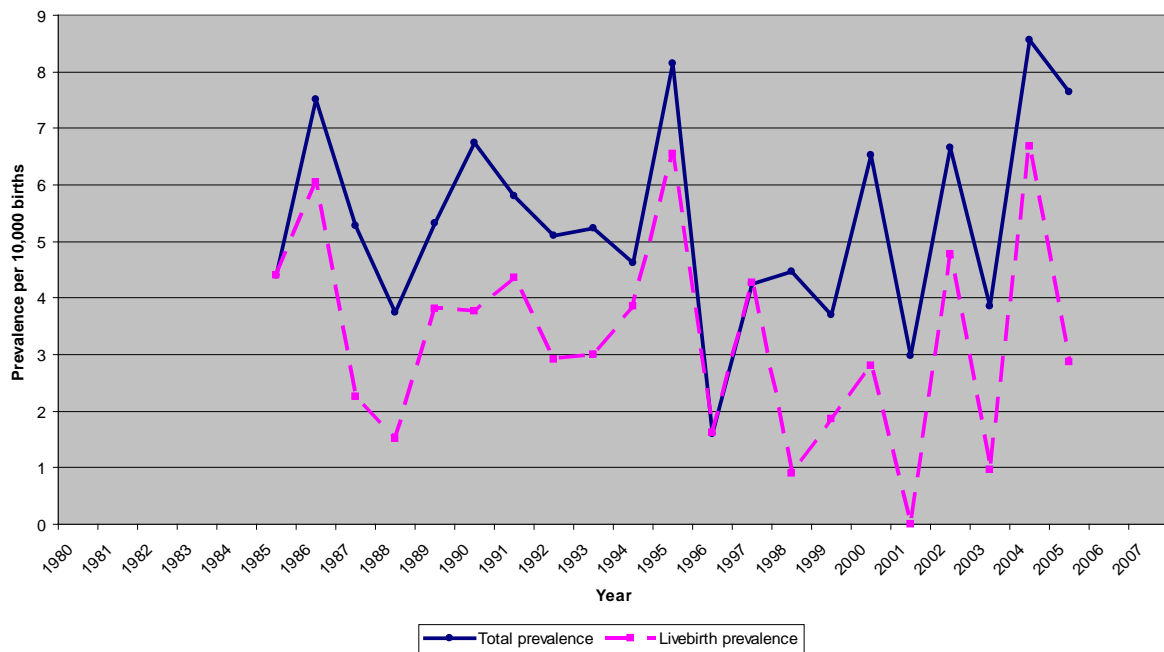
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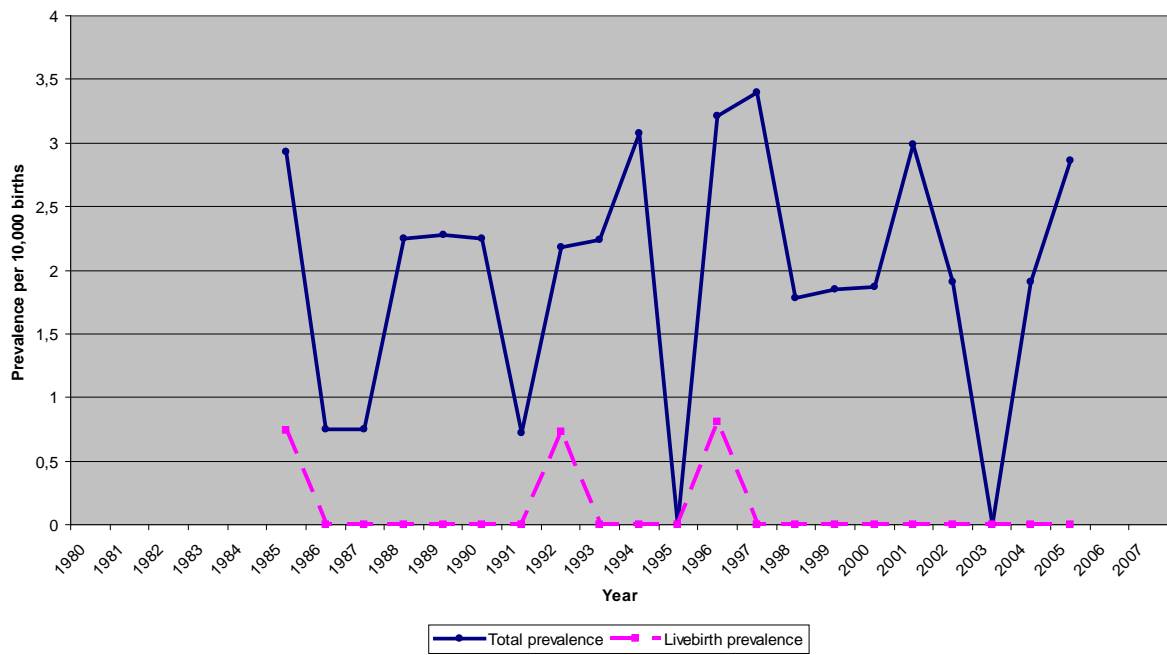
Austria (Styria): Total and Livebirth Prevalence Rates for Neural Tube Defects



Austria (Styria): Total and Livebirth Prevalence Rates for Spina Bifida



Austria (Styria): Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Belgium

Prof Yves Gillerot, Andre Baguette and Vera Nelen

Folic Acid Supplementation Policy

In Belgium there is no official recommendation for periconceptional folic acid supplementation. However, the unofficial policy is for all women planning a pregnancy to take 0.4 mg folic acid daily and for women at high risk of having a pregnancy affected by a neural tube defect to take 4 mg of folic acid daily. This should be taken 2 or 3 weeks before conception and during the first 3 months of pregnancy.

Food Fortification Policy

There is no official folic acid food fortification policy in Belgium. However, fortified products such as breakfast cereals are available for consumption.

Health Education Initiatives

In 2005, the ONE (Office de la naissance et de l'enfance (Office of Birth and Childhood)) in association with the ASBBF (Association Spina Bifida Belge Francophone), ran a health education campaign which included leaflets, a website, and information on radio and television. Letters about the benefits of periconceptional folic acid were sent to family physicians and gynaecologists in the French speaking area of Belgium. Information on why and when to take periconceptional folic acid is also on the website of the Flemish counterpart of ONE "Kind en Gezin (Child and family)".

In 2009 a health education campaign, including leaflets and posters, started in the province of Antwerp. The campaign was announced in the press and focused on gynecologists, family doctors, pharmacies, midwives and child welfare.

Knowledge and Uptake of Folic Acid

In 2006, a questionnaire regarding use of folic acid was administered to 195 breast feeding women in the first week after delivery.¹ They had all delivered their first baby and had been recruited for a study on pollutants in mothers' milk. The results are in Table 1.

Table 1 % of women using folic acid

	Flanders N= 104	Wallonia N= 71	Brussels N= 20	Total N= 195
Before and during pregnancy	26	21	25	24
Only before pregnancy	13	6	0	9
Only during pregnancy	52	44	40	48
Total	90	70	65	81

Proportion of Pregnancies that are Planned

No information provided

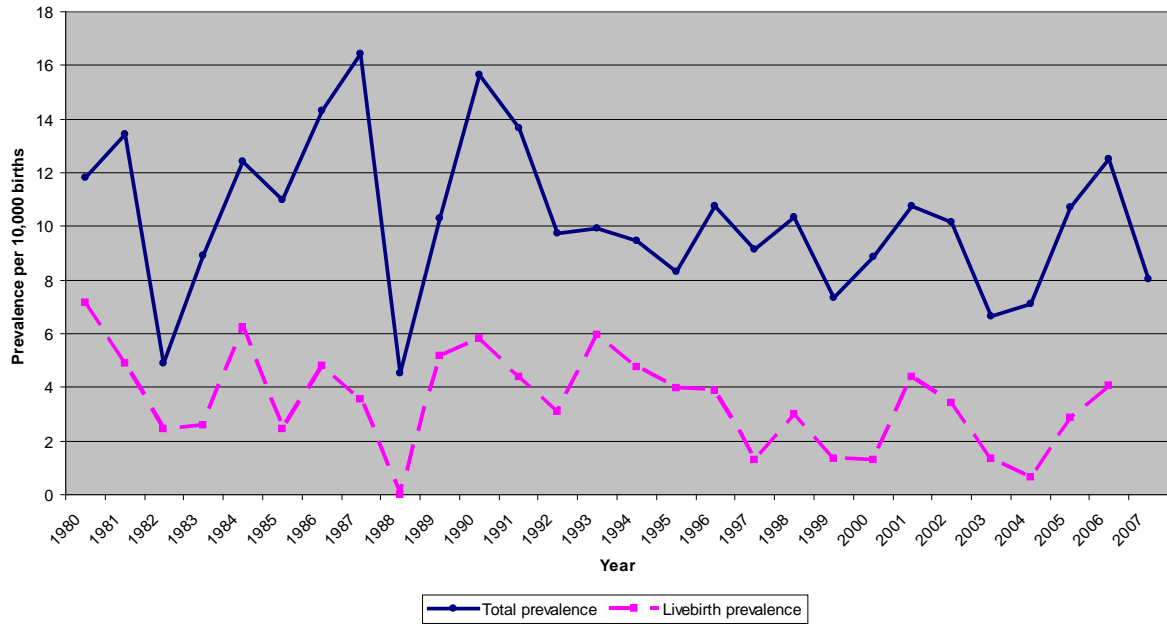
Laws Regarding Termination of Pregnancy

Termination of pregnancy is legal up to the gestational age of 12 weeks. Beyond the period of twelve weeks, the termination of pregnancy may be practised only when the pursuit of the pregnancy severely endangers the health of the woman or when it is certain that the unborn child will be affected by a disorder of a particular gravity, recognized as incurable at the time of the diagnosis in which case there is no gestational age limit.²

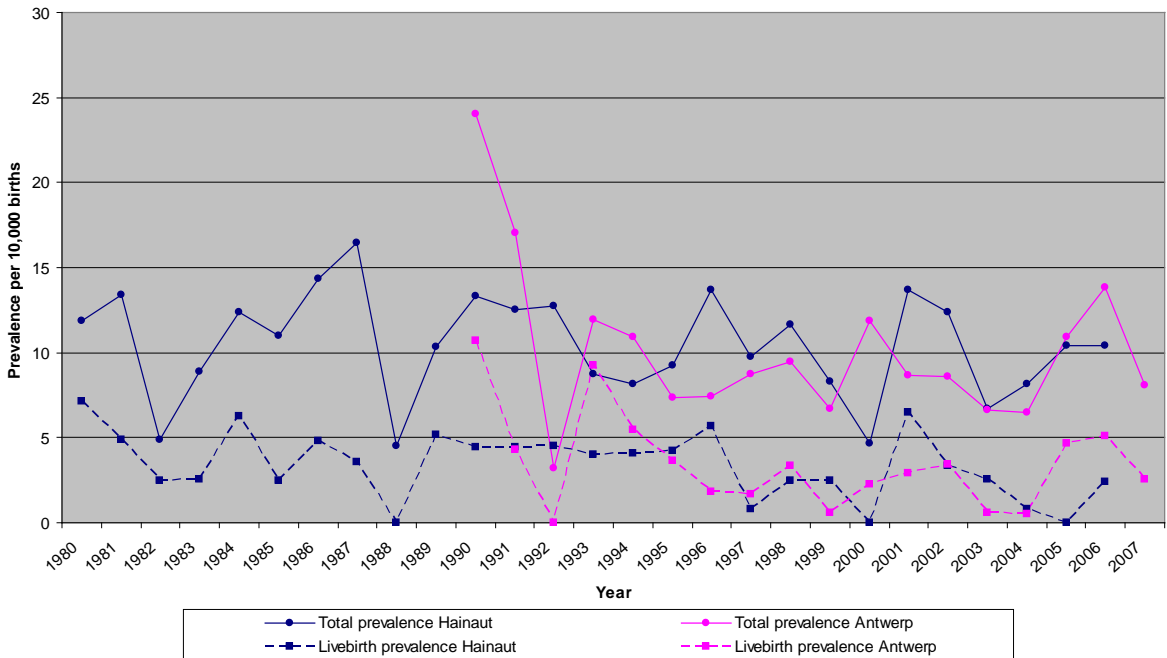
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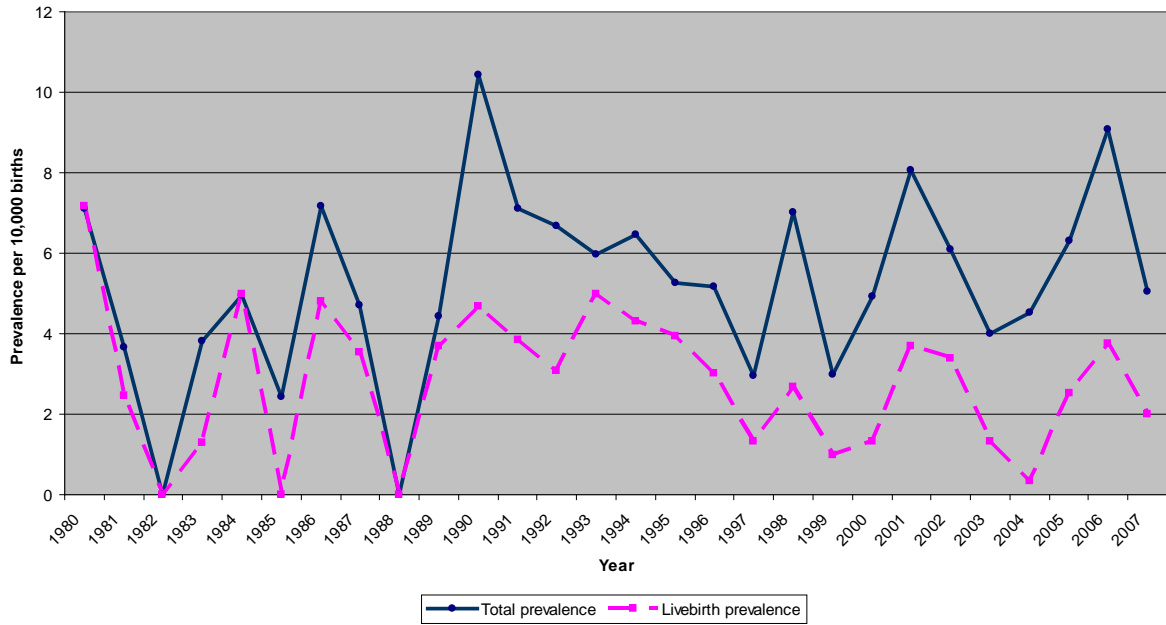
Belgium (Hainaut and Antwerp): Total and Livebirth Prevalence Rates for Neural Tube Defects (2 registries together)



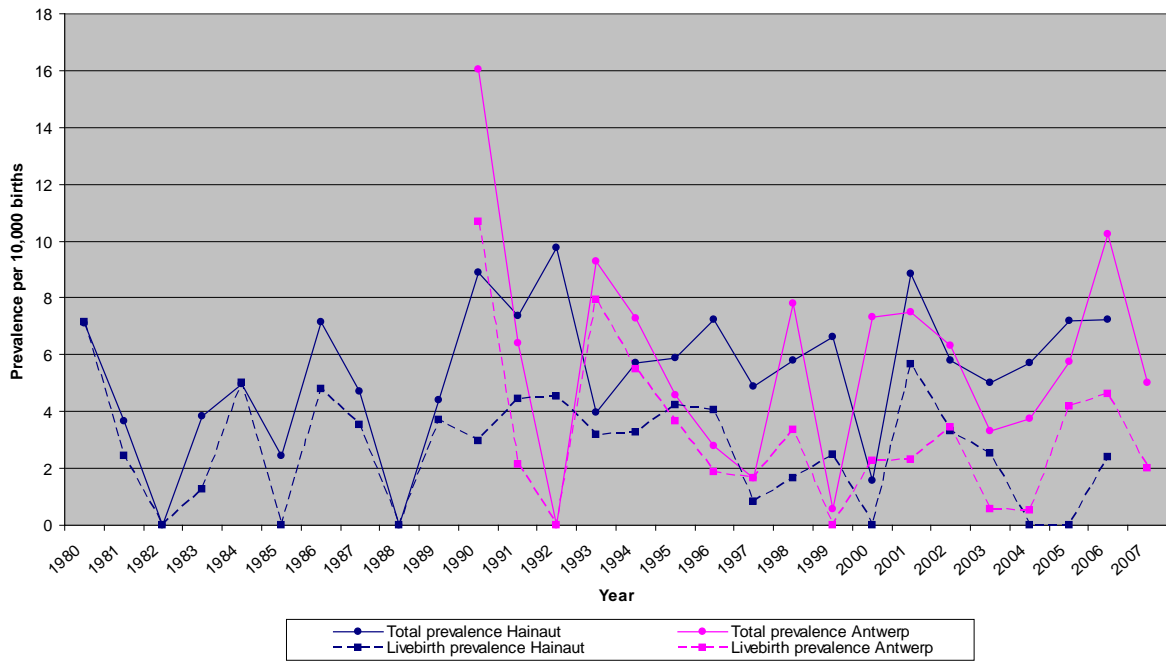
Belgium (Hainaut and Antwerp): Total and Livebirth Prevalence Rates for Neural Tube Defects



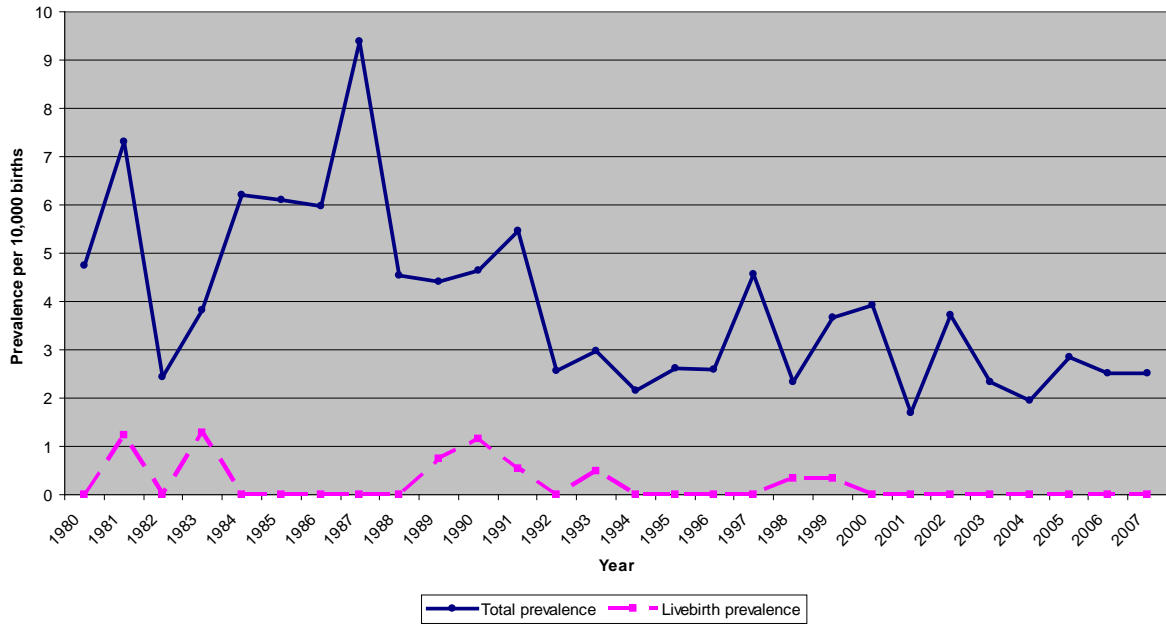
**Belgium (Hainaut and Antwerp): Total and Livebirth Prevalence Rates for Spina Bifida
(2 registries together)**



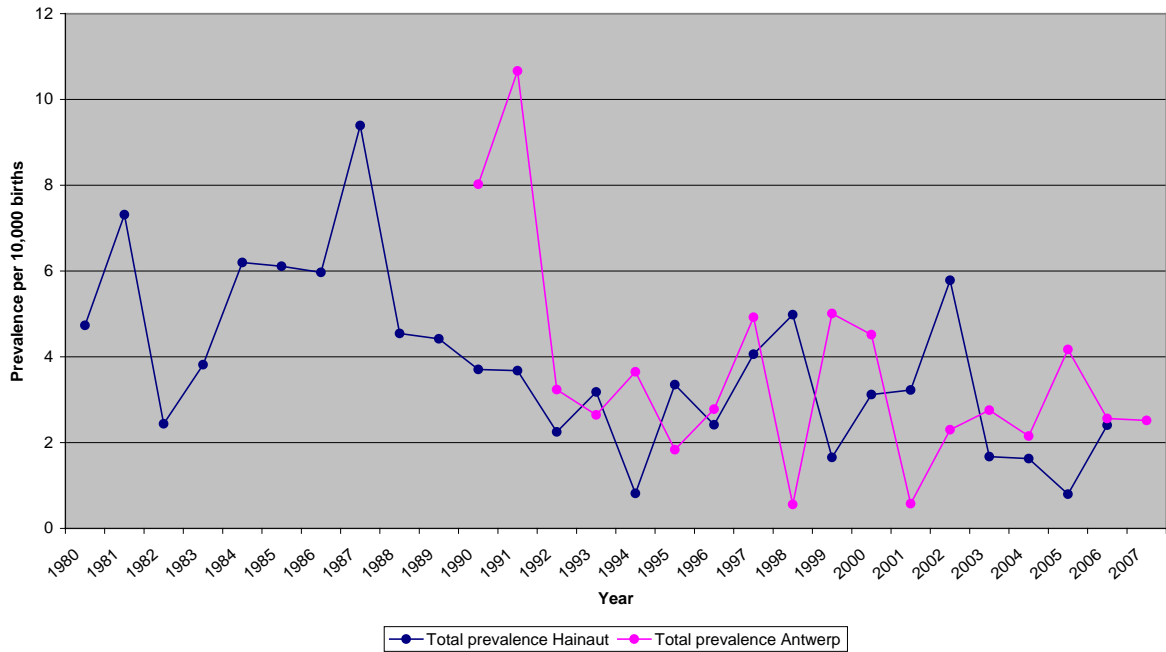
Belgium (Hainaut and Antwerp): Total and Livebirth Prevalence Rates for Spina Bifida



Belgium (Hainaut and Antwerp): Total and Livebirth Prevalence Rates for Anencephaly (2 registries together)



Belgium (Hainaut and Antwerp): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Croatia

Dr Visnja Tokic, Dr Ingeborg Barisic, Dr Romana Gjergja

Folic Acid Supplementation Policy

There is no official folic acid supplementation policy in Croatia and none is being planned. Most gynaecologists and paediatricians in Croatia advise every woman to take folic acid (0.4 mg per day) at least 4 weeks before starting a pregnancy until the 12th week of pregnancy. For women who have had a previous pregnancy affected by a neural tube defect, the dosage is 4 mg per day for the above-mentioned period. There are few folic acid supplementation products: FOLIC PLUS – (400 µg in 3 tablets) Natural Wealth, FOLIC ACID CAPS (800 µg) - Twinlab, PRENATAL tablets (800 µg) – Natural Wealth, PRE-NATAL caps (400 µg in 2 capsules), FOLACIN (5 mg) – Jadran Galenski Laboratorij. There is no funding for folic acid products during pregnancy; pregnant women have to pay for it themselves.

Food Fortification Policy

There is no mandatory food fortification in Croatia. Of course, one can get fortified food from other European countries, and it is not prohibited to have and to sell it in shops, but there are no statistics or studies on that issue.

Health Education Initiatives

There is no official health education initiative in Croatia, but there are many initiatives by the media (TV, Internet, journals, gynecologists and pediatricians, especially private ones). An example is in the Maternity Unit “Sveti Duh” in the city of Zagreb; there is a “Club of pregnant women” and they discuss their habits and nutrition during the pregnancy. A major function of that Club is to educate women about healthy nutrition, for instance, the importance of taking ample folic acid. The Internet page is: www.klubtrudnica.net

There are some useful Croatian sites on the Internet:

- www.poliklinika-harni.hr
- www.mameibebe.net
- www.vasezdravlje.com
- www.iskon.hr/bebe

Knowledge and Uptake of Folic Acid

The studies on dietary habits and folic acid supplementation in Croatia are limited; there are a few studies relating to anaemia in children, congenital heart diseases, neurological disease in children and arteriosclerosis. In 2003 we administered a questionnaire to pregnant women in "Sveti Duh Hospital" in Zagreb (unpublished data): 495 pregnant women completed the questionnaire during their attendance at the prenatal clinic. Median age was 30.8 years (± 3.7). 74% (368/495) of women were aware of the role of folic acid in the prevention of birth defects. The sources of the information were: the media (53%), health professionals (39%) and friends (9%). 64% of women were informed too late: 48% during the first pregnancy and 16% after the first pregnancy. 71% of women (349/495) expressed the need for more information on folic acid supplementation in pregnancy. 69% (343/495) of women were taking folic acid, but only 20% of them (70/343) during the appropriate periconceptional period. This was despite the fact that 75% (371/495) of the pregnancies were planned. Most of the women (71%) could not specify the daily dosage taken. As a group, women who were not taking folic acid were less educated than women who were taking it. 20% of women not taking folic acid had graduated from faculty or high school, while 41% of women who were taking it had graduated from faculty or high school. ($p < 0.01$). Parity, marital and economic status did not influence folic acid intake. Out of 371 planned pregnancies, folic acid was taken during the appropriate time period by only 19% of women (70/371), while 27% (100/371) did not take folic acid supplementation at all.

In a more recent study (2006),¹ Pucarín-Cvetković et al looked at 100 women of childbearing-age (range 20-30 years), mean age 24 ± 3.7 . The subjects were residents of Zagreb and its surroundings. The results based on the data obtained through 24-h recall showed that the mean intake of naturally occurring food folate and folic acid from fortified cereals was $156 \pm 72.2 \mu\text{g/day}$. The mean value of the serum folate was within the normal range: 7-28 nmol/L – no clinical deficit was identified. Differences were found ($p < 0.001$) between the subjects who consumed folic acid supplements in drinks and tablets and subjects who did not. Differences were also found between subjects who took folic acid supplements in drinks or tablets and subjects who took folate only through foodstuffs, and did not consume folic acid supplements ($p = 0.040$).

Proportion of Pregnancies that are Planned

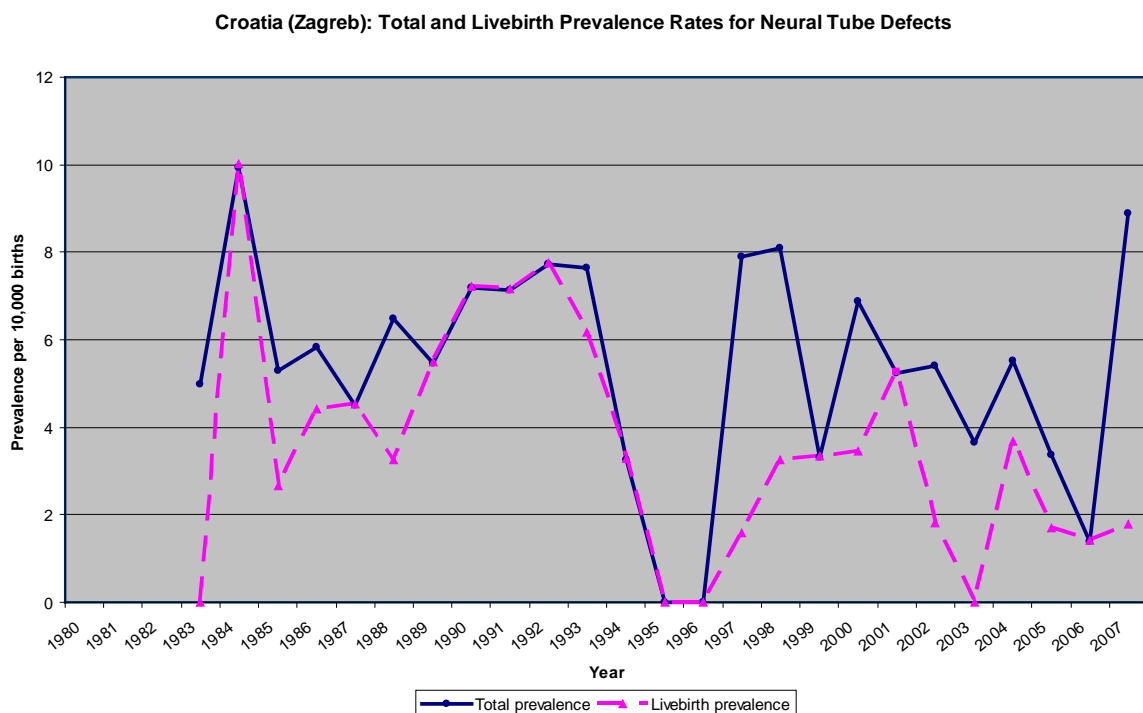
In one small unpublished study, 75% of pregnancies were planned. No other information is available.

Laws Regarding Termination of Pregnancy

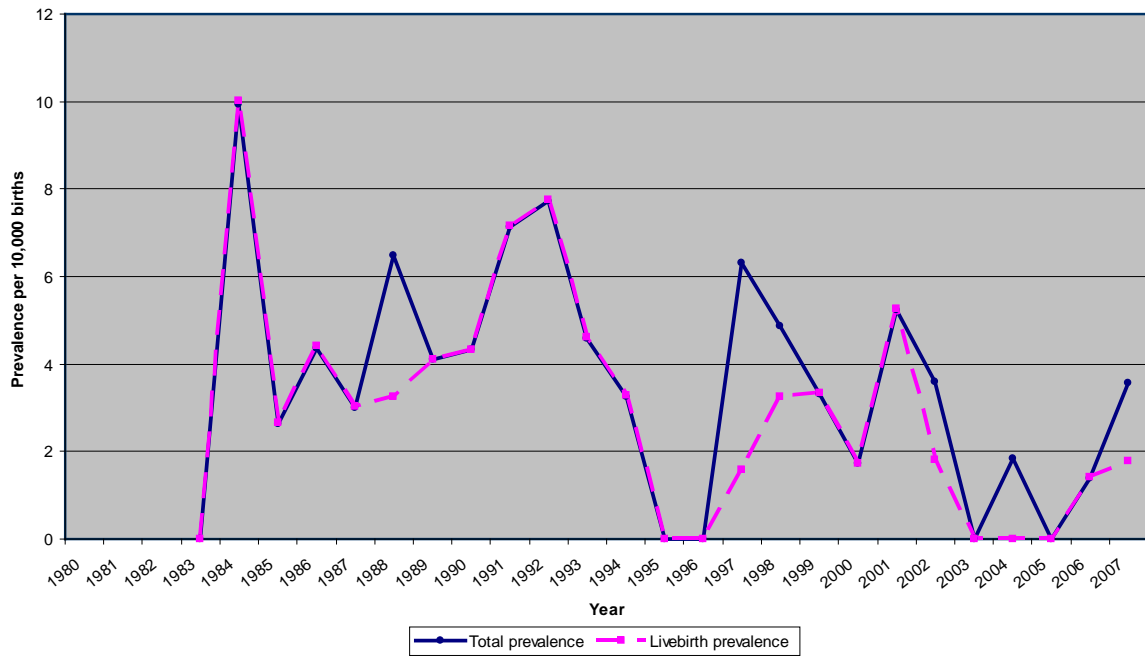
Termination of pregnancy for fetal abnormality is legal up to 24 weeks of gestation in Croatia. After 24 weeks gestation it is not legal, but if a life-threatening anomaly is found on ultrasound scan after 24 weeks, there is some possibility of termination of pregnancy if it is approved by the Hospital Commission.

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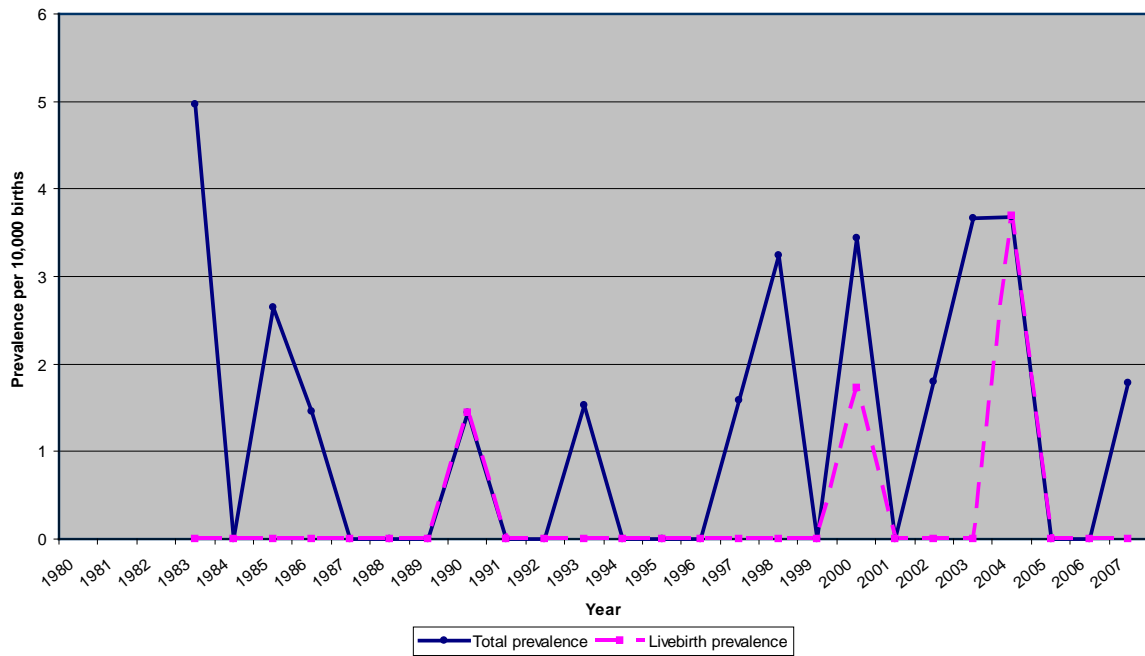
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Croatia (Zagreb): Total and Livebirth Prevalence Rates for Spina Bifida



Croatia (Zagreb): Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Denmark

Dr Marianne Christiansen

Folic Acid Supplementation Policy

The official folic acid supplementation policy in Denmark was introduced in March 1997 by the Danish Veterinary and Food Administration. It is as follows: Women planning a pregnancy are recommended to take a multivitamin tablet or a folic acid tablet containing 400 µg of folic acid per day, or to take in 400 µg of folic acid per day through diet, if possible. In the official recommendations, it is mentioned that for practical reasons the recommendation is to take a folic acid supplementation of 400 µg per day since achieving 400 µg of folic acid through the diet would require a change of diet for most women. The supplementation should begin when the pregnancy is planned and continue until 3 months of gestation. Women with increased risk of having a pregnancy with a neural tube defect due to malabsorption, long-term use of certain medications, diabetes mellitus or neural tube defects in relatives are recommended a folic acid supplement of 400 µg per day through multivitamin / folic acid tablets. Available preparations include Folsyre[®] 0.4 mg folic acid, "Gravitamin" containing 0.4mg folic acid amongst other vitamins, and "Gravid" containing 0.4mg folic acid amongst other vitamins.

Women who have previously had a fetus with a neural tube defect, who themselves have a neural tube defect or whose partner has a neural tube defect are recommended to take 5 mg of folic acid per day. This supplementation is recommended from when the pregnancy is planned and until 2 months of gestation. The available supplementation is "Folimet" 5 mg folic acid.

The official policy was declared by the Danish Veterinary and Food Administration after a working group had made a report on the issue.¹ The official policy differs slightly from the recommendations given in the report regarding the time period in which pregnant women should take supplementation. The policy is also stated in the Directives of Antenatal and Maternity Care given by the Danish National Board of Health 1998.²

Food Fortification Policy

In 2002 the Danish Veterinary and Food Administration established a working group to re-evaluate the issue of folic acid fortification of food. In April 2003 this group published a report recommending that the existing official recommendations regarding supplementation should be followed and that mandatory folic acid fortification of food should be introduced in Denmark. However, no action has been taken yet and the official policy established in 1997 remains unchanged; there is no mandatory folic acid fortification of food in Denmark.

Health Education Initiatives

There is an official health education initiative in Denmark to inform women about the role of folic acid in reducing the risk for neural tube defects: The Danish Veterinary and Food Administration have had press releases with information about the policy; the first was on March 3, 1997, another on June 11, 1999. Leaflets addressing women planning pregnancy have been published by the Danish Veterinary and Food Administration and distributed to general practitioners, specialists in gynaecology and obstetrics, gynaecological / obstetrical departments of the Danish hospitals, pharmacies and drugstores. The leaflets were first distributed in 1999 and again in 2001. In 2001 the number of leaflets distributed was 105,000 (the number of total births in Denmark per year is approximately 65,000). Publications from the National Board of Health addressing women planning a pregnancy and pregnant women also contain information about the official folic acid recommendations. There have been no paper or television advertisements, but the issue has been covered in some newspaper articles, television programs about health issues and in magazines concerning health, pregnancy and children. The Danish Veterinary and Food Administration has started an ongoing campaign with flyers, go-cards and posters to download from their website.

Knowledge and Uptake of Folic Acid

In 2004, a paper called "Low compliance with recommendations on folic acid use in relation to pregnancy: is there a need for fortification?" (4) was published in Public Health Nutrition. It was a cohort study on pregnant women in Denmark. 22,000 pregnant women were recruited for The Danish National Birth Cohort between November 2000 and February 2002. Use of dietary supplements was recorded. Compliance with the recommendation was related to the information campaign that

took place during the second half of 2001. An increase was seen in the proportion of women complying with the recommendation in the study period and this coincided with the information campaign events. However, even at the end of the period, only 22.3% of the women who had planned their pregnancy fully complied with the recommendation. No increase at all was seen in periconceptual folic acid use among women with unplanned pregnancies.

Regarding the dietary habits of women of child bearing age, the working group under the Veterinary and Food Administration (1) have calculated the intake of folate in Denmark using data from the Danish Dietary Survey performed in 1995. The results were that women of child-bearing age in Denmark have a mean intake of 248 µg folate per day through the diet; only 5% get 400 µg or more.

Proportion of Pregnancies which are Planned

No national study has been published from Denmark on the proportion of pregnancies which are planned. In the Danish version of the report done by the working group under the Danish Veterinary and Food Administration (1) it is assumed that the number is a little higher than in the United States where approximately half of the pregnancies are planned, since compliance with contraception in Denmark is rather high. However a regional study in Denmark was published in 2001.⁵ The study population (n=3516) was recruited among pregnant women attending Odense University Hospital, Funen County (the region covered by the EUROCAT register), in the period November 1994-January 1996. In this study 68% of the women with accepted pregnancies stated that the pregnancy was planned. The representativity of this study sample was judged by comparing the age distribution and the parity profile of the women in the study population with the national figures. No pronounced difference was found, indicating that the study sample can be considered a representative sub sample of the Danish population.

