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European Surveillance of Congenital Anomalies

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Special Report:

Special Report:

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

December 2005

Part I: Overview
Part II: Country-Specific Chapters
Part III: Appendices

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RECOMMENDATIONS

1) 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.

2) 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.

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 malformation

SUMMARY

Background

Approximately 4,500 pregnancies every year in Europe result in a livebirth, stillbirth or termination of pregnancy of a baby/fetus affected by a Neural Tube Defects (NTD), mainly anencephaly and spina bifida. With the publication in 1991 of the MRC Vitamin Study, periconceptional folic acid supplementation was shown to be an effective method of preventing potentially two thirds of cases. In the EUROCAT Special Report 2003, we reviewed progress up to the end of the year 2000 in European countries in terms of developing and implementing public health policies to raise periconceptional folate status, and analysed data on the prevalence of neural tube defects from 36 congenital anomaly registries in 17 countries 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 consideration being given by governments to fortifying a staple food with folic acid.

We recognise that the folic acid / neural tube defect story is still being written, and this current report is an update of both folic acid policies and neural tube defect rates. The report will be updated annually.

Methods

EUROCAT is now a network of 43 congenital anomaly registries in 20 European countries collaborating in the epidemiological surveillance of congenital anomalies. Representatives from eighteen countries participating in EUROCAT provided information about policy, health education campaigns and surveys of folic acid supplement uptake in their country. NTD rates (including livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis) were extracted from the EUROCAT Central Registry database for 1980-2002.

Results

We found that there have been some changes in policy and practice since our report in 2003. In Italy, where there was no official supplementation policy at the end of 2002 and no official interest, there is now a lively Folic Acid Network which has succeeded in achieving a supplementation policy and a health education drive. In Belgium, the Association Spina Bifida Belge Francophone was so disturbed by the official indifference revealed in the 2003

EUROCAT Report that they are instigating a health education campaign. In Spain there has been an increase in health education about folic acid. Ireland and Denmark report some movement towards mandatory fortification, but this has not yet happened.

At the beginning of 2005, an official governmental recommendation that women planning a pregnancy should take 0.4 mg of folic acid supplementation daily was in operation in eleven of the eighteen countries. The earliest countries to introduce an official supplementation policy were the UK, Ireland and Netherlands in 1992-3 and the latest was Italy in 2004. In the remaining 7 participating countries, no official government recommendation about supplementation was in place; however, professional bodies had recommended supplementation, and two countries had an official policy of encouraging women to increase their dietary intake of folate periconceptionally. Nine of the eighteen countries had official health education initiatives (either ongoing or in the past): UK, Ireland, France, Italy, Spain, Poland, Netherlands, Norway and Denmark.

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.

The situation regarding low uptake of supplementation advice is reflected in the lack of a clear decline in the prevalence of neural tube defects across Europe. Nevertheless, there was some evidence that in countries with a supplementation policy, a small decline in prevalence had taken place. In UK and Ireland, it was difficult to distinguish any effect of supplementation policy against the background of a strongly declining NTD prevalence throughout the 1980s and 1990s, predating folic acid advice.

Conclusion

The potential for preventing NTDs by periconceptional folic acid supplementation is still far from being fulfilled in Europe. Only a public health policy including folic acid fortification of a staple food is likely to result in large-scale prevention of NTDs while avoiding widening socio-economic inequalities in NTD prevalence.

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 neural tube defects has been described in the scientific literature for more than three decades (Scott et al, 1995). Since the early 1980s a number of intervention trials examining the effects of periconceptional folic acid on the incidence 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) Vitamin Study (MRC Vitamin Study Research Group, 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 examines the periconceptional folic acid policies and implementation strategies across Europe since 1991 and the reported prevalence rates of neural tube defects until the end of 2002. Contributions from EUROCAT (European Surveillance of Congenital Anomalies) members representing 18 countries 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 neural tube defects up to the end of 2002 is examined in relation to policies on folic acid supplementation across Europe.

Although there is increasing evidence to suggest that folic acid may also protect against other congenital anomalies (Botto, Olney and Erickson 2004) this 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. BACKGROUND

2.1 What are Neural Tube Defects?

The development of the brain and spinal cord is observable at approximately 18 days after conception as a localised thickening of cells collectively known as the neural plate. Following elongation and subsequent formation of the neural tube, closure at the midbrain/cervical region occurs at about day 21 and closure at the cephalic end at about day 26. The closed neural tube then stimulates the development of the bony structures of the vertebral column and the skull. The group of congenital malformations known as NTD are the collective set of malformations which occur if the bone fails to form above any unclosed region of the neural tube. One of the main difficulties regarding the prevention of neural tube defects lies in the fact that NTD occur before most women know they are pregnant.

The location of the defect along the neuraxis determines the specific anomaly presented: if the cephalic end of the tube is affected, the outcome is the lethal condition anencephalus, or more rarely encephalocele or iniencephalus; if any of the remainder is affected, the outcome is spina bifida. Many neonates with spina bifida and encephalocele survive but the vast majority have lifelong moderate or severe disability including lower limb paralysis, poor bladder control, and intellectual impairment.

2.2 Geographic, Temporal and Socio-economic Variation in the Prevalence of NTD

There is marked geographic variation in the prevalence of NTD (Little and Elwood, 1992) with the UK and Ireland exhibiting the highest rates in Europe for many decades (Penrose, 1957; EUROCAT Working Group, 1991). There has been a decline in many parts of the world in the prevalence of neural tube defects. This decline appears to have begun earlier in some places than in others, for example: 1950s in the Netherlands (Romijn and Treffers, 1983), and 1970s in the UK (Kadir et al, 1999). While the decline in birth prevalence in UK and Ireland since the early 1980s is partly due to prenatal diagnosis and selective termination of affected pregnancies, decreasing total prevalence is still seen when terminated pregnancies are included (EUROCAT Working Group 91).

Data are available from several countries up to the mid-1970s which demonstrate a higher prevalence of NTD in babies of women of low socio-economic status: (Elwood and Nevin 1973; Anderson et al 1958; Field 1978; Hemminki et al 1981; Naggan and MacMahon 1967). This association may have become weaker more recently, (Vrijheid et al 2000), but there is evidence emerging that women of higher socio-economic status are much more likely to take periconceptional folic acid than are women of lower socio-economic status (de Jong-van den Berg et al 2005, Relton et al 2005, Sen et al 2001; de Walle et al 1999;) and the predicted effect of this is that over time the difference in NTD pregnancy rates between mothers from higher and lower socio-economic backgrounds will increase.

2.3 What is Folic Acid?

The term folate refers to a family of compounds which have common vitamin activity and have a double aromatic ring of a pteridine attached to a *p*-aminobenzoate and a glutamate. Folic acid (pteroyl glutamic acid) is the synthetic form of folate (one of the B-vitamin group). It is highly bio-available, stable to heat exposure (eg. during cooking), and not present in nature. In order that folic acid can function enzymatically it must be converted *in vivo* to the natural forms – first to the dihydro and subsequently the tetrahydro form, both reactions being catalysed by the enzyme dihydrofolate reductase (Scott & Weir, 1994).

2.4 Sources of Folic Acid

Folate is found in a wide variety of foods, but liver is the only particularly good source (see Table 1). Cruciferous vegetables such as cabbage, cauliflower and broccoli are rich in natural folate; however, few women have sufficiently high intakes of these foods to offer optimal protection for the fetus. The relatively low bio-availability of natural folate adds to the problem; natural food folate is only half as bio-available as folic acid. (Gregory et al, 1991).

It can be seen from Figure 1 that the folate-rich foods shown in Table 1 do not necessarily contribute the most to overall intake of folate in a population (McNulty, 1997). The main food sources of folate consumed in the UK (as determined in the Dietary and Nutritional Survey of British adults) are shown in Figure 1 below. The paucity of foods eaten on a regular basis which are folate-rich, leads to a problem in

achieving the higher folate status thought to be necessary to reduce the risk of development of NTD in the fetus during pregnancy (Cuskelly et al, 1996).

Mean dietary intake of folate is considerably less than the recommended amount for prevention of NTD in those countries reporting mean values in Part 2 of this report.