Laws Regarding Termination of Pregnancy

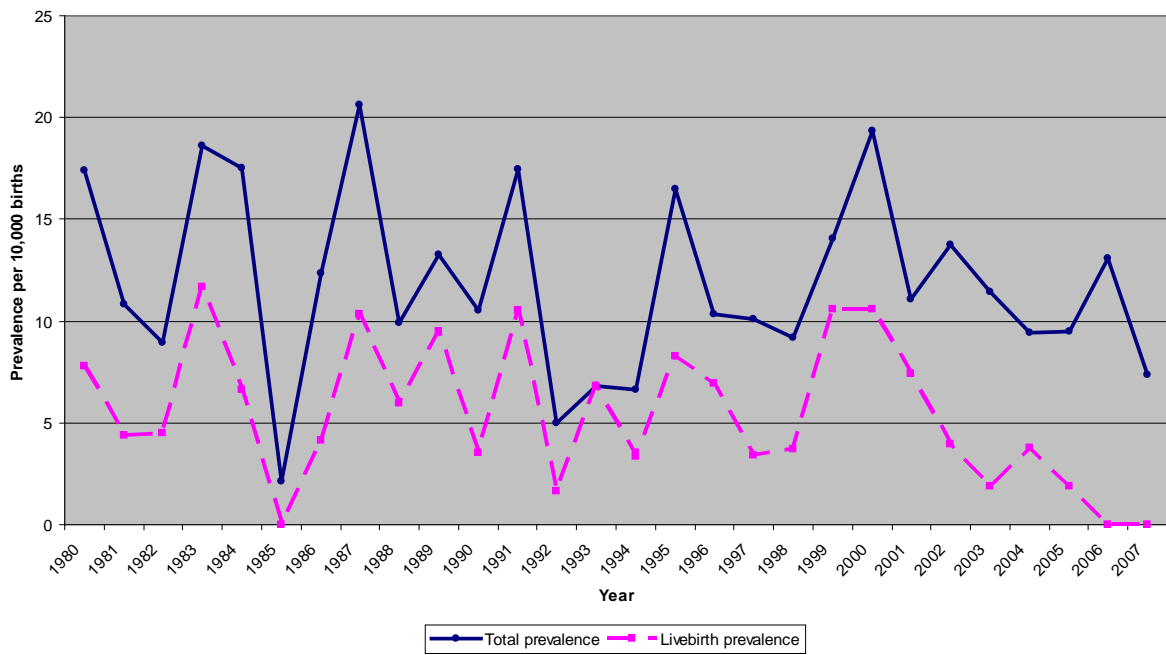
Women in Denmark have the right to have a termination of pregnancy before 12 weeks of gestation. After 12 weeks a woman can have her pregnancy terminated after obtaining permission from a special committee of two doctors and an employee at the Social Centre (one committee in each County). If a severe congenital anomaly

is diagnosed, the upper gestational age for termination is usually 22 weeks. Termination may be permitted later, but only if the congenital anomaly is so severe that survival by birth would be impossible.

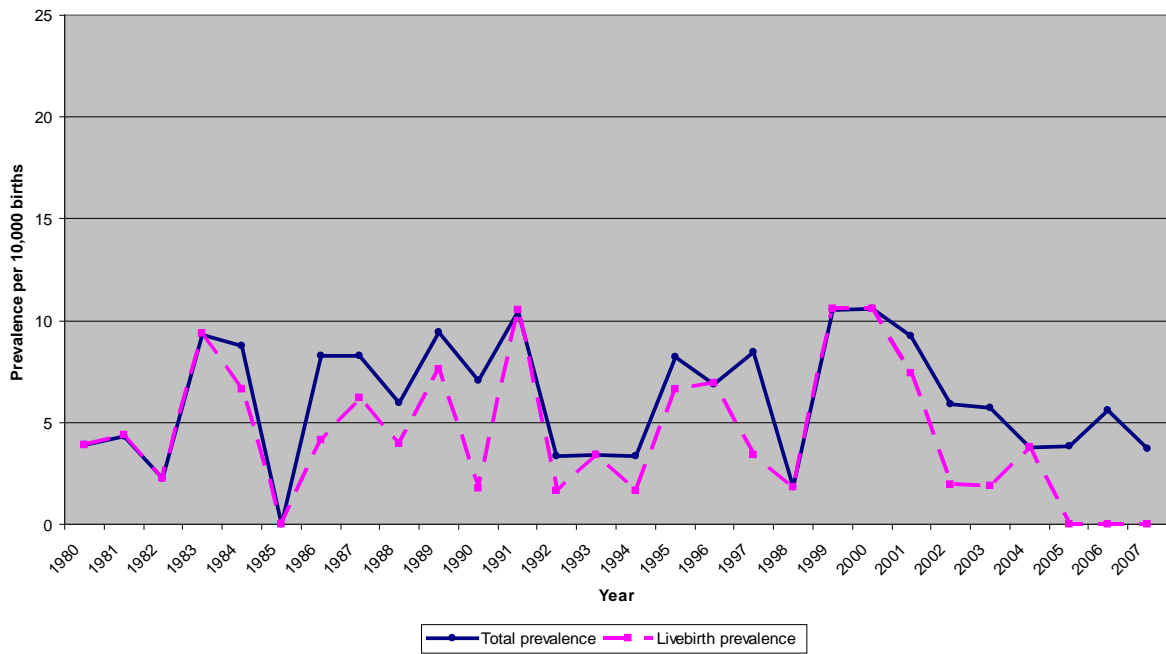
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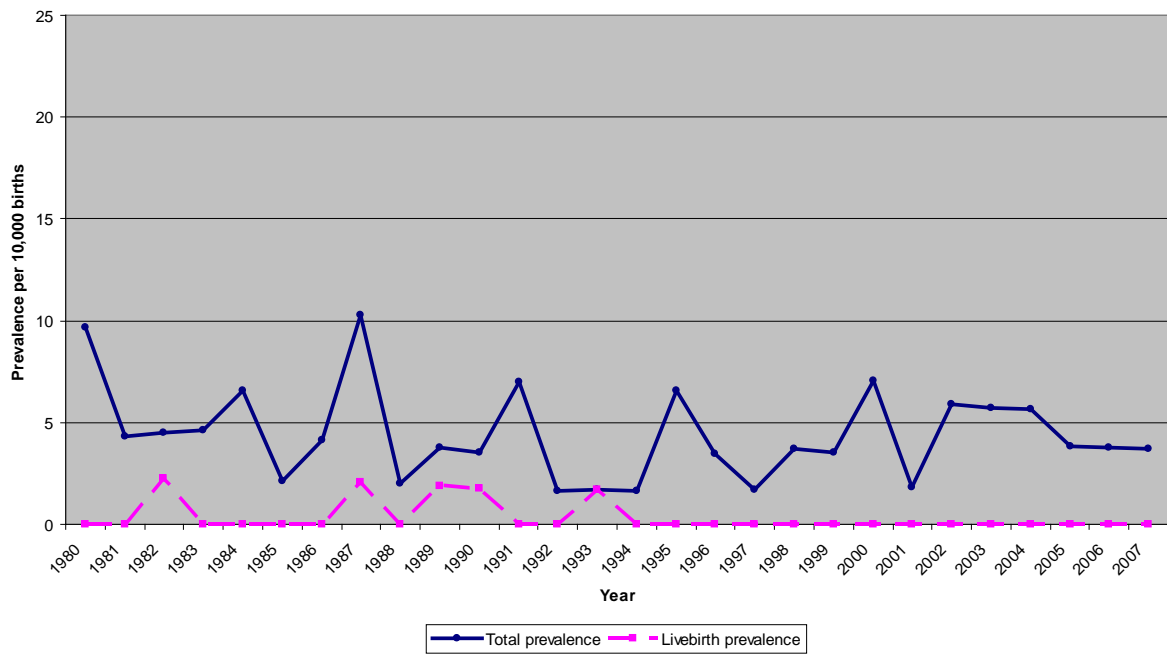
Denmark (Odense): Total and Livebirth Prevalence Rates for Neural Tube Defects



Denmark (Odense): Total and Livebirth Prevalence Rates for Spina Bifida



Denmark (Odense): Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Finland

Dr Annukka Ritvanen

Folic Acid Supplementation Policy

In 1994 the Finnish Ministry of Social Affairs and Health set up an expert group to prepare a National Recommendation on Periconceptional Use of Folic Acid. The recommendations, issued in 1995, were sent to all medical professionals, health care centres, hospitals and pharmaceutical companies.¹ The recommendations were also published in the leading Finnish scientific medical paper in 1996.² The recommendations were reviewed by an expert group of the Ministry of Social Affairs and Health in 2004, and in the autumn of 2004 the new recommendations on folic acid were published as part of a National Nutrition Recommendation for small children and pregnant and breast feeding mothers. The main changes in the new recommendations, compared with the old ones from 1995, are in the first section concerning ordinary pregnancies. The 1995 recommendation was purely dietary, while in the 2004 recommendation a supplement of a 0.4 mg folic acid tablet is recommended for those with an unbalanced diet poor in folate content.

The present official recommendation on folic acid supplementation has three sections:

1. Prevention of first occurrence of NTD in ordinary pregnancies

The recommendation is to take 0.4 mg folate daily in diet periconceptionally.

- A normal, balanced low-fat and low-sugar diet, with abundant fresh vegetables, berries and fruit as well as wholemeal products, rich in folate, is recommended for all women planning a pregnancy and in early pregnancy, in order to obtain folate equivalent to at least 0.4 mg folic acid daily.
- A daily supplement of a 0.4 mg folic acid tablet, to be used periconceptionally, is recommended for all women planning a pregnancy and in early pregnancy, whose diet does not contain enough fresh vegetables, berries, fruit or wholemeal products.
- A daily supplement of a 0.4 mg folic acid tablet can also be taken periconceptionally by women with balanced, folate-rich diet, if they want to make sure they will obtain an adequate amount of folic acid.

2. Prevention of first occurrence of NTD in special situations

The recommendation is to take a daily supplement of a 0.4 mg folic acid tablet periconceptionally.

- In addition to a balanced diet, a daily supplement of a 0.4 mg folic acid tablet, to be used periconceptionally, is recommended for women who are planning a pregnancy and who may, for various reasons, have potential folate deficiency in early pregnancy.
- Potential folate deficiency may occur, if the mother has a very unbalanced diet, treatment with antiepileptics (phenytoin and barbiturates), long-term treatment with sulphonamides, celiac disease or other severe intestinal malabsorption or heavy alcohol consumption.
- Folic acid supplementation may also be considered, if the mother has, insulin dependent diabetes, clomiphene treatment, valproate or carbamazepine treatment or neural tube defects among more distant relatives.

3. Prevention of recurrence of NTD

The recommendation is to take a 4 mg folic acid tablet daily, periconceptionally

- There is an increased risk (2–3%) of fetal NTD in the following situations:
 - a) the parents have had a common child or fetus with NTD.
 - b) either parent has had a child or fetus with NTD with another partner
 - c) either the mother or the father has had NTD him/herself.
- The use of a 4 mg folic acid supplement as tablets should take place under the control of a doctor, and this supplement is only available with a doctor's prescription. Before starting this supplementation, or if needed also during the supplementation, the maternal serum B12 level should be checked in order to make sure that there is no deficiency of vitamin B12. The reason for this is that an amount of 1mg folic acid can conceal megaloblastic anaemia, associated with deficiency of vitamin B12, and thus prevent the detection of deficiency of this vitamin.
- Folic acid supplementation does not give complete protection against fetal NTD, so in pregnancies in high risk families, prenatal screening

and diagnosis should be offered to women. Women who want prenatal investigations should be referred to a prenatal diagnostic unit in a university hospital early in pregnancy.

- The Social Insurance Institution does not reimburse preventive folic acid supplementation.
- Folic acid supplementation is started, when contraception is stopped or at the latest, at the beginning of the menstrual period after which a pregnancy is hoped for, and the supplementation will be continued until the end of the 12th week of pregnancy (i.e. starting 4 weeks before conception and continuing until the end of the 12th week of pregnancy).

The expert group of STM still considered that the balanced diet, according to the National Nutrition Recommendation, usually guarantees an adequate supply of folate, and that routine folic acid supplementation is not needed. It has, however, been observed that the average intake of folate by Finnish women (224 µg) is less than the Finnish Nutrition Recommendation (400 µg for pregnant women and those planning a pregnancy and 300 µg for other women). The expert group considered that a minimum of 5 to 6 portions of vegetables, berries and fruit should be eaten daily. If the mother eats very few fresh vegetables, berries and fruit, she should be advised to increase her intake of them in order to improve the balance of her diet and to ensure intake of the recommended amount of folate.³

The expert group also reported that the easiest way to implement supplementation of 0.4 mg folic acid is to use a multivitamin preparation with an adequate amount of folic acid. There are a few preparations in the Finnish market which, taken according to instructions, give a daily supply of 0.4 mg folic acid. Preparations with lower concentrations of folic acid are not recommended for use, as by increasing the dosage, the supply of other nutrients becomes too high.

A recommendation on folic acid supplementation published by the National Research and Development Centre for Welfare and Health STAKES in 1999 was approximately the same as the present recommendation.⁴

Food Fortification Policy

Fortification of food products with folic acid was not considered justifiable in Finland (STM 1995). Fortification of food products with folic acid has been monitored by the Finnish Food Safety Authority (previously National Food Agency) with the support of the Ministry of Social Affairs and Health and under the direction of a broad-based group of experts. The report of the expert group, published in December 2001, did not recommend fortification of basic food products with folic acid.⁵

Health Education Initiatives

There has been no health education initiative on folic acid supplementation in Finland, but information is being given at schools and by the maternity clinics and child welfare clinics. The issue has been widely presented in women's magazines.

Folic Acid Knowledge and Uptake

A study was carried out in the year 2000 in 114 public maternity clinics around Finland. Public Health nurses or midwives completed a questionnaire with the women during their first visit to the maternity clinic. 547 women participated in the study; 6 % of the women refused. The women had their first antenatal visit on average during the ninth gestational week. 65 % of respondents had heard about folic acid; young and less educated women had heard of it less often than others. The women had received information on the effect of folic acid on pregnancy and fetuses from newspapers and magazines, public maternity clinics and health care centres, and from schools and other educational institutions. Drug advertisements and friends were a more common source of information than were doctors and pharmacists. 10 % of women knew about the effects of folic acid on pregnancy and the fetus. 29 % of women could list at least one food product containing folic acid. 45 % of women had used at least one preparation containing vitamins and / or trace elements before and / or in early pregnancy. 34 % of women had consumed a folic acid supplement (19% of them before pregnancy and /or in early pregnancy).⁶

Proportion of Pregnancies which are Planned

547 women were interviewed by a midwife / nurse during their first prenatal care visit at approximately 9 weeks gestation. Data were collected over a one month period in 114 maternity centres in Finland in the year 2000. 6 % of the women refused to participate. Between 37 % and 86 % of the pregnancies were planned, depending on

the interpretation of the concept of “planned”. 60 % of the women changed their life style in early pregnancy. However, 75 % of these changes were made only after the woman found out about her pregnancy.⁷

What women thought about getting pregnant prior to the pregnancy, by age of mother (%)

	<25	25-29	30-34	≥35	All
I wished to get pregnant as soon as possible	33	39	41	32	37
I thought the pregnancy may begin by its own time	48	53	47	45	49
I wished to get pregnant later	9	4	2	5	5
I did not want to get pregnant	4	1	3	3	2
I didn't think about it	3	3	4	9	4
Getting pregnant or the time was not important	4	1	3	6	3

According to a recent study in Northern Finland the percentage of wanted pregnancies seems to be high even among primiparous mothers.⁸

Laws Regarding Termination of Pregnancy

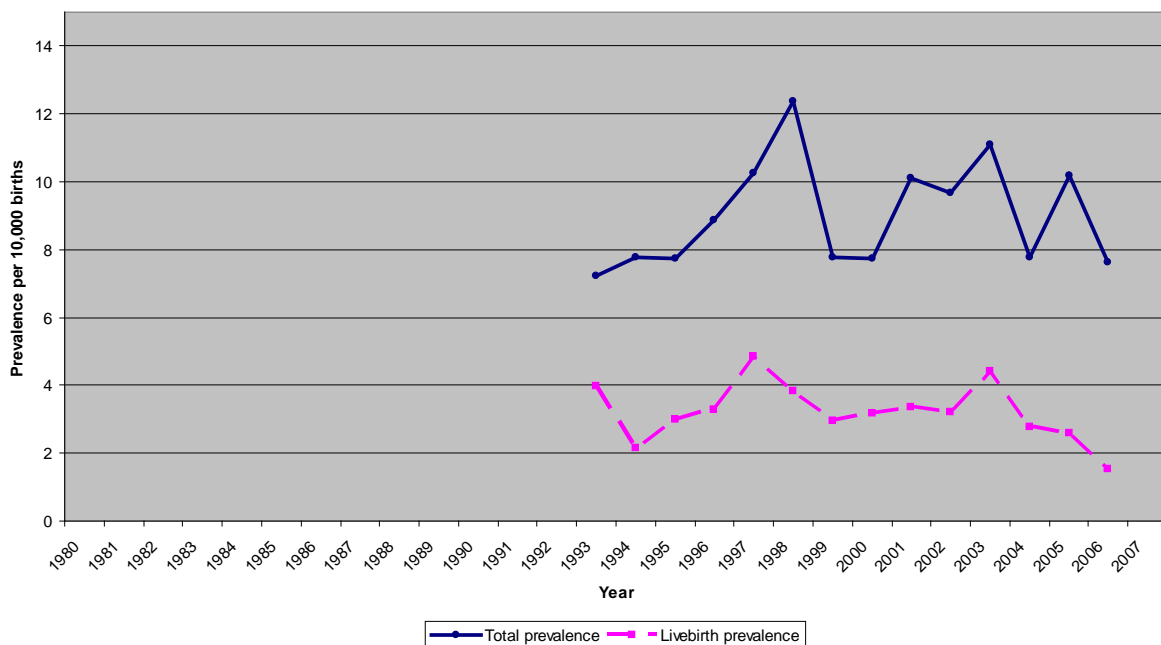
Termination of pregnancy is allowed up to 12 weeks gestation (12+0 gw) for many indications by permission of one or two doctors and up to 20 weeks (20+0 gw) by special permission of the National Supervisory Authority for Welfare and Health (Valvira). If the mother's life is in danger, the pregnancy can be terminated at any gestational age. Termination for severe fetal abnormality can be done up to 24 weeks only by special permission of the National Supervisory Authority for Welfare and Health (Valvira).

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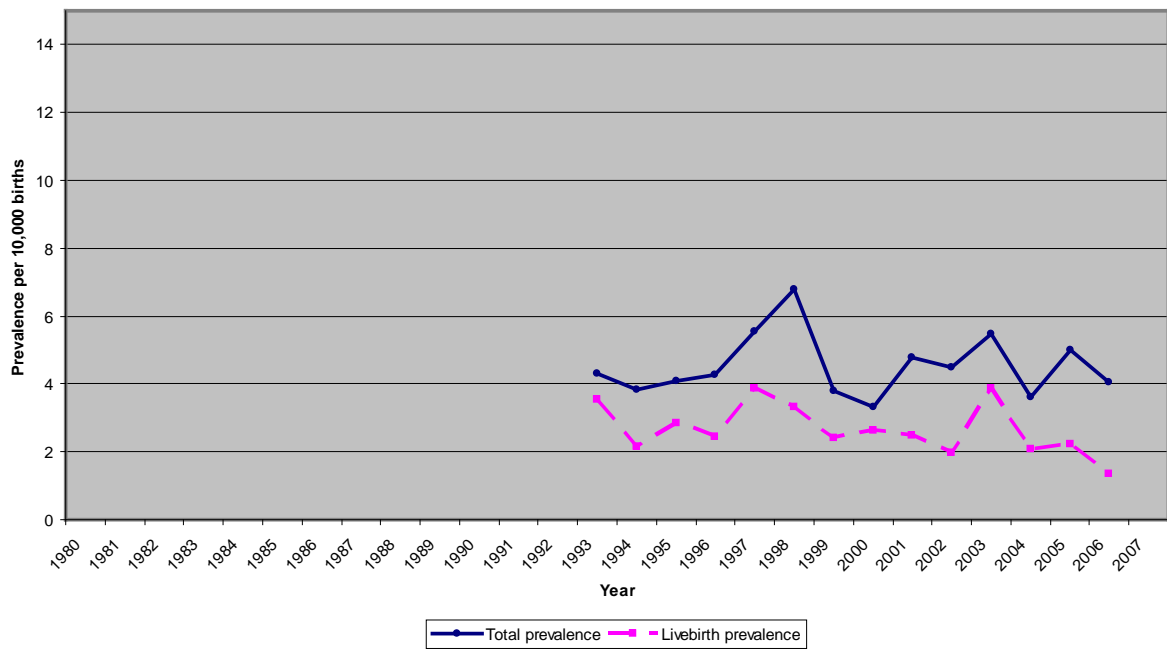
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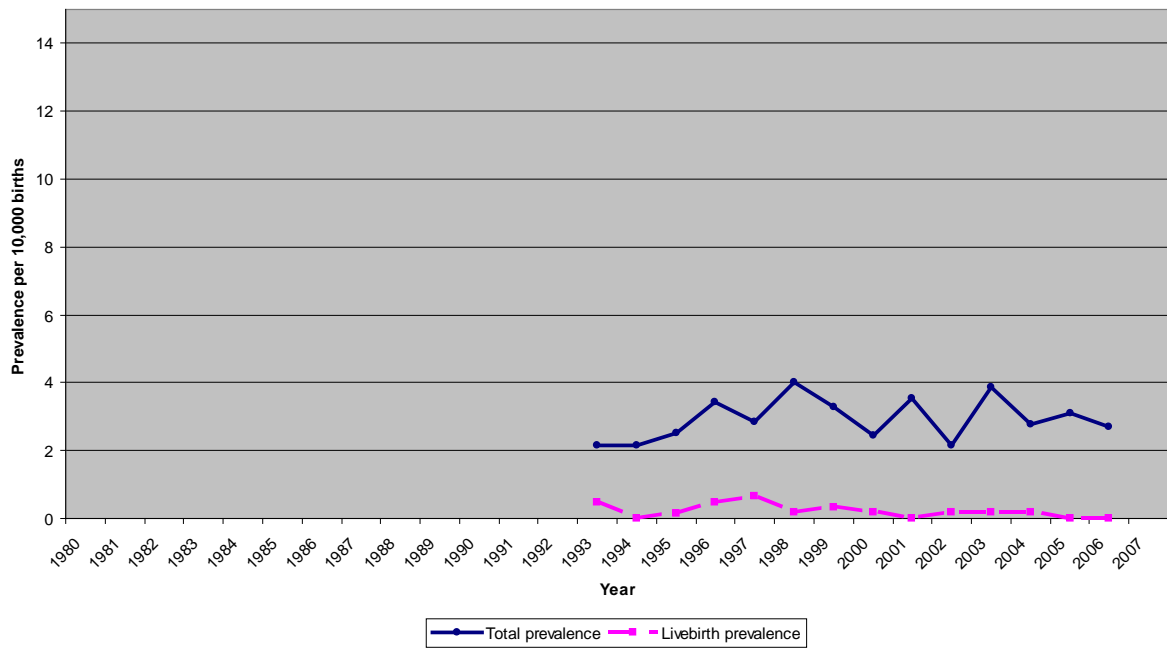
Finland: Total and Livebirth Prevalence Rates for Neural Tube Defects



Finland: Total and Livebirth Prevalence Rate for Spina Bifida



Finland: Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for France

Dr Janine Goujard and Elisabeth Robert-Gnansia

Policy on Folic Acid Supplementation

In 1995, the French Pediatric Society published a recommendation to pregnant women to take a daily dose of 0.2 mg daily of folic acid supplements. They also advised women of child-bearing age to increase folate intake through diet.

A second awareness was raised in 1997 by the National College of Obstetrics and Gynecology. They advised the same folic acid supplementation level of 0.2 mg daily during the periconceptional period, reinforcing the position of the French Pediatric Society. The folic acid status of the French women was considered to be good. However, encouragement was given for a multi-vitamin therapy at a daily dose of 400 µg of folic acid in high-risk situations (teenagers, discontinuation of oral contraception, alcoholic women, women of low social economic class).

In 1999, the State Secretary of Health set up an expert group to prepare national recommendations which were issued in August 2000. The advice for most women planning a pregnancy was a daily dose of 0.4 mg of folic acid from 4 weeks before conception to 8 weeks after conception. In February 2003, two pharmaceutical companies marketed the first tablets ever sold in France containing the exact dosage of 0.4 mg of folic acid alone. The Ministry of health agreed to refund women for 65% of the cost for these tablets when they are prescribed to prevent malformations.

For women with a previous NTD pregnancy and women taking antiepileptic medication, the recommendation was 5 mg folic acid daily; this dosage has been marketed for many years.

Food Fortification Policy

There is no mandatory food fortification. However, some fortified breakfast cereals are available (around 160-170 mg /100 g, more for "Cornflakes: 300 mg /100 g") in most supermarkets.

Health Education Initiatives

In 2000, recommendations for a diet rich in folate, calcium, iodine and iron were made in an illustrated leaflet addressed to women of child-bearing age. In this booklet, there is a small paragraph for women planning pregnancy, saying that folic acid is needed to “prevent intra uterine growth retardation and various severe malformations of the baby “.

In 2004, the French “Association Spina Bifida” edited 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.

The pharmaceutical companies marketing 0.4 mg folic acid tablets have organized conferences and training programmes for gynaecologists across the country in order to stimulate prescription of folic acid by physicians.

Advice about periconceptional folic acid has been spread via TV and newspapers.

Knowledge and Uptake of Folic Acid

Two studies using the same protocol were done in public and private obstetric units in Paris in 1995 and 1999. The 1999 study (2) carried out on 735 women interviewed 2 or 3 days after the delivery showed that 55.1 % (405/735) had heard of folic acid but most often with no knowledge of its effect. 24.3% (177/728) reported the use of one of the products containing folic acid (with or without additional multivitamins or minerals) present on a list with the pictures of the boxes. But only 1.0% (8/735) took the folic acid in the recommended period. Even these results were better than those of the 1995 survey (1) in which only 0.5 % - 3/733- took folic acid during the recommended period. Clearly, the messages from the “non official” recommendations issued in the country in 1995 and 1997 were not heard.

In a recent study in Brittany, more than 200 women were surveyed after delivery. 10% reported taking periconceptional folic acid correctly. A further 30% took it during pregnancy only (personal communication Dr. Hubert Journel)

Proportion of pregnancies which are planned

No information is available.

Laws Regarding Termination of Pregnancy

There is no upper gestational age limit on termination of pregnancy for fetal abnormality with approval by experts if “there is a high probability that the fetus is affected by a particularly severe condition with no effective therapy available at the time of prenatal diagnosis” (law of July 1994).

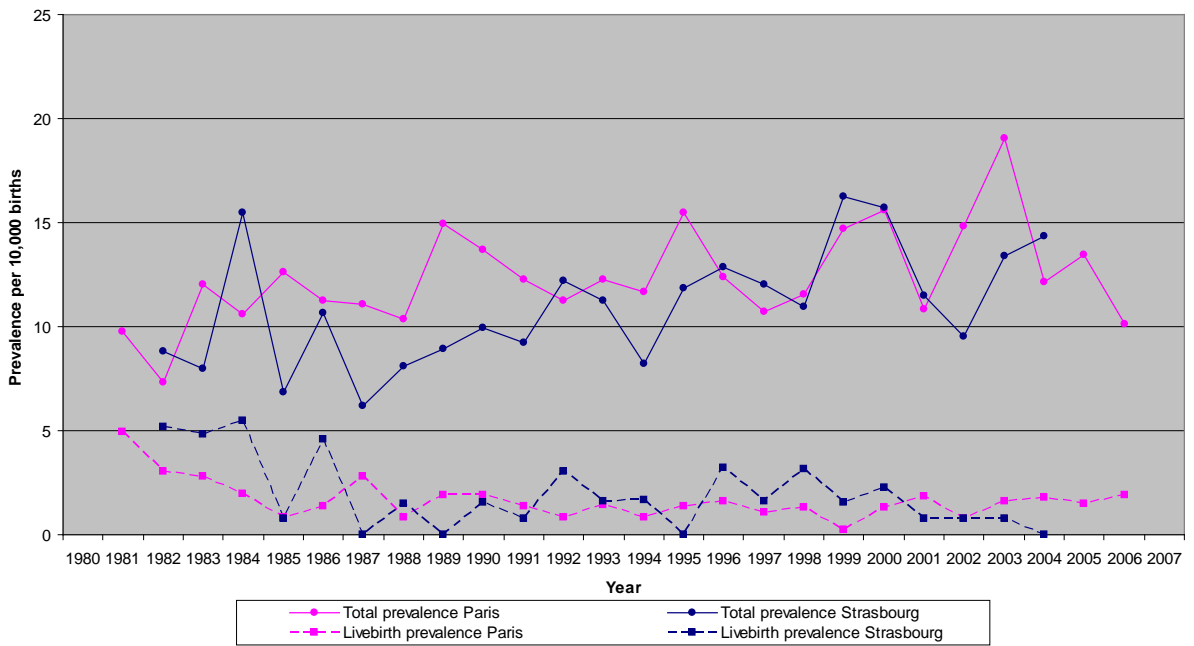
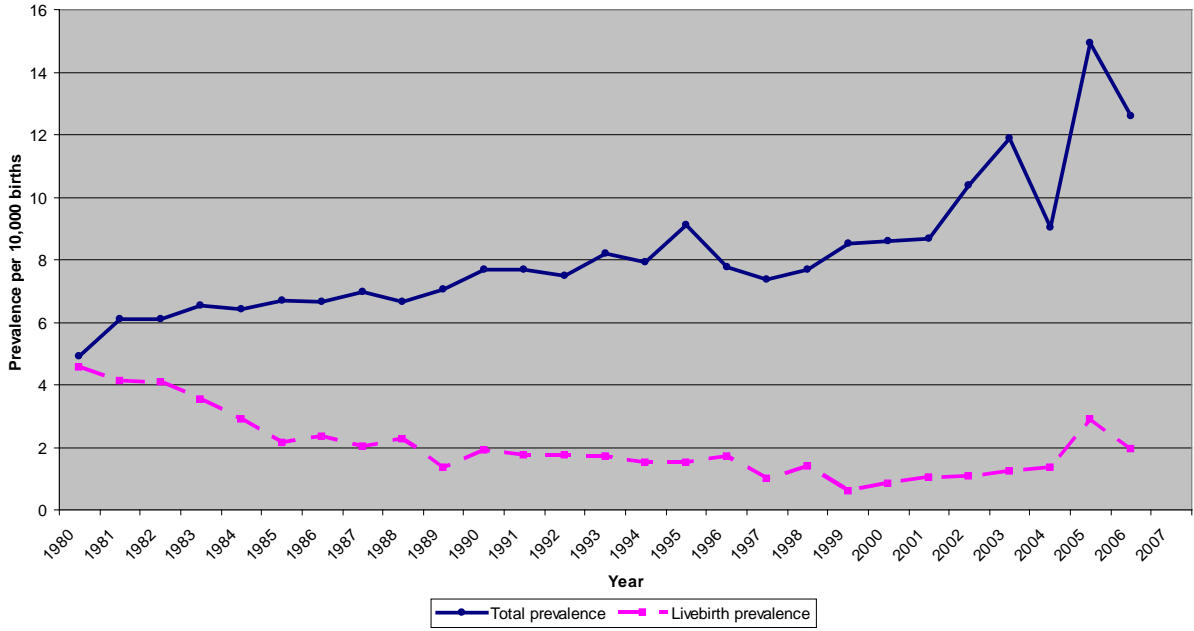
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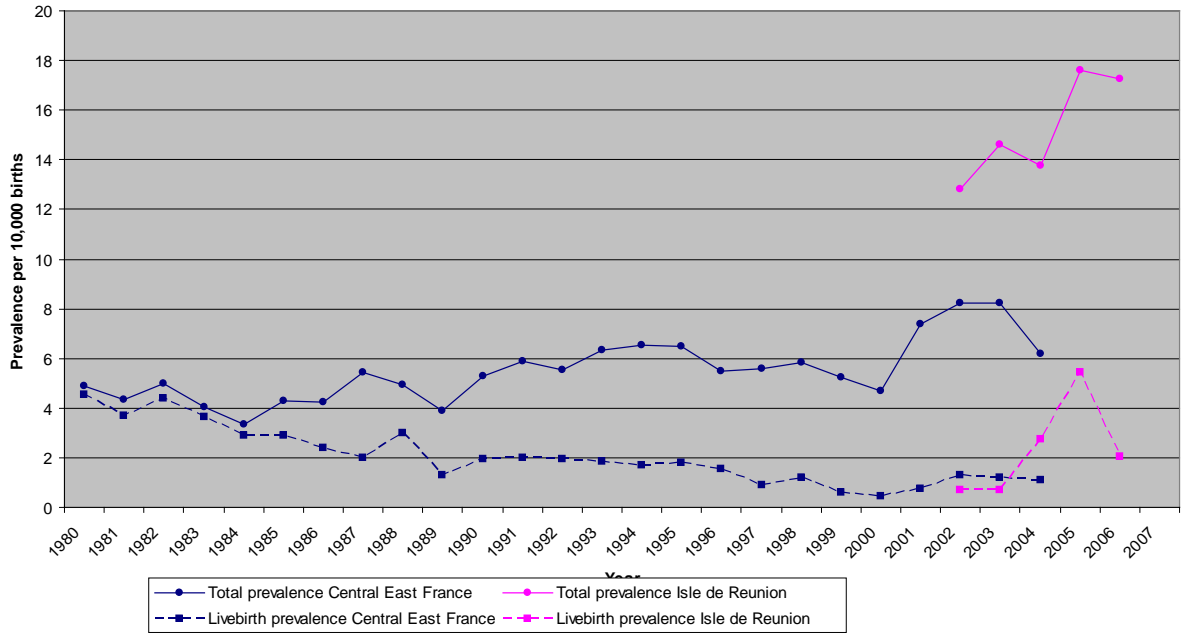
Additional Reading: Three chapters in books addressed to the French medical establishment have been written

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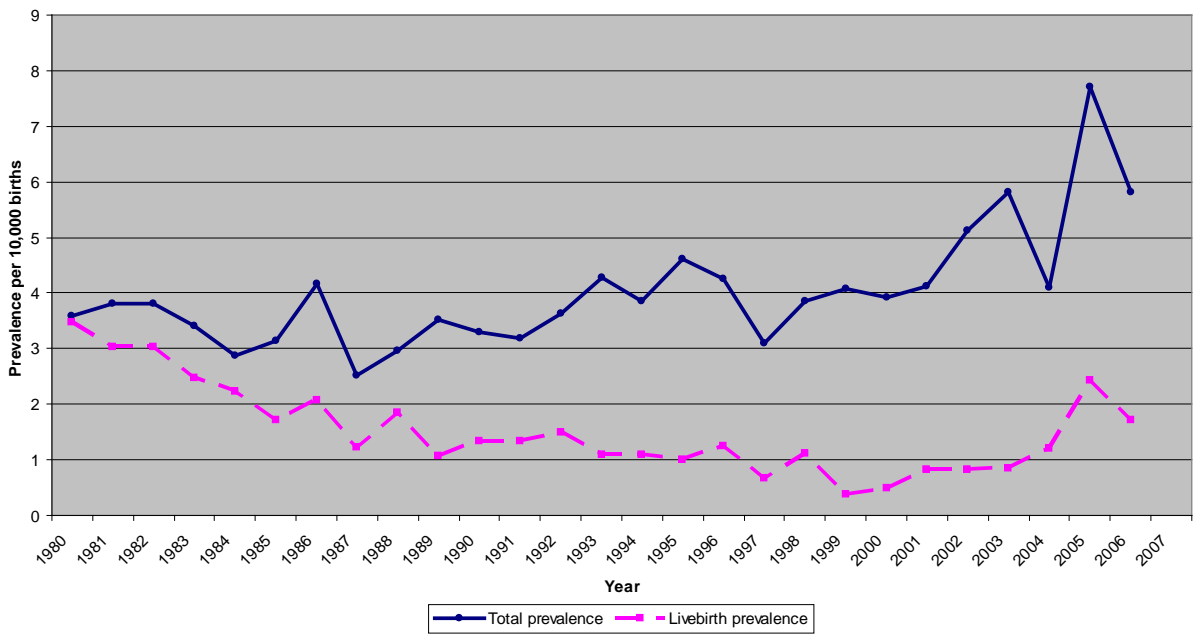
France (Strasbourg, Paris, Central East France, Isle de Reunion): Total and Livebirth Prevalence Rates for Neural Tube Defects (all 4 registries together)