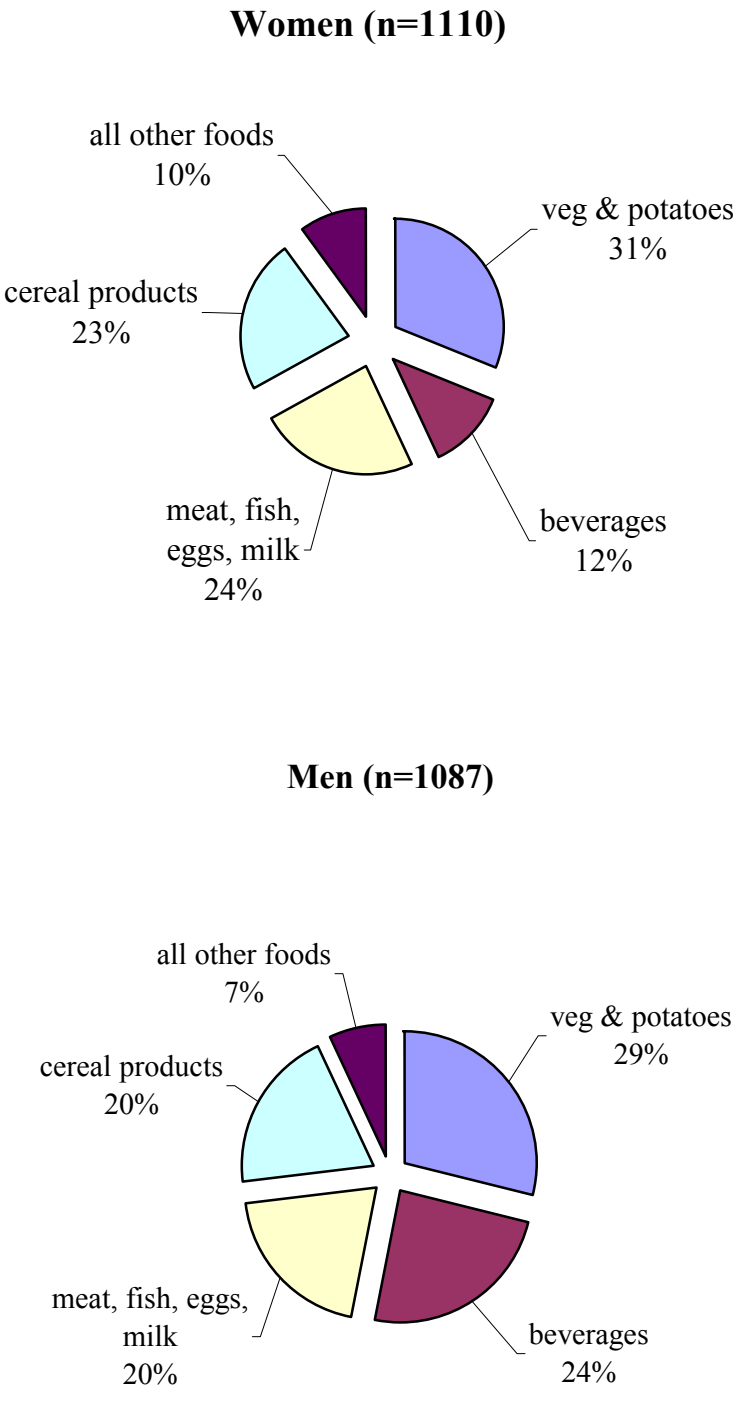
Table 1: Folate Content* of Selected Foods

Average portion	**μg of folate**	**Folic acid equivalent**
Chicken liver (grilled or fried)	500	250
Asparagus	193	96
Fortified breakfast cereal	83	41
Spinach	81	40
Broccoli	54	27
Green beans	50	25
Marmite	40	20
Orange juice	32	16
Baked beans	30	15
Fruit yoghurt	24	12

*Holland et al (1991)

Data from the UK National Food Survey indicate that average dietary folate intakes in Britain have increased substantially since the mid 1980s (the current average daily intake is 311μg for men and 213μg for women) coinciding with the increased proportion of breakfast cereal manufacturers introducing voluntary fortification with vitamins (including folic acid) between the years 1985 and 1991. In addition, bread voluntarily fortified with folic acid first became available in the UK in 1991. National food survey data suggest that steady increases occurred in the consumption of fruit juice and fruits in British households during the past three decades (Rayner, Mockford and Boaz, 1998).

Figure 1: Main Food Sources of Folate*



* MAFF (1994)

2.5 Folic Acid and Neural Tube Defects: The Evidence for a Protective Effect

The possibility that maternal folate status might be implicated in NTD was raised in 1965 when Hibbard and Smithells showed that a test indicating lack of folate or disturbed folate metabolism (the FIGLU test) was more often positive in women carrying a fetus with an NTD than in controls (Hibbard and Smithells, 1965). This finding stimulated a number of studies investigating the role of folic acid in relation to NTDs.

a) Recurrence studies

In 1980 Smithells et al reported on a multi-centre (5 UK centres) non-randomised prospective trial of periconceptional multivitamin supplementation (containing folic acid) for the prevention of recurrence of NTD (i.e. mothers who have had a baby with NTD having another baby with NTD). This study found a statistically significant difference between the recurrence risk in supplemented women (0.6%) and that of the controls (5.0%). The lack of randomisation made interpretation of these results difficult. Laurence et al (1981) reported on the results of another intervention study for the prevention of recurrence of NTD. This was a small, randomised controlled trial in which the study group took 4mg folic acid daily while the control group took a placebo. While supplemented women had fewer recurrences, the small size and methodological weaknesses left the question still open.

The MRC vitamin study (1984-1991) conclusively demonstrated a substantial reduction of the recurrence risk for NTD with periconceptional folic acid treatment. This was an international, multi-centre, double-blind randomised trial involving 33 centres of which 17 were in the UK (MRC Vitamin Study Research Group, 1991). The recurrence rate in the folic acid groups was 1.0% and in the non folic acid groups it was 3.5%, yielding an odds ratio of 0.29 (95% CI: 0.12-0.71). This represents a 72% protective effect of folic acid for recurrence among women with a previously affected pregnancy.

b) Occurrence studies

Since 95% of NTD are first occurrences rather than recurrences (Department of Health (DOH), 1992), the results in 1992 of the randomised controlled occurrence trial carried out in Hungary were very important. Czeizel and Dudás published the first results in 1992 with further analysis following in 1993 and 1996. There were no NTD in the multivitamin group and six in the trace element group (Fisher's exact p=0.014). Although unlikely to alter the conclusions of this study, it must be pointed out that the design of the trial does not allow the contribution of the various components of the vitamin tablet administered to be distinguished as there were only two arms (vitamin supplement including folic acid, other vitamins and trace elements versus a trace elements only arm).

In addition to the intervention trials, there have been a number of observational studies. A protective effect of folic acid or dietary folate was found by most of them (Mulinare et al, 1988; Milunsky et al, 1989; Bower and Stanley, 1989; Werler et al, 1993; Berry et al, 1999). One study (Mills et al, 1989) did not find a protective effect of folic acid. While the overwhelming body of literature is supportive of the positive role of folic acid for the prevention of NTD, more cautious views have also been expressed (Kalter 2000).

2.6 Folic Acid and Other Congenital Anomalies: The Evidence for a Protective Effect

There is increasing evidence to suggest that folic acid may also protect against other congenital anomalies such as orofacial clefts (Tolarova and Harris 1995, Shaw et al, 1995a, 1998b; Hayes et al 1996, Czeizel et al, 1999; Mills et al 1999, Werler et al, 1999; Itikala et al, 2001), cardiac defects (Shaw et al, 1995b; Botto et al, 1996; Scanlon et al 1998, Botto et al, 2000), urinary tract defects (Li et al, 1995; Werler et al, 1999) and limb reduction defects (Shaw et al, 1995b; Yang et al, 1997), Further studies are required in order to establish whether and to what degree folic acid offers protection against congenital anomalies other than NTD.

2.7 Gene-nutrient Interaction (MTHFR and Folate)

Methylene tetrahydrofolate reductase (MTHFR) is a critical enzyme involved in folate metabolism. There is good evidence that the C677T polymorphism of the

MTHFR gene is associated with an increased risk of NTD (van der Put et al, 1995; van der Put et al, 1996, Wald and Noble 1999). This is a very good example of a gene-nutrient interaction, where the absence of an environmental factor (either folate or folic acid) combined with an abnormal gene (MTHFR) can cause a NTD. In terms of the biochemical effects of the C677T polymorphism of MTHFR, homozygotes show reduced enzymatic activity (Frosst et al, 1995) and this leads to low serum and red cell folate (Molloy et al, 1997) and increased levels of plasma homocysteine (Kang et al, 1993; Engbersen et al, 1995; Kluijtmans et al, 1996). The percentages of various populations homozygous for that MTHFR polymorphism are described elsewhere (Fletcher and Kessling, 1998, Botto and Yang 2000). It has been proposed that folic acid supplementation offers some protection against NTDs in fetuses of homozygotes by partially correcting for the lower activity of the variant form of the enzyme (Whitehead et al , 1995; Shaw et al, 1998b). However, the benefits of increasing folate status are not confined only to women with that MTHFR mutation.

3. THE PUBLIC HEALTH RESPONSE TO EVIDENCE CONCERNING THE PROTECTIVE EFFECT OF FOLIC ACID

3.1 Possible Methods of Increasing Folate Status

There are three possible ways in which the recommendation of increasing folate status in women of childbearing age can be achieved:

1) Increased intake of foods naturally rich in folate
2) Folic acid supplementation
3) Fortification of food with folic acid

Cuskelly et al (1996) addressed the question of the relative effectiveness of these three options in an intervention study in healthy young women. They measured change in red cell folate concentration (considered to be the best indicator of folate status) in response to a 12-week intervention study in which women were randomly assigned to one of the following groups: a) folic acid supplements (400µg per day), b) folic acid-fortified food (400µg per day), c) dietary advice (qualitative) or d) none of the above. Although women in all four groups increased their folate/folic acid intakes, this change was reflected in increased folate status in *only* those women assigned to folic acid supplements or fortified food.

3.2 Increase Intake of Natural Folate

In order to achieve the recommended extra 400µg, a 3-fold increase in typical intakes of the vitamin would be required (Subar et al, 1989; Gregory et al, 1990; Irish Universities Nutrition Alliance, 2001). Achieving this target by food folate alone would require major dietary modifications unlikely to be accomplished by most women planning a pregnancy, not to mention those women not planning to become pregnant (McNulty et al, 2000).

McKillop et al (2002) indicated the importance of cooking method, especially for green vegetables, a particularly good source of folate. Boiling was found to decrease the folate content to 49% and 44% of the original amount for spinach and broccoli respectively. Steaming of spinach and broccoli, in contrast, resulted in no significant

decrease in folate content. Thus, dietary changes would need to concern both which foods were eaten and whether / how they were cooked.

3.3 Periconceptional Folic Acid Policies in European Countries

Table 2 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, eleven of the eighteen countries contributing 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). Of the other 7 countries: Portugal recommends that health workers should educate women about the benefits of folic acid; Malta and Finland 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 (Table 2) 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 II. There is little evidence as to how often health education campaigns need to be repeated for a sustained effect.

Table 2: Current[1] Folic Acid Supplementation Policy in European Countries

Country	Periconceptional Folic Acid Policy [2]				Health Education Campaign	Selection of recent studies of folic acid use described in the Country-Specific chapters	
	Status	Year current policy introduced	Low risk women	Women with previously affected pregnancy		Year of study	% Women Using Folic Acid
Netherlands	Official	1993	0.5 mg	5 mg	1995	1998	63% some of advised period 36% for entire advised period
UK	Official	1992	0.4 mg	4 mg	1995	2001	45% preconceptionally
Ireland	Official	1993	0.4 mg	5 mg	1993 and 2000/2001 with Ulster	1997-8	30% preconceptionally
Denmark	Official	1997	0.4 mg	5 mg	1999 and 2001	2000-2	22% of women who planned pregnancies took supplements at correct time
Poland [3]	Official	1997	1.0 mg	4 mg	Yes, but no date given	2001	19% of all women aged 18-45 13% of non-pregnant women aged 18-45
Norway [4]	Official	1998	0.4 mg	4 mg	1998 (website)	2000	46% periconceptionally
France	Official	2000	0.4 mg	4 mg	2000 and 2004	1999	1% at recommended time (1 month before until 2 months after conception)
Italy	Official	2004	0.4mg	-	2004 regional	1999 2002	3% periconceptionally 5.7% periconceptionally
Switzerland	Official	1996	0.4 mg	4 or 5 mg	Being prepared		
Spain	Official	2001	0.4 mg	4 mg	Yes 2001	2000 2004	4.5% - 17% took FA at recommended time (many studies)
Sweden	Official	1996	0.4mg	4-5mg	No	1997	8% of pregnant women took FA
Malta	Official	1994	Women planning a pregnancy should increase dietary intake of folate		No	1999	15% periconceptionally a further 59% at GA <12 weeks
Finland [5]	Official	1995	dietary	4 mg	Unofficial	2000	19% took FA before or in early pregnancy
Portugal	Official	1998	Health workers should educate women about benefits of folic acid		No		
Germany	Unofficial	1994	0.4 mg	4 mg	No	2000	4.3% preconceptionally
Austria	Unofficial	1998	0.4 mg	4 mg	No	1998	10% at GA <12 weeks
Belgium	Unofficial	-	0.4 mg	4 mg	Being prepared		
Croatia	Unofficial	-	0.4 mg	4 mg	Unofficial	2003	19% of women with planned pregnancies in the study took FA at appropriate time

1. Policy as of December 2004
2. Recommended dose is as supplements unless otherwise stated
3. Poland recommends that all women of child bearing age take a supplement of 0.4 mg, increasing to 1 mg when planning a pregnancy.
4. Norway recommends >0.4 mg for moderate risk women
5. Since 2004, Finland recommends 0.4 mg folic acid supplementation for women with moderate risk, those with a poor diet or those wishing to be sure they are taking enough folate.

3.4 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 2. Details are given in the individual country chapters in Part 2 of this report. A fully informative survey needs to be based on a representative sample of pregnant women, and must contain information about when in relation to conception the folic acid was taken. Unfortunately, many studies that have been done do not meet these minimum criteria. Details of the methodology of each survey, where available, are given in Part II, and figures shown in Table 2 should be interpreted in the light of these details. Readers should note that the studies vary widely in every way and that results cannot be directly compared. Table 2 provides a very imperfect starting off point for looking at compliance in different countries.

In all countries, only a minority of women were found to have taken folic acid supplements during the entire advised periconceptional period. The highest uptake was recorded in Netherlands, UK, Ireland and Norway with 30-46% periconceptional uptake. Extremely low uptakes of less than 5% were found in France, Spain, Germany and Italy. It should be noted that the countries in which the highest uptake rates were found were those with official health education initiatives.

3.5 Pregnancy Planning Behaviour

The low uptake of periconceptional folic acid supplements may be because a large proportion of women do not plan their pregnancies and, of those who do plan the pregnancy, many are either unaware of the benefits of periconceptional folic acid, unaware of when they should take it or disinclined to take it (Clark and Fisk 1994; Scott et al, 1994; de Walle et al, 1999). It has been shown that women often modify their behaviour only after pregnancy has been confirmed and this usually occurs after the critical embryonic development of the neural tube is complete (Morin et al, 2002). A group in the Netherlands is attempting to get the message to women prior to conception by using pharmacists as the educators. Initial results are promising. (Meijer et al 2005)

Estimates of the proportion of pregnancies which are 'planned' in different countries are shown in Table 3. Since surveys which have asked women whether their pregnancy was planned have not generally employed a definition of "planned", it is difficult to make meaningful comparisons of reported pregnancy planning behaviour between countries. The concept of 'planning' needed in relation to periconceptional folic acid supplementation refers to a conscious decision to stop contraception together with consideration by the woman of possible health and lifestyle changes needed to achieve conception and/or a healthy pregnancy. It may or may not include a consultation with a health professional. The concept of pregnancy 'planning' held by women almost certainly differs from this, and is influenced by social status and cultural factors.

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 (Food and Drug Administration, 1996; Sayers et al 1997; de Walle et al, 1998), potentially leading to widening of socio-economic inequalities in NTD prevalence.

Table 3: Proportion of Pregnancies Thought to be 'Planned'*

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

*none of the authors were confident that their information was accurate. All were either estimates or based on very limited data and with no definition of planning.

3.6 Fortification of Food with Folic Acid

Mandatory fortification of a staple food (usually flour) with folic acid has been seriously considered in seven countries contributing to this report (Denmark, Germany, Ireland, Norway, Poland, Switzerland, and the UK) and the case for it is still being reviewed. As of January 2005 it had not been implemented in any European country although it is now widespread in North and South America and in much of the Middle East.

Food voluntarily fortified with folic acid (mainly breakfast cereals) is available in many European countries. In a recent 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 et al, 2001). It may be difficult in some countries 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.

4. NTD PREVALENCE RATES IN EUROPE 1980-2002

NTD prevalence rates over time by country can be found in the Country Specific Chapters of Part II. Registry descriptions can be found in Appendix 3. The majority of registries are population-based and register affected fetuses / babies in livebirths, stillbirths 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 4.