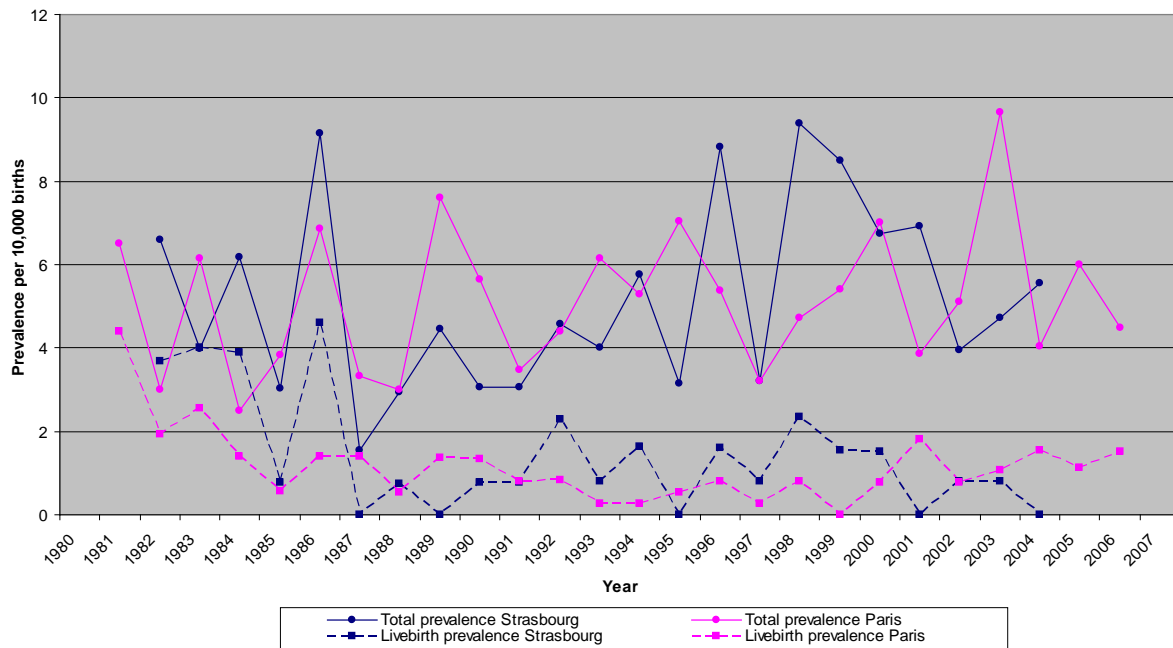
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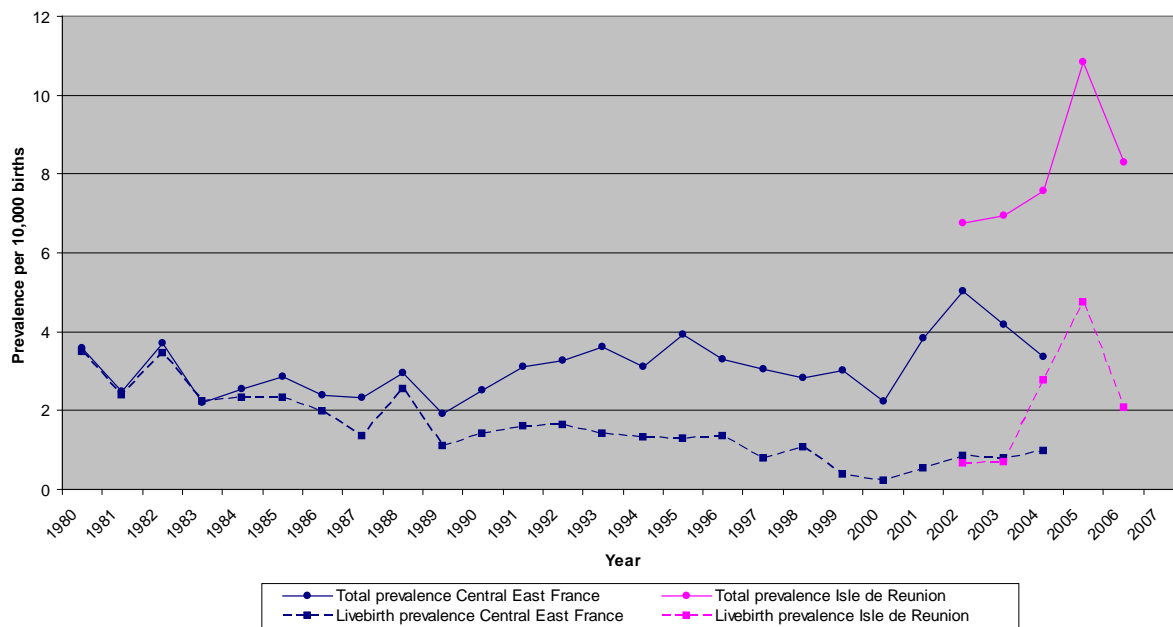
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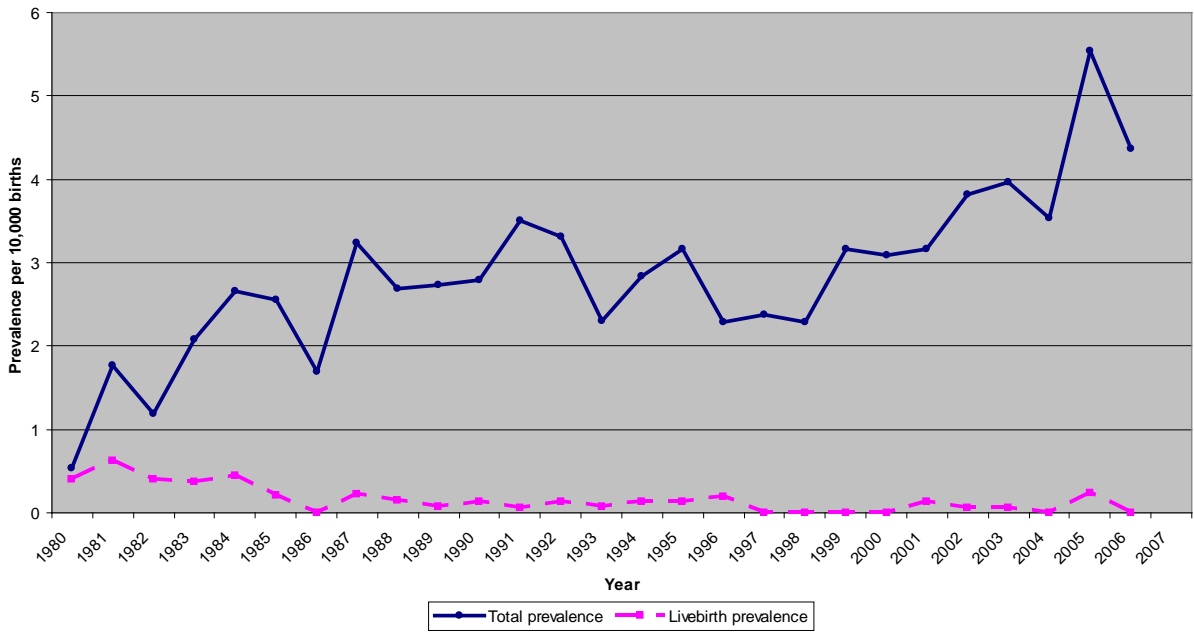
France (Strasbourg, Paris): Total and Livebirth Prevalence Rates for Spina bifida



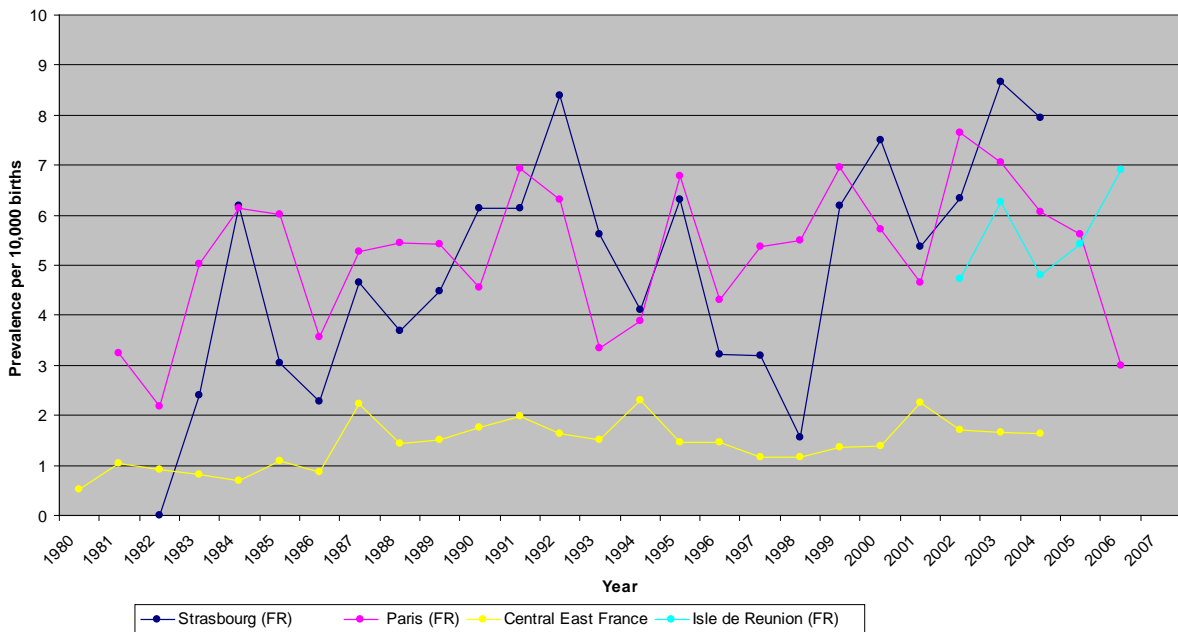
France (Central East France, Isle de Reunion): Total and Livebirth Prevalence Rates for Spina Bifida



France (Strasbourg, Paris, Central East France, Isle de Reunion): Total and Livebirth Prevalence Rates for Anencephaly (all 4 registries together)



France (Strasbourg, Paris, Central East France, Isle de Reunion): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Germany

Dr Simone Pöttsch, Prof Volker Steinbicker (emeritus)

Folic Acid Supplementation Policy

While many bodies have made recommendations regarding folic acid intake for women planning a pregnancy, there are no official governmental guidelines on this point in Germany.

In 1994/95 recommendations published by the German Nutrition Society, 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 advised 0.4 mg folic acid daily for women planning a pregnancy, and 4 mg of folic acid daily for women with a previous pregnancy affected with a neural tube defect (NTD). The recommendations specified a period starting four weeks prior to pregnancy and lasting till the end of the first trimester (Koletzko 1994, Koletzko 1995).

In 2000 the Societies of Nutrition in Germany (DGE), Austria (ÖGE) and Switzerland (SVE, SGE) published the “Reference Values for Nutrient Intake” for the German speaking countries (Deutsche Gesellschaft für Ernährung 2000). The reference values for folic acid intake can be found in table 1.

Table 1: Reference values for folic acid intake (Deutsche Gesellschaft für Ernährung 2000)

Age groups	Folic acid (µg equivalent daily)
Infants	
0 – 4 months	60
4 – 12 months	80
Children	
1 – 4 years	200
4 – under 7 years	300
7 – under 10 years	300
10 – under 13 years	400
13 – under 15 years	400

Adolescents and adults	
15 – under 19 years	400
19 – under 25 years	400
15 – under 65 years	400
51 – under 65 years	400
65 years and elder	400
Pregnant women	600
Breastfeeding women	600

Food Fortification Policy

In 2006 the German Society for Nutrition (DGE) published a position paper containing strategies to improve folic acid supplementation in Germany. Therein the DGE argues for the supplementation of flour with 0.15 mg folic acid/ 100 g flour to achieve an additional intake of 0.135 mg/d for men and 0.106 mg/d for women (Deutsche Gesellschaft für Ernährung 2006).

In Germany folic acid is classified as a supplementary food, and hence does not fall under drug approval requirements. The Nutritive Value Declaration Regulation (Nährwertkennzeichnungsverordnung) (Thamm 1999) claims that 100 g of flour should be fortified with up to 15 per cent of the recommended daily dose of 0.2 mg of folic acid. However, the maximum daily intake must not exceed three times the recommended daily dose (i.e. 0.6 mg folic acid).

In Germany no authorisation is required for the fortification of foods for general consumption with folic acid. As many manufacturers have used this option in recent years, there is now a wide range of foods enriched with folic acid brought on the market (Bundesinstitut für Risikoforschung 2005).

A major problem in marketing food enriched with folic acid is the fact that in Germany it is not allowed to refer to potentially beneficial effects on health for advertisement purposes, e.g. "... contributes to the prevention of NTD". (Law on Food and Articles of Consumption - Lebensmittel- und Bedarfsgegenstandsgesetz) (Thamm 1999).

Among the medical societies in Germany, only the Society of Paediatrics and Adolescent Medicine has published a recommendation for flour enriched with folate (Koletzko 2000). Some foodstuffs, such as bread, cereal grains and fruit juice, are fortified with folic acid. However, there is still no official list in Germany.

On 8 May 2000, a meeting of experts took place in Berlin where the necessity of improving the measures for preventing NTD was discussed. Participants in the meeting included physicians, representatives of malformation registries, politicians, representatives of the food industry, consumer federations, scientists, pharmaceutical companies, and others. However, this meeting failed to establish a common position regarding the fortification of food with folic acid. Instead, the participants decided to form a working group to this end.

In autumn 2003 the “Folic Acid and Health Working Group” (www.ak-folsaeure.de) was formed in which representatives of professional medical societies, scientific institutions, the food industry, parents’ initiatives and the Swiss Federal Commission for Nutrition work together. The German Federal Ministry for Health and the Federal Ministry of Consumer Protection, Food and Agriculture send their observers to meetings of this group. The work focuses on introducing folic acid fortification of basic food in Germany. As a first step, a consensus paper was published in the German medical journal "Deutsches Ärzteblatt" in 2004 (Koletzko 2004). The consensus paper is highly appreciated among German physicians.

In 2005, the Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung - BfR) published a final report referring to the provision of folic acid for the German population. Because of gaps in the knowledge about the risk assessment, the authors recommended that folic acid supplementation for women of childbearing age should be 0.4 mg/d. Furthermore the BfR postulated additional information campaigns in the population and highlighted the point that the effectiveness of supplementation of wheat or salt with folic acid has not been proven yet (Bundesinstitut für Risikobewertung 2005).

Health Education Initiatives

There has been no official health education initiative. Departments of the Federal Ministry of Health, Federal Ministry of Consumer Protection, Food and Agriculture,

and the German Nutrition Society are aiming to improve health knowledge and raise awareness of the population. Although they all have analysed the effects of folic acid intake, a concerted action for improving knowledge in this field has not been launched to date.

Knowledge and Uptake of Folic Acid in Women

- In 2000 a study in Munich was performed by Egen, comprising two inquiries: (i) during the first inquiry 346 women were interviewed after delivery in 1996, (ii) the second inquiry interviewing 402 women was performed in 1998.
- Between 1996 and 1998 an information campaign had taken place. The study results revealed a periconceptual folic acid intake of 400 µg per day in seven women (2%) in 1996, whereas this number was 20 (5%) in 1998 (Egen 1999).
- In the Federal State of Saxony-Anhalt an inquiry was made in maternity hospitals in 1998. A total of 567 women were interviewed after childbirth about whether they had taken folic acid prior to or after confirmed conception. Only 34 women (6%) reported to have taken folic acid prior to conception. A second inquiry was conducted in 2000, comprising a total of 1,224 women after delivery. The total number of women who had taken folic acid prior to conception amounted to only 53 (4.3%) (Heinz 2001).

Knowledge about Vitamins and the Nutritional Behaviour of Students

An inquiry about the nutritional behaviour and knowledge about vitamins among 4,332 students aged 16-21 in the Federal State of Saxony-Anhalt revealed that only 4.5% of those interviewed were aware that folic acid is a vitamin and only 0.7% of the students knew the function of folic acid in the organism. Boys and girls did not differ in their knowledge. In contrast, more than 95% of those interviewed knew that alcohol, nicotine and X-rays should be avoided during pregnancy, information, which is taught in school lessons. This suggests that information about folic acid and pregnancy should also be given at school (Seelig 2005; Pöttsch et al. 2006).

Knowledge and Practice of Health Care Professionals in Recommending a Supplementary Folic Acid Intake

From October 1997 to March 1999 the first German Health Survey was carried out (German National Health Interview and Examination Survey) (Bundesgesundheitsurvey 1999, Mensink 1998). One point of this study was

"Subjective Statements on the Daily Intake of Drugs from Selected Drug Groups". For women between 18 and 45 years of age the following ranking of drug use was established: (i) in the western federal states 30% oral contraceptives, 11.5% thyroid drugs, 8.1% vitamins; (ii) in the eastern federal states 47% oral contraceptives, 10% thyroid drugs, 5.5% vitamins (Knopf 1999).

Gynaecologists

- In 1998 the Malformation Monitoring System Saxony-Anhalt performed an anonymous inquiry among 234 gynaecologists regarding pre- and post-conceptional administration of folic acid. The questionnaire was returned by 104 gynaecologists (44.4%). 76.9% of them said they would supply folic acid after confirmation of conception, whereas 87.5% would recommend preconceptional intake.
- In 1996 a total of 27 gynaecologists in Munich were interviewed about their attitude towards prophylactic folic acid supplementation. Nine gynaecologists (38%) recommended taking folic acid preconceptionally, two (8%) recommended taking folic acid at the beginning of pregnancy, four (17%) recommended taking folic acid only in cases within a family history of NTD, whereas nine (37%) did not give any recommendation at all.
- Following an intervention campaign in 1998, 20 (74%) gynaecologists recommended taking preconceptional folic acid, four (15%) recommended taking folic acid with the beginning of pregnancy and three (11%) only in case of a family history of NTD (N = 27) (Egen 2000).

Pharmacists

- In 1996 Egen interviewed 21 pharmacists in Munich about their recommendations for prophylactic folic acid. Eight pharmacists (38%) recommended taking folic acid in the beginning of pregnancy, whereas five (24%) did not give any recommendation, and eight pharmacists (38%) recommended a periconceptional intake (Egen 2000).
- In 2000, Malformation Monitoring Saxony-Anhalt conducted an anonymous inquiry among 598 pharmacists with regard to prophylactic folic acid. Only 104 (17.4%) of the interviewed pharmacists returned the questionnaire, of which 82 (79%) recommended both a pre- and post-conceptional folic acid intake. Twelve pharmacists (11.5%) recommended taking folic acid preconceptionally, and eight

(7.7%) recommended it only in the post-conceptional phase. Two pharmacists (1.8%) did not give any recommendation at all (Kästner 2001).

Nutritional Habits and Other Supplementary Vitamins

A large part of the population in Germany does not reach the recommended folate intake.

- The German Nutrition Report 2004 stated that the daily intake of folic acid among women aged 19 to 24 years was 198 µg/d in the western and 184 µg/d in the eastern federal states. The average daily intake of 215 µg/d among all women is still below the reference value of 400 µg/d (Deutsche Gesellschaft für Ernährung 2004).
- In the German National Health Interview and Examination Survey (Bundesgesundheitsurvey 1999, Mensink 1998) a total of 1,266 women between 18 and 40 years of age were interviewed. The average daily folic acid intake was 119 µg free folic acid equivalents. In 80.6% of all women the daily intake of folic acid was less than 150 µg. 8.1% of the women in the western federal states (N = 1,231) and 5.5% of the women in the eastern federal states (N = 601) between 18 and 45 years of age were taking multivitamin tablets and 0.6% of them were taking folic acid tablets (Heinz 2001).
- The Bavarian Food Consumer Study (Bayerische Verzehrstudie 1995) found out that the average daily folic acid intake for women was 0.08 mg folic acid equivalents (Bayerisches Staatsministerium für Ernährung, Landwirtschaft und Forsten 1997).

Women's Sources of Information about Folic Acid

The German National Health Interview and Examination Survey (N = 562) (Bundesgesundheitsurvey 1999, Mensink 1999) found out that women received their information about folic acid from the following sources:

- 29.3% physicians
- 28.1% journals
- 14.8% TV
- 9.1% friends
- 8.5% newspaper
- 7.1% health insurance
- 3.1% radio

Egen (1999) interviewed 35 women and found they received their information from the following sources:

- 77% gynecologists
- 14% self-information
- 6% professionals
- 3% genetic counselling

Investigations in Saxony-Anhalt (2000) (Heinz 2001) found out that women received their information from the following sources (table 2):

Table 2: Women's sources of information about folic acid in Saxony-Anhalt (Heinz 2001)

Sources of information	Prior to pregnancy		During pregnancy	
	N = 227	Rate in per cent	N = 1,057	Rate in per cent
Physicians	137	60.4	784	74.2
Radio/ TV/ magazines	44	19.4	51	4.8
Books	33	14.5	61	5.7
Friends	30	13.2	47	4.4
Others	17	7.5	28	2.7
Partner	13	5.7	28	2.6
Relatives	13	5.7	25	2.4
Pharmacists	11	4.8	27	2.6
Information centre	0	0	6	0.6

Proportion of Pregnancies which are planned

- Egen conducted a study comprising 131 women right after delivery, of which 94 (72%) confirmed that they had planned their pregnancy. In 1998 Egen again interviewed 118 women after delivery. 80 (68%) out of them had planned their pregnancy (Egen 1999).

- In 1998 a study was performed in Saxony-Anhalt, comprising 567 women after delivery who were asked whether or not their pregnancy had been intended. A total of 391 (69%) of the women confirmed that their pregnancy had been planned. Again, in 2000 a study was conducted in Saxony-Anhalt in the course of which 1,224 newly delivered women were interviewed. 806 (66%) answered that their pregnancy had been planned.
- Declaration of the final report of the Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung) referring to the supply of the German population with folic acid: 40-50% unplanned pregnancies are estimated (no source known).

Molecular-Genetic Investigations

Within the German National Health Interview and Examination Survey (Bundesgesundheitsurvey 1999) 994 women were checked for the presence of a C677T mutation. 421 women (42.4%) did not carry this mutation. 455 women (45.7%) were heterozygous and 118 (11.9%) were homozygous for the C677T mutation. These women exhibited a significantly higher homocysteine level (Thamm M – personal information).

Laws Regarding Termination of Pregnancy

In Germany, termination of pregnancy is allowed irrespective of gestational age, if the pregnancy implies a serious threat to the pregnant woman's physical or mental health, or if the fetus is affected by malformations.

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Additional Summary on folic acid/metafoline for Germany

Dr Annette Queißer-Luft and short explanation folic acid versus 5-Methyl-Tetrahydrofolat (from Prof. Dr. K. Pietrzik, Rheinische Frierich-Wilhelms-Universität, Bonn)

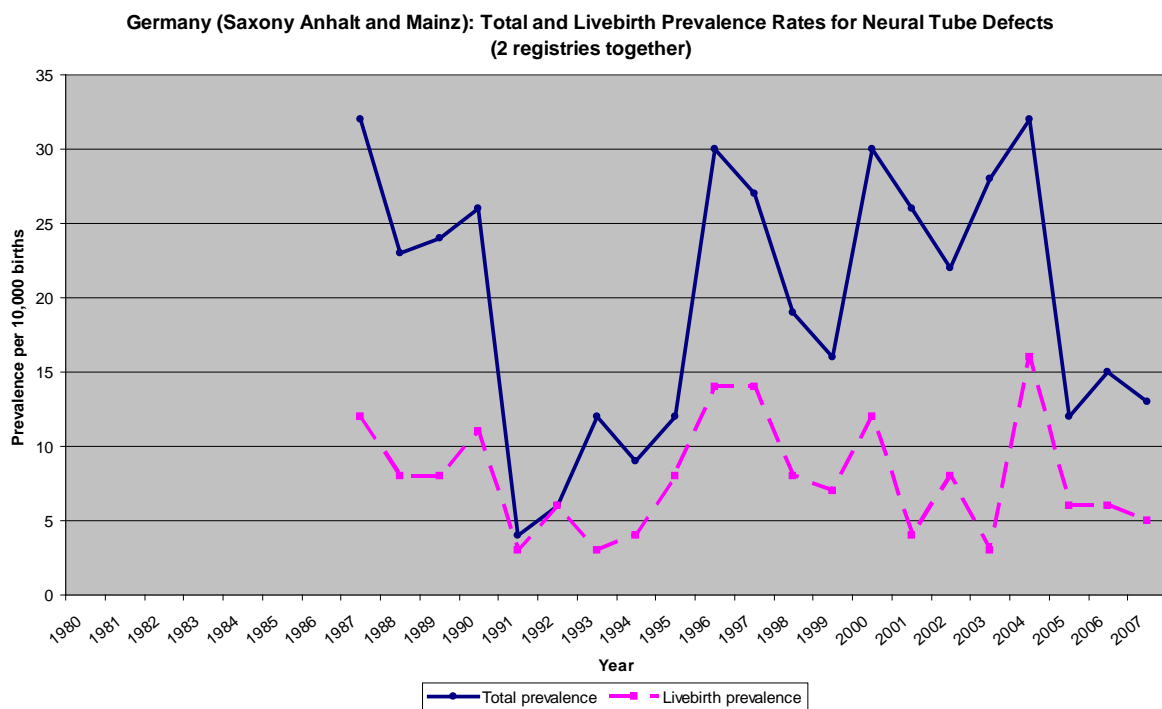
The intake of folate via normal foods and the folate status of (parts of) the European population are below the reference values. At the same time, the incidence of neural tube defects (NTD) in Europe is considered unacceptably high. Earlier studies have shown a preventive effect of folic acid on the occurrence of NTDs. Therefore, to increase the intake of folate/ folic acid is a major public health objective in Europe.

Up to now, women of childbearing age were advised to take supplements with a minimum of 400 µg folic acid from four weeks before to two to three months after conception. However, only a small percentage of women follow this advice. Therefore, in many European countries fortification of flour or another staple food with folic acid has been considered an alternative strategy.

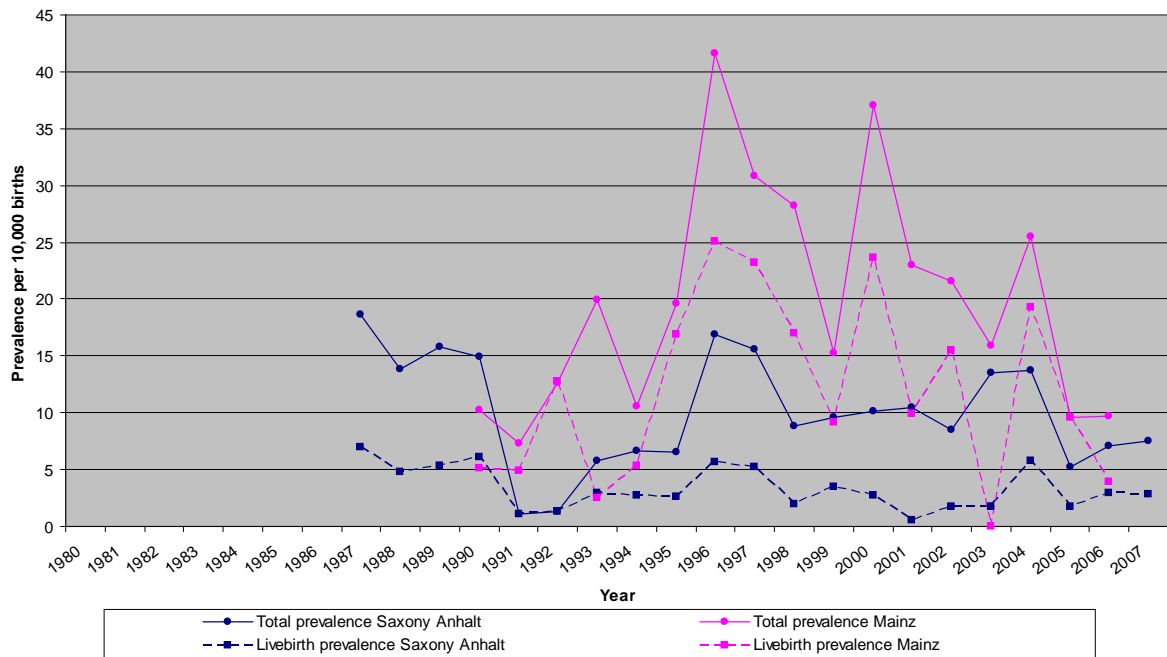
The daily peri-conceptional intake of additional 400µg folic acid is recommended to prevent NTDs. Various studies showed risk reductions between 35 to 70% for NTDs. Multivitamins containing 800µg folic acid showed a close to 100% for NTD and a significant decrease for congenital heart defects and defects of the urinary tract. Concerning major birth defects prevention these products seem to be superior.

Taking into account the recent development (increasing use of folic acid i.e. by fortifying food like cereal and fruit juices) long term overdoses, more than 1mg tolerable upper intake level, have to be avoided due to the masking of haematological symptoms of a vitamin B₁₂ deficiency. For this purpose natural folate [5-Methyl-Tetrahydrofolate (5-MTHF)] would be the best choice. At first a masking of a B₁₂- deficiency is highly unlikely and second it is the biological active form of the vitamin in the human body. This is of main importance for people with an enzymatic polymorphism of the folate metabolism, resulting in a lower 5-MTHFR production. Approximately 10% of any population show a homozygote MTHFR 677C→T-polymorphism, resulting in a 75% decrease of MTHFR activity. Thus the supply of this “missing” substance would have the strongest impact in terms of a broad prevention strategy. As homozygote constellations do have a higher risk for NTDs and also the risk for heterozygote persons is slightly increased, a beneficial folate supply through 5-MTHF intake could be the optimal result for 50% of the population.

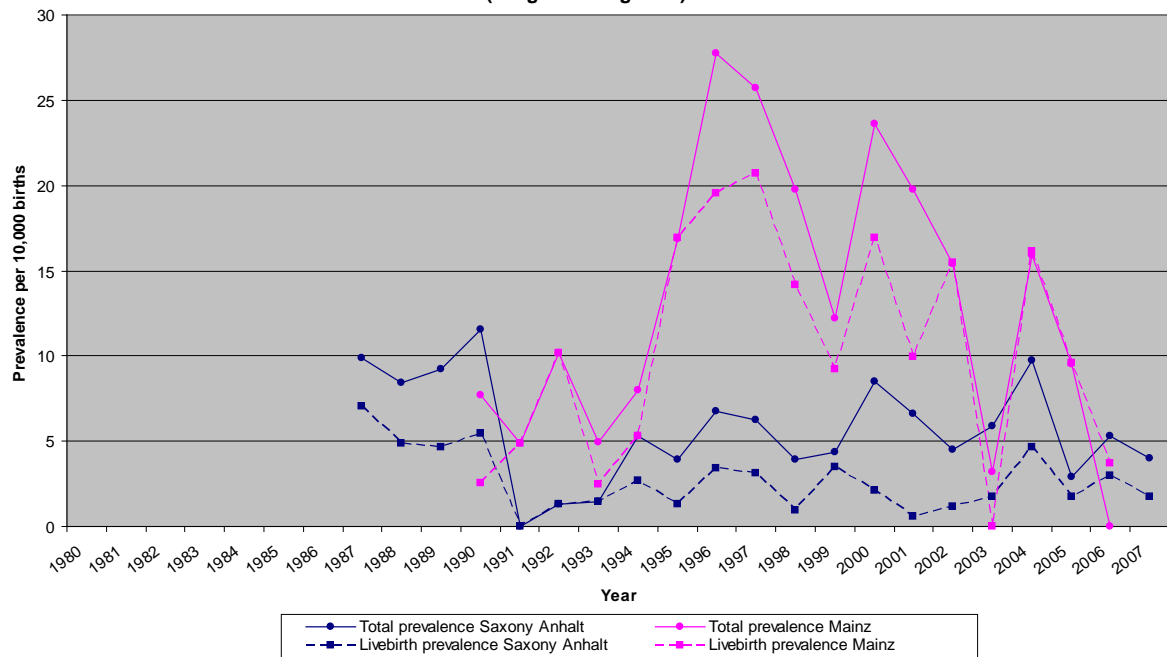
Well respected studies on bioavailability and reduction of Homocysteine levels proved 5-MTHF (Calcium L-Methylfolate) to be equivalent to folic acid. Long term studies on the elevation of the Erythrocytic folate levels even resulted in a significant superiority of the active form.



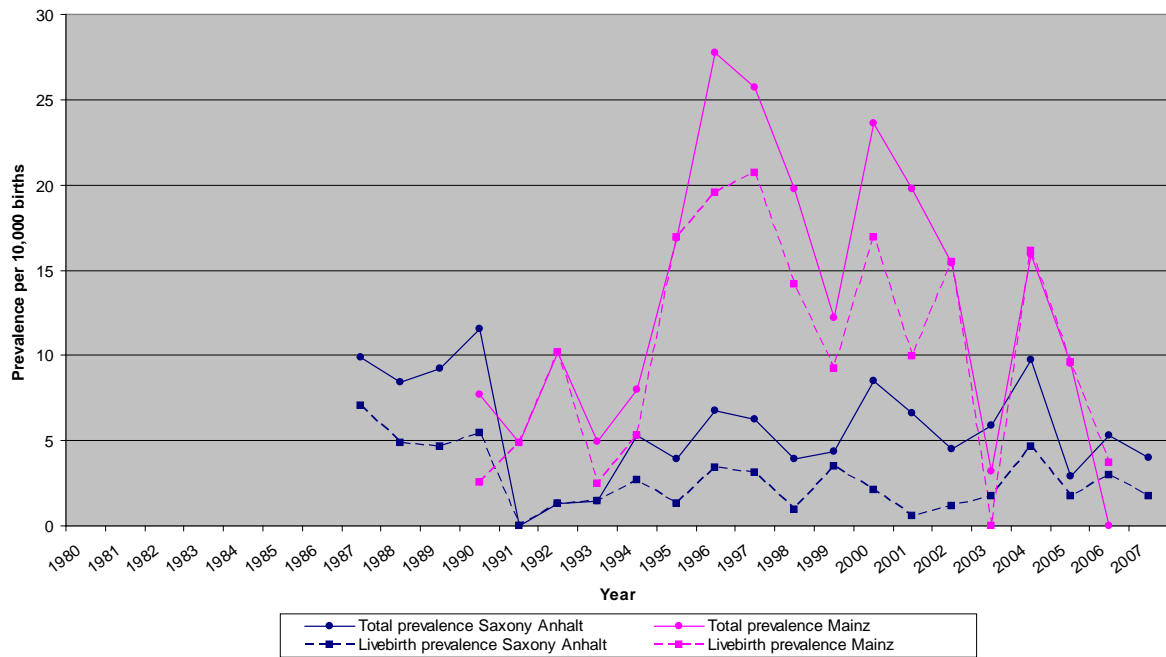
Germany (Saxony Anhalt and Mainz): Total and Livebirth Prevalence Rates for Neural Tube Defects



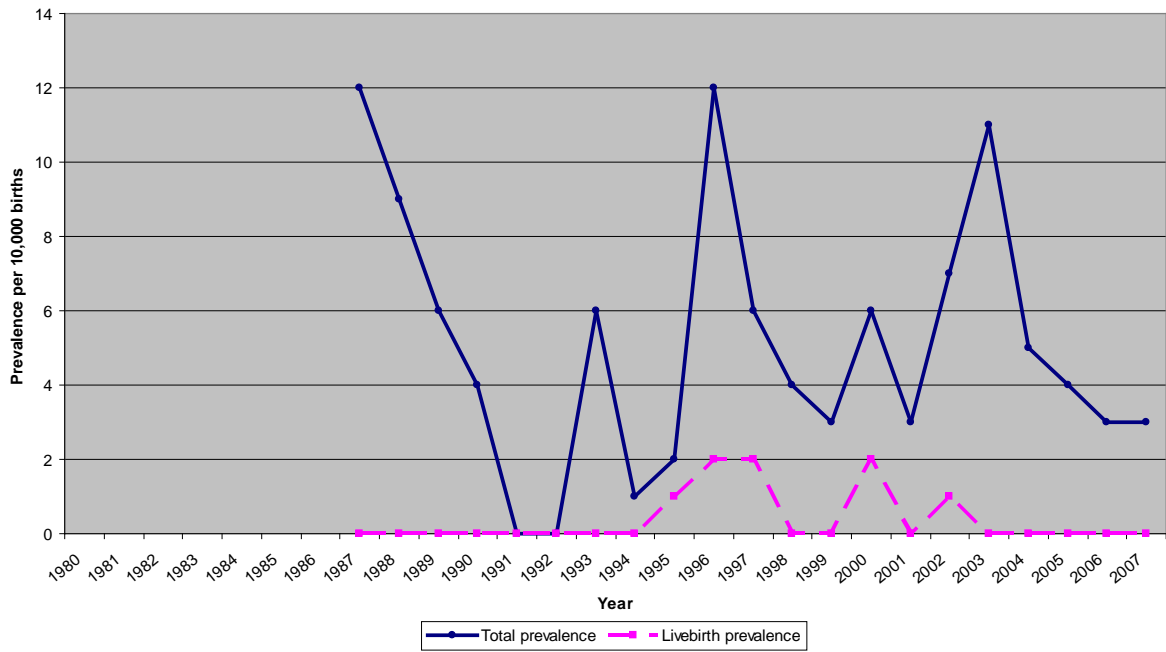
Germany (Saxony Anhalt and Mainz): Total and Livebirth Prevalence Rates for Spina Bifida (2 registries together)



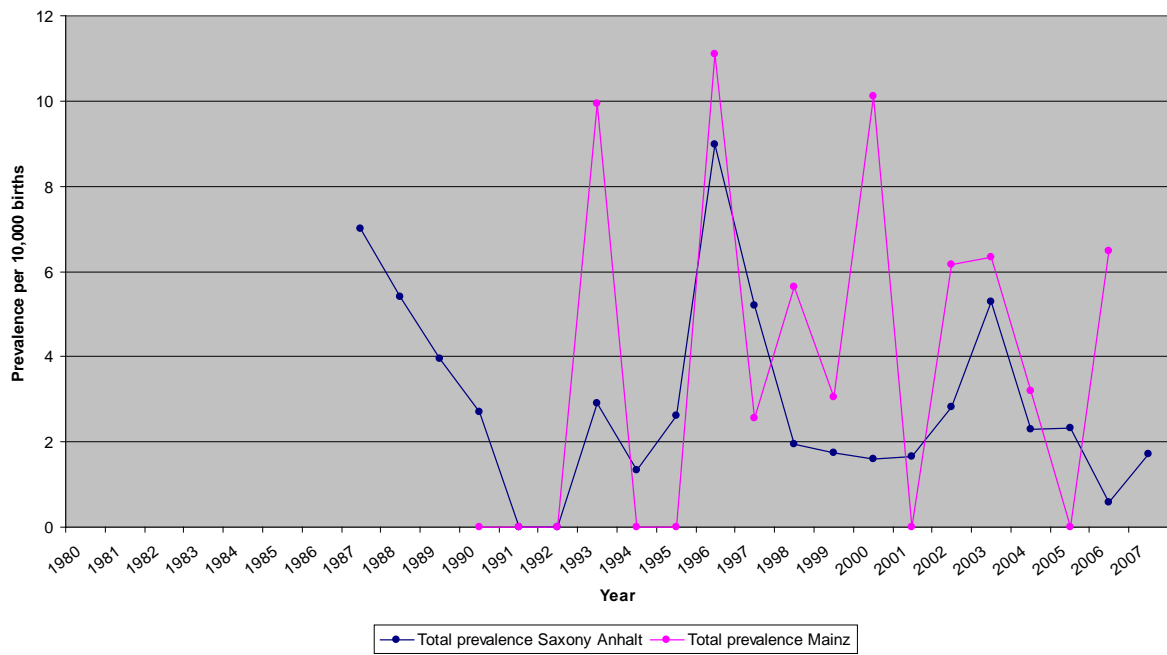
Germany (Saxony Anhalt and Mainz): Total and Livebirth Prevalence Rates for Spina Bifida



Germany (Saxony Anhalt and Mainz): Total and Livebirth Prevalence Rates for Anencephaly (2 registries together)



Germany (Saxony Anhalt and Mainz): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Hungary

By Janos Sandor

Folic Acid Supplementation Policy

In 1996, the National Institute for Health Promotion released a recommendation for women planning a pregnancy. The recommendation was for women to take a supplement of 0.4 mg/day folic acid during the preparation for pregnancy.

In 1998, The National Board of Hungarian Gynaecologists issued guidelines for vitamin and mineral supplementation during pregnancy. They recommended 0.4 mg/day folic acid throughout pregnancy in order to prevent neural tube defects.¹ They did not mention preconceptional folic acid.

Food Fortification Policy

There is no mandatory food fortification in Hungary, and the fortification of a staple food is not planned in the near future. The authorization and production of fortified foods is allowed and is under legal regulation, but there is no available database about fortified foods at the moment. A wide variety of imported breakfast cereals are available. In 1998 a special kind of bread fortified with folic acid became accessible with very limited success. In the absence of supporting health education, the lack of interest led to its disappearance it from the market.

Health Education Initiatives

In Hungary, public health nurses support women preparing for pregnancy, during pregnancy and after delivery. This service is provided free of charge and is financed by municipalities. Since the early 1980s, these nurses have been required to direct the attention of women to the fact that folic acid supplementation is effective in the prevention of anaemia. More recently, they have begun to tell women about the benefits of folic acid in helping to prevent congenital anomalies.