Table 4: 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	24 weeks	24 weeks
Croatia	Yes	24 weeks	No upper limit
Denmark	Yes	24 weeks	28 weeks
Finland	Yes	24 weeks	24 weeks
France	Yes	No upper limit	No upper limit
Germany	Yes	No upper limit	No upper limit
Ireland	No	Not legal	Not legal
Italy	Yes	24 weeks	24 weeks
Malta	No	Not legal	Not legal
Netherlands	Yes	24 weeks	28 weeks
Norway	Yes	18 weeks	No upper limit
Poland	Yes	Viability	No upper limit
Portugal	Yes	24 weeks	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

Information as of January 2005

[1] Except Northern Ireland

4.1 Methods

Data for all cases of NTD were extracted from the EUROCAT Central Registry database 1980-2002.

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 were calculated for anencephalus, spina bifida and all NTD combined. Cases with both anencephalus and spina bifida were classified as having anencephalus.

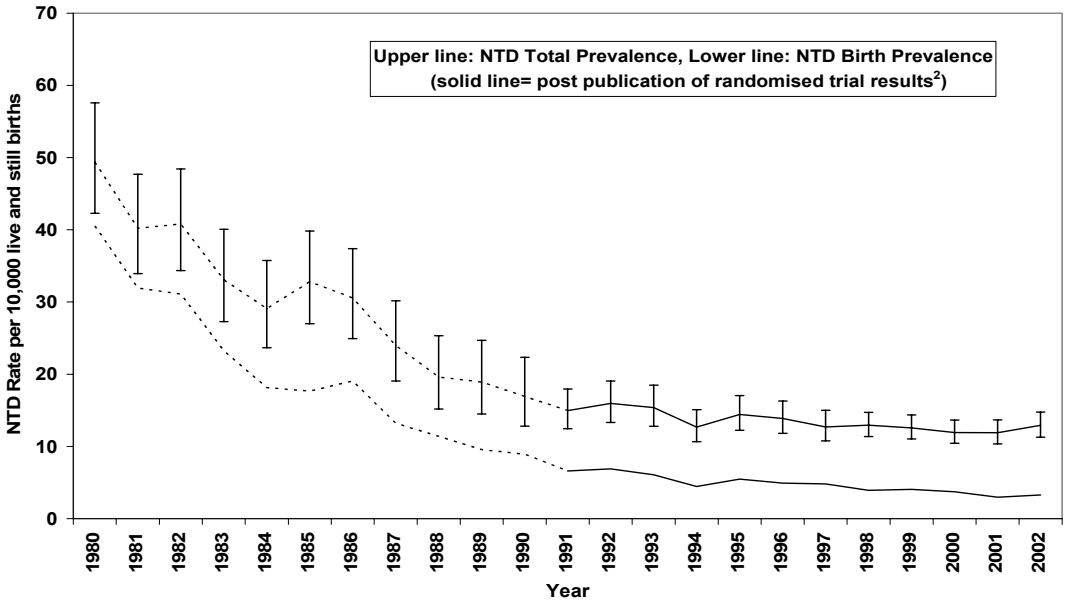
Data from UK and Ireland were analysed separately from data from the rest of Europe due to the historically higher prevalence of NTD in UK and Ireland, and the well-documented steep decline in prevalence in the UK and Ireland prior to the 1990s (EUROCAT Working Group 91).

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 and in Busby et al 2005 a and b.

4.2 Results

In the UK and Ireland, where periconceptional folic acid supplementation policies (PFAS) were introduced in 1992 and 1993 respectively and where there have been active health education campaigns, all registers combined show a 30% overall mean reduction in NTD total prevalence in 2000-2002 compared with 1989-1991.

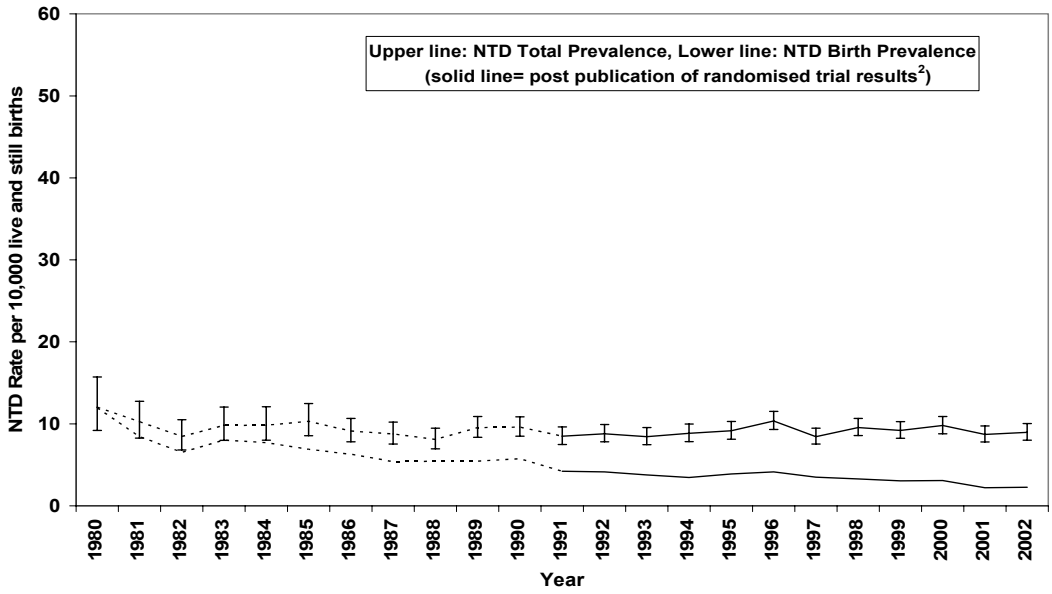
Figure 2: NTD rates in UK and Ireland over time



Busby A, Abramsky L, Armstrong B, Dolk H, et al **(2005a)**, **"**Preventing Neural Tube Defects in Europe: A Missed Opportunity", *Reproductive Toxicology,* Vol 20, pp 393-402 (reprinted with permission from Elsevier).

In Continental Europe, all registries combined showed a non-significant reduction in NTD total prevalence (2%) for countries with a PFAS policy and 8% for those without. However, in Northern Netherlands, where PFAS policy was introduced early (1993) and an active health education campaign has been ongoing, there is a 43% reduction in NTD prevalence rates in 2000-2002 compared to 1989-1991.

Figure 3: NTD rates in Continental Europe over time



Busby A, Abramsky L, Armstrong B, Dolk H, et al **(2005a)**, **"**Preventing Neural Tube Defects in Europe: A Missed Opportunity", *Reproductive Toxicology*, Vol 20, pp 393-402.

For statistic analysis of the results and discussion, see Busby et al, 2005a and b.

4.3 Discussion

In UK and Ireland it is difficult to distinguish the effect of 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 British and Irish diet (see Sources of Folate above).

In Continental Europe, notwithstanding the significant decrease in NTD prevalence rates in Northern Netherlands, the decrease for all registries combined is slight and non-significant.

While live birth prevalence has decreased considerably in countries without a folic acid supplementation policy due to the increase in prenatal diagnosis and termination of pregnancy 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 needed.

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 neural tube defects. Information on NTD prevalence should be supplemented where possible by surveys of periconceptional folic acid supplementation in the population, and by monitoring of serum levels of folic acid.

Overall in Europe, despite the considerable promise of primary prevention of NTD by raising folic acid levels periconceptionally, little progress has been made, and few of the 4,500 affected pregnancies every year in Europe are being prevented. Folic acid fortification of staple foods is likely to be the only way that significant prevention of neural tube defects will be achieved.

5. THE CASE FOR FORTIFICATION OF STAPLE FOODS IN EUROPE

The previous section has shown the disappointing progress of NTD prevention in Europe, even in countries which have a clear supplementation policy implemented by a health education campaign. 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.

Spina bifida (including many avoidable cases) carries a high lifetime burden to the affected individual and family and a high economic cost for services. In addition to individuals surviving with spina bifida, there are large numbers of terminations of pregnancy and perinatal losses affected by NTD, causing great distress (Statham 2003; van Mourik 2003) and using health service resources. Evidence continues to mount about the beneficial effects of folic acid for the prevention of other congenital anomalies, cardiovascular disease (Boushey et al, 1995), and cancer. (Branda and Blickenderfer, 1993; Kim et al, 1997; Jacob et al, 1998; Choi and Mason, 2000). Fortification of food with folic acid might therefore have very far-reaching public health benefits beyond prevention of NTDs.

In the US, mandatory fortification of enriched grain products at a level of 1.4 μg per g of product (Food and Drug Administration, 1996) was introduced in 1998. This level of fortification was projected to result in an additional 100 μg per day of folic acid in the population intake. Studies carried out subsequent to the introduction of fortification report increased mean levels of folic acid in serum from 4.8 ng/ml before fortification to 14.8 ng/ml after fortification (Centers for Disease Control and Prevention, 2000). Choumenkovitch et al (2002) estimated that folic acid intake increased by a mean of 190 (95% CI: 176-204) μg per day for non-supplement users and total folate intake increased by a mean of 323 (95% CI: 296-350) μg dietary folate equivalents per day using data collected from participants of the Framingham

Offspring Cohort Study. As manufacturers of breakfast cereal have also increased the fortification level in many products in recent years in the US, it is not clear how much of the rise in folate status is due to mandatory fortification and how much to the increase in voluntary fortification which was introduced. A 25% lowering of NTD rates in the US since the introduction of mandatory fortification has been reported (CDC, MMWR, May 7, 2004; Williams et al 2002). Calls have been made for a further increase in the level of fortification (Oakley, 1999), however, others have urged that more information should be available regarding both the benefits and hazards of fortification before this should be considered (Mills, 2000).

Mandatory fortification has also been introduced in Canada, and in many countries in Central and South American and the Middle East. In Canada and Chile, increased serum folate levels have been found following the introduction of mandatory fortification (Hirsch et al, 2002; Ray et al, 2002). NTD rates have declined by about 50% in both countries since fortification. (Liu et al 2004, Lopez et al 2005; Hertrampf E, Cortes F, 2004).

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, to the extent that many countries have been exceedingly slow to develop a primary prevention policy and some have still not developed one. This lack of recognition may stem from the fact that the great majority of neural tube defect 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 and Jong-van den Berg 2005).

There has been concern regarding the potential risk of masking the symptoms of pernicious anaemia caused by vitamin B_{12} deficiency. If undiagnosed, there is potential for irreversible neurological damage in those at high risk of this deficiency, namely the elderly (Savage and Lindenbaum, 1995). However, it is argued that B_{12} deficiency can be diagnosed simply with or without the presence of anaemia (Bower

and 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.

There have been some reports of possible increases in twinning associated with periconceptional folic acid (Czeizel et al, 1994; Werler et al, 1997; Ericson et al, 2001). Most of the women in these studies used multivitamins and not folic acid alone. In fact, the increased occurrence of multiple births was not supported in another early, randomised trial of folic acid (Kirke et al, 1992) and has not been confirmed in a more recent, large population-based cohort study with folic acid in China (Li et al, 2003).

The association between folic acid supplementation and twinning is thought by many researchers to be due to the confounding effect of folic acid supplementation being much more common among women using assisted reproductive technology and the fact that use of this technology may be significantly under-reported. (Berry, Kihlberg and Devine 2005)

Although there is evidence that folate may be protective against the development of new cancers, there is concern at the possibility that folic acid may enhance the development of undiagnosed pre-malignant and malignant lesions. This issue was reviewed by Kim in 2004.

6. CONCLUSIONS

- The evidence that the majority of NTD are preventable by increasing folate status before conception is very strong. Evidence is also accumulating that the protective effect may extend to other congenital anomalies.
- Government response to this evidence has been variable in Europe. Many countries have been slow to introduce policies, and some still have no policy regarding periconceptional folic acid supplementation.
- Only half of the countries contributing to this report have implemented health education campaigns designed to reach all women before conception.
- The majority of women in countries surveyed are not taking folic acid supplements periconceptionally.
- In countries without a policy regarding folic acid supplementation, there has been no discernible decrease in the total prevalence of neural tube defects.
- In countries with a policy to recommend periconceptional folic acid supplementation, there is evidence of some decrease in prevalence, but to a disappointing degree compared to the potential for prevention. In UK and Ireland, it is not clear if the decrease in prevalence is simply a continuation of the pre-existing decline in prevalence already evident in the 1980s.
- 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 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, renewed 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
  - introduce mandatory folic acid fortification of a staple food
- The objective of preventing the majority of NTD is unlikely to be achieved without mandatory fortification of a staple food, which 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.

- As countries change their policies and practices regarding prevention of NTD, continued monitoring of NTD prevalence is vitally important, using the data of population based registers of congenital anomalies with high ascertainment of cases among livebirths, stillbirths and termination of pregnancy for fetal abnormality

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REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR AUSTRIA

Prof Andrea Berghold, Prof Häusler

Folic Acid Supplementation Policy

In Austria, there is no official government recommendation for periconceptional folic acid supplementation, but a recommendation was published by the Austrian Pediatric Society and the Austrian Society of Prenatal and Perinatal Medicine in 1998.[1] 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 8th week. For women with a high risk for recurrence of a neural tube defect, a periconceptional folic acid supplementation of 4 mg per day was recommended.

Food Fortification Policy

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

Health Education Initiatives

No official health education initiative to inform women about the role of folic acid in reducing the risk for neural tube defects has been carried out and none is planned for the near future in Austria.

Knowledge and Uptake of Folic Acid

A study carried out in the obstetric unit of St Pölten hospital in Lower Austria, [2] looked at knowledge and uptake of periconceptional folic acid supplementation among recently delivered women. All women whose babies were born between 1.12.1997 and 31.3.1998 were included in the study. They were interviewed using a standardized questionnaire. 238 women participated in the study and 234 questionnaires were used for the analysis. 57 (24%) women used folic acid; however 33 out of 57 did not start use until after the 12th week of gestation. 61 out of 161 (38%) who answered this question knew of the preventive effect of folic acid in respect of 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

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 the case of non-lethal malformations, most doctors in Austria agree to terminate pregnancies only before viability (< 25 weeks gestational age). In the case of lethal malformations they will agree to terminate pregnancies after viability.