Knowledge and Uptake of Folic Acid

The most recent investigations on folic acid intake are the following:

69% of Hungarian pregnant women regularly take products containing folic acid (usually multivitamins). 93% of them start the intake after the 7th week of pregnancy.

(45.85% start in 1st trimester, 41.68% in 2nd trimester, and 12.46% in 3rd trimester)
The daily dose is under 0.5 mg for 85% of pregnant women.²

The Dietary survey in Hungary (2003-2004) investigated the nutritional habits of a representative sample. A nested sample was investigated according to vitamin intake as well. This sub-sample consisted of 587 women over 18.³

Daily folate intake ($\mu\text{g}/\text{day}$) in Hungary among women

Age group	Mean	SD	N
18-34	132.3	47.5	176
35-59	132.3	47.5	176
60+	124.6	42.9	235
18+	131	46.9	587

Proportion of Pregnancies that are Planned

67.4% of pregnancies in Hungary were found to be planned in a study published in 2006.⁴ The figures broken down by maternal age were as follows:

15-19 year: 48.3%

20-24 year: 54.2%

25-29 year: 62.5%

30-34 year: 67.1%

35-39 year: 67.4%

40-44 year: 66.1%

45-49 year: 64.6%

Laws Regarding Termination of Pregnancy

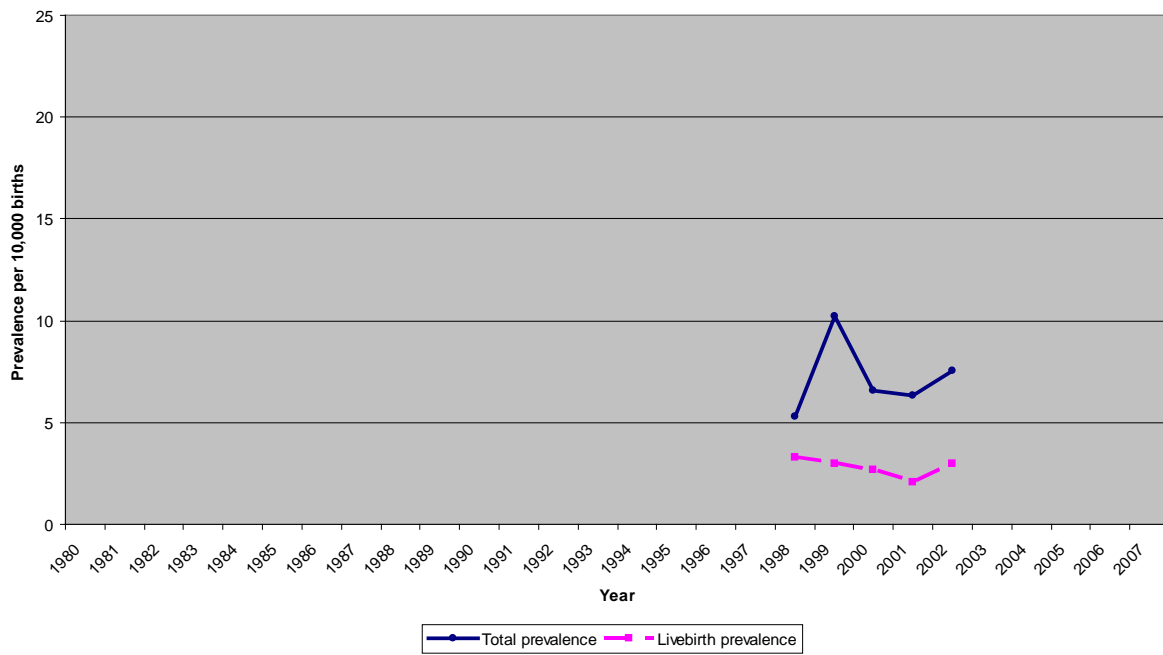
Induced abortion is regulated by the 1992 Act Number LXXIX on the protection of foetal life which modified the 1973 regulations. According to the 1992 act, a pregnancy may be interrupted if it seriously endangers the health of the mother or the foetus, if the pregnancy is the consequence of a crime or if the mother is in a grave crisis situation. According to the definition of the Decree of the Ministry of Health No 18/2000(June 29) a grave crisis situation occurs when it causes bodily or mental impairment or socially intolerable situation.⁵

If the probability of a genetic or congenital impairment is above 50%, then termination of pregnancy is allowed until a gestational age of 20 weeks. If the diagnosis requires more time, then this period can be extended until 24 weeks. Finally, if the intrauterine diagnosis is a disease or condition which is incompatible with life, there is no gestational age limit on termination of pregnancy.

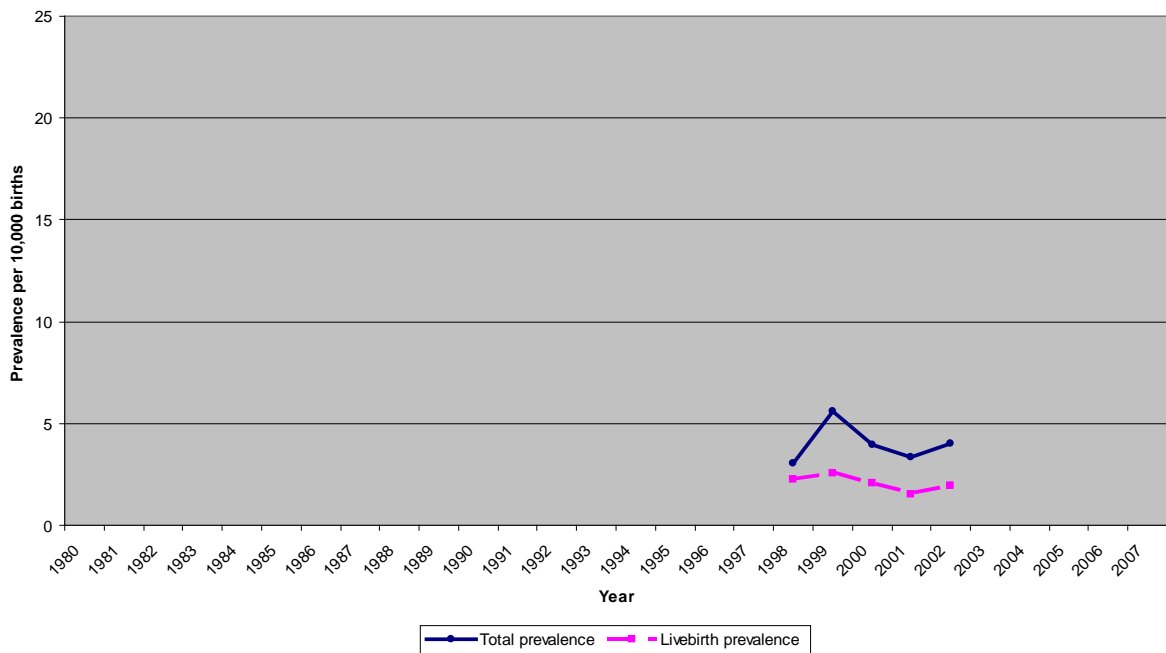
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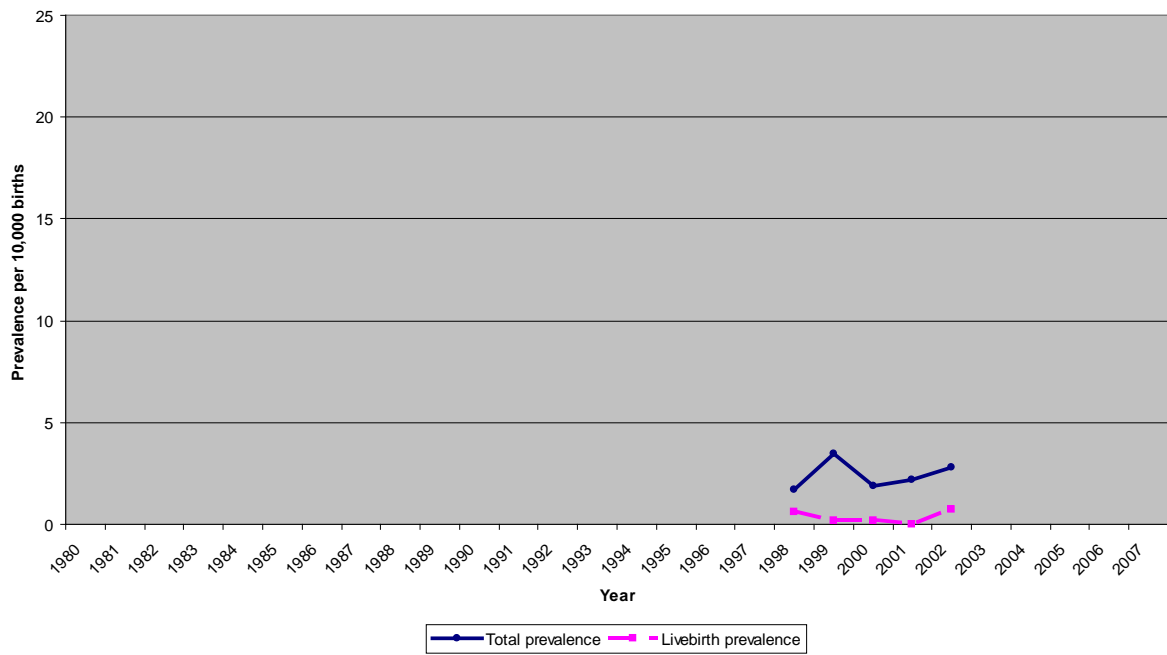
Hungary: Total and Livebirth Prevalence Rates for Neural Tube Defects



Hungary: Total and Livebirth Prevalence Rates for Spina Bifida



Hungary: Total and Livebirth Prevalence Rates for Anencephaly



Report on Folic Acid Supplementation for Republic of Ireland

Dr Robert McDonnell

Folic Acid Supplementation Policy

Recommendations were made by the Irish Department of Health and Children in 1993 that if there is any possibility of pregnancy, a woman should take an additional 400 µg of folic acid daily prior to conception and during the first twelve weeks of pregnancy. The preferred means of supplementation is by a daily folic acid tablet. The policy is promoted through the Department's Health Promotion Unit by way of leaflets and promotion campaigns.

Food Fortification Policy

Voluntary fortification of foods (particularly cereal and milk) by food producers has been in existence for a number of years, and it was expected that mandatory fortification will be implemented in 2008 (see below).

In a 1998 report to the Minister for Health¹, the Food Safety Advisory Board of Ireland (an official body) recommended that food fortification should be considered as a complimentary measure to supplementation (rather than an alternative).

In 2004, a report by the Nutrition Sub-committee of the Food Safety Authority of Ireland (which has replaced the Food Safety Advisory Board) undertook a risk benefit analysis of fortification in Ireland and concluded that folic acid fortification at 200µg /100g would have a significant effect in preventing NTD without resulting in an appreciable risk of adverse health effects from high intakes in any population subgroup. In 2005 the Department of Health and Children set up a national committee to examine folic acid food fortification (www.folicacid.ie).

In May 2006, the Report of the National Committee on Folic Acid Food Fortification² was launched by the Food Safety Authority of Ireland (FSAI) and the Irish Department of Health & Children (DoHC). This made a number of recommendations, the first of which was the fortification of all bread (with the exception of minor bread products) on a mandatory basis with folic acid at a level which provides 120 µg per 100g of bread as consumed. The report and its recommendations were adopted as government policy. Following this, the FSAI established a Folic Acid Implementation

Group in November 2006 to progress and implement the Report's recommendations. The report is available via link: <http://www.fsai.ie/assets/0/86/204/ca0a6f81-e3a1-4e7c-8284-bc363f8ed091.pdf>

However, in 2008, the FSAI recommended postponement of fortification, following preparatory studies by the implementation group which showed that the rate of NTD affected births had decreased further. In addition, there had also been a significant increase in folic acid intake in the Irish diet as a result of increased voluntary fortification by food producers in recent years. In the interim period in which fortification is postponed, further monitoring of folic acid supplement intake and rate of NTD would take place to see if the situation had further changed. The report of the implementation group is available via the link:

<http://www.fsai.ie/assets/0/86/204/cc3c2261-7dc8-4225-bf79-9a47fbc2287b.pdf>

Health Education Initiatives

The Health Promotion Unit of the Irish Department of Health and Children has undertaken much of this work at a national level. A folic acid promotional campaign has been in operation since the official recommendations on folic acid came into being in 1993. There are periodic national media campaigns prompting folic acid supplement intake in women of child-bearing age. The Health Promotion Unit of the Irish Department of Health has undertaken much of this work at a national level. At a more local level, health promotion units and public health departments in the regions promote folic acid through a variety of channels, generally on an on-going basis. The 2006 Report of the National Committee on Folic Acid Food Fortification recommended the launch of a National Health Promotion Programme in relation to all aspects of folic acid promotion. The details are available in the Report.²

Folic Acid Knowledge and Uptake

There have been studies on folic acid awareness and uptake since 1995. The table below summarizes the results of studies of women attending their first ante-natal visit in maternity hospitals in Dublin.³⁻⁹ The sample sizes in the studies from 1996-2000 were of 300 respondents each, using the same questionnaire, with core questions as shown in the table. These studies mainly asked about daily folic acid tablet intake, without explicitly asking about vitamin intake. The table below shows that since 1998, almost all mothers have heard of folic acid; and by 2002, more than three

quarters knew that it could prevent NTD. However, less than 25% of women were taking periconceptional folic acid by 1998 and this had not changed by 2002.

Studies of Folic Acid Knowledge and Uptake in Ireland 1996-2002

Year	1996	1997	1998	1999	2000	2001	2002
Heard of folic acid	54%	76%	88%	91%	92%	94%	95%
Knew folic acid can prevent spina bifida / NTD	21%	44%	57%	64%	67%	83%	77%
Took folic acid periconceptionally	6%	16%	21%	22%	18%	24%	23%

As it was expected that fortification would take place by 2008, further studies were deferred. However, with the postponement of fortification in 2008, new studies of folic acid supplement intake were planned with the first taking place in mid -2009.

Health Care Professionals

Although there has not been a survey among health care professionals, it is likely that virtually all are aware of the recommendations considering the high profile folic acid promotion campaigns that have taken place, and the high level of knowledge among women of child-bearing age, the source of which is frequently a health professional.

Proportion of Pregnancies which are Planned

The studies quoted in the above table have found that the proportion of women planning their pregnancy has been stable from 1996-2002 at 40-45%.

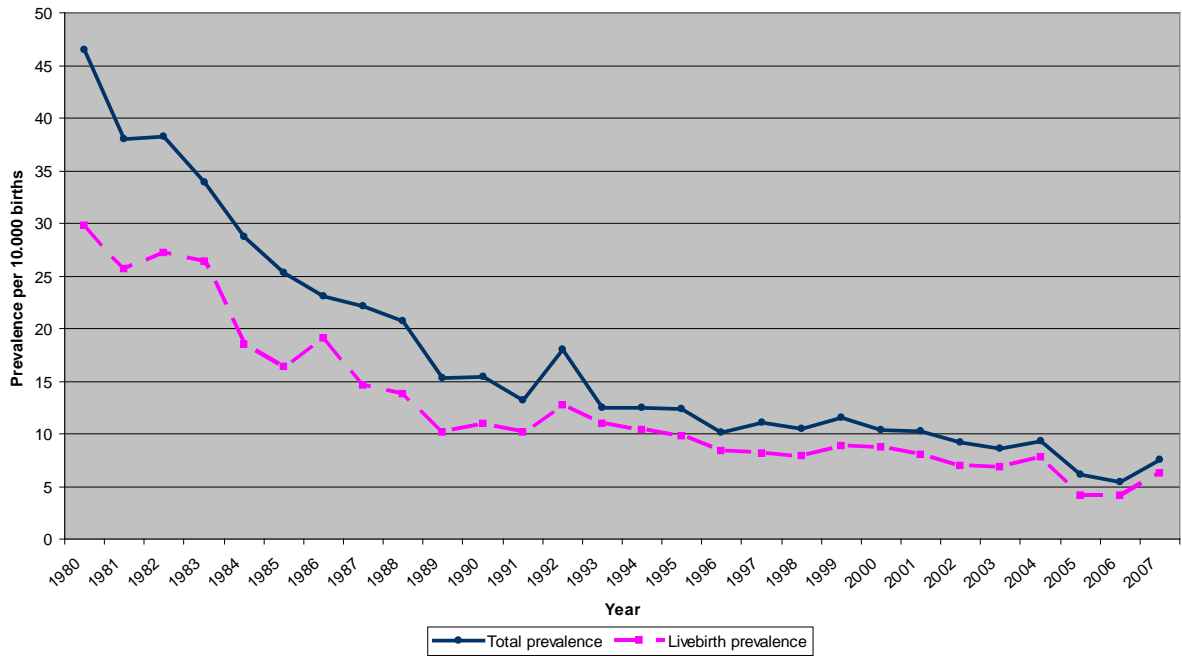
Laws Regarding Termination of Pregnancy

Termination of pregnancy is not legal in Ireland except in the most extreme circumstances. It is never allowed because of fetal abnormality. The number of women who may go abroad for terminations because of fetal abnormality is not known.

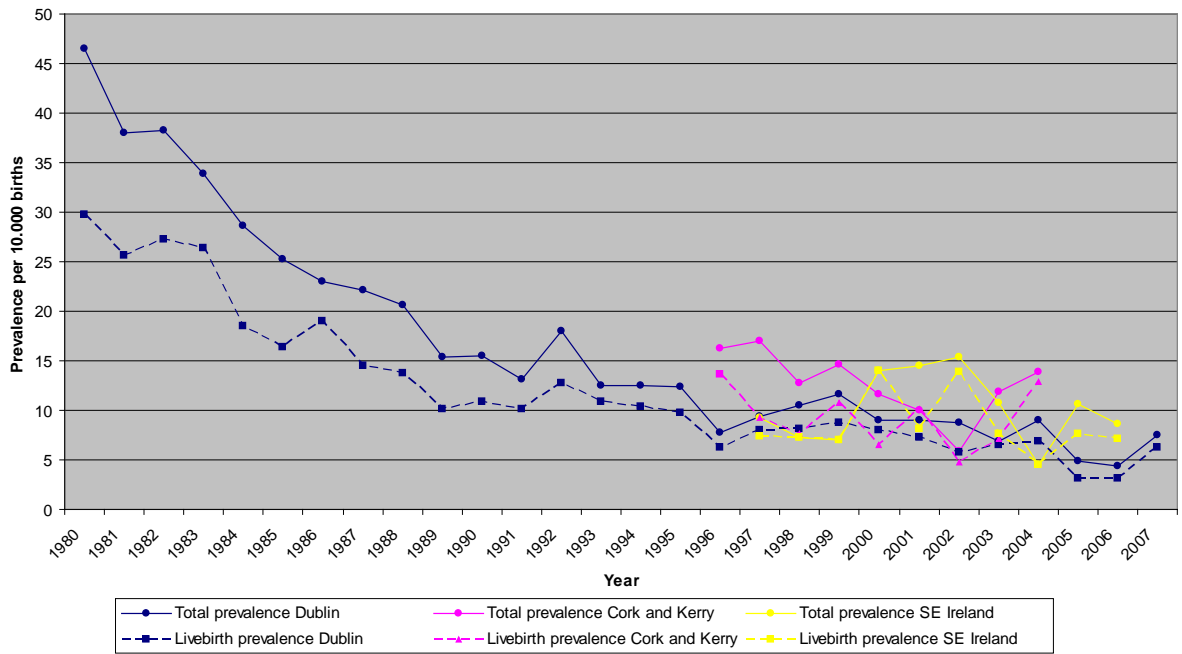
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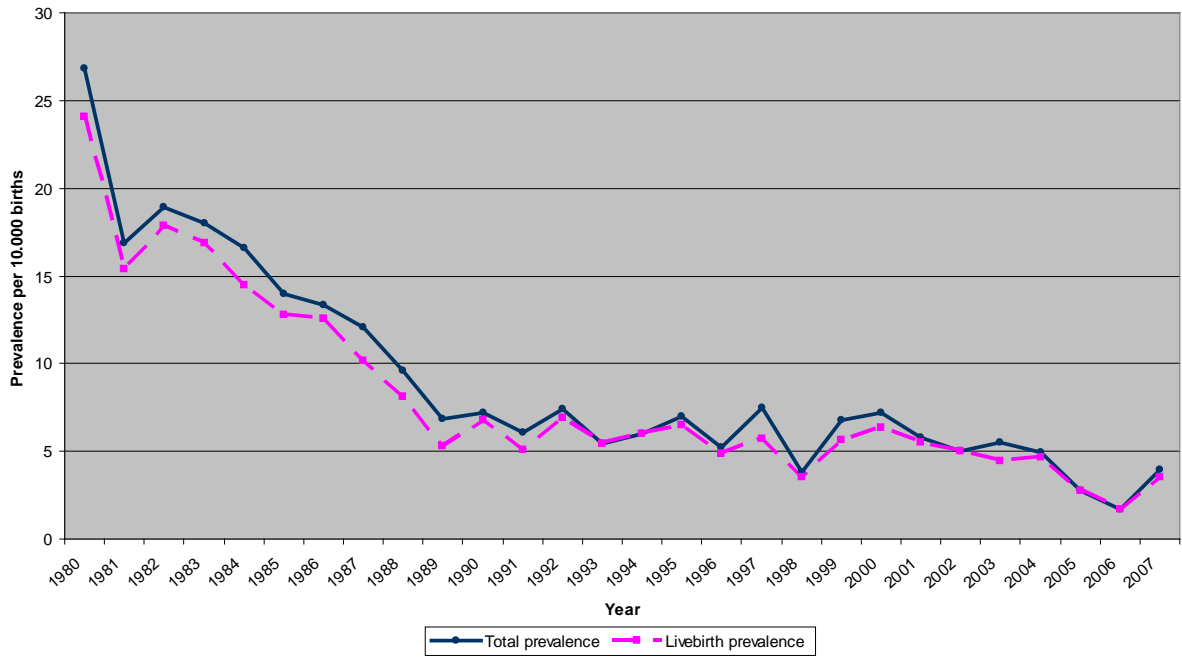
Ireland (Dublin and Cork&Kerry and SE Ireland): Total and Livebirth Prevalence Rates for Neural Tube Defects (all 3 registries together)



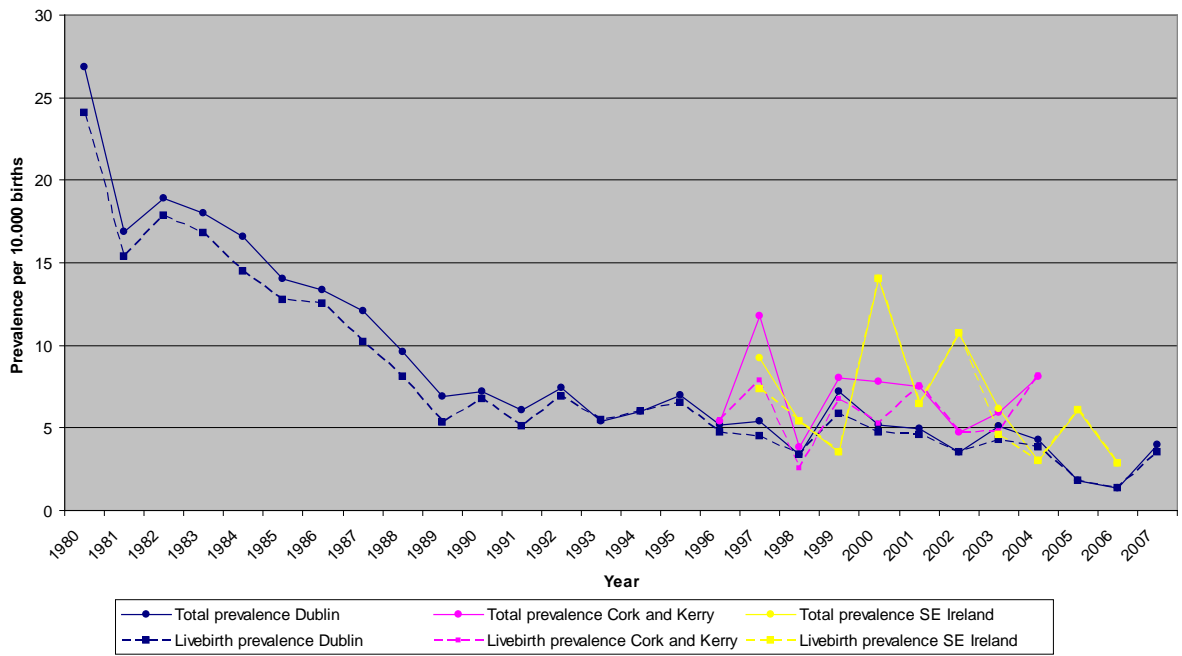
Ireland (Dublin and Cork&Kerry and SE Ireland): Total and Livebirth Prevalence Rates for Neural Tube Defects



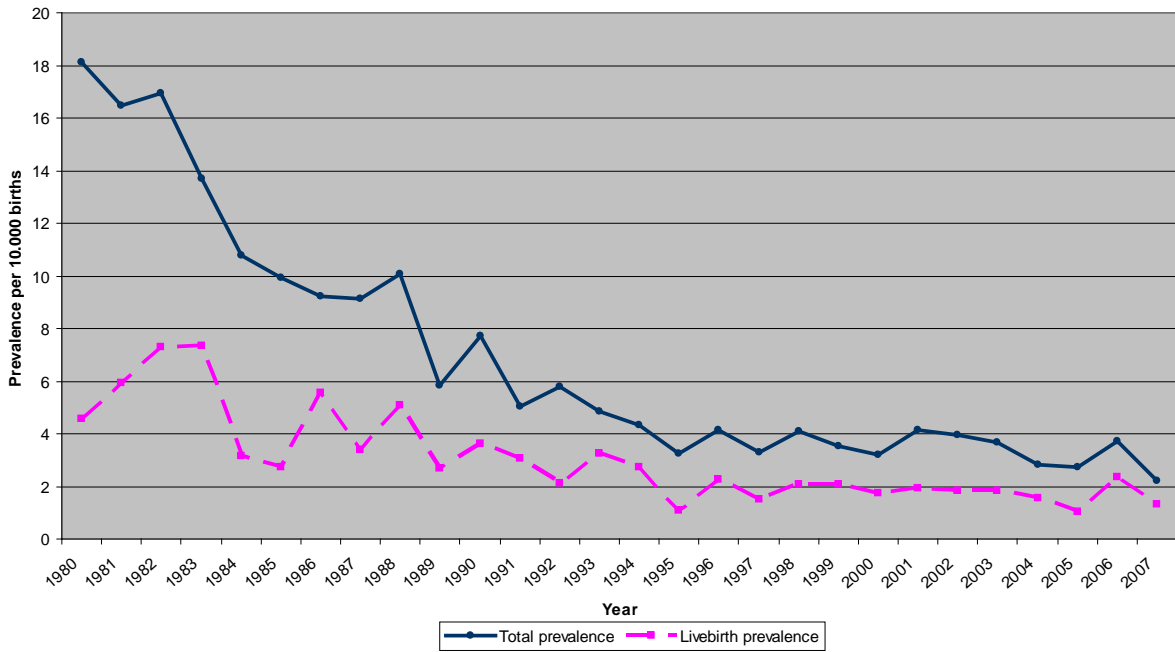
Ireland (Dublin and Cork&Kerry and SE Ireland): Total and Livebirth Prevalence Rates for Spina Bifida (all 3 registries together)



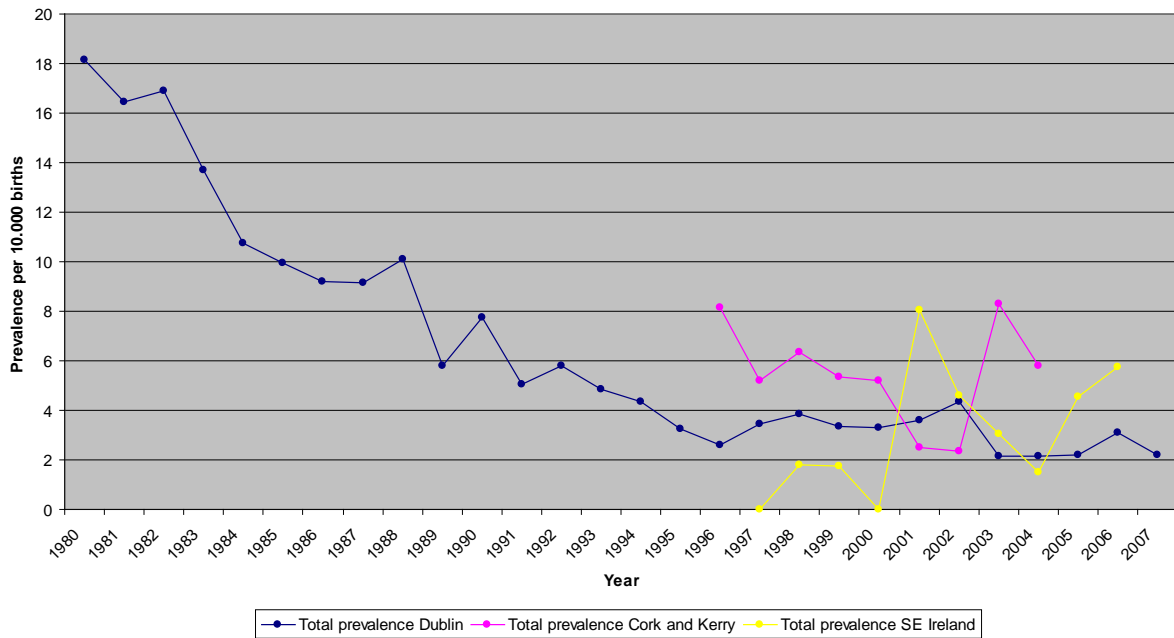
Ireland (Dublin and Cork&Kerry and SE Ireland): Total and Livebirth Prevalence Rates for Spina Bifida



Ireland (Dublin and Cork&Kerry and SE Ireland): Total and Livebirth Prevalence Rates for Anencephaly (all 3 registries together)



Ireland (Dublin and Cork&Kerry and SE Ireland): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Italy

This document was prepared and approved by the Scientific Committee of the Italian Network for Folic Acid Promotion for the primary prevention of birth defects and the Italian Registers of Congenital Malformations

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Folic Acid Supplementation Policy

The Italian Network for Folic Acid Promotion for the primary prevention of birth defects was established in 2004 with the aim to propose and agree recommendations regarding folic acid supplementation. The Network brings together research institutions, patient organizations, scientific societies, universities, doctors, health personnel and other institutions in order to promote collaboration and share strategies for action. The objectives of the Network, in addition to the main topic of primary prevention of birth defects with folic acid, have been extended to include the nutritional aspects and approaches to promote proper dietary intake of folate, in agreement with the evolution of the subject at European and international level. The network now involves over 200 members and is coordinated by the National Centre for Rare Diseases (CNMR) of the Institute of Health (ISS).

The summary recommendation on Folic Acid Supplementation Policy was approved in November 2004 and is as follows:

It was recommended that all fertile women that plan a pregnancy, or do not actively exclude the possibility, take at least 0.4mg a day of folic acid. It is fundamental that it is taken starting at least a month before conception and for all of the first trimester of pregnancy.

The recommendation, together with more details (why, how much, when, foot notes explaining the choice, and a list of scientific publications that support the recommendation) is accessible at <http://www.cnmr.iss.it/>

Every year since the birth of the Network a national workshop (now Congress) is organized to present the activities and achievements in various fields: research on genetic and environmental risk factors of malformations, epidemiological surveillance, risk-benefit assessment of strategies to promote adequate folic acid intake, communication and public information and training of health professionals. In order to widen discussion and collaboration international experts have been invited to participate.

Implementation

The first major result of the Network is the production and dissemination of material both scientific and informative available on the website [www.iss.it/cnmr/folic acid](http://www.iss.it/cnmr/folicacid). The scientific documents capitalize the interdisciplinary nature of the Network, with attention given to interactions between folate and other factors (genetic / food / environmental) and the role of folate nutrition. The Italian Registers of Congenital Malformations are developing a shared system of data collection and processing of reports that will allow the longitudinal evaluation of the impact of prevention activities. From the analysis of trends the registries show a declining trend in the prevalence of malformations linked to folic acid, probably indicative of the effectiveness of increased supplementation with folic acid. A positive relationship established with the Ministry of Labour, Health and Social Policy ensures network activities have a positive impact on medico-social services at the national level.

The 2009 edition of the conference was important in consolidating the messages, the strategic objectives and collaborative relationships between institutions related to the Network. Actions in progress include:

- research on genetic susceptibility factors (polymorphisms of genes and microRNAs) involved in the pathogenesis of non-syndromic orofacial clefts, another group of birth defects associated with folate levels in pregnancy
- identification of new horizons for example:
 - 1) research on probiotic foods naturally rich in folate, as an alternative to products fortified with synthetic folic acid;

2) the opportunity to expand the future objectives and activities of the network to give an even broader scope for the prevention of birth defects through proper eating habits and life

Folic Acid Supplements on Sale

As a result of the work of the Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects a 0.4mg tablet was registered, declared refundable (Class A) and marketed. Monitoring what proportion of women use each type of supplementation is difficult due to the fact that some are sold as prescription drugs, others as over the counter preparations and yet others as multi vitamins or food supplements. Results presented at the Network meeting in Rome on Oct 5 2007¹ report that while there is a positive trend towards the correct use of folic acid few patients and doctors are aware of the correct dosage and timing.

Food Fortification Policy

Periconceptional supplementation is seen as the central element in a strategy that also includes the increase of knowledge, promotion of dietary habits based on scientific evidence and the exploitation of women's empowerment in the management of personal health and life choices.

An unquestionable merit of the Network has been the ability to critically evaluate, through the collection and updating of scientific data, risks and benefits of widespread fortification of foods with folic acid. The Network has developed, discussed and disseminated the scientific community's doubts about the safety of an uncontrolled increase in intake of folic acid in the whole population, and in particular on the possible effect of tumour promotion in the population over 60. The position of the ISS and the Network has been reported by EFSA ESCO² on fortification with folic acid highlights the serious gaps in knowledge that make it difficult to evaluate risk-benefit and impose an attitude of caution

A study of folate intake in many sections of the Italian population is underway. The results will serve as a basis for planning communication activities and promotion and assessing the possibility of voluntary fortification of certain products.

Health Education Initiatives

The Italian Network for the promotion of Folic acid in congenital malformation prevention remains the coordinating body for health education initiatives. An intensive communication work program has included the production and distribution of brochures, posters and pamphlets at the national level, available at the Network's website <http://www.iss.it/cnmr> .

Recent initiatives include:

- The commitment of the associations of social and health workers, in particular, the activities of the spontaneous movement of Italian Pharmacists to involve pharmacists in promoting folic acid supplementation and the association of obstetricians in non-hospital training of medical personnel. These activities should be extended beyond the pilot projects, enhancing national coverage: currently only fifteen provinces are actively involved as volunteers.
- NHS staff training, at national and local level in gynaecology and obstetrics and food-nutrition areas, through active collaboration of the network and co-ordination by CNMR. The on line course has seen a broad and active participation (20 tutors and 1300 participants).
- Projects specifically aimed at the promotion of correct dietary habits in adolescents at the national level (eg "Folate: building blocks for life")
- Participation of associations the campaign "I can not conceive life without folic acid," sponsored in May by ASBI in collaboration with COOP Italy with the aim of conveying the message of supplementation "in everyday life" spreading the recommendation in Italian supermarkets

Knowledge and Uptake about Folic Acid

The percentage of Italian women who take folic acid in the periconceptional period has increased markedly, but focus on the weakest members of society is needed. The correct intake of folic acid in Italian women is now 13 to 33%, a considerable advance from less than 5-10% in 2004-5 (data from the project "The Birth Pathway: promotion and quality assessment of operating models ", coordinated by M. Grandolfo, ISS). Progress is still insufficient and action plans are needed for more effective communication and greater reach.

Proportion of pregnancies which are planned

A pilot study on 200 women in 2005 showed 61% had planned their pregnancies³
This is in line with previously reported data giving 63% of pregnancies in Italy as planned.⁴

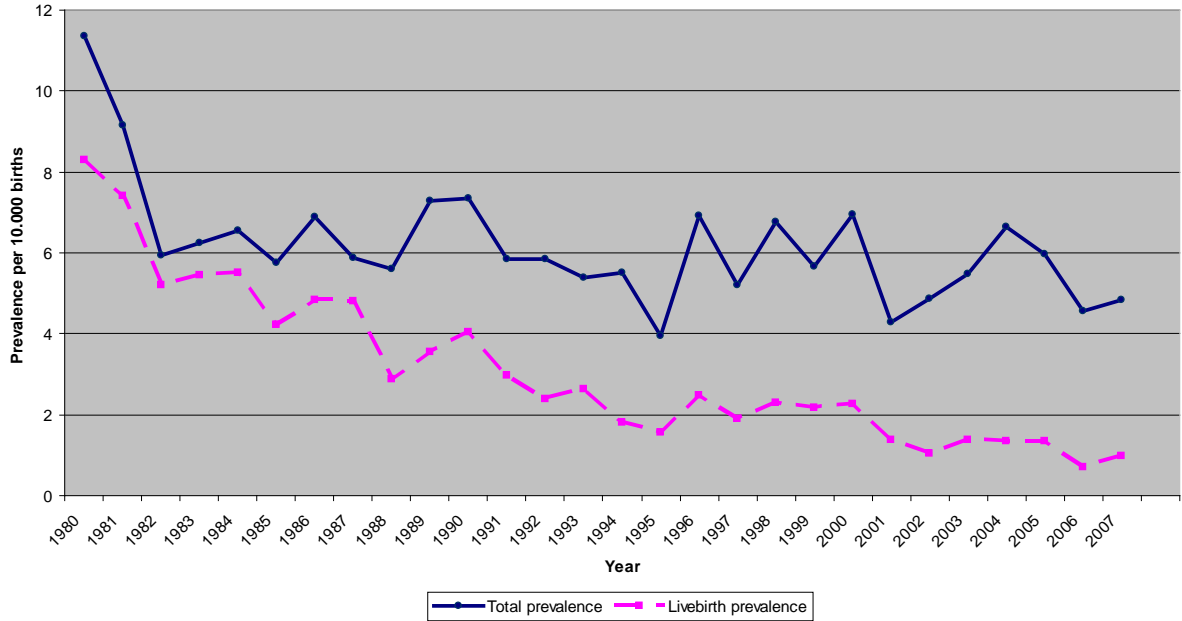
Laws Regarding Termination of Pregnancy

Voluntary termination of pregnancy became legal in Italy in 1984. Termination due to a congenital anomaly is usually performed until gestational age of 23-24 weeks. A psychiatric report is required. Termination of pregnancy is allowed only in NHS hospitals, not in private clinics.