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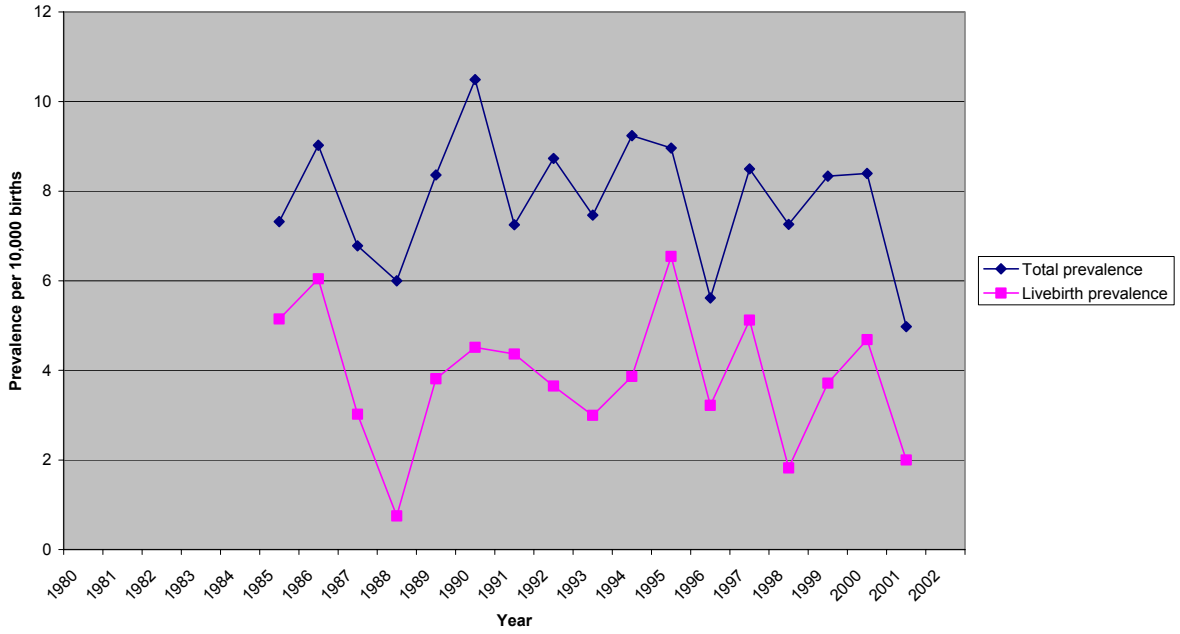
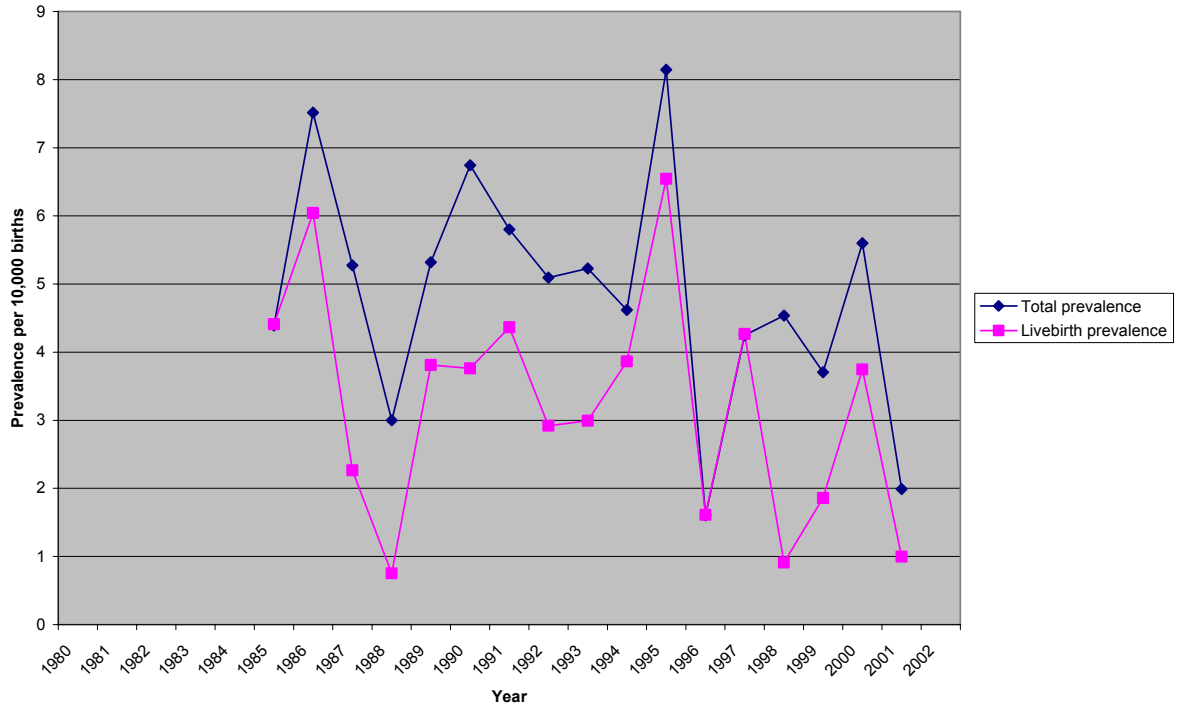
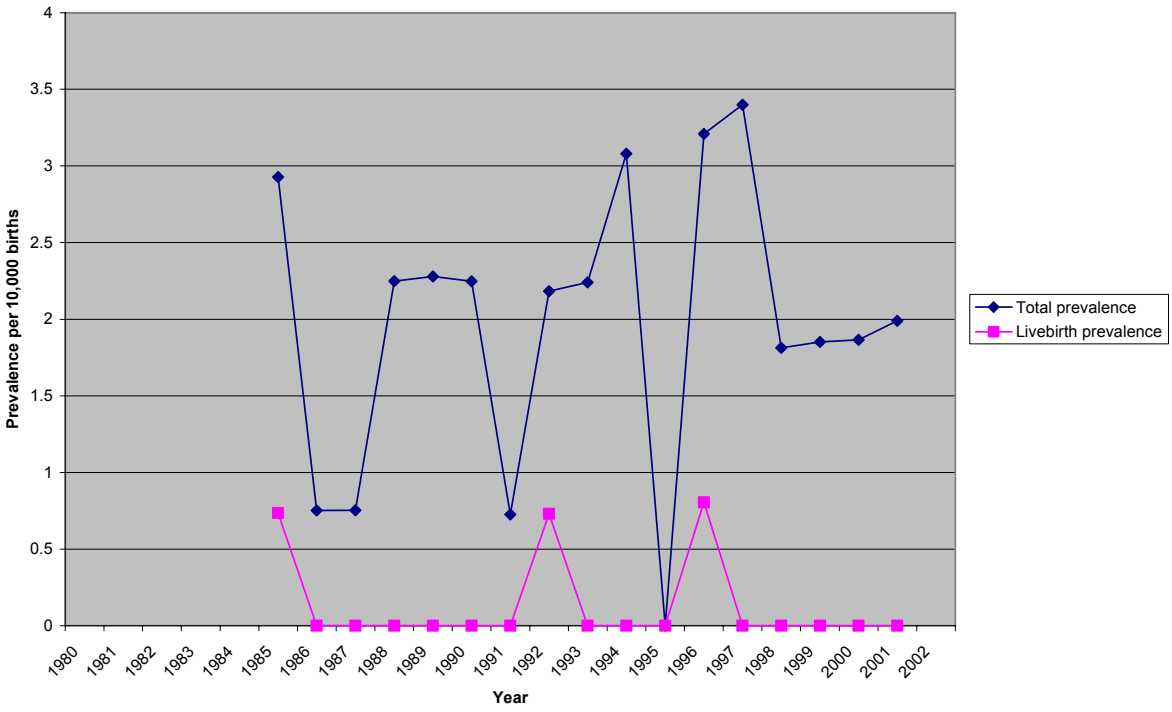
Austria (Styria): Total and Livebirth Prevalence Rates for Neural Tube Defects



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



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



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR BELGIUM

Prof Yves Gillerot and Andre Baguette

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

No information provided

Health Education Initiatives

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), is currently (December 2004) preparing a health education campaign which will include leaflets, a website, and information on radio and television. Letters about the benefits of periconceptional folic acid will be sent to family physicians and gynaecologists in the French speaking area of Belgium. This initiative has come about largely as a result of the first EUROCAT Special Report which highlighted the low priority given to preventing NTDs in Belgium.

Knowledge and Uptake of Folic Acid

No information provided

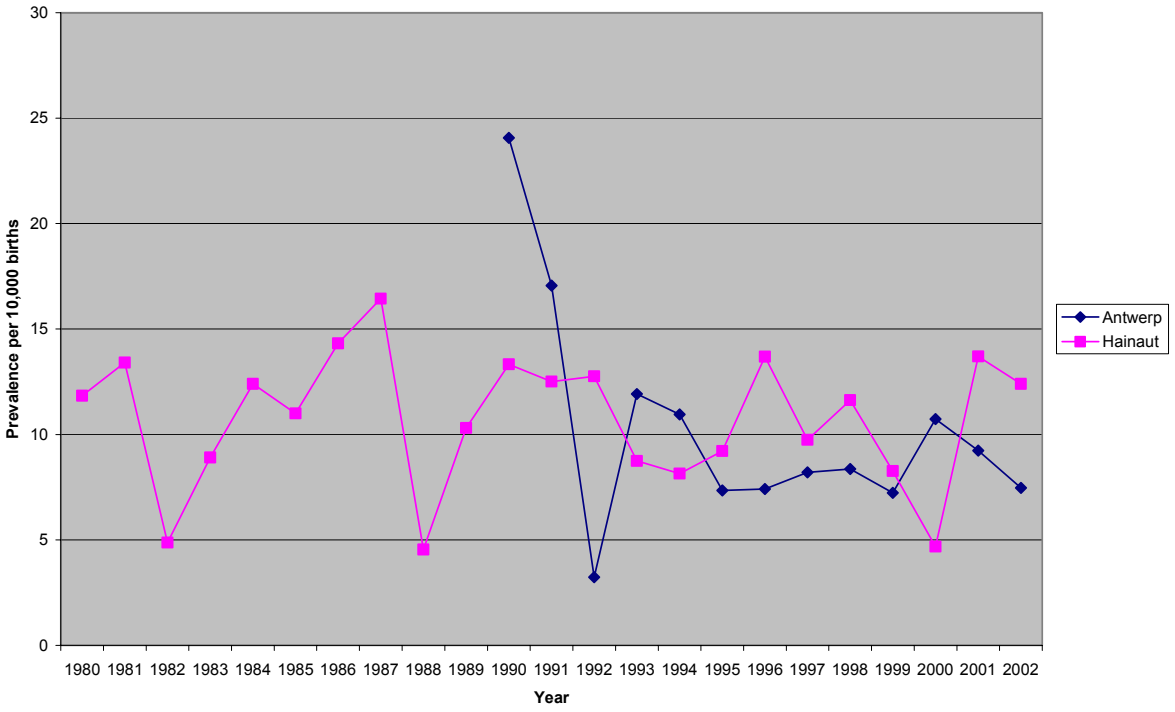
Proportion of Pregnancies that are Planned