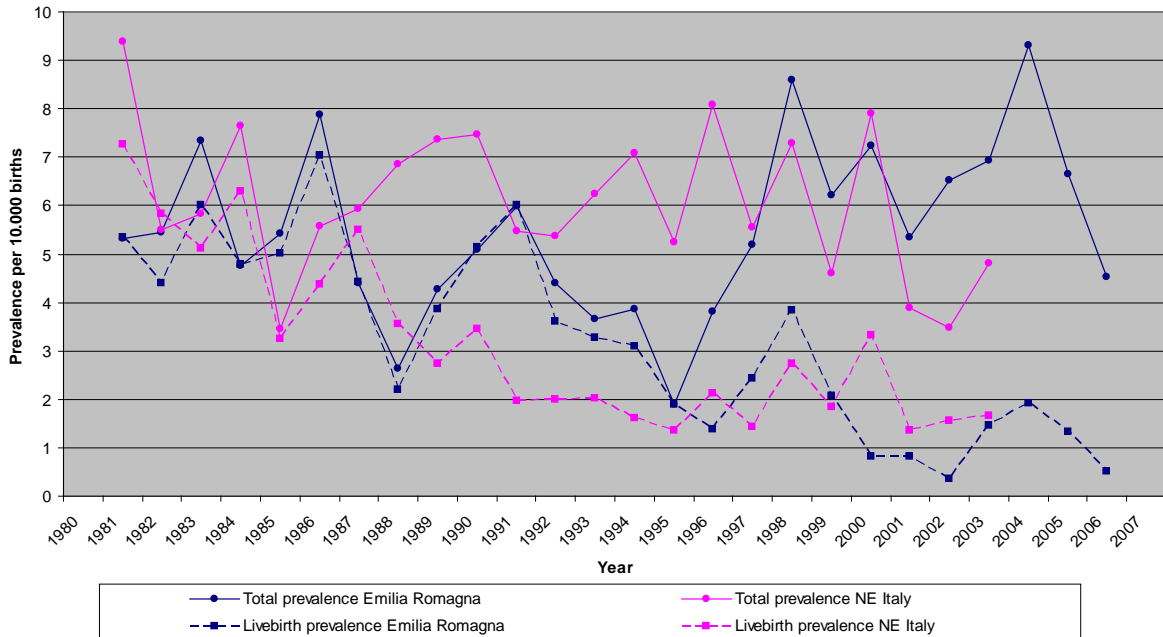
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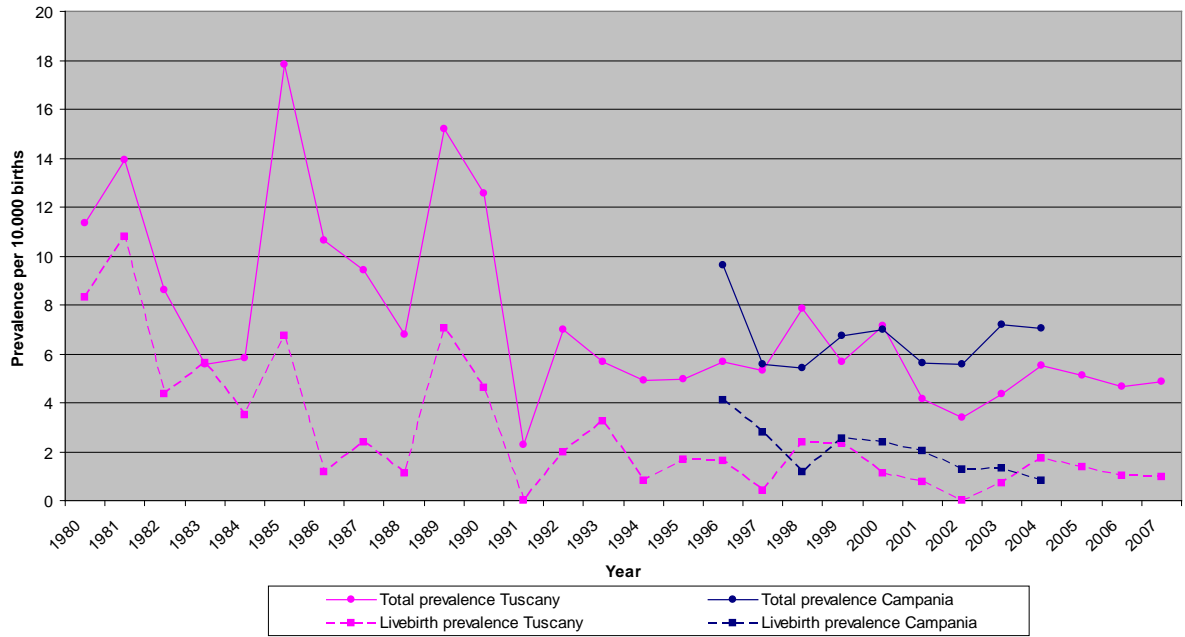
Italy (Emilia Romagna, North East Italy, Campania and Tuscany): Total and Livebirth Prevalence Rates for Neural Tube Defects (all 4 registries together)



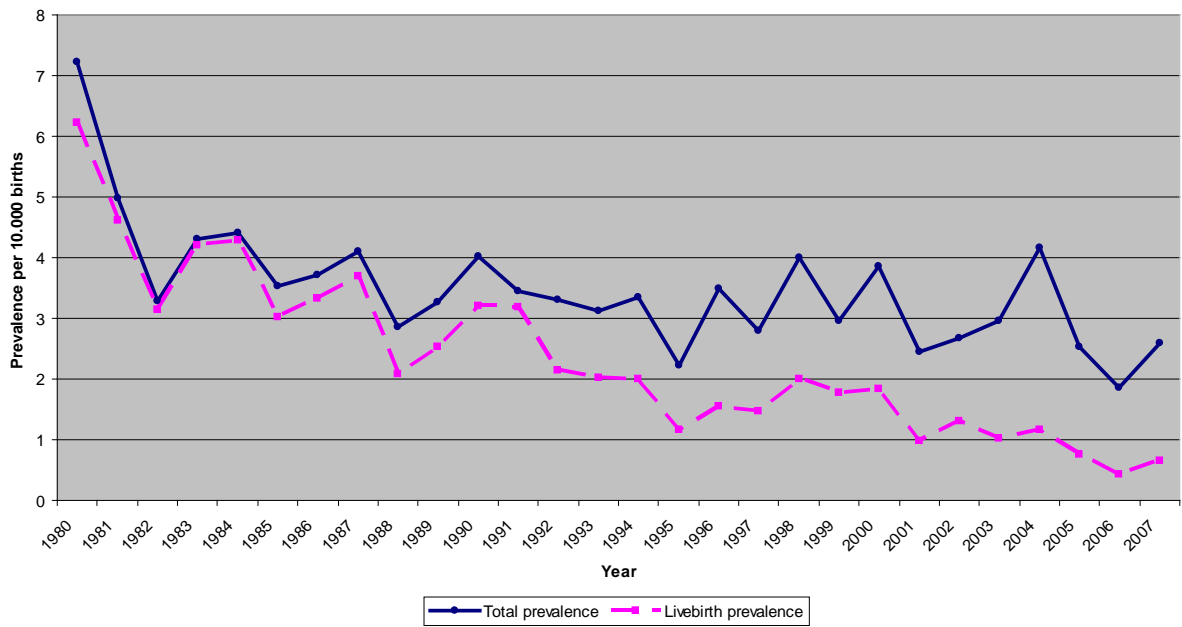
Italy (Emilia Romagna, North East Italy): Total and Livebirth Prevalence Rates for Neural Tube Defects



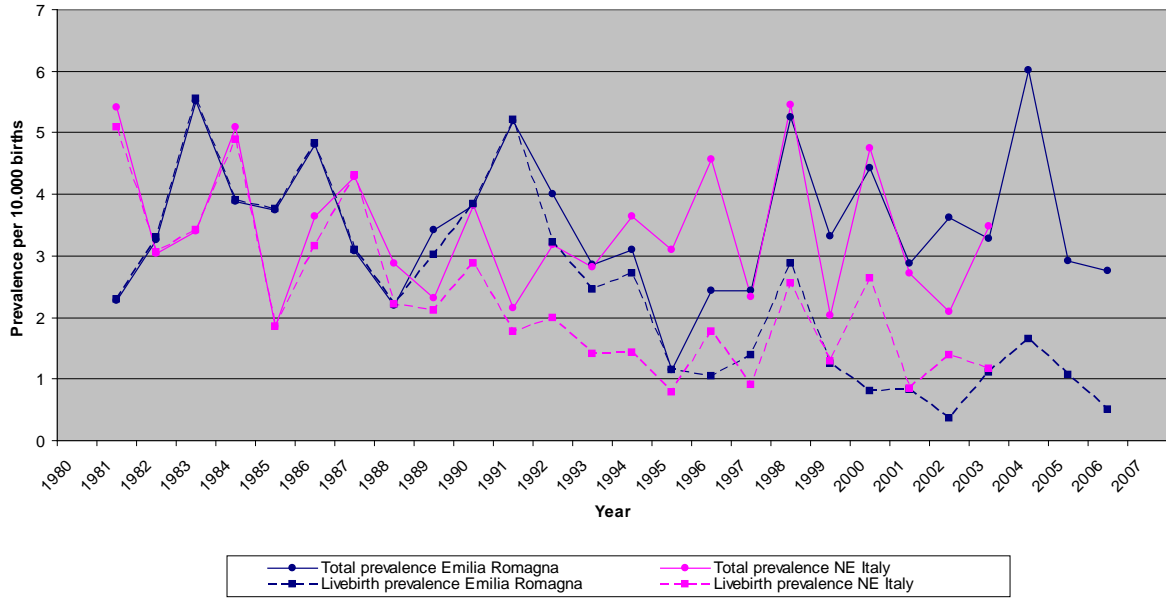
Italy (Campania and Tuscany): Total and Livebirths Prevalence Rates for Neural Tube Defects



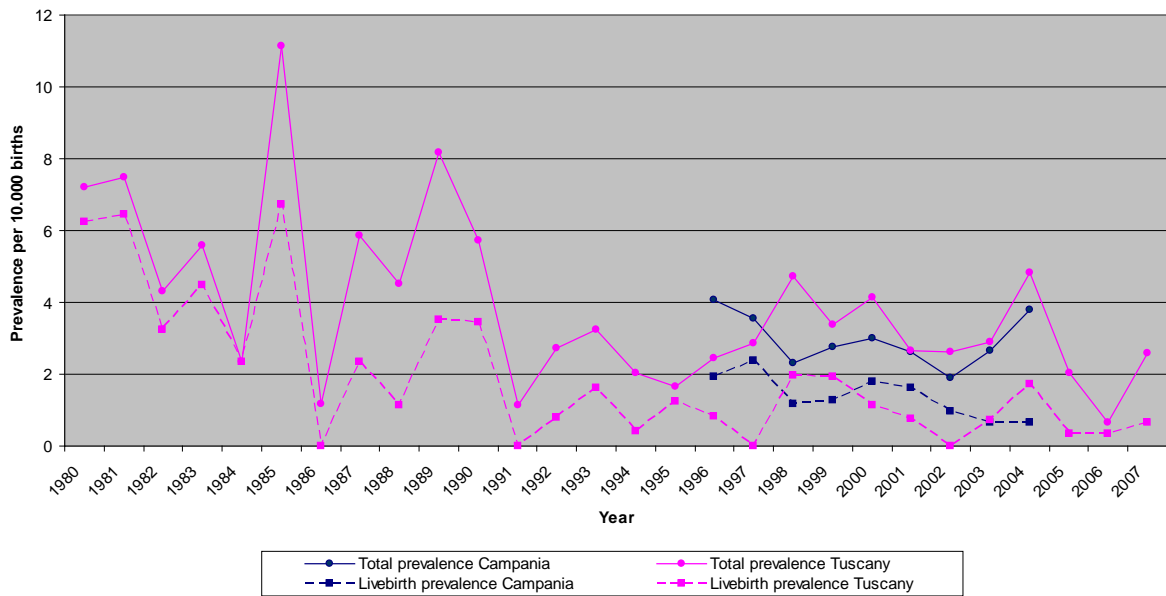
Italy (Emilia Romagna, North East Italy, Campania and Tuscany): Total and Livebirth Prevalence Rates for Spina Bifida (all 4 registries together)



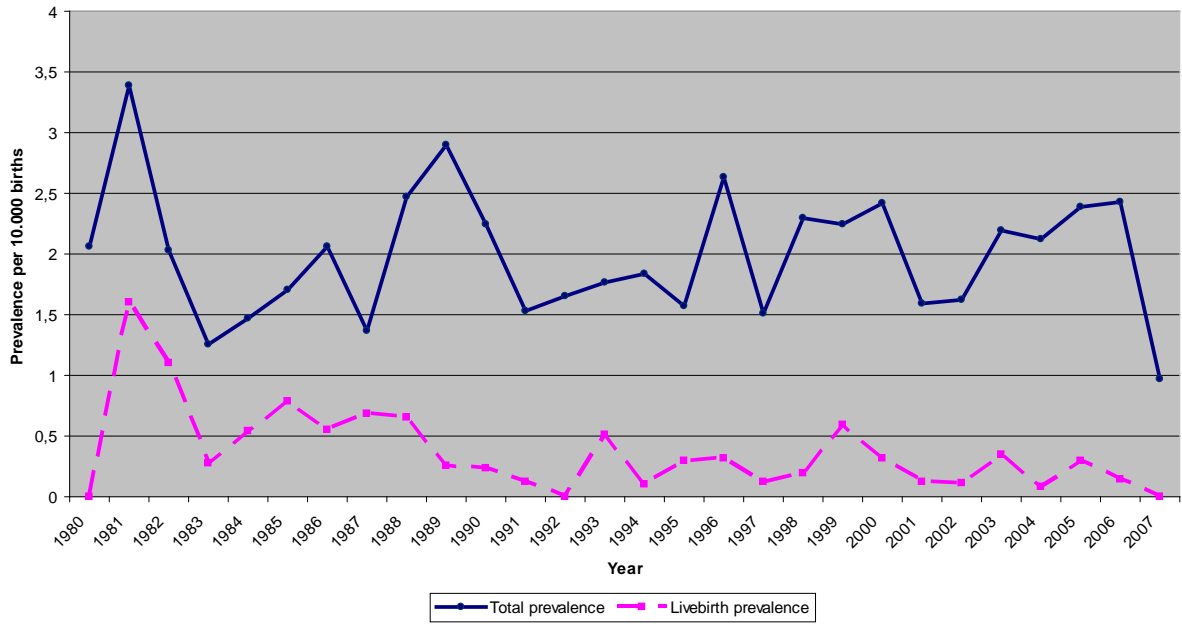
Italy (Emilia Romagna, North East Italy): Total and Livebirth Prevalence Rates for Spina Bifida



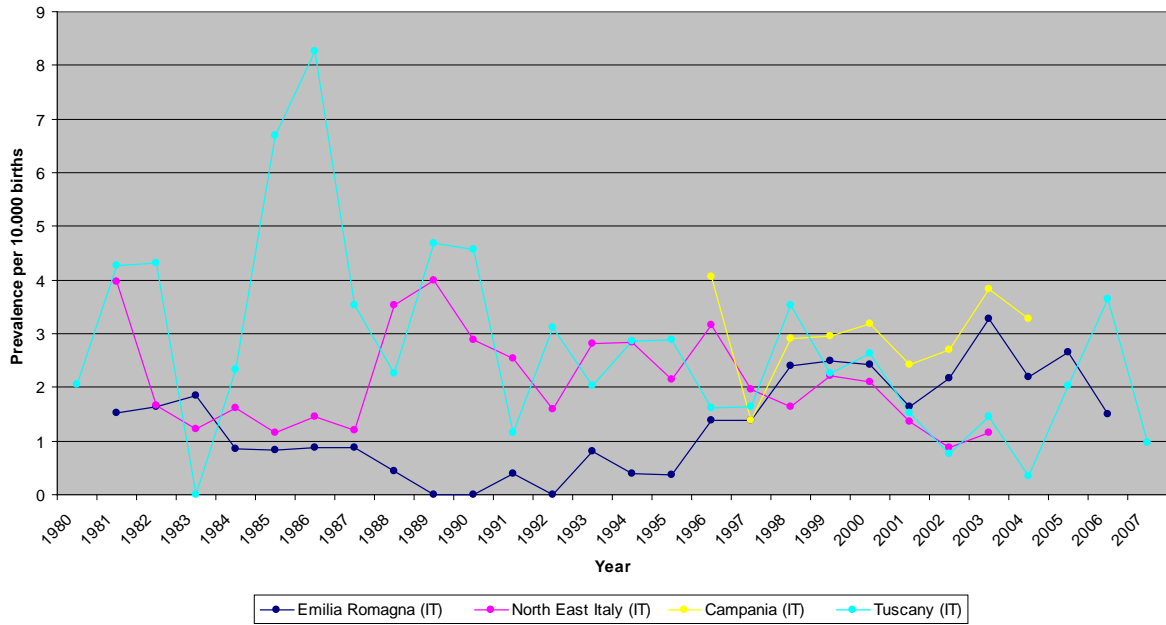
Italy (Campania and Tuscany): Total and Livebirth Prevalence Rates for Spina Bifida



Italy (Emilia Romagna, North East Italy, Campania and Tuscany): Total and Livebirth Prevalence Rates for Anencephaly (all 4 registries together)



Italy (Emilia Romagna, North East Italy, Campania and Tuscany): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Malta

Dr Miriam Gatt

Folic Acid Supplementation Policy

In Malta an official policy regarding increasing folate in the diet was introduced in 1994. The policy advises that pregnant women and women intending to become pregnant should increase their intake of foods rich in folate. This is a Department of Health Circular No. 36/94

Food Fortification Policy

There is no official food fortification policy and none is currently being planned. However, a wide variety of imported fortified cereals and malted drinks are available. Fortified breads are not readily available.

Health Education Initiatives

No official Department of Health Promotion campaigns directed at periconceptional folic acid supplementation have been undertaken but GPs, gynecologists, midwives and organised antenatal courses inform women of the benefits of folic acid. The official dietary policy mentioned above was aimed to inform and educate health professionals.

Folic Acid Awareness and Uptake

A study regarding folic acid awareness in Maltese mothers was undertaken between October 1999 and February 2000 (Gatt 2000). The results were published as a report from the Malta Congenital Anomalies Register. Of the mothers interviewed in the study, 72% had known that folic acid was important in pregnancy. 15% of mothers took folic acid supplementation prior to pregnancy; another 59% of mothers started folic acid after conception but before 12 weeks of gestation. 35% said that they had changed their diet during pregnancy, increasing their folate intake.

Proportion of Pregnancies which are Planned

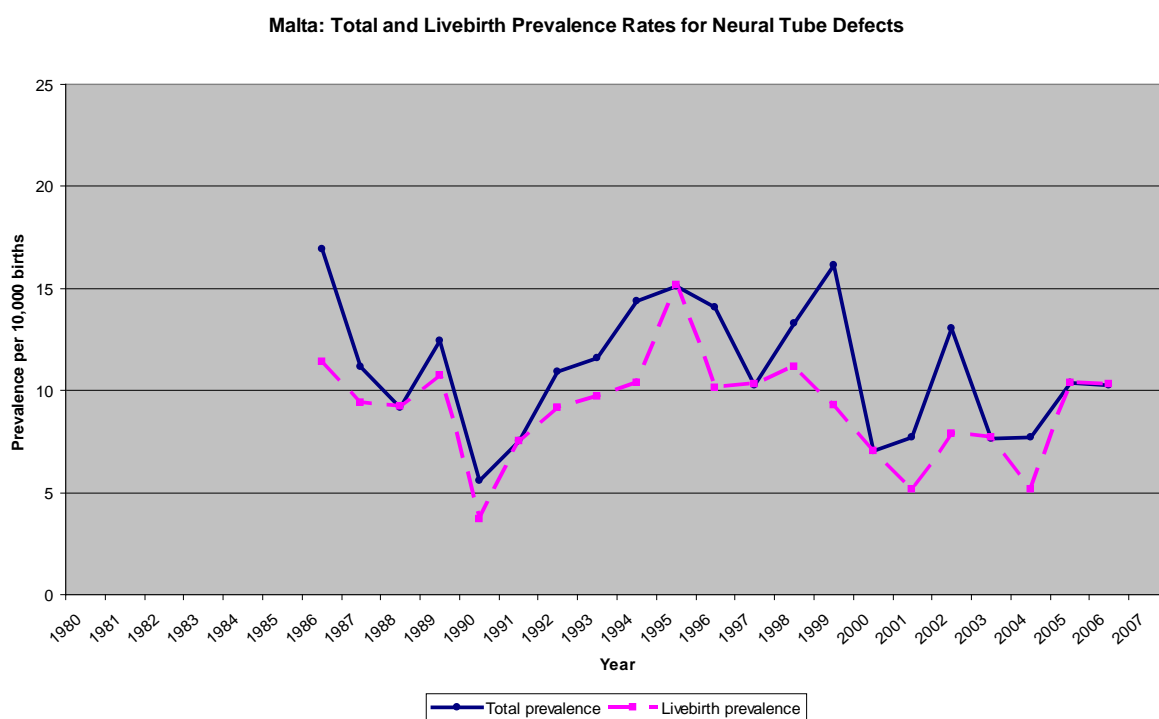
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Laws Regarding Termination of Pregnancy

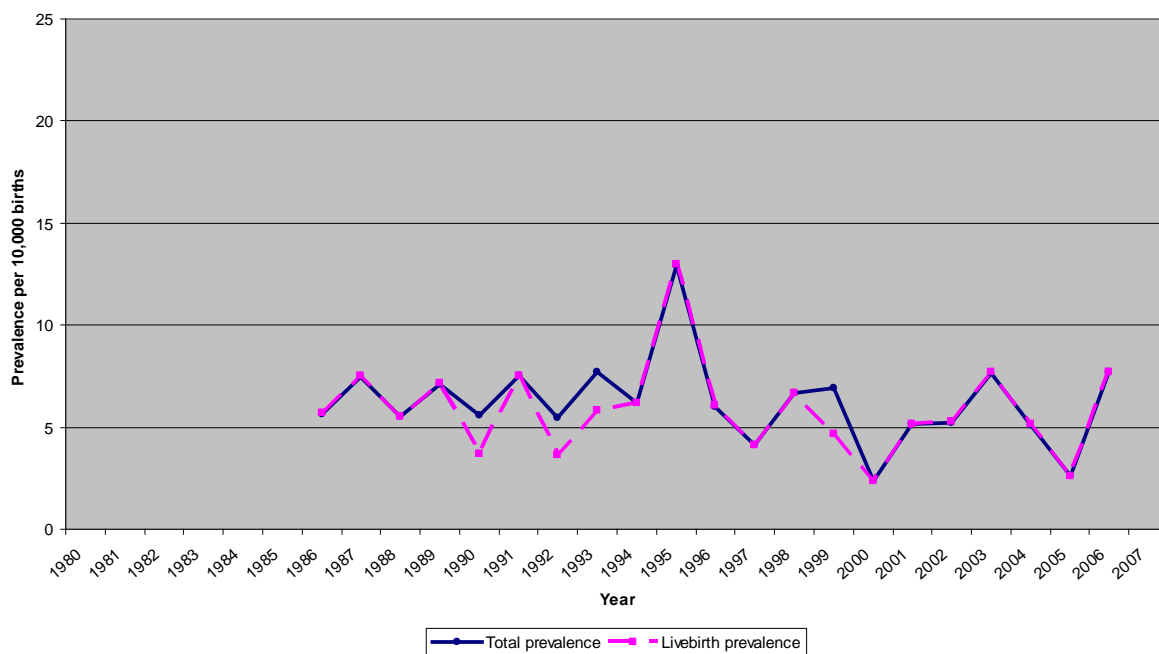
In Malta, termination of pregnancy is not legal.

References:

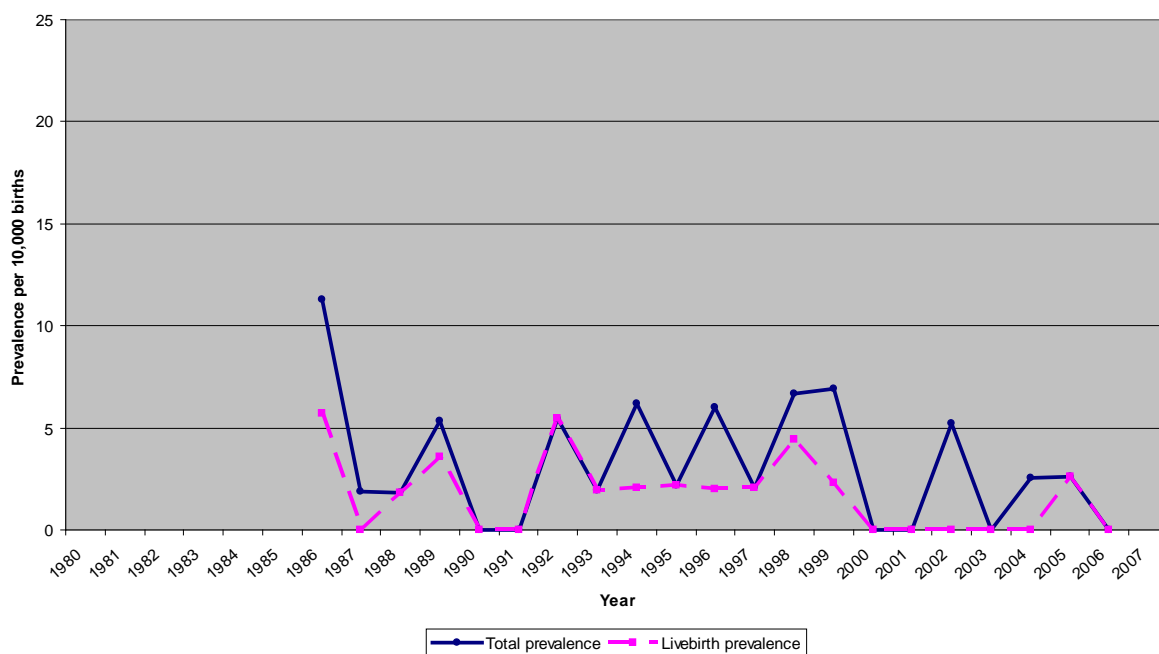
Gatt M (2000) Periconceptional Folic Acid Supplementation in Malta, in 'Half Yearly Report of Malta Congenital Anomalies Register July – December 1999, Malta Congenital Anomalies Registry, Department of Health Information. [Available: <http://www.sahha.gov.mt/showdoc.aspx?id=43&filesource=4&file=hyjuly-dec1999.pdf>)



Malta: Total and Livebirth Prevalence Rates for Spina Bifida



Malta: Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for the Netherlands

Dr HEK de Walle

Folic Acid Supplementation Policy

In 1993 the official Dutch advice was that all women wishing to become pregnant should take a folic acid supplement of 0.5 mg per day. Women with a previous NTD affected pregnancy are advised to consume 5 mg per day. The official status for that policy was the Ministry of Health Welfare and Sports¹.

Food Fortification Policy

Since 1996 different types of food have been fortified with vitamins and minerals in the Netherlands. For example, extra calcium is added to milk and some vitamins are added to (expensive brands of) marmalade. Initially, folic acid was not one of the vitamins added to food because of the risk of masking a vitamin B₁₂ deficiency.

In 2001, the Dutch Health Council issued a report² which did not advise fortification of staple foods such as flour, but advised fortification of products that could be specifically aimed at the target population (ie. women who want to become pregnant). No suggestions were made as to what these products should be or what the recommended amount of folic acid to be added to these products would be.

For the last couple of years folic acid has been added to some cereals such as Kellogg's cornflakes and to some margarines. This has been made possible due to a recent change in regulations regarding micronutrients after the advocate-general of the European Court of Justice decided that fortification of special foods must be allowed in the Netherlands.

In 2008 a new group of the Dutch Health Council will look at the issue of fortification again. A point in favour of fortification is that 60-70% of all the people in the Netherlands do not reach the 200-300 micrograms of folate per day that is recommended.

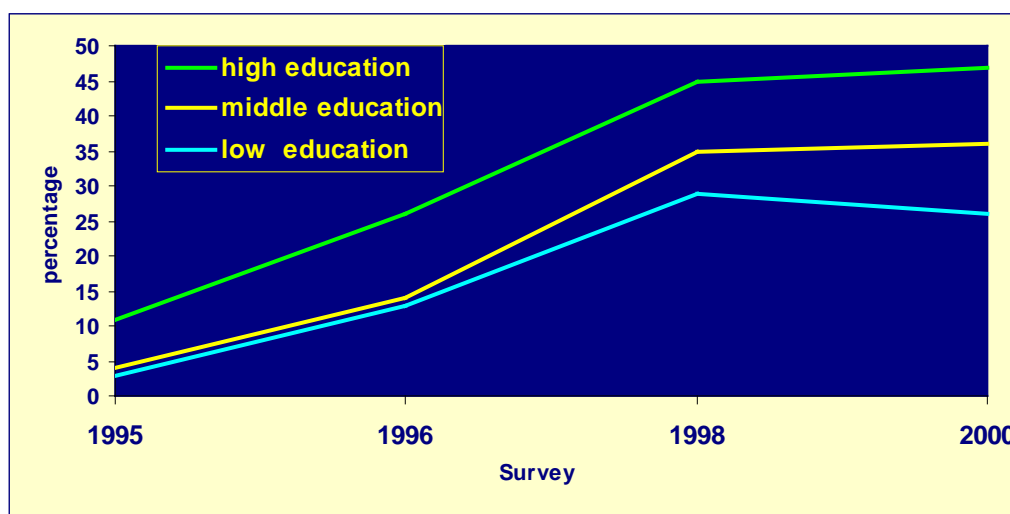
Health Education Initiatives

A campaign was aimed at all women of childbearing age but with a special emphasis on reaching women with a low socio-economic status. General targets of the campaign were that 70% of women planning a pregnancy should know the recommended period to use folic acid and that 65% of women who knew of the advice before pregnancy should use folic acid during the entire recommended period³. This campaign was carried out in 1995.

Currently, the Dutch Ministry of Health are running four projects concerning folic acid. Three of them are interventions: in the pharmacy, via the midwives and ‘well baby clinics’. The fourth project is to give, on a large scale, as much information as possible about folic acid. This includes digital and written information and is carried out by the Dutch “Erfocentrum” (Centre for congenital and hereditary diseases). The website on folic acid is: <http://www.slikeerstfoliumzuur.nl/>

Folic Acid Awareness and Uptake

Figure 1 The use of folic acid during the entire advised period according to educational level



The level of knowledge about folic acid increased satisfactorily in the five years after the campaign. However, the percentage that used it in the advised period did not follow the same trend. Figure 1 shows how socio-economic status is related to use of folic acid during the last five years in which we did the four surveys⁴⁻⁸. It is clear that

the goal of the campaign that the 65% of the women who were aware of the folic acid advice before their pregnancy should use folic acid during the entire recommended period is not reached in any of the surveys (36% of women surveyed in 1999 used folic acid during the entire recommended time). Socio-economic differences with respect to knowledge and use of folic acid remained statistically significant in all the surveys. This means that another goal of the public campaign, the reduction of socio-economic differences with respect to the use of folic acid, was not reached. It is disappointing to conclude this was also true in the regions where an extra intervention was made to reach women with a low education. Striking examples are the billboards with the folic acid message, which were placed in public areas and in buses. The more highly educated women remembered this information much better than the group for whom it was intended.

In a more recent study,⁹ we evaluated women's awareness of and use of folic acid in 2003 and looked at the trend of folic acid use among pregnant Dutch women between 1995 and 2003 with regard to socio-economic status (SES). *Method:* We conducted 2-yearly cross-sectional studies among pregnant women who filled in a questionnaire during the first or second antenatal visit. The highest achieved level of education was taken as a proxy for SES. *Results:* In 2003 the general level of folic acid awareness was high but with significant differences relating to SES; a quarter of the lower educated women did not know about folic acid before pregnancy. Of the subjects with a lower SES, 20% knew the correct period of use compared with nearly 50% in the higher SES group. Worryingly, the reported correct use of folic acid among the lower educated women has actually decreased over the past 3 years (22% in 2003), while it has increased for the higher SES groups (59% in 2003), implying larger discrepancies in health between the lower and higher SES groups. *Conclusion:* In 2003, 8 years after a mass media campaign, awareness and use of folic acid were increased considerably in comparison with the start of the campaign. However, differences in knowledge and use of folic acid with respect to the level of education had increased by 2003. A once-only campaign has a short-term effect especially for lower educated women. Strategies to promote folic acid use in daily structural health care systems are needed.

Pharmacists' Role in Folic Acid Education

About 70% of Dutch women use oral contraceptives sometime before the first pregnancy. For this reason they visit their pharmacy regularly, which provides a great opportunity to educate them about folic acid. In 2002, a pilot study was performed to investigate the feasibility of a proactive intervention through pharmacies and the attitude of the target population towards this education¹⁰. The study showed the intervention was feasible and the target population was positive about the information received. Evaluation of the intervention showed that the use of folic acid was higher among women using the intervention pharmacies compared to those using the reference pharmacies. The difference was more marked among women with a first pregnancy¹¹. In view of the success of this intervention, it was decided to implement it more widely.

Proportion of Pregnancies which are Planned

The Netherlands has a high percentage of planned pregnancies¹². In our surveys the percentage of planned pregnancies was high (around 85%) and it was not related to the socio-economic status of the respondents. However, the concept of "planned" in the way the respondents are using it might be different from the way it is interpreted by researchers.

Our study shows that in the Northern Netherlands, in 2000, women were aware of the importance and the correct time frame of using folic acid. However, not all of them took folic acid in the periconceptual period. This was not because of a negative attitude towards taking folic acid but, according to the most often mentioned reason, because although the pregnancy was planned they conceived sooner than expected.

Laws Regarding Termination of Pregnancy

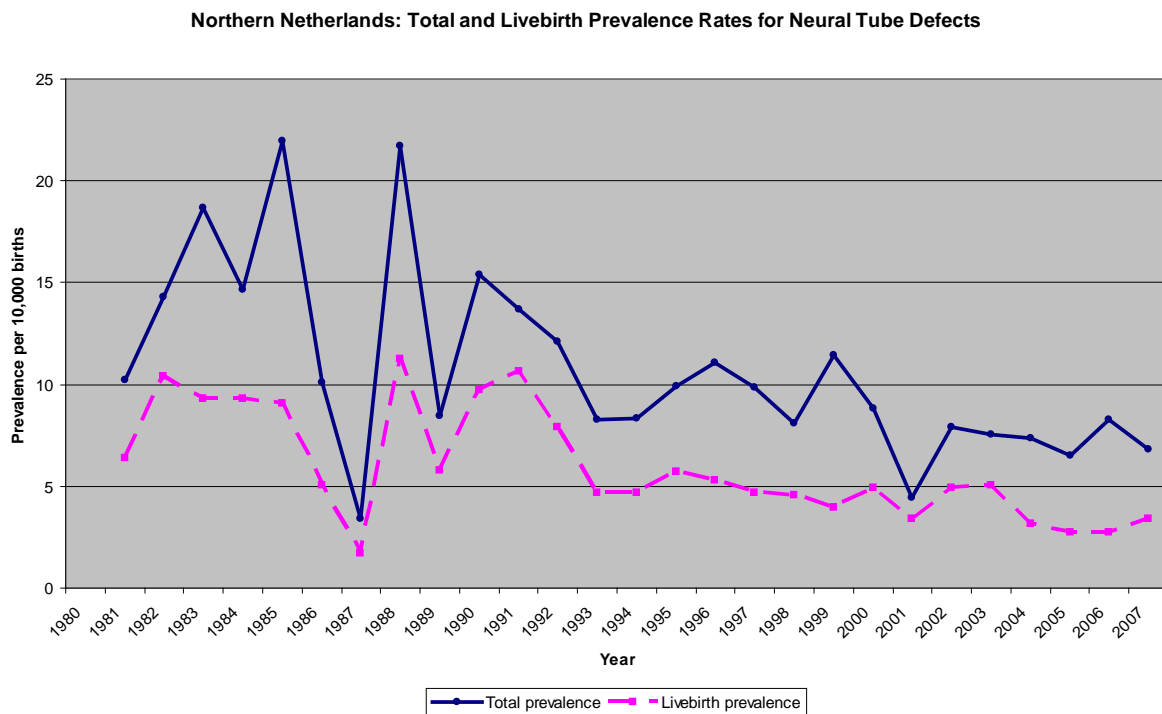
In the Netherlands, termination of pregnancy for fetal abnormality is allowed until 24 weeks of pregnancy. Parents have to be informed about all the facts concerning their situation and have the sole power to decide whether to terminate the pregnancy in a controlled facility. After 24 weeks of pregnancy, termination is only permitted in the case of a fetus with a disorder not compatible with life and a woman who has major mental problems with carrying on with the pregnancy. The decision has to be

reviewed by a multidisciplinary committee and has to be reported to the counsel for the prosecution.

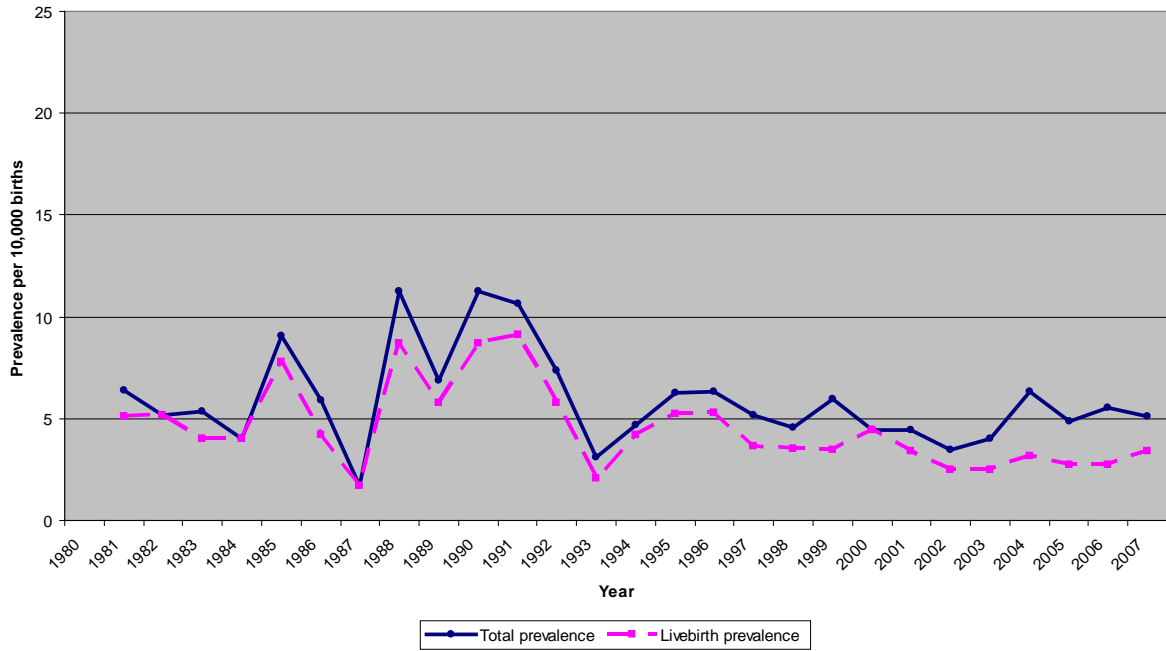
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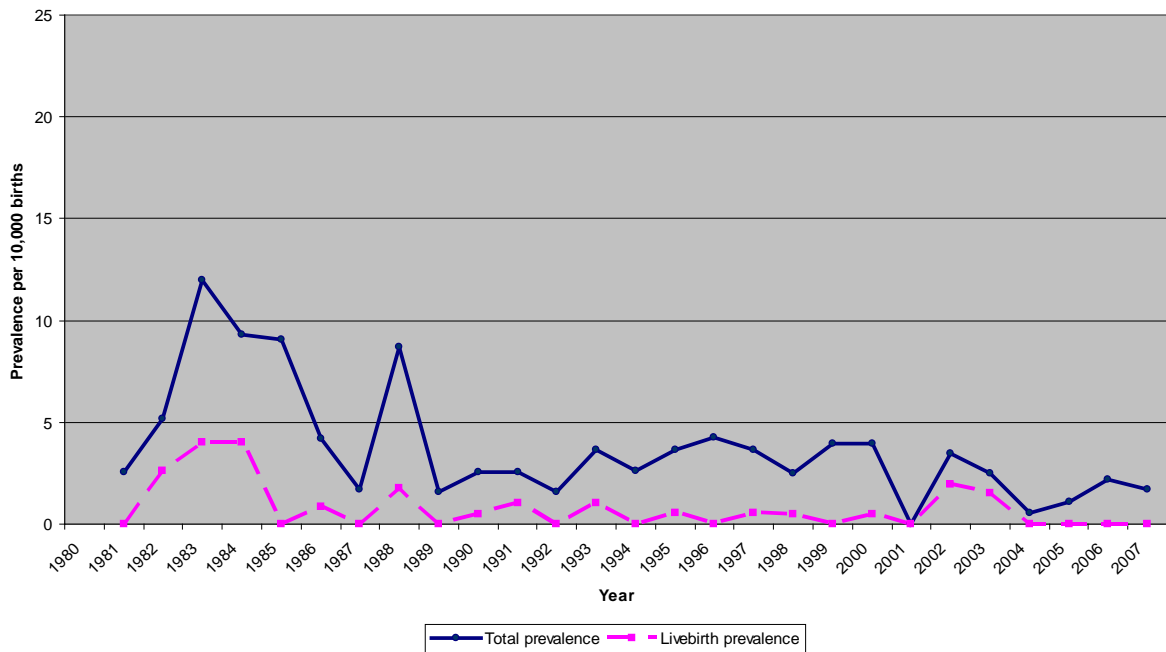
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Northern Netherlands: Total and Livebirth Prevalence Rates for Spina Bifida



Northern Netherlands: Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation in Norway

Dr Anne Kjersti Daltveit

Folic Acid Supplementation Policy

The official folic acid supplementation policy in Norway, issued in the spring of 1998 by the National Council on Nutrition and Physical Activity, is that women who are planning a pregnancy or who may become pregnant are recommended to have a total intake of at least 400 µg of folic acid per day. Since an intake of 400 µg through the diet is unlikely to be achieved by many women, and since there are reasons to believe that supplementation is more efficient than diet in reducing the risk, the practical recommendation is to take a folic acid supplement of 400 µg per day. The supplementation should begin prior to the first month before conception and continue until 2-3 months of gestation.

Women with an increased need for folic acid due to disease or medication (eg anti-epileptic medication), and women with neural tube defects in their own or their partner's family, are recommended to confer with their doctor about a supplement of more than 400 µg per day. The supplementation should begin prior to the first month before conception and continue until 2-3 months of gestation.

Women who have previously had a fetus with a neural tube defect as well as women who themselves or their partner have a neural tube defect are recommended to take 4 mg of folic acid supplement per day. The supplementation should begin prior to the first month before conception and continue until 2-3 months of gestation.

After the first 2-3 months of pregnancy, pregnant and breastfeeding women are recommended to have a total intake of folic acid of 400 µg per day. It is suggested that a common level of dietary intake of folic acid among Norwegian women in the child-bearing age is about 200 µg per day. It is therefore recommended that women continue with a folic acid supplement of 200 µg per day during the last 6 months of pregnancy and during the breastfeeding period.

Women of child-bearing age are recommended to have a dietary intake of folic acid of 300 µg per day. With the exception of recommendations regarding pregnancy and breastfeeding, women of child-bearing age are not recommended to take folic acid supplementation.

The above recommendations were issued in the spring of 1998 by the National Council on Nutrition and Physical Activity (1998). Before 1998, the official recommendations were those issued by the Board of Health in February 1993. These first recommendations did not recommend the use of supplements for any women other than those at risk of recurrence, but stated that women of child-bearing age should consume 400 µg through their diet.

Food Fortification Policy

A working group was established in 1997 by the National Council on Nutrition and Physical Activity to suggest recommendations and means of increasing the intake of folic acid among women of child bearing age. The working group's recommendation was that food fortification with folic acid should not be implemented; it maintained that women should be recommended to have a supplementary intake of folic acid in the periconceptual period (Rapport nr. 1/1998). This decision was reviewed by a working group appointed by the Norwegian Directorate for Health and Social Affairs. Their report was published in December 2004. It found that the policy of recommending periconceptual folic acid supplementation had not yielded satisfactory results. It recommended that consideration be given to mandatory fortification with folic acid of a staple food.

Health Education Initiatives

An official Health Education Initiative began in Norway in autumn 1998 to inform women about the role of folic acid in reducing the risk for neural tube defects. The Norwegian Agency for Health and Social Welfare (formerly National Council on Nutrition and Physical Activity) has a public web site (1998). At the web site there is information on the occurrence of neural tube defects in Norway, recommended daily intake of folic acid, folate content in different foods, when to take supplementation of folic acid in connection with pregnancy, potential side effects related to high intake of

vitamin A through multivitamin supplementation, and needs of special groups such as epileptic women.

Leaflets published by the Norwegian Agency for Health and Social Welfare (formerly National Council on Nutrition and Physical Activity) are distributed to women by general practitioners, specialists in gynaecology and obstetrics, midwives, health care centres for mother and child, drugstores, and pharmacies. Also posters and post cards are distributed, and there have been advertisements in women's magazines and other relevant magazines.

Health personnel are requested to inform women about folic acid and pregnancy at the time of giving guidance on contraceptive devices, doing pregnancy tests, removing an intrauterine device, selling of pregnancy tests, and selling of contraceptive devices. The Norwegian Agency for Health and Social Welfare has distributed a guide for health personnel with these items.

The national recommendations for periconceptional folic acid supplementation are now included in the updated official guidelines for antenatal care in Norway

Folic Acid Awareness and Uptake

Following the recommendations issued in the spring of 1998, a random sample of 1500 Norwegian women of reproductive age was selected for study of their awareness of recommendations regarding folic acid supplementation and of their uptake of the advice. Among the 1500 women, telephone interviews were carried out with 1146 women in the autumn of 1998. (Vollset & Lande 2000) The study was repeated in 2000. (Daltveit ,Vollset , Lande , Oien, 2004)

The folic acid recommendation issued by the National Council on Nutrition and Physical Activity in March 1998 was known by 22% of women in 1998 increasing to 32% in 2000. Supplementation with folic acid before conception or early in pregnancy, when that pregnancy was less than one year ago, was reported by 10% of women in 1998 increasing to 46% in 2000. Intention to follow the recommendations on folic acid supplementation in a future pregnancy was reported by 56% of women in 1998 increasing to 68% in 2000. Intention to follow

recommendations on consumption of folate rich food in a future pregnancy was reported by 75% of women in 1998 and again in 2000. The women were also asked about other vitamin supplementation. Supplementation of other vitamins or minerals before or early in pregnancy among women in whom the last pregnancy was less than one year ago, was reported by (numbers for 2000 in parenthesis) 57% (79%) for any vitamin or mineral supplementation, 29% (30%) for multivitamins, 5% (11%) for vitamin B, 28%(20%) for iron, and 21% (32%) for cod liver oil.

A further study of folic acid supplement use among pregnant women: the Norwegian Mother and Child Cohort Study was published in 2006 (Nilsen et al 2006). In addition to a description of use of folic acid supplementation before and throughout pregnancy, socio-demographic differences in use were studied. An important finding was that most women started folic acid supplementation too late with respect to the prevention of neural tube defects.

A study of epileptic women found that women of childbearing age treated with anti epileptic drugs received folic acid supplementation, particularly those who were taking P450-inducing anti epileptic drugs. (Kampman 2007)

Proportion of Pregnancies which are Planned

There is little knowledge in Norway about the proportion of pregnancies that are planned. In the Norwegian Mother and Child Cohort Study (www.fhi.no), preliminary unpublished data suggest that 76% of the pregnancies were planned. However, the response rate was low, and the true proportion of pregnancies that were planned is thought to be somewhat lower, somewhere between 50% and 75%.

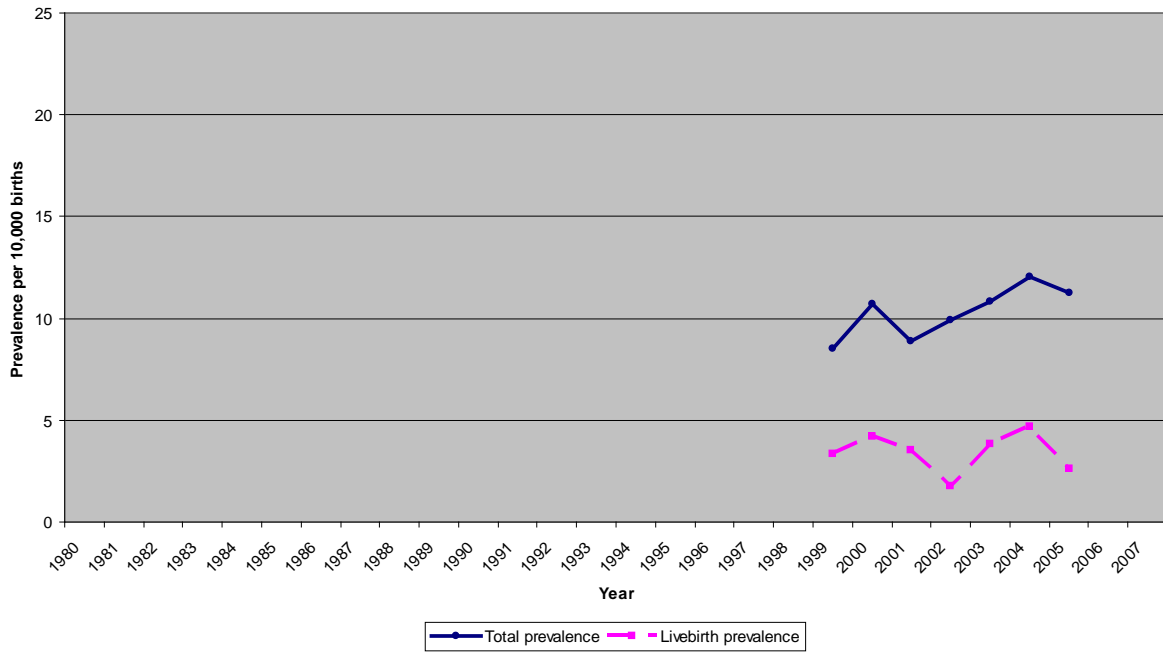
Laws Regarding Termination of Pregnancy

Induced abortion is legal at a woman's request up to 12 completed weeks of gestation. Induced abortion is legal on specified medical and social indications above 12 completed weeks and up to 18 completed weeks, and the decision is made by an abortion board. After 18 completed weeks, induced abortion is legal if the pregnancy represents a serious risk to the mother, or if the fetus suffers from a condition incompatible with life. In those cases there is no gestational age limit.

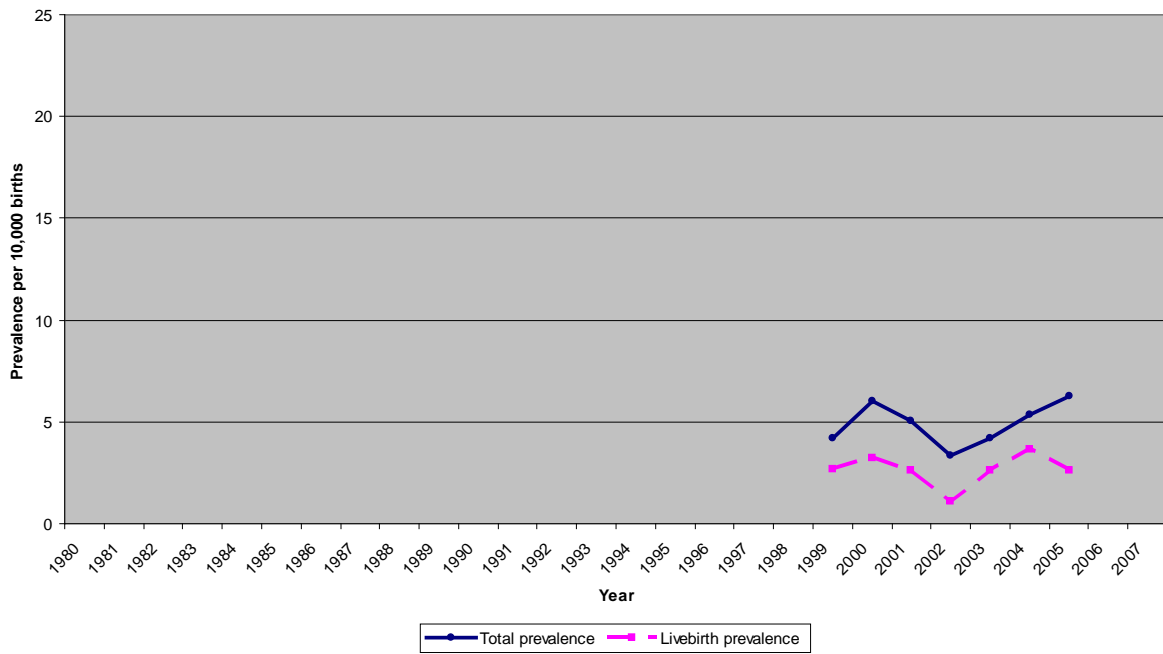
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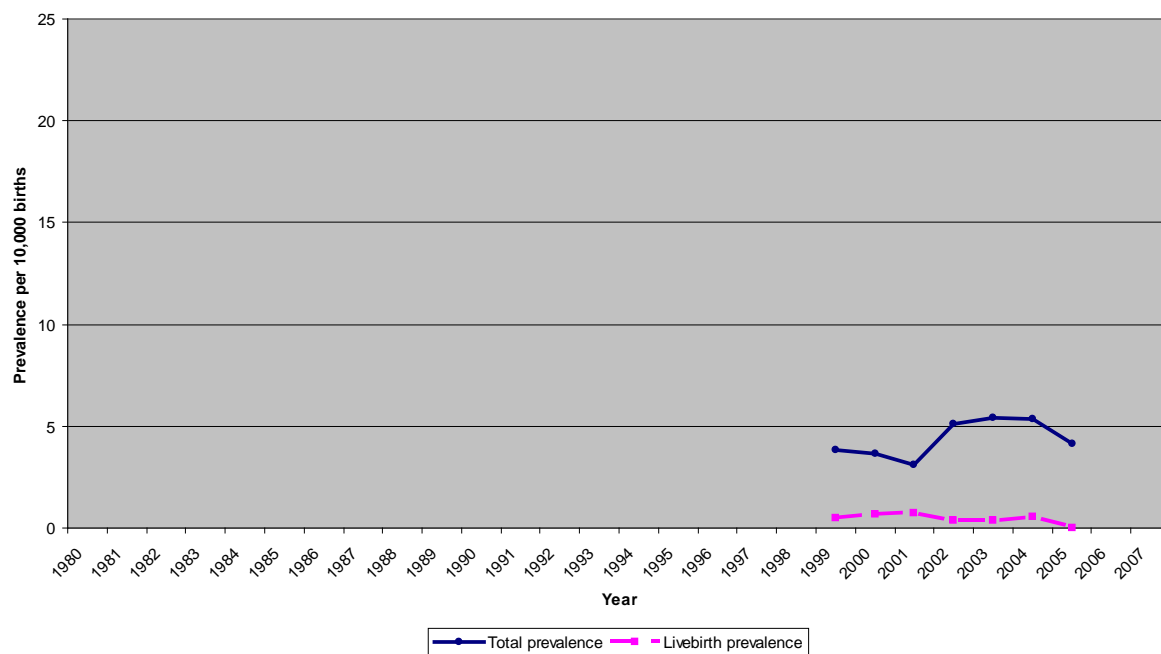
Norway: Total and Livebirth Prevalence Rates for Neural Tube Defects



Norway: Total and Livebirth Prevalence Rates for Spina Bifida



Norway: Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Poland

Dr Anna Latos-Bielenska

Folic Acid Supplementation Policy

In 1997 there was a nation wide government program regarding periconceptional folic acid supplementation. The program "Primary Prophylaxis of Neural Tube Defects", was headed by Professor Zbigniew Brzezinski, from the Department of Epidemiology, Institute of Mother and Child, Warsaw. The original recommendation was that all women of child bearing age should take 0.4 mg of folic acid daily and that women planning a pregnancy should take 0.8 mg daily. The current recommendation is altered, and all women of child bearing age, including those planning a pregnancy, are advised to take 0.4 mg of folic acid daily.

Food Fortification Policy

Food fortification is planned for the Lublin Province in which there are approximately 30,000 births per year.

Health Education Initiatives

An educational program is aimed at women, health care professionals and children over fifteen years of age.

The Polish Registry of Congenital Malformations has arranged that mothers of children with congenital malformations are sent a letter with information about the indications for genetic counselling and about the benefit of folic acid. Mothers delivering a child with a NTD are informed about the need to take 4 mg folic acid/day while trying to conceive a pregnancy.

There are web sites on folic acid:

www.kwasfoliowy.pl/

www.genetyka-ginekolog.pl

Knowledge and Uptake of Folic Acid

Folic acid supplementation was taken by 15% of women aged 18-45 in 1999 and by 19% of women aged 18-45 in 2000; by 11% of non-pregnant women aged 18-45 in 1999 and by 13% of non-pregnant women aged 18-45 in 2001; by 9% of women

under 20 years of age in 1999 and by 16 % of women under 20 in 2001. Thus, folic acid supplementation rates had gone up for all three categories within the space of two years. 57% of women took other vitamin supplements. (Primary Prophylaxis 2000)

Data has since been collected by the Polish Registry of Congenital Malformations. It has been not published yet but has been presented at conferences in Poland. The proportion of women taking folic acid during pregnancy was found to be 64% in 2003, 63% in 2004 and 70% in 2005. The proportion of women taking folic acid before pregnancy was found to be 5.5% in 2003, 7.4% in 2004, 10.6% in 2005.

Proportion of Pregnancies which are Planned

The proportion of pregnancies which are planned in Poland is low.

Laws Regarding Termination of Pregnancy

In Poland termination of pregnancy is allowed in the following instances:

1. the pregnancy is dangerous for the life of the mother (up to 12 weeks gestational age).
2. the pregnancy is the result of a crime (up to 12 weeks gestational age)
3. the fetus is seriously and irreversibly damaged (up to 23 weeks gestational age)

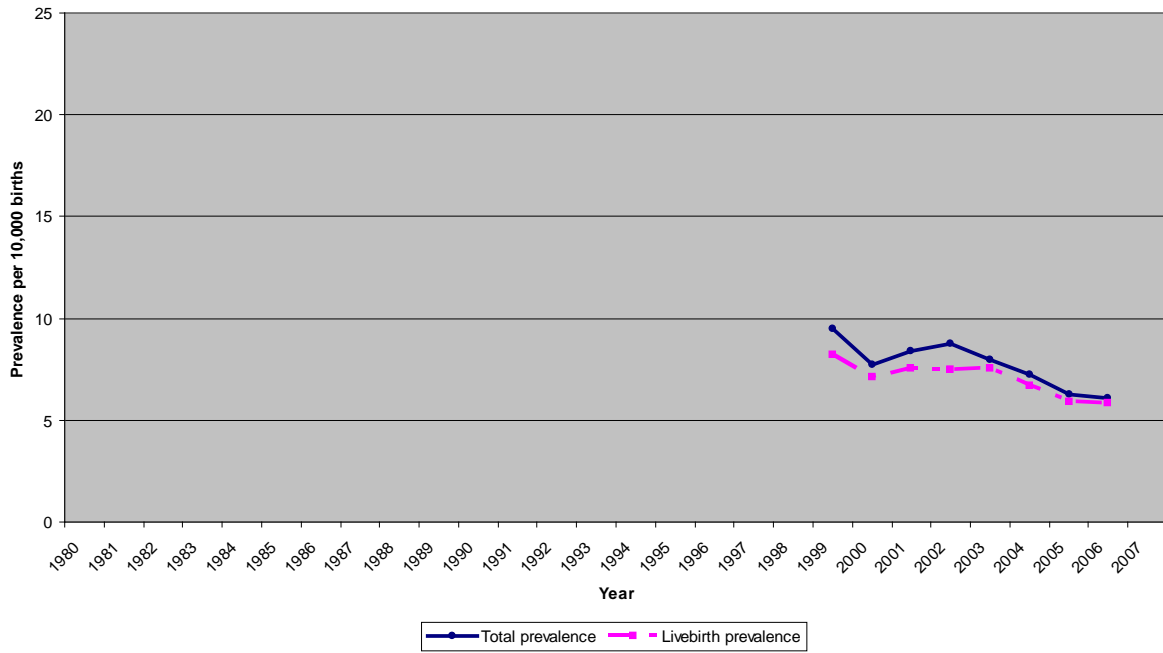
The gestational age limit for termination of pregnancy is under 23 weeks.

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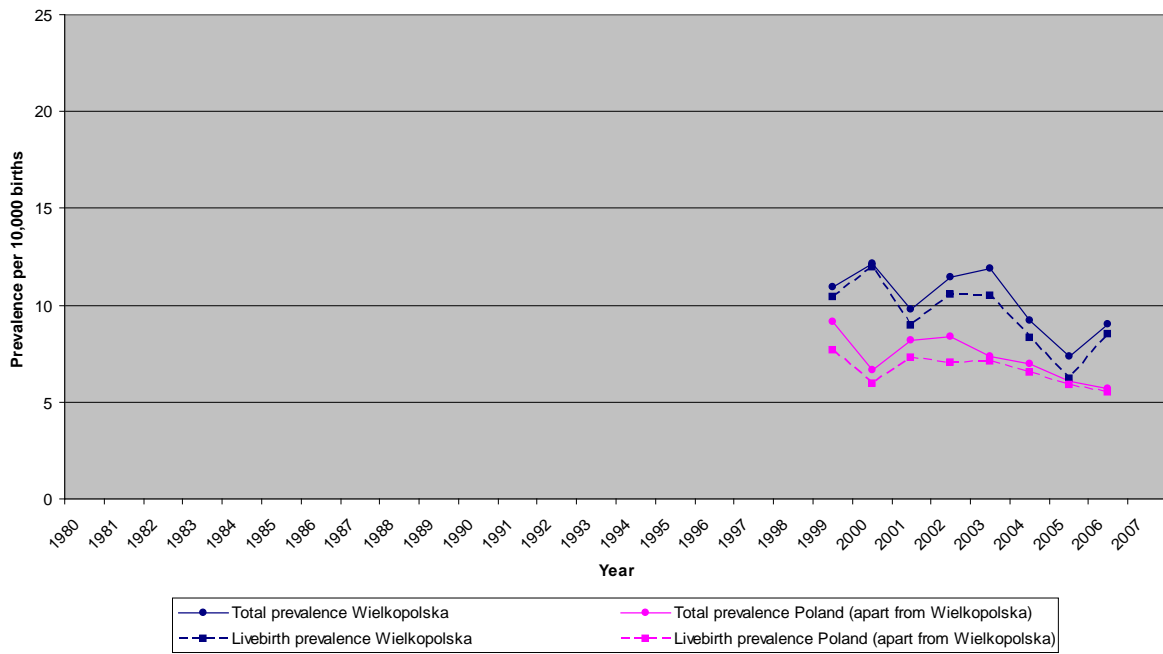
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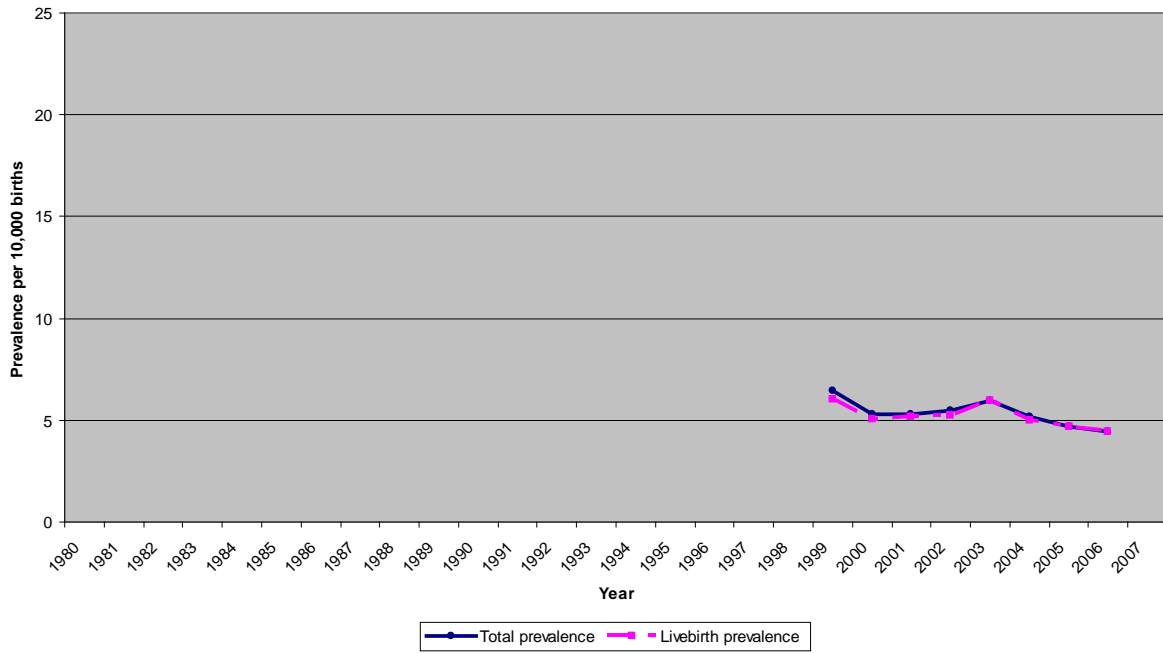
Poland: Total and Livebirth Prevalence Rates for Neural Tube Defects



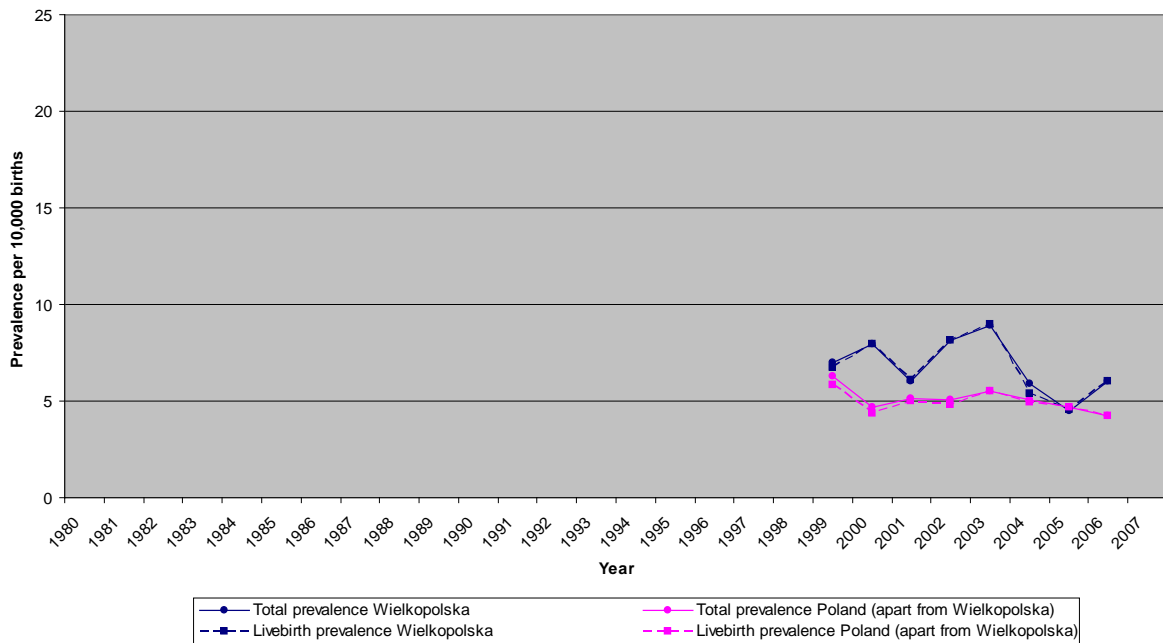
Poland: Total and Livebirth Prevalence Rates for Neural Tube Defects



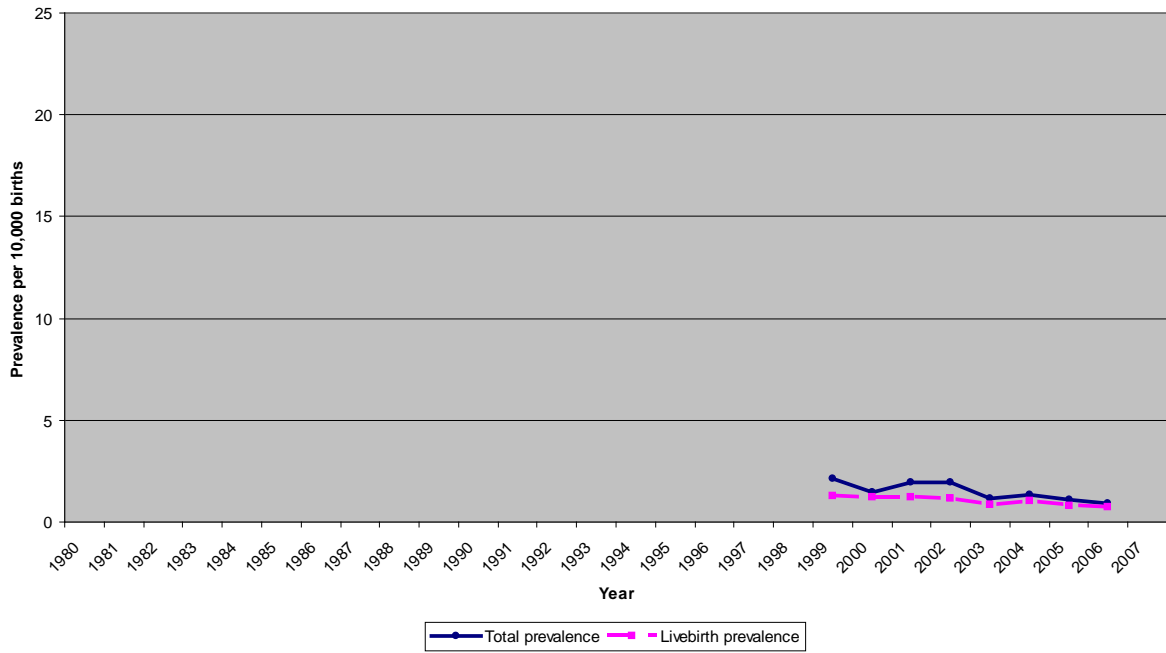
Poland: Total and Livebirth Prevalence Rates for Spina Bifida



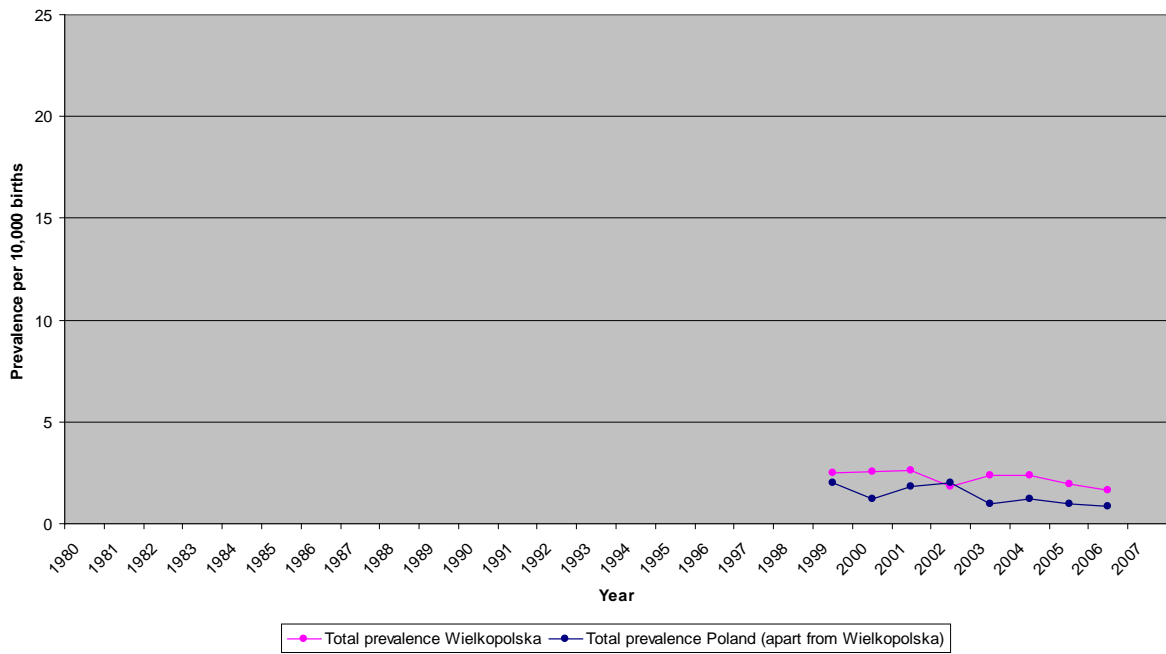
Poland: Total and Livebirth Prevalence Rates for Spina Bifida



Poland: Total and Livebirth Prevalence Rates for Anencephaly



Poland (Wielkopolska and the rest of Poland) Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Portugal

Dr Paula Braz and Carlos Matias Dias

Folic Acid Supplementation Policy

In March 1998 there was a recommendation from the General Directorate of Health (guideline number 2/DSMIA) to all health care professionals, to inform the childbearing population about the importance of folic acid. There was no information about dosage.

In January 2006, these recommendations were updated by the General Directorate of Health (guideline number 2/DSMIA). All health professionals are instructed to inform the childbearing population to start folic acid at least two months before stopping contraception.

Folic acid supplements are available on prescription in Portuguese pharmacies:

0.4mg dose - multivitamin pill (Centrum, Prenatal)

0.3mg -1mg dose – combination with ferritin

5mg dose - monopreparation pill (Folicil, Acfol, Lederfoline, Raycept)

Food Fortification Policy

There is no food fortification policy, but one of the most important commercial firms in Portugal for milk products (Mimosa) decided five years ago to fortify milk with 50µg/100ml of folic acid.

Health Education Initiatives

The Portuguese Association, Spina Bifida and Hydrocephalus, (ASBIHP) initiated an educational project to promote the importance of folic acid in the prevention of NTD. This project, which took place during 2003 and 2004, was targeted at universities and health professionals. The same association also conducts a project called “Olá Bebê” (Hello Baby) to support parents with a new baby with NTD.

The Internet site of ASBIHP has information on folic acid;

www.asbihp.org

Knowledge and Uptake of Folic Acid

Machado and Feijóo, in their study (2006)¹, found that 77.5% of women aged 24-44 years old knew about folic acid, but only 20% were able to describe folic acid as an effective method to reduce NTD. 15.4% of all respondents knew that supplementation with folic acid should begin before conception.

In 2005, Braz² found an increase in the proportion of women taking folic acid prior to pregnancy since 1998. In 2005, 23.9% (CI 95% 14,0;33,8) of women in her study took folic acid prior to pregnancy. There was a significant association ($p < 0,001$) between appropriate intake and the pregnancy being planned.

Proportion of Pregnancies which are Planned

In one survey,³ 54.5% of all women surveyed who had ever been pregnant reported having consulted an MD while preparing for their last pregnancy.

Laws Regarding Termination of Pregnancy

Termination of pregnancy is legal in Portugal until 24 weeks gestation for major congenital anomalies, rape, and risk to the mother's health. It is legal up to term if an anomaly is incompatible with life. There is a technical committee in each obstetric unit in which terminations are performed which decides in each case if the procedure is legal.

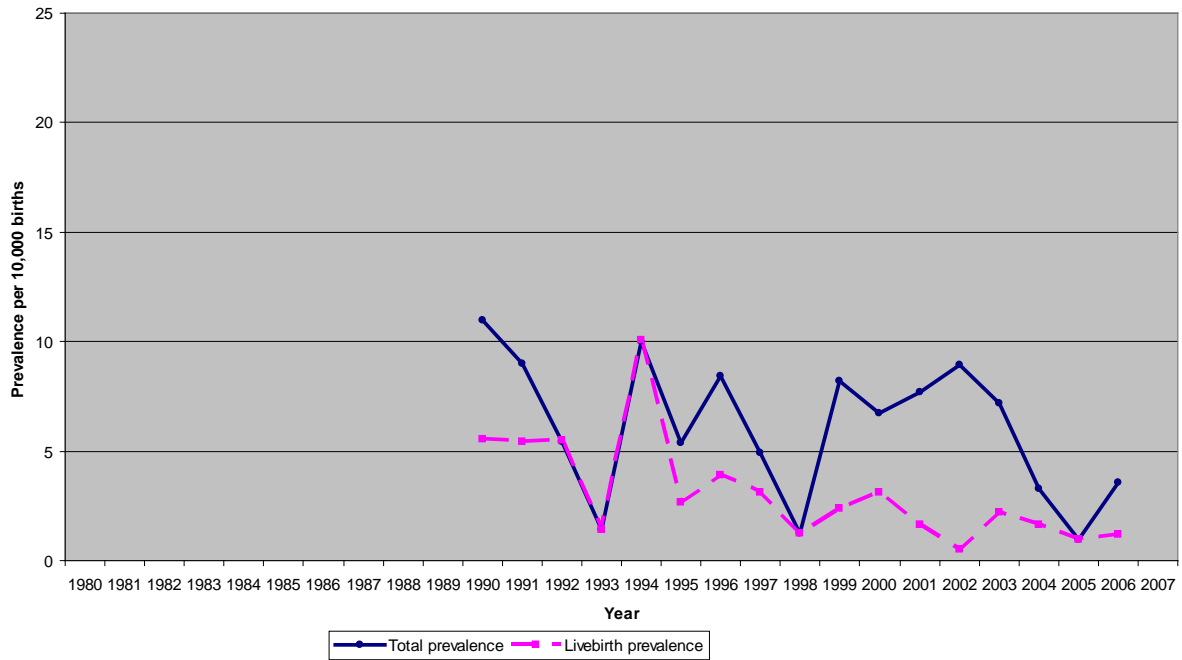
In April 2007, a new law was passed allowing termination of pregnancy until 10 weeks of gestation if a woman does not wish to be pregnant. This law did not affect the regulations regarding termination of pregnancy due to major congenital anomalies, rape, and risk to the mother's health.