No information provided

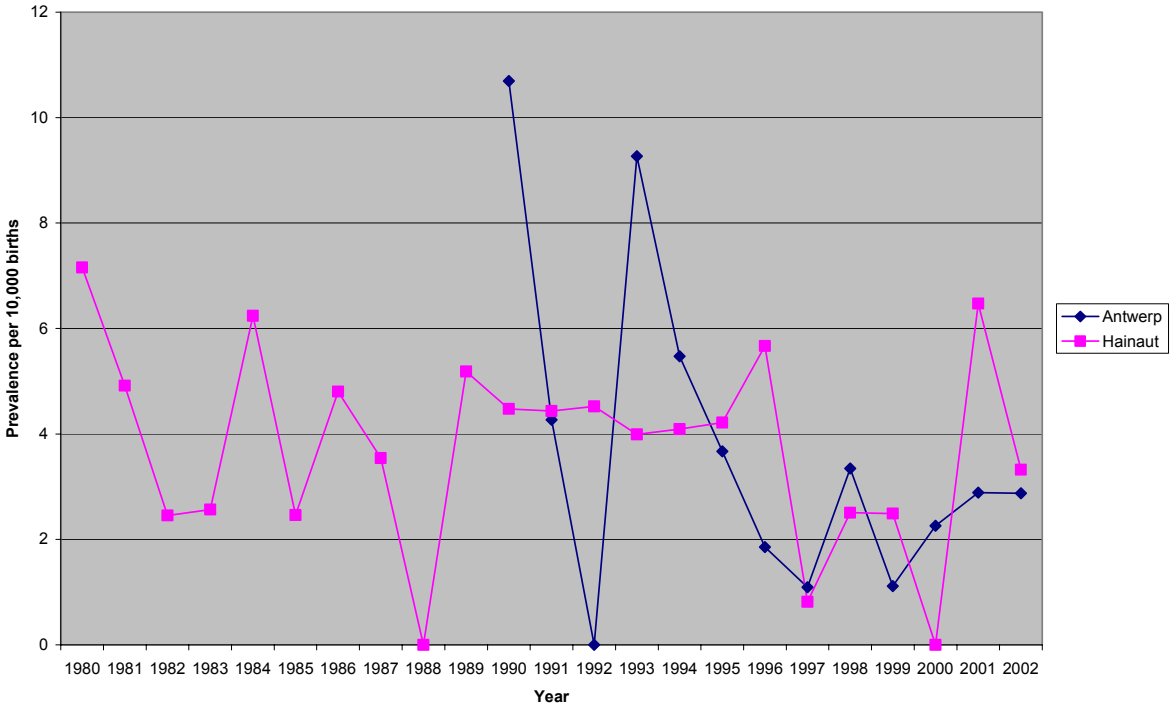
Laws Regarding Termination of Pregnancy

Termination of pregnancy for fetal abnormality is legal up to the gestational age of 24 weeks.

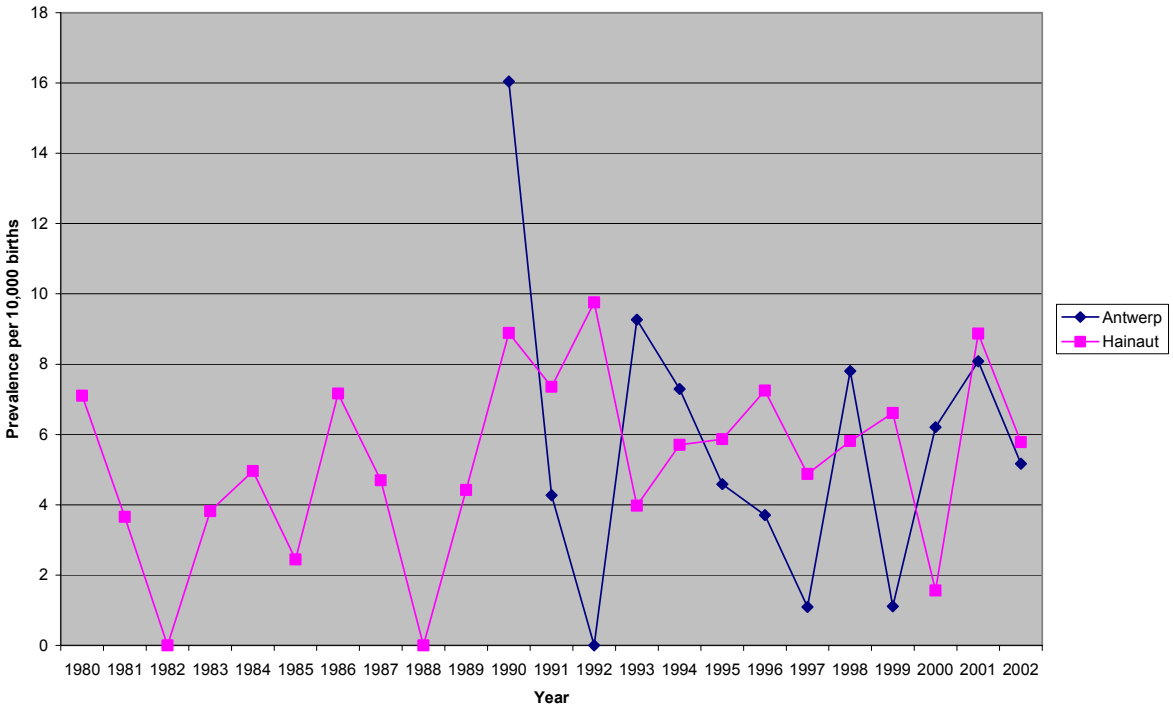
Belgium (Antwerp and Hainaut): Total Prevalence Rates for Neural Tube Defects



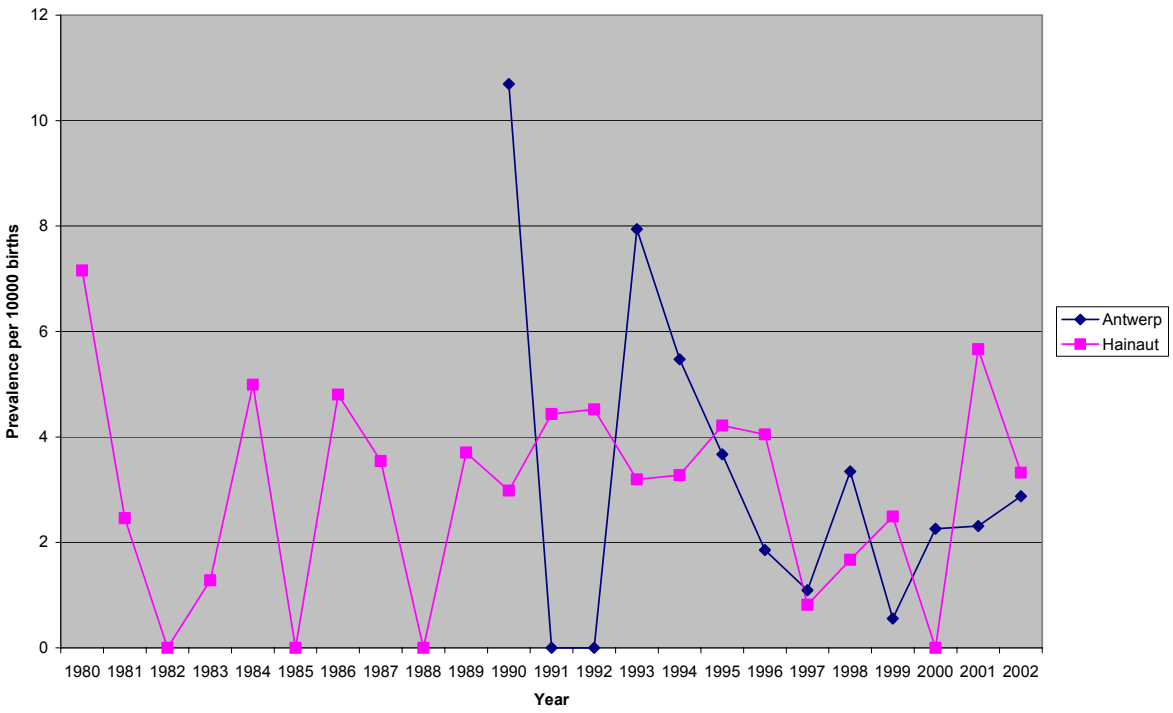
Belgium (Antwerp and Hainaut): Livebirth Prevalence Rates for Neural Tube Defects