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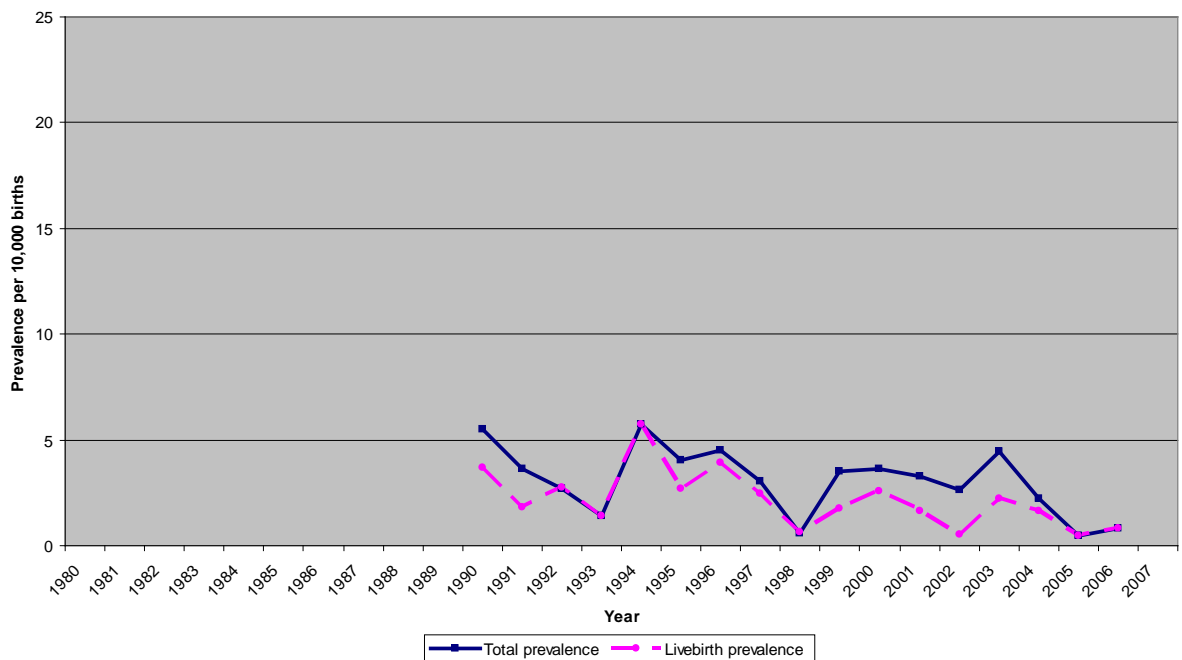
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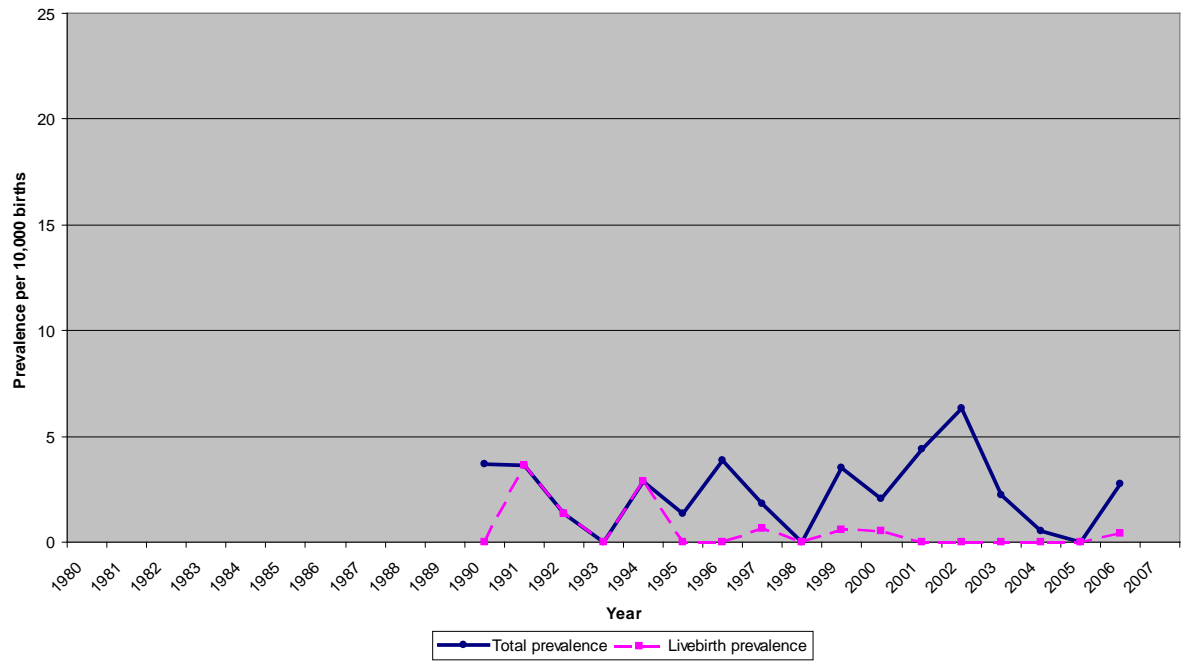
Portugal (South Portugal): Total and Livebirth Prevalence Rates for Neural Tube Defects



Portugal (South Portugal): Total and Livebirth Prevalence Rates for Spina Bifida



Portugal (South Portugal): Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Slovenia

Dr Ksenija Ogrizek Pelkič

Folic Acid Supplementation Policy

In Slovenia, there is no official government recommendation for periconceptional folic acid supplementation, but a recommendation was published by the Slovenian Association for Perinatal Medicine in 1998. They recommended that all women wishing to become pregnant should take periconceptional folic acid supplementation of 0.4 mg per day before conception. Women who were already pregnant should start taking folic acid supplementation during the first four weeks of gestation and continue until the 12th week. Women with increased risk of having a pregnancy with a neural tube defect due to malabsorption, long-term use of certain medications, diabetes mellitus or neural tube defects in relatives are recommended a folic acid supplement of 4 mg per day until the end of pregnancy.

There is no funding for folic acid products during pregnancy; pregnant women have to pay for it themselves.

Food Fortification Policy

There is no official food fortification policy in Slovenia. We have sent a letter to the Minister for Health requesting that action towards fortification of a staple food with folic acid be set in motion (september 2007).

Health Education Initiatives

There is no official health education initiative in Slovenia, but there are many initiatives by the Slovenian Association for Perinatal Medicine. Leaflets addressing women planning pregnancy have been published and distributed to general practitioners, specialists in gynaecology and obstetrics, and gynaecological/obstetrical departments of the Slovenian hospitals. There have been no paper or television advertisements, but the issue has been covered in some newspaper articles and in magazines concerning health, pregnancy and children. Some Slovenian sites on the Internet are used to educate women about healthy nutrition and about the importance of taking ample folic acid (www.med.over.net, www.ringaraja.net). The initiative is still ongoing.

Knowledge and Uptake of Folic Acid

In Slovenia a study was carried out and published in 2001 (1). This study found that 79% of the pregnant women questioned knew about folic acid, but only 7% were aware of the benefits of supplementation. 52% of them were taking folic acid during the last pregnancy. 27% took it before conception. Only 14% of all pregnant women took folic acid correctly.

In 2007 we administered a questionnaire to pregnant women in a prenatal clinic in the Maribor teaching hospital (unpublished data): 350 pregnant women completed the questionnaire. 88% of the women were taking folic acid, but only 31.5% of them during the appropriate periconceptional period. An increase was seen in the proportion of women complying with the recommendation in the study period and this coincided with the information campaign events.

Proportion of Pregnancies that are Planned

The proportion of pregnancies that are planned in Slovenia is unknown.

Laws Regarding Termination of Pregnancy

The national law is that up till 10 weeks of gestational age every woman may opt for termination of pregnancy without special permission. After 10th week termination of pregnancy for fetal anomaly can be performed after permission from a regional committee (two doctors and one employee at the Social centre). The upper gestation limit for fetal anomaly is not set.

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Report on Periconceptional Folic Acid Supplementation For Spain

Dr Isabel Portillo and Dr Blanca Gener

Folic Acid Supplementation Policy

In 2003, the Ministry of Health updated its advice regarding use of periconceptional folic acid supplementation to reduce the risk of having a child affected with an NTD. This is available in the web and links with other National Recommendations⁽¹⁾.

These recommendations are in line with the policy introduced in 2001 advising the intake of folic acid prior to pregnancy: All women who are considering a pregnancy and have no previous pregnancy affected by NTD should take 0.4 mg per day of folic acid at least one month before conception and during the first three months of pregnancy; Women planning a pregnancy who have already had a pregnancy affected with NTD should take a dose of 4 mg per day of folic acid at least one month before conception and during the first three months of pregnancy⁽²⁾. However, the 2003 document advises that more emphasis should be placed on dissemination of information.

In the Basque Country, recommendations are included in the Health Promotion webpage and also in all patient information leaflets for pregnant women, as well as medical record⁽³⁾.

The Spanish Society of Gynaecology and Obstetrics (SEGO) continues the promotion of folic acid supplements in accord with international and national patterns (daily dose of 0.4 mg in low risk and 4mg in high risk taken periconceptionally). Also they recommend not using multivitamin tablets in order to achieve the desired doses of folic acid, because in order to do this an excess of other vitamins (e.g. vitamins A and D) might be taken, and this could be dangerous both for the fetus and the mother.

Food Fortification Policy

At this time, there is no mandatory fortification of food with folic acid. However, there is voluntary fortification of most breakfast cereals.

Knowledge and Uptake of Folic Acid

Studies of Prevalence of folic acid intake

In Spain, the average daily intake of folic acid in the adult female population was estimated to be 211.7 µg (108) by Aranceta et al, (1994)⁽⁴⁾ in the Basque Country and to be 392 µg (131) in Valencia Country (Vioque et al, 2000)⁽⁵⁾. These studies were based on the Nutritional Inquiry of 1994 and on blood tests. In the Basque and Valencia countries, percentages of women who took the appropriate amount of folate (400µg per day) were low (10% and 40% respectively). Also the observational study of Ballesteros et al (1999)⁽⁶⁾ in Cantabria Community found that only 12% of pregnant women in the first trimester had optimum levels of serum folate. Population studies done in Catalonia by Garcia et al (2002)⁽⁷⁾ found that 12.9% women aged 18-34 years had sub optimal serum folate levels. More recently, Martinez-Frias et al (2007) found that of 16,761 newly delivered women with non-malformed infants, 17% took folic acid prior to conception, while a further 71% took it after conception. ⁽⁸⁾.

Studies of Prophylaxis Assessment

Study	Design	Intake of periconceptual folic acid supplements	Knowledge of benefits of folic acid	Recommendations
Gilbert et al (2000) ⁽⁹⁾	Retrospective 651 mothers attended in Hospital Mallorca 1998	4.5% of the prescribed preventions were sufficient and they were more frequent in private medicine (12%) than in public medicine (3.4%) (p= 0.036).	85.2 % of midwives and 45.7% of gynaecologists recommended prophylaxis when the mother first attended the antenatal clinic or before (p<0.001).	Involvement of Gynaecologists, midwives, and Public institutions

Martínez-Frías et al ⁽¹⁰⁾ (2003)	Retrospective Mothers of controls ECEMC database (1980-2002): 28522 Mothers of controls 2001 and first trimester 2002: 1338. Spanish hospitals	Increased intake of folic acid since 1992 (80%). 2002 10.62% of women took folic acid prior to pregnancy. Dosage higher (>4.5mg per day) than recommendations. 100% mothers with low educational level did not take any supplementation More than 15% of mothers with high educational level took supplements of folic acid		Primary Care physician to be involved in prevention of NTD. Cultural and social barriers to be addressed Fortification of staple food such as flour.
García et al ⁽¹¹⁾ (2003)	Observational 346 pregnant women in Madrid referred to hospital for delivery 1999-2000	17% (CI 95% 13.2-21.4) of women took periconceptional folic acid. Appropriate intake was significantly associated with marital status and with prescription by primary care physician no association with social or educational level	34% (CI 95% 29.2-40.1) of women were able to describe folic acid as efficacious method to reduce NTD	The role of Primary Care physician to prevent NTD
Gutierrez et al ⁽¹²⁾ (2003)	Observational Sample of 928 pregnant women <35 years. Economic analysis of prescription in 101 women Zaragoza Unknown period	15,4% of women took supplementation with folic acid correctly. There was significant association (p<0,001) between appropriate intake and planned pregnancy. 2.4% of women took supplementation of multivitamins not recommended. 32% of women did not take any folic acid supplementation no association with social or educational level.	72, 6% of women knew that periconceptional folic acid supplementation can prevent NTD	Prescription of commercial folic acid (400µ) supplement with sufficient B12 to prevent deficit of B12
Perez-Vázquez et al ⁽¹³⁾ (2003)	Observational 148 pregnant women in Pontevedra Unknown period	15.5% (CI 95% 10.3-22.1%) of women took appropriate dosage. 86% (CI 95% 73-86%) were planned pregnancies	41% (CI 95% 33-50%) of women did not know benefits of folic acid	Information campaigns to care providers and general population

Coll et al (2004) ⁽¹⁴⁾	Retrospective 1000 consecutive women who delivered in Hospital in Barcelona 2000	6.9% of women took appropriate dosage	85.7% of women had not been informed by care providers 50.6% were aware of benefits of folic acid.	Information about folic acid should be given in primary care and preconceptional counselling
Martinez-Frias et al 2007 ⁸⁾	Retrospective 16,761 recently delivered mothers of non-malformed infants	17.% took FA prior to conception. 71% took FA once pregnant. Most of them took high dose (= \geq 4mg)		

Reviews by Spanish Authors

In recent years, some authors have published articles referring to folic acid supplementation and the need to strengthen policies to improve intake. Four references should be mentioned: Madueño and Muñoz (2001)⁽¹⁵⁾, Capitán and Carrera (2001)⁽¹⁶⁾ and Carrera (2003)⁽¹⁷⁾, Martinez-Frias (2007)⁽¹⁸⁾ All of them stress the need to improve information to care providers and the general population.

Aranceta et al (2001)⁽¹⁹⁾ and Ortega et al (2001)⁽²⁰⁾ carried out reviews at an international level.

Health Education Initiatives

Since 2001 pharmaceutical companies and Public Health departments have carried out health campaigns to inform health professionals about the recommendations for periconceptional folic acid supplementation (Madrid, Valencia, Navarra, Murcia, Extremadura and the Basque Country).

A new official centre was created in 2002 at the Carlos III Institute which is a part of Ministry of Health, “Centro de Investigación de Anomalías Congénitas (CIAC)”, connected to the ECEMC project (Estudio Colaborativo Español de Malformaciones Congénitas). Some pamphlets for the general population about prevention of NTDs with folic acid are available from the web⁽²¹⁾.

In some autonomous communities the Public Health Departments have been making “records” about recommendations (internal papers, webs) for doctors and nurses and also local campaigns and leaflets for general people.

Proportion of pregnancies that are planned

There are no reliable national figures about the number that are planned. A survey in Barcelona from 1994 to 2006 found that between half and two thirds of pregnancies surveyed were planned.

Laws Regarding Termination of Pregnancy

Termination of pregnancy in Spain is allowed up to 22 weeks of gestation if the fetus is expected to be born with severe physical or intellectual defects (unspecified). Two doctors must sign that any of those indications is present. This gestational age limit was confirmed in 2004 by the Spanish Governmental Authorities.

Authorised compounds of Folic Acid

There are a total of 23 proprietary preparations with folic acid (3 with folic acid only, and the rest in combination with other vitamins or minerals), containing varying dosages between 75 micrograms and 5 milligrams of folic acid. The price per day ranges from 0.04 to 0.13 € and is 60% subsidized by the Health System. A further 18 folinic acid compounds (calcic folinate or levofolinate) are also licensed for sale, and their use during pregnancy is accepted (even with the higher dosages, varying between 1.08 and 350 milligrams). The price for these is 9 times higher than for folic acid and is subsidized by more than 60% by the Health System. In 1999 the Basque Society of Gynaecology together with the Health Department issued recommendations about periconceptual intake of folic acid and also discouraged gynaecologists from prescribing levofolonic acid. It would be advisable to monitor the use of levofolonic acid for periconceptual care.

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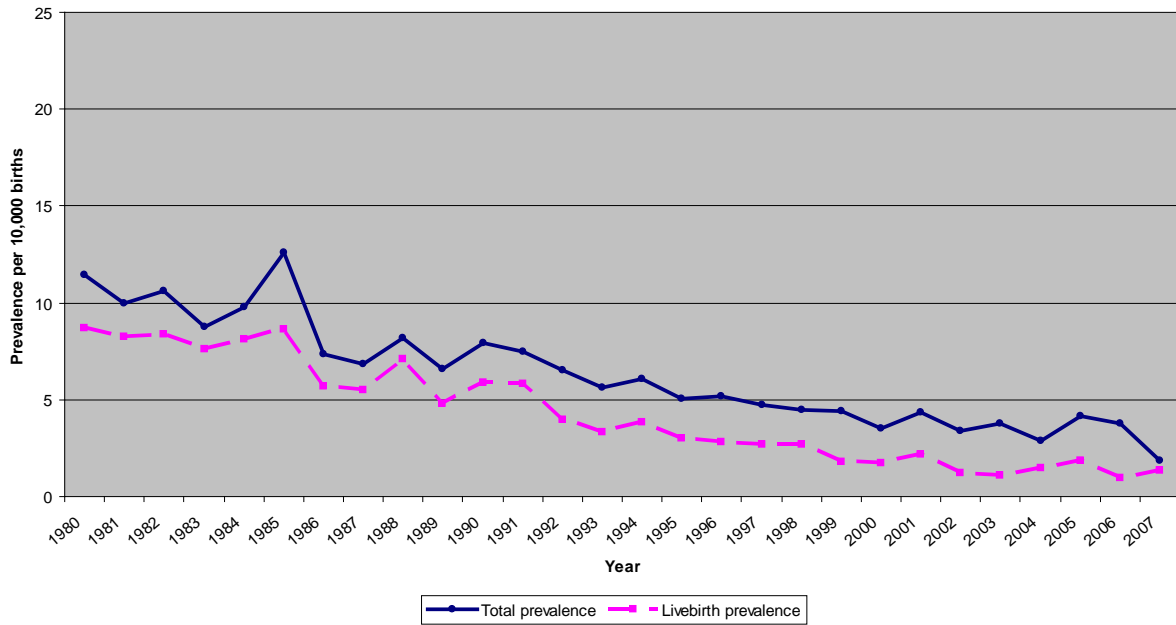
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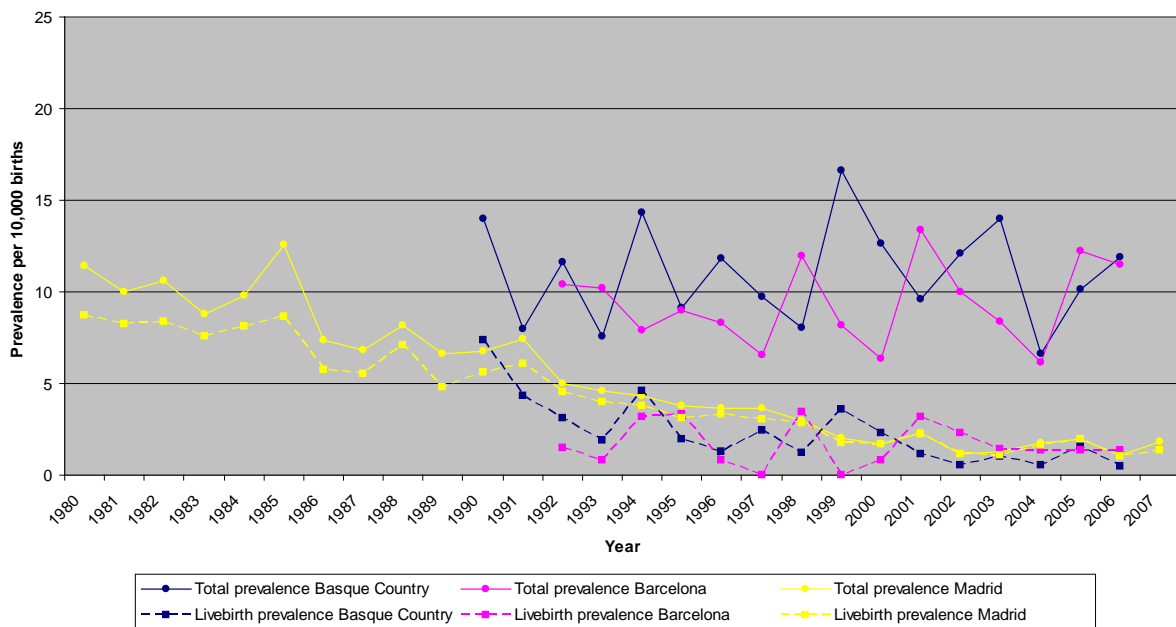
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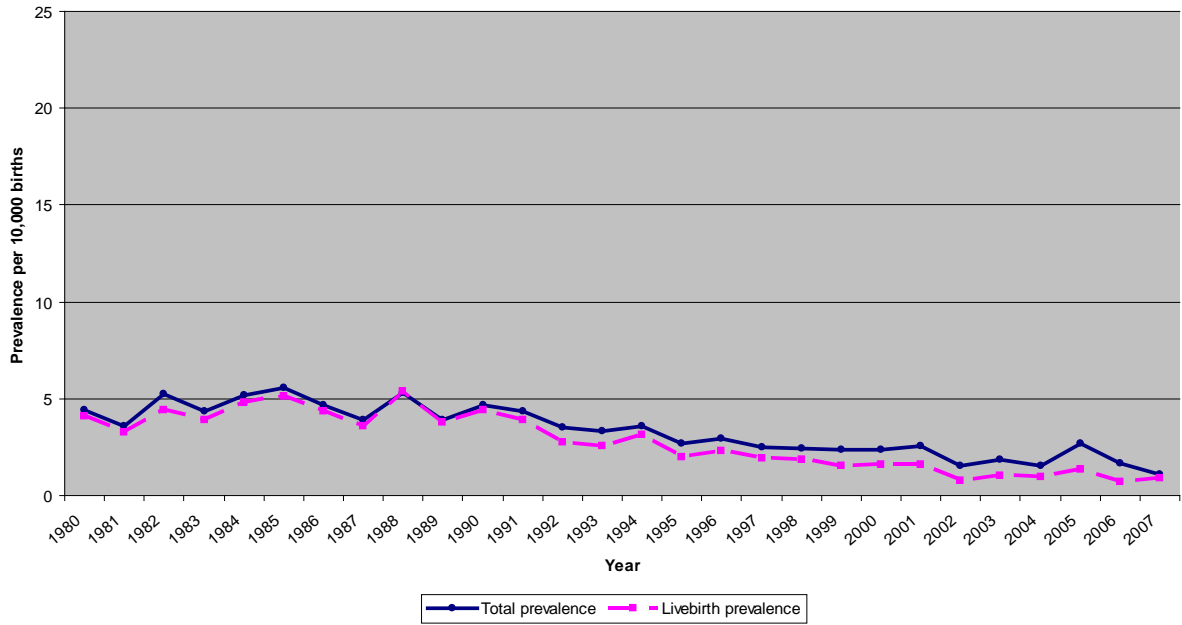
Spain (Basque Country, Barcelona and Madrid): Total and Livebirth Prevalence Rates for Neural Tube Defects (all 3 registries together)



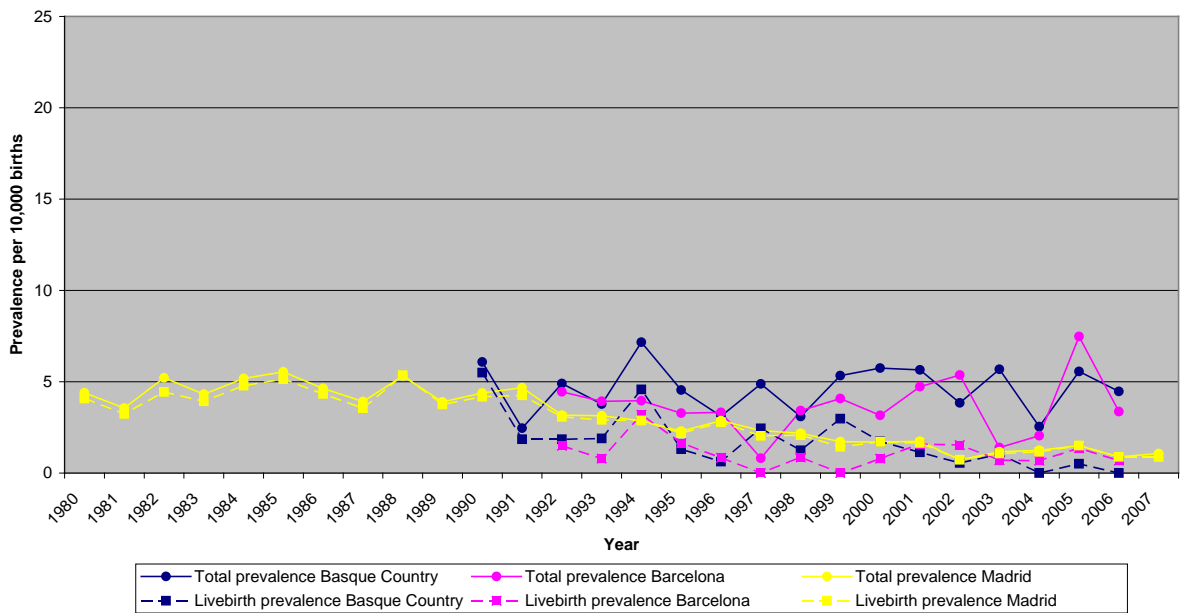
Spain (Basque Country, Barcelona and Madrid): Total and Livebirth Prevalence Rates for Neural Tube Defects



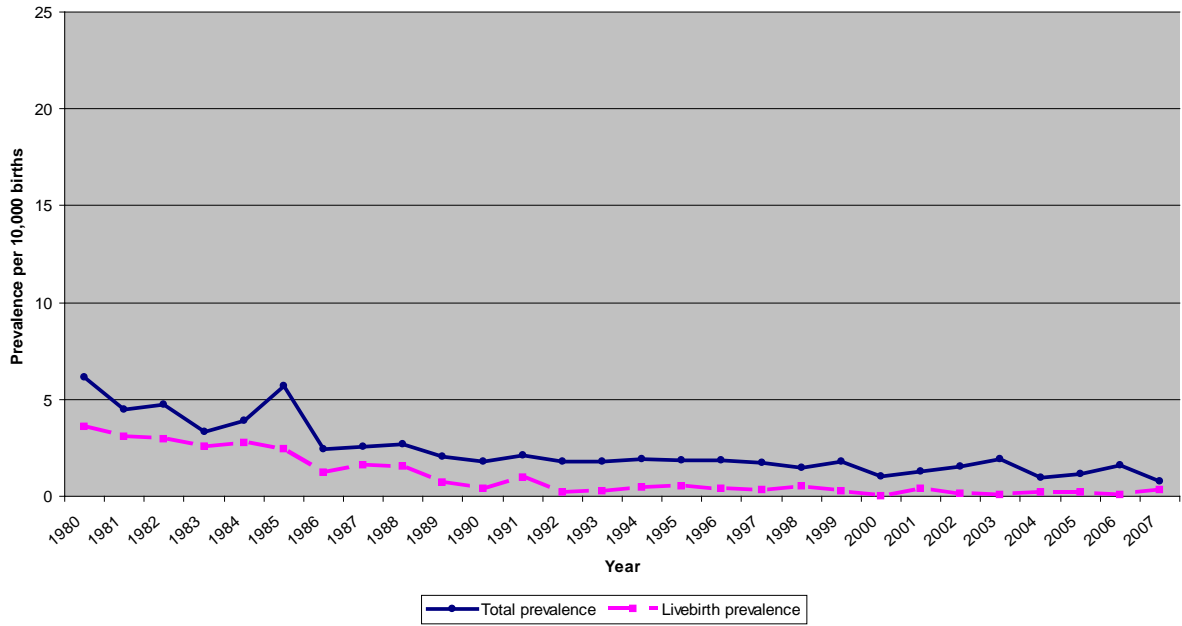
Spain (Basque Country, Barcelona and Madrid): Total and Livebirth Prevalence Rates for Spina Bifida (all 3 registries together)



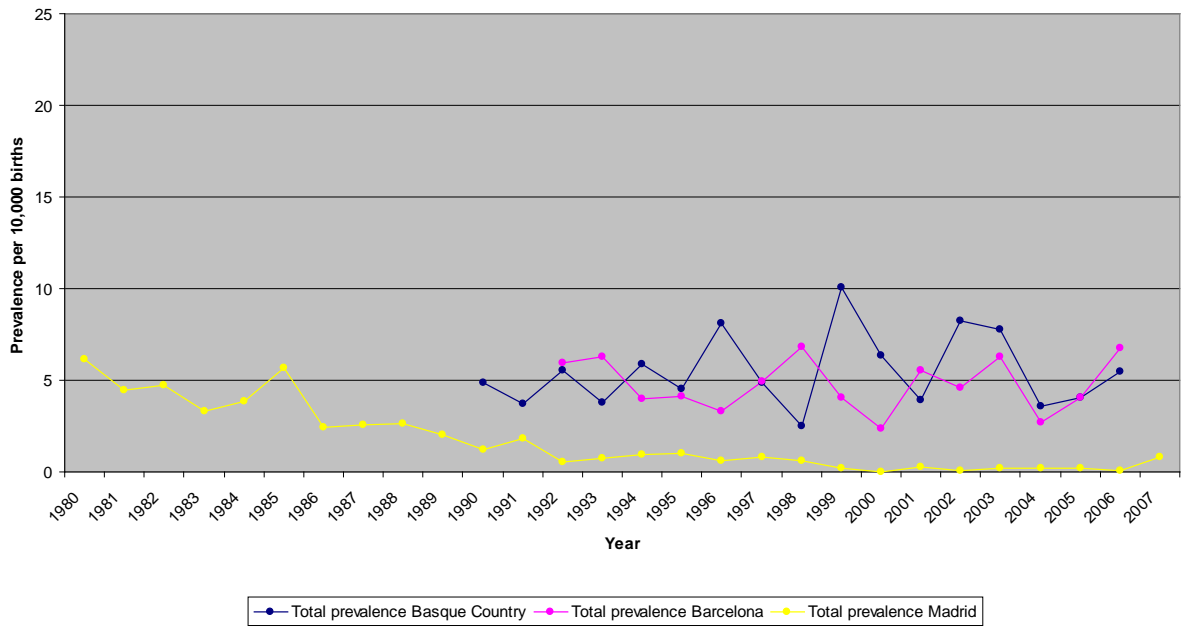
Spain (Basque Country, Barcelona and Madrid): Total and Livebirth Prevalence Rates for Spina Bifida



Spain (Basque Country, Barcelona and Madrid): Total and Livebirth Prevalence Rates for Anencephaly (all 3 registries together)



Spain (Basque Country, Barcelona and Madrid): Total Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation For Sweden

Göran Annerén and Birgitta Ollars

Folic Acid Supplementation Policy

The National Board of Health and Welfare issued recommendations regarding dietary folate and periconceptional folic acid supplementation in 1996¹ and again in 2001.² Women who are planning a pregnancy or who may become pregnant are recommended to have a total intake of at least 400 µg of folate per day. Since an intake of 400 µg through the diet is unlikely to be achieved by many women, the official recommendation is to take a folic acid supplement of 400 µg per day. The supplementation should begin one month prior to conception and continue until the end of the first trimester.

Women who have previously had a foetus with a neural tube defect (NTD), women who themselves or whose partner have a NTD or a close relative with a NTD, women with an increased need for folic acid due to disease or medication, such as anti-epileptic medication, are recommended to take 4-5 mg of folic acid supplement per day. The supplementation should begin one month prior to conception and continue until 2-3 months of gestation. This recommendation for women at high risk was issued in 1991.³

In September 2007, The Board of the National Food Administration, in Sweden, made the strategic decision to distribute folic acid supplements free of charge to women in the age range 18-45 years, plus complementary information measures. The decision involves, in the first instance, activities during a five-year period. The first year will be taken up with planning and detailed decisions concerning the activities. Thereafter, all women in the age range 18-45 years will be sent an annual letter with information on the link between folic acid and the risk of spina bifida, plus the offer of free folic acid tablets. The results will be continuously assessed.

Food Fortification Policy

The Board of National Food Administration reached a decision in 2007 that

compulsory enrichment would be inappropriate in view of the uncertainty regarding the increased risk of cancer due to high intake of folic acid. The National Food Administration will continue to monitor the scientific discussion on folic acid in the future. The European Food Safety Authority (EFSA) together with the National Food Administration will arrange a scientific meeting on the question of folic acid and cancer in Sweden in the beginning of 2008.

Health Education Initiatives

No official Health Education Initiative has been performed in Sweden to inform women about the role of folic acid in reducing the risk for neural tube defects. However, this is about to change since the 2007 decision by the Board of the National Food Administration means that all women in the age range 18-45 years will be sent an annual letter with information on the link between folic acid and the risk of spina bifida, plus the offer of free folic acid tablets.

Knowledge and Uptake about Folic Acid

To our knowledge no national epidemiological studies have been conducted. About 8% of pregnant women used periconceptional supplementation in 1997 but this figure is probably an under estimate.⁴

Dietary studies in Sweden indicate that only a small group of women of childbearing age achieve the daily recommended intake of 400 micrograms of folic acid or dietary equivalent at present.

Proportion of Pregnancies that are Planned

There is little knowledge in Sweden about the proportion of pregnancies that are planned. Probably the situation in Sweden is similar to that in Norway where they reported that between 50 and 75% of all pregnancies were planned.

Laws Regarding Termination of Pregnancy

Induced abortion is legal at a woman's request up to 18 completed weeks of gestation. Induced abortion is legal on specified medical and social indications between 18 and 22 completed weeks, and the decision is made by an ethical committee at the National Board of Health and Welfare.

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Report on Periconceptional Folic Acid Supplementation for Switzerland

Dr Marie-Claude Addor and Monika Eichholzer

Switzerland is a federal country comprising 26 cantons. Most responsibilities in the health field are vested in the Cantonal Public Health Services. On the federal level, there is a Federal Office of Public Health whose guidelines now have a large audience and are used as the legal basis.

Folic Acid Supplementation Policy

In the early 1990s, the Public Health Officer for the canton of Vaud, at the request of the University Department of Gynecology and Obstetrics, asked the Federal Office of Public Health to support the idea of a national recommendation concerning folic acid and the prevention of neural tube defects (NTD).

The recommendations for primary prevention, issued in 2002, are as follows:

- 0.4 mg folic acid supplementation (with or without other vitamins) should be taken daily from four weeks before conception until twelve weeks after.
- All women of child bearing age without safe contraception should consume a folate rich diet (fresh fruits and vegetables, whole grain products and fortified food eg cereals and breakfast beverages).
- Women who have had a previous pregnancy affected by a neural tube defect are advised to take the following supplements periconceptionally:
 - 4-5 mg folic acid daily, monopreparation (Folvite, Ac. Folicum, Foli-Rivo)
 - polyvitamins = 0.4-1 mg folic acid (vit A ≤ 8000 UI)

Food Fortification Policy

Voluntary fortification of food with folic acid is legal, but mandatory fortification has not been introduced.

In 1997, Wiederkehr et al submitted to the Swiss representative assembly a proposal for the mandatory fortification of flour with folic acid for the prevention of neural tube defects. In 2000, the Federal Office of Public Health began studying the folate

situation in Switzerland (4) and in 2002 a working group of the Swiss Nutrition Council submitted a report for the Federal Government with scientific recommendations(5). They recommended that flour should be fortified on a mandatory basis by 3 mg folic acid and 10 micrograms of vitamin B12 per kg of flour in order to obtain a supplementary daily intake of folic acid of 275 micrograms and about 1 microgram of B12 per day and said this was the most efficacious, sure and economic way to prevent NTD. This recommendation was supported by the Swiss Nutrition Council but not by the Federal Office of Public Health.

A further report was issued in November 2006 saying that there is no legal basis for mandatory fortification in the Swiss law (6)

Health Education Initiatives

In 2005, a working group of the Federal Office of Public Health prepared a booklet and a leaflet for women in childbearing age. Some booklets, edited by pharmacists “vitamin info” will be available in waiting rooms of gynaecologists in 2008.

Uptake and Knowledge of Folic Acid.

According to market research, awareness of folic acid in the population increased from 38% in 1999 to 58% in 2003. Jans-Ruggli and Baerlocher looked at a sample of 505 pregnant women in three hospitals in Eastern Switzerland between September 2002 and October 2003. (7) They found that 97.5% of women in their study women took a folic acid supplement during pregnancy, but only 37% took it at the correct time to prevent NTDs. Women of Western European origin were better informed about folic acid than were women from Eastern countries (Balcan and Turkey). Older women were better informed than younger women.

In Switzerland, the daily dietary intake of folate has been estimated to be 275 µg or less.

Proportion of Pregnancies that are Planned

The percentage of pregnancies that are planned in Switzerland is thought to be very low, and there are very few “preconceptional consultations”. However, in the Jans-Ruggli, Baerlocher study, 80% of the pregnancies were said to be planned.

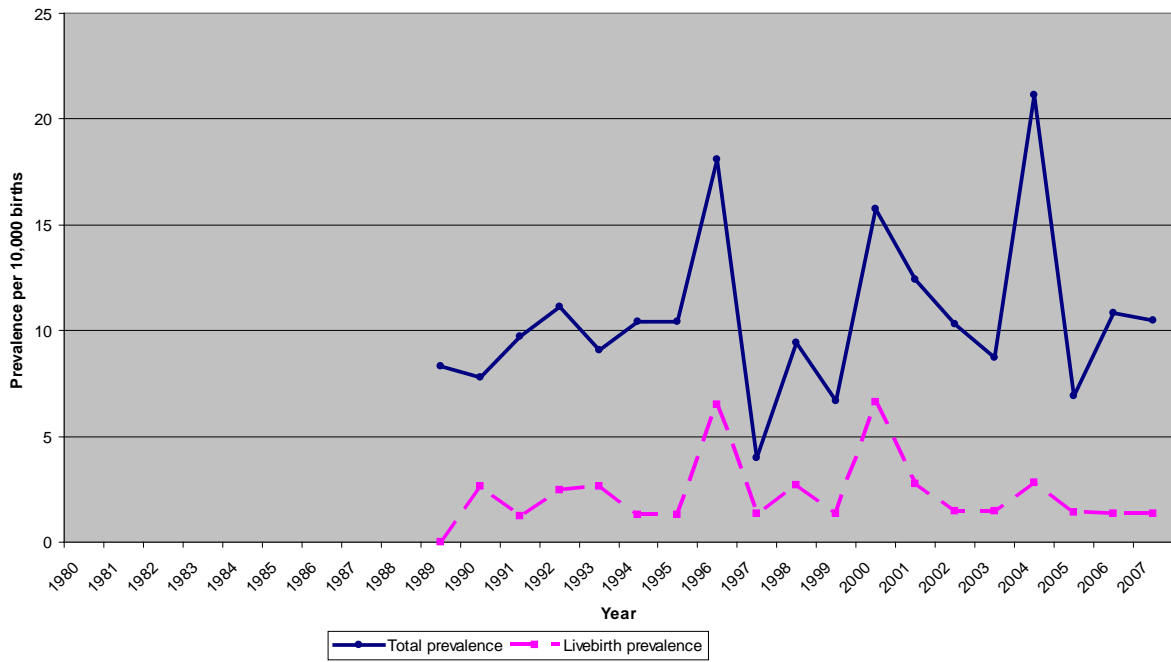
Laws Regarding Termination of Pregnancy

According to the Swiss penal code, there is no gestational age limit for termination of pregnancy. However, in practice it is performed until the 24th week of gestation.

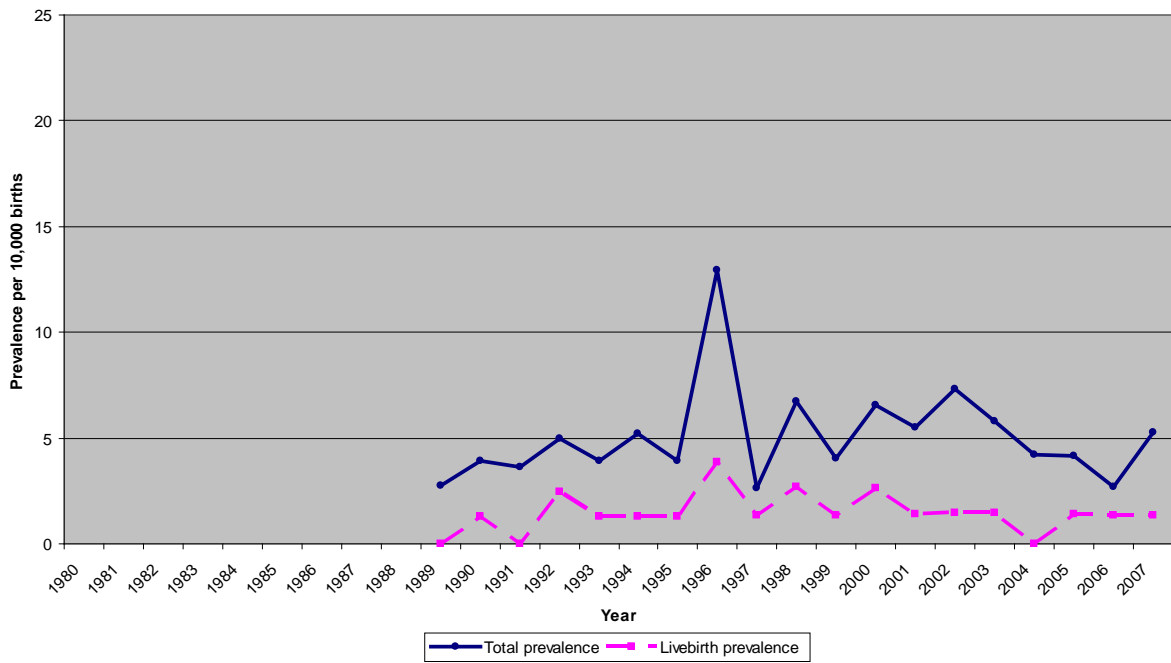
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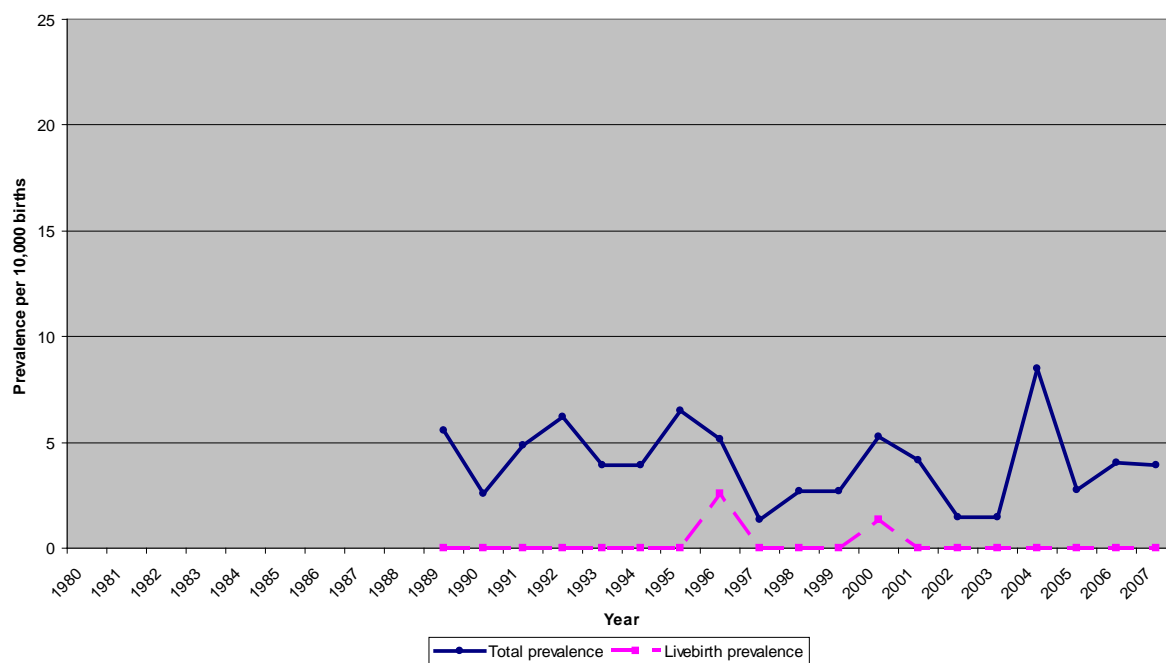
Switzerland (Vaud): Total and Livebirth Prevalence Rates for Neural Tube Defects



Switzerland (Vaud): Total and Livebirth Prevalence Rates for Spina Bifida



Switzerland (Vaud): Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for Ukraine

Dr Natalya Zymak-Zakutnya

Folic Acid Supplementation Policy

In Ukraine an official policy regarding increasing folate in the diet was introduced on December 28, 2002. The policy advises to take 0.4 mg in 3 months before conception till 16 weeks of pregnancy¹.

This is a Ministry of Health Care of Ukraine Order No. 503 "On Improvement of Outpatient Obstetric-gynecologic Aid in Ukraine" (28.12.2002).

Food Fortification Policy

There is no official food fortification policy. There are imported fortified cereals and malted drinks, but not widely available. Fortified breads are not readily available.

Health Education Initiatives

No official Department of Health Care Promotion campaigns have been undertaken but GPs, gynecologists, midwives organised antenatal courses to inform women of the benefits of folic acid. The official dietary policy mentioned above was aimed to inform and educate health professionals.

A number of initiatives were launched by non-profit organizations, e.g.:

- Educational project "One way to life's harmony - without birth defects - is folic acid", November 3, 2001 (Rivne, Ukraine), held by Ukrainian - American Birth Defects Program (UABDP), NGO Ukrainian Alliance for the Prevention of Birth Defects and political consolidation "Women for Future";
- International conference "Fortification of food with vitamin B9 with the aim of neural tube defects prevention", November 27-29, 2006 (Kyiv).
- 1st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects, August 27-30, 2008 (Budapest) - analysis and discussion of the promotion of women's health before, during and beyond pregnancy, and the role of preconception health and health care in the prevention of birth defects in the Central and Eastern European region. Ukrainian participants presented results of a folic acid related survey: Survey of Pre-conception Health and Birth Defects Prevention Knowledge and Attitudes in Ukraine¹.

Folic Acid Awareness and Uptake

A study regarding folic acid and pregnancy risk factors awareness in Ukrainian mothers was undertaken in Jan- May 2008. The results were presented at 1st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects, August 27-30, 2008, Budapest². The aim was to assess knowledge and attitudes regarding pre-conception health and birth defects prevention in Ukraine. This pilot survey was held in six heterogenous regions (northwest, Rivne and Volyn oblasts; west, Transcarpathia oblast; south, Kherson oblast; and central-west, Khmelnytsky and Cherkasy oblasts).

A questionnaire was designed by OMNI-Net partners with consideration to previous surveys conducted by the March of Dimes and other agencies. Pregnant women seeking family planning or medical genetic services were asked to volunteer anonymously information about their ethnicity, health, previous pregnancies and negative pregnancy outcome risk factors. Information was recorded by health care personnel.

Proportion of pregnancies which are planned

No information available.

Laws Regarding Termination of Pregnancy

Termination of pregnancy is legal and performed by a physician when:

- 1) a pregnancy poses danger to health or life of a pregnant women;
- 2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease;
- 3) there is a plausible suspicion the pregnancy has arisen from a prohibited act.

Gestational age limit – from January 2007 – before 22 weeks³.

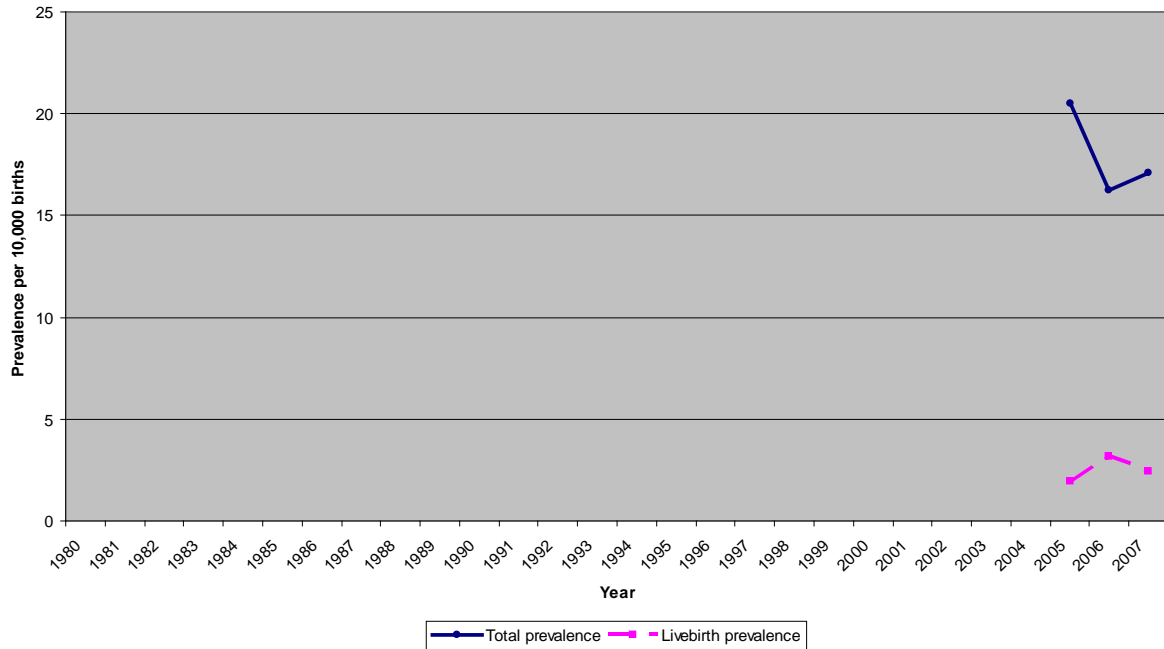
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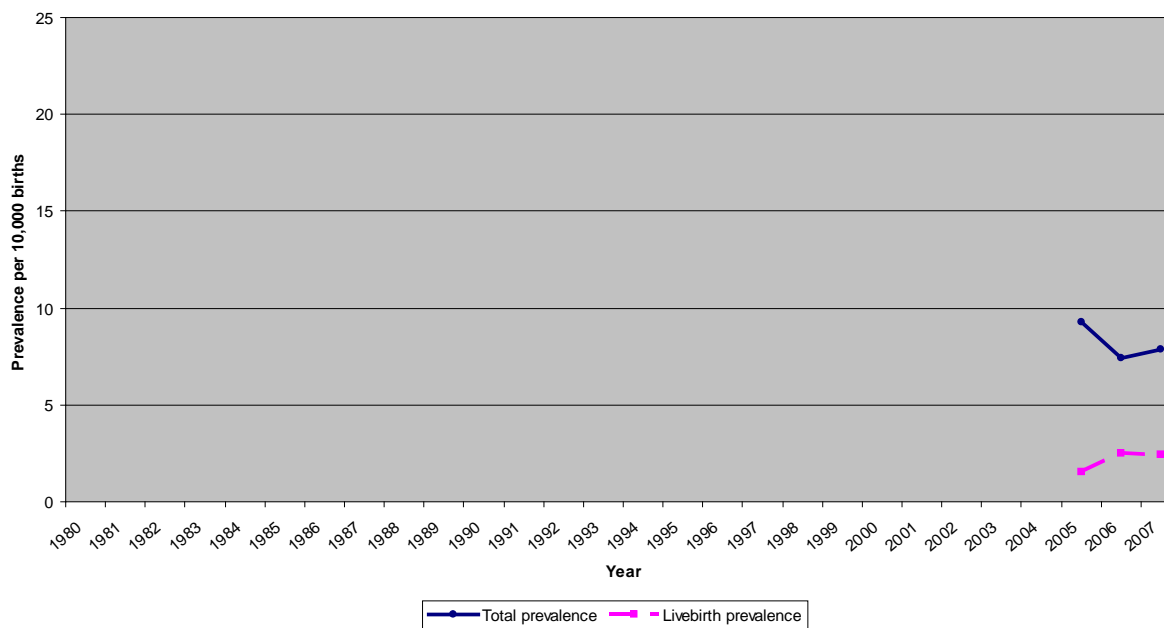
Abstract Book: 1st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects, p. 95, August 2008, Budapest.

- Decree No.144 "On Implementation of Article 281 of Civil Code of Ukraine", Cabinet of Ministers of Ukraine, February, 15, 2006.

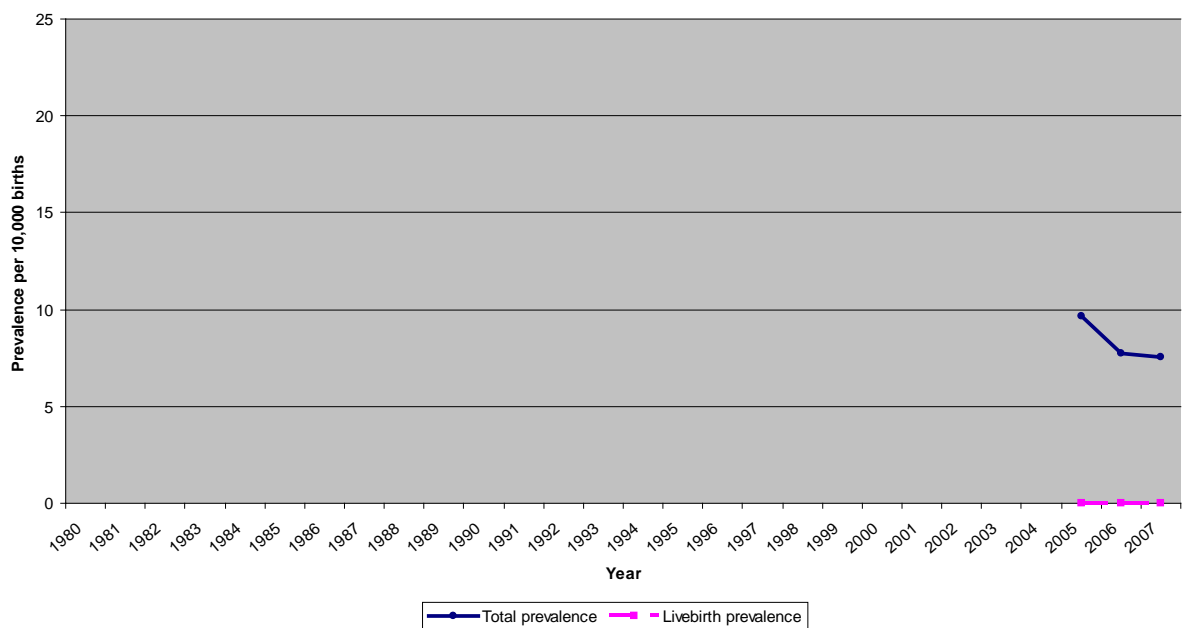
Ukraine: Total and Livebirth Prevalence Rates for Neural Tube Defects



Ukraine: Total and Livebirth Prevalence Rates for Spina Bifida



Ukraine: Total and Livebirth Prevalence Rates for Anencephaly



Report on Periconceptional Folic Acid Supplementation for the United Kingdom

Dr Grace Edwards and Lenore Abramsky

Folic Acid Supplementation Policy

The Medical Research Council Vitamin Study confirmed the role of periconceptional folic acid supplementation in reducing the risk of a fetal neural tube defect.¹ As a result, in 1992 the Department of Health in conjunction with the Scottish Office, the Welsh Office and the Northern Ireland office produced a report recommending that folic acid supplementation should be taken by all women contemplating pregnancy. The report recommended that all women take 400 µg of folic acid per day when planning a pregnancy. Women who had had a baby with a previous neural tube defect were advised to take 5 mg per day before conception and until 12 weeks of pregnancy.² These recommendations are still in place.

Food Fortification Policy

Mandatory fortification of flour in the United Kingdom has been recommended by the Food Standards Agency but not yet implemented. It is expected to be implemented in 2008. Most breakfast cereals have been voluntarily fortified for many years with vitamins such as B vitamins, including folic acid, and minerals such as iron. There is no standardized amount and there are varying levels of fortification with folic acid.

Health Education Initiatives

In 1995 a three year UK campaign led by the Health Education Authority (HEA) was launched to improve folate status awareness in women of child bearing age. This campaign highlighted ways of improving folate status before conception and up to 12 weeks of pregnancy by increasing folic acid intake from foods and supplements. This was a large and expensive campaign with advertisements on television, in newspaper, magazines and professional journals. Although the campaign raised awareness in women from 9% in 1995 to 68% in 1998, only 38% of women surveyed in 1998 took folic acid around the time of conception.³

It should be noted that Northern Ireland was not covered by the television advertising campaign launched by the HEA in 1995. However, a Northern Ireland television

advertising campaign was broadcast as part of a public information initiative developed by the Health Promotion Agency for Northern Ireland and launched in 1998.

Knowledge and Uptake of Folic Acid

Numerous studies have been undertaken in the UK and Ireland and all have shown that while the majority of women have now heard of folic acid and know something about its protective effect, fewer than half of them take it prior to conception. Most of the studies have looked at the association of demographic and lifestyle variables with uptake and have found that uptake is lower among young women, smokers, those with less formal education, of lower social class, and from ethnic minorities.⁴⁻⁹

Some work has been undertaken in the United Kingdom to measure the changes in dietary folate consumption.^{10,11} Murphy et al found that dietary folate consumption had increased by 1.6% per annum in Scotland and 1.4% in England from 1980 to 1996. This increase was thought to have been linked with the introduction of folate fortification of cereals.

In Northern Ireland anecdotal evidence from antenatal clinics indicates an increase in uptake of folic acid supplements.

Proportion of Pregnancies which are Planned

A study by While found that up to one live birth out of every three was unplanned.¹² These findings were supported by research in Merseyside, England where forty percent of women reported that their pregnancies were unplanned¹³ and by research in other parts of Britain⁶

Laws Regarding Termination of Pregnancy

Under the 1967 Abortion Act (amended in 1990) abortion is legal in England, Scotland and Wales at gestational age up to 24 weeks provided that two doctors certify that a woman's mental or physical health (or that of her children) is at greater risk if she continues with the pregnancy than if she has a termination. At the time of

writing (October 2007), the UK parliament is considering the possibility of removing the need for two doctors to certify that the criteria for permitting a termination are met and is also considering the possibility of lowering the gestational age limit to 22 weeks. There is no gestational age limit for termination of pregnancy because of serious fetal abnormality or because there is a risk of permanent injury to a woman's health or life. The 1967 Abortion act does not apply in Northern Ireland.

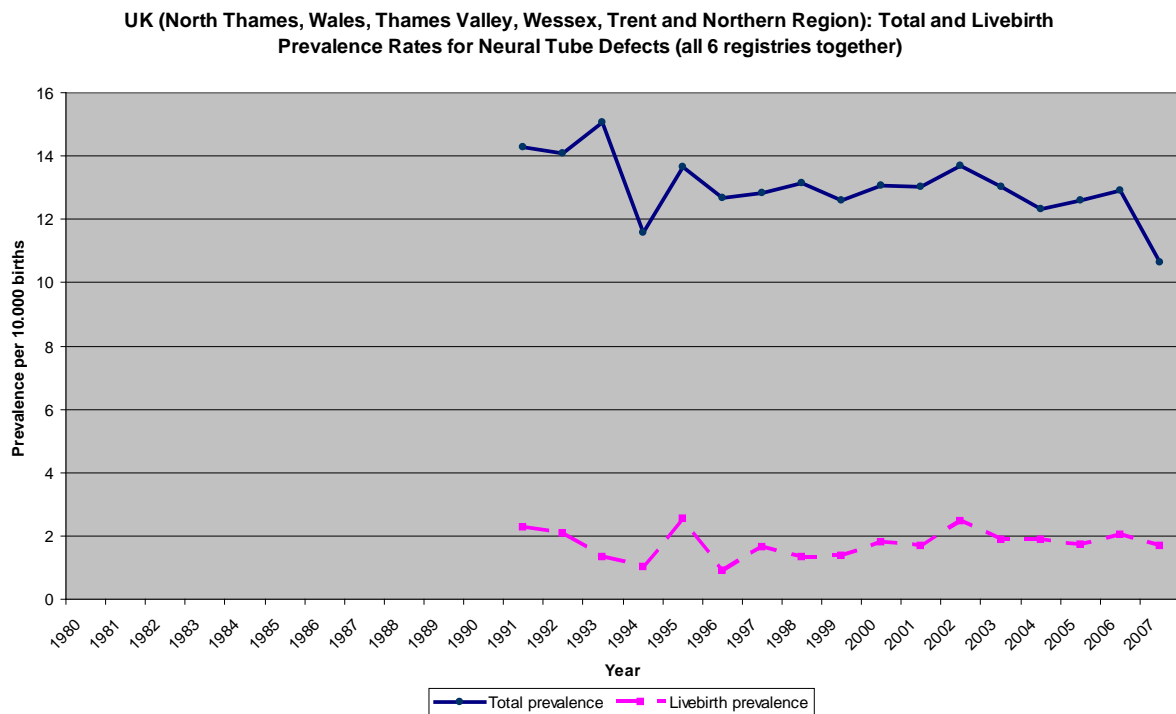
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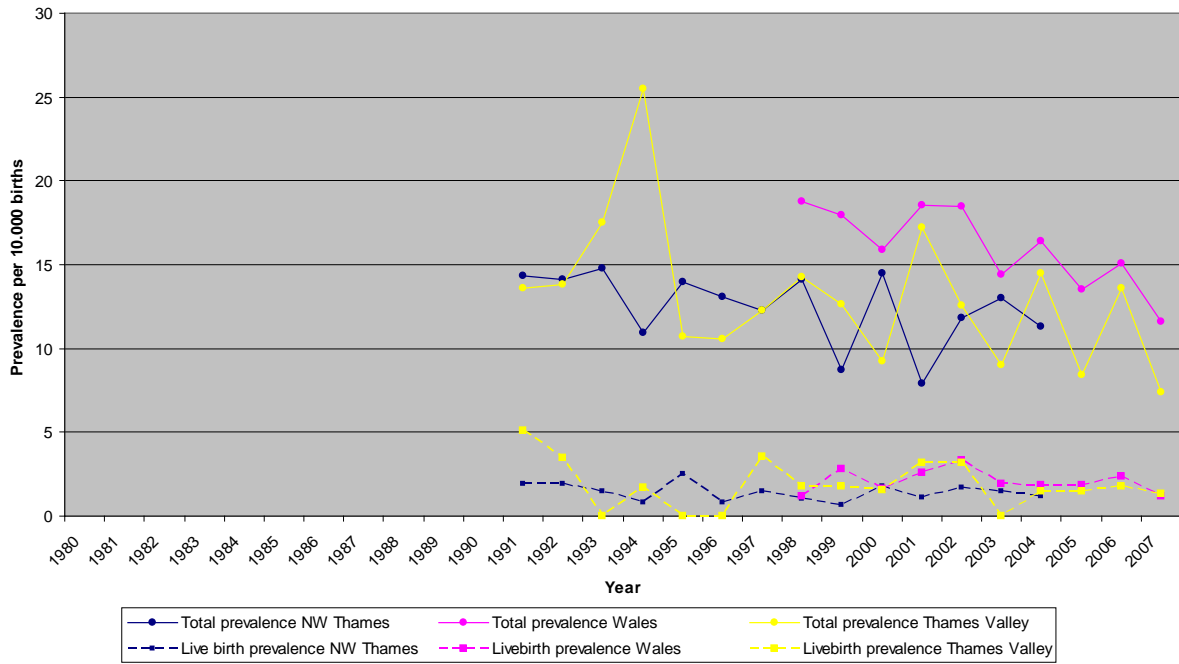
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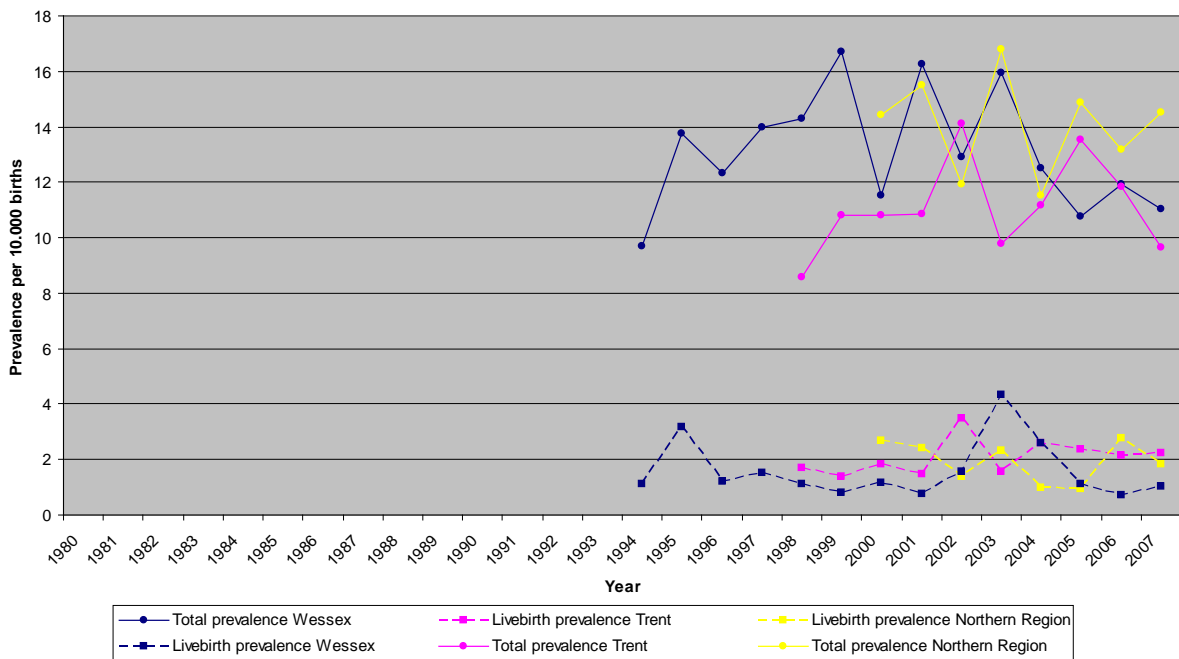
Thanks to Margaret Slane of the Health Promotion Agency in Northern Ireland and Margaret Boyle, Senior Medical Officer, Department of Health, Social Services and Personal Safety Northern Ireland for their input about the situation in Northern Ireland.



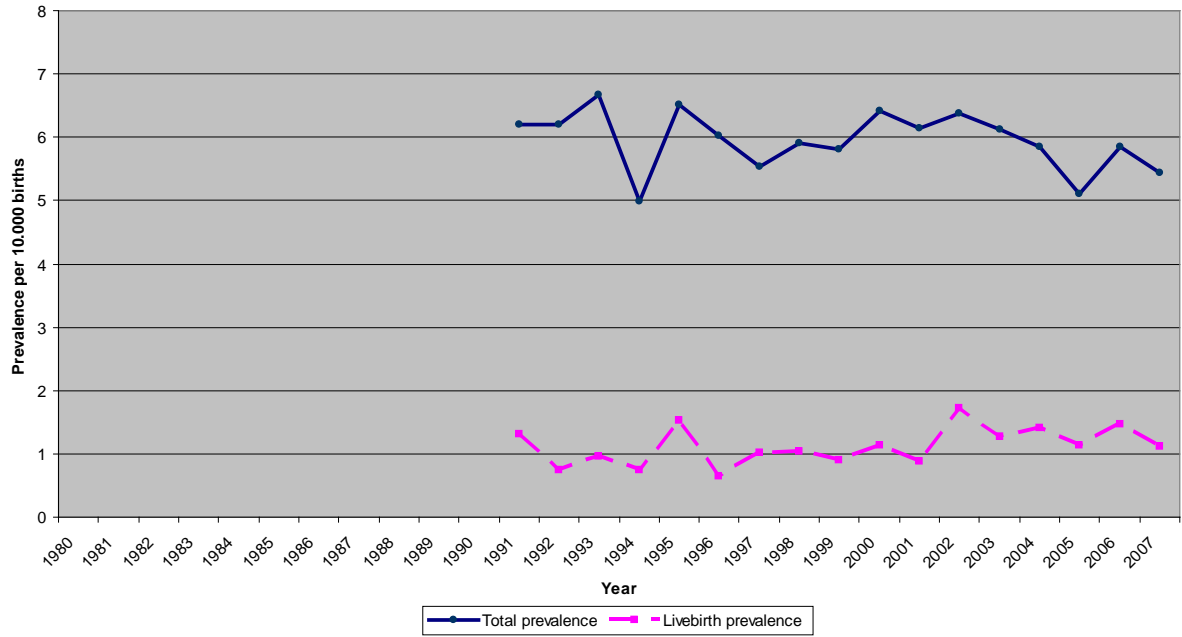
UK (North Thames, Wales, Thames Valley): Total and Livebirth Prevalence Rates for Neural Tube Defects



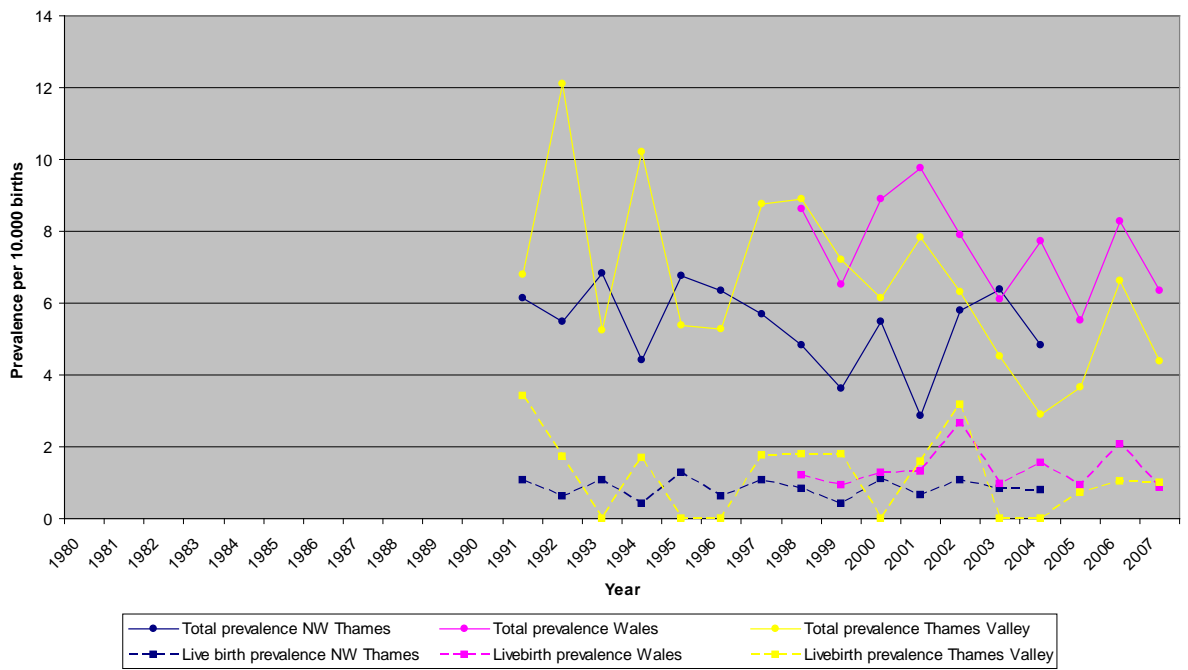
UK (Wessex, Trent and Northern Region): Total and Livebirth Prevalence Rates for Neural Tube Defects



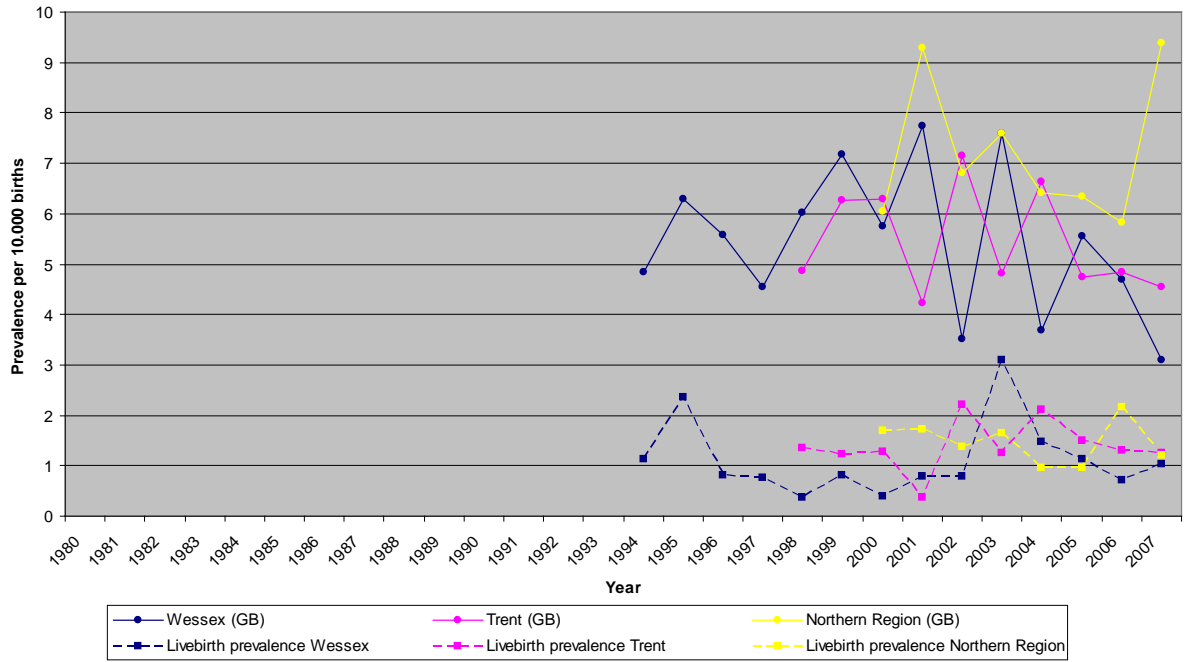
UK (North Thames, Wales, Thames Valley, Wessex, Trent and Northern Region): Total and Livebirth Prevalence Rates for Spina Bifida (all 6 registries together)



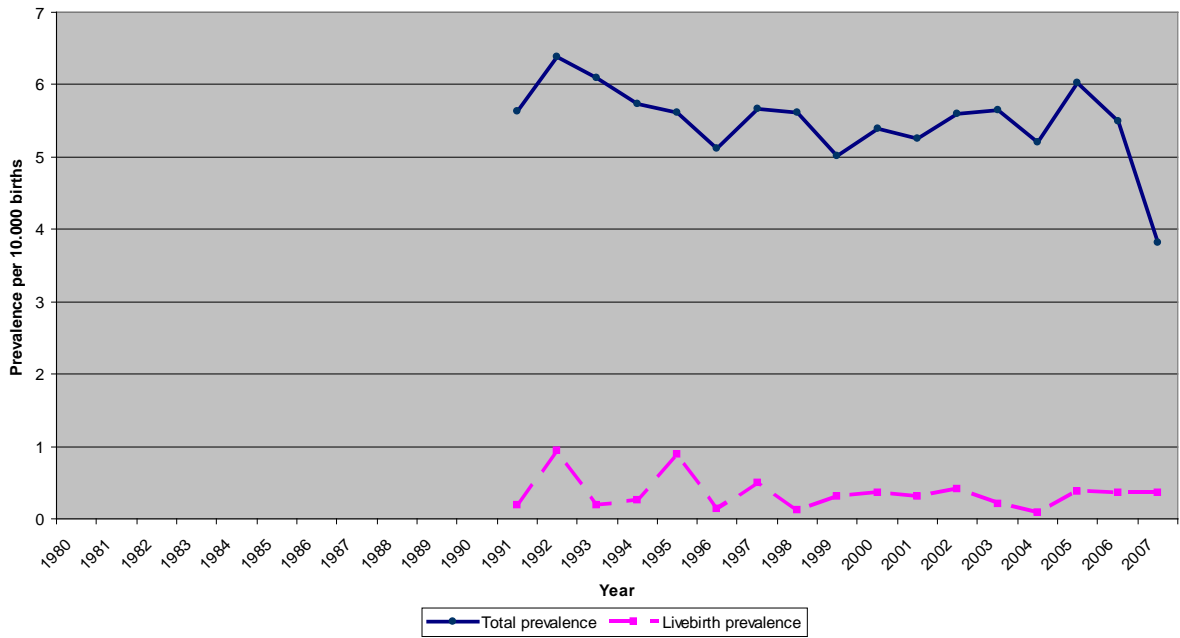
UK (North Thames, Wales, Thames Valley): Total and Livebirth Prevalence Rates for Spina Bifida



UK (Wessex, Trent, Northern Region): Total and Livebirth Prevalence Rates for Spina Bifida



UK (North Thames, Wales, Thames Valley, Wessex, Trent and Northern Region): Total and Livebirth Prevalence Rates for Anencephaly (all 6 registries together)



UK (North Thames, Wales, Thames Valley, Wessex, Trent and Northern Region): Total Prevalence Rates for Anencephaly