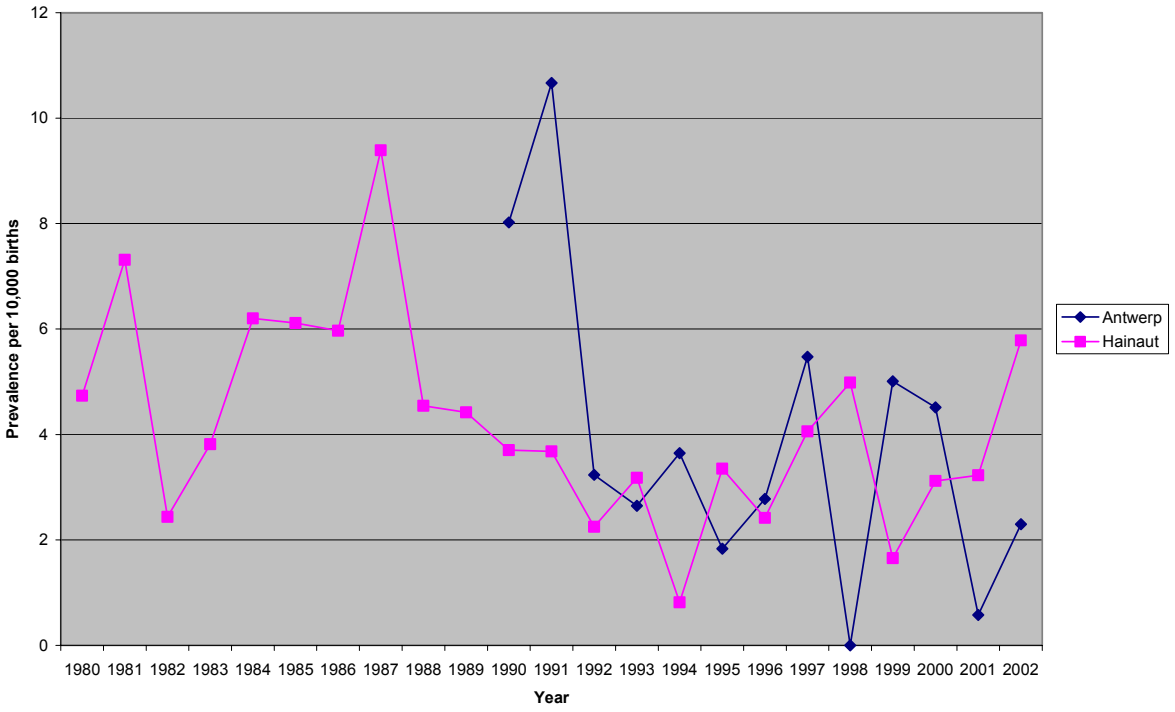
Begium (Antwerp and Hainaut): Total Prevalence Rates for Spina Bifida



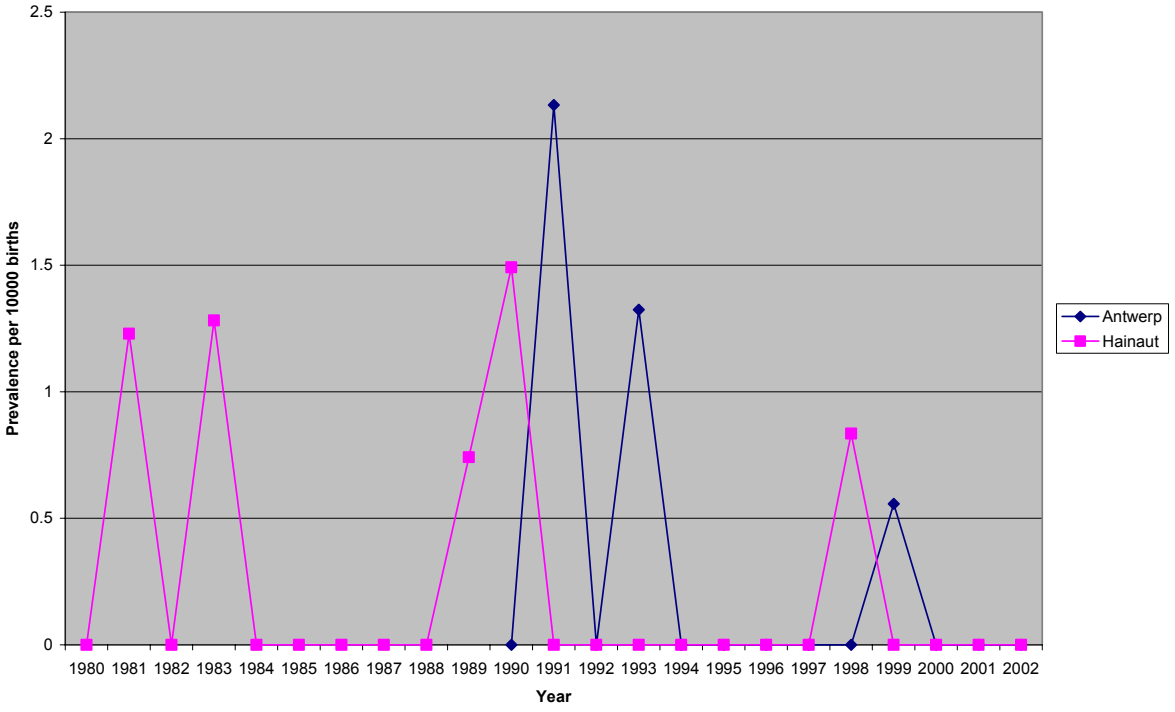
Belgium (Antwerp and Hainaut): Livebirth Prevalence Rates for Spina Bifida



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



Belgium (Antwerp and Hainaut): Livebirth Prevalence rates for Anencephalus



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR CROATIA

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; the few studies there are relate to anaemia in children, congenital heart diseases, neurological disease in children and arteriosclerosis. So far, there are no published studies on the awareness of the childbearing population of recommendations regarding periconceptional folic acid supplementation. In 2003 we administered a questionnaire to pregnant women in “Sveti Duh Hospital” in Zagreb (upublished 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.

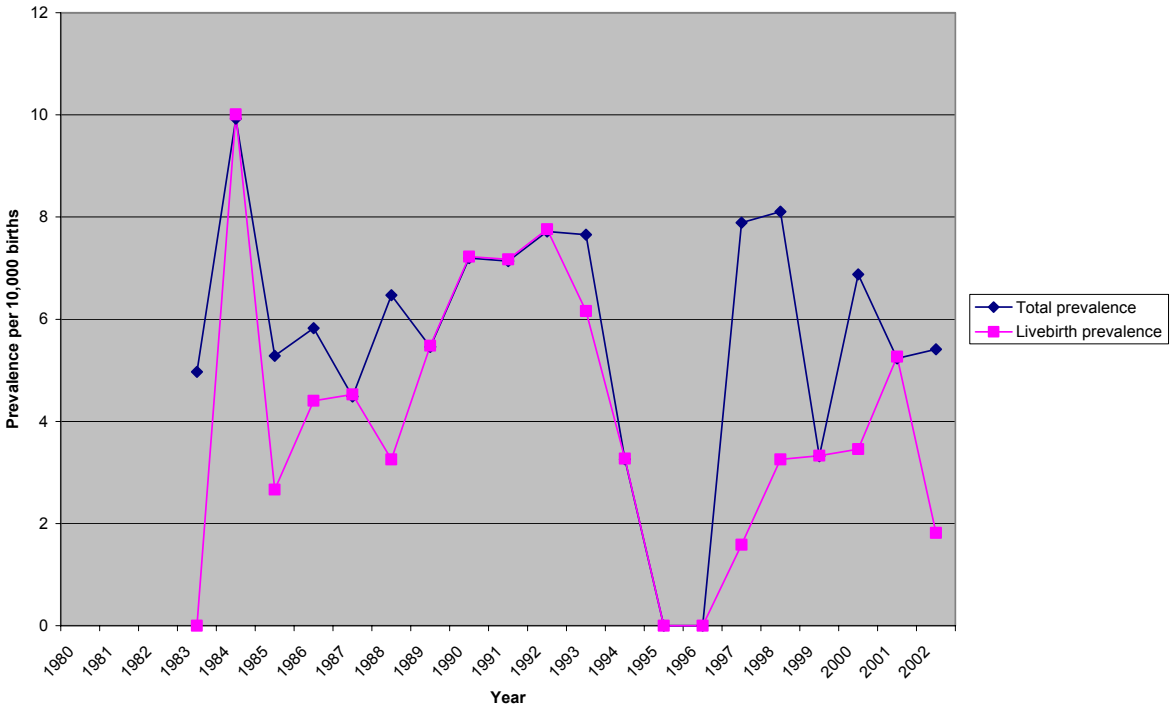
Proportion of Pregnancies that are Planned

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

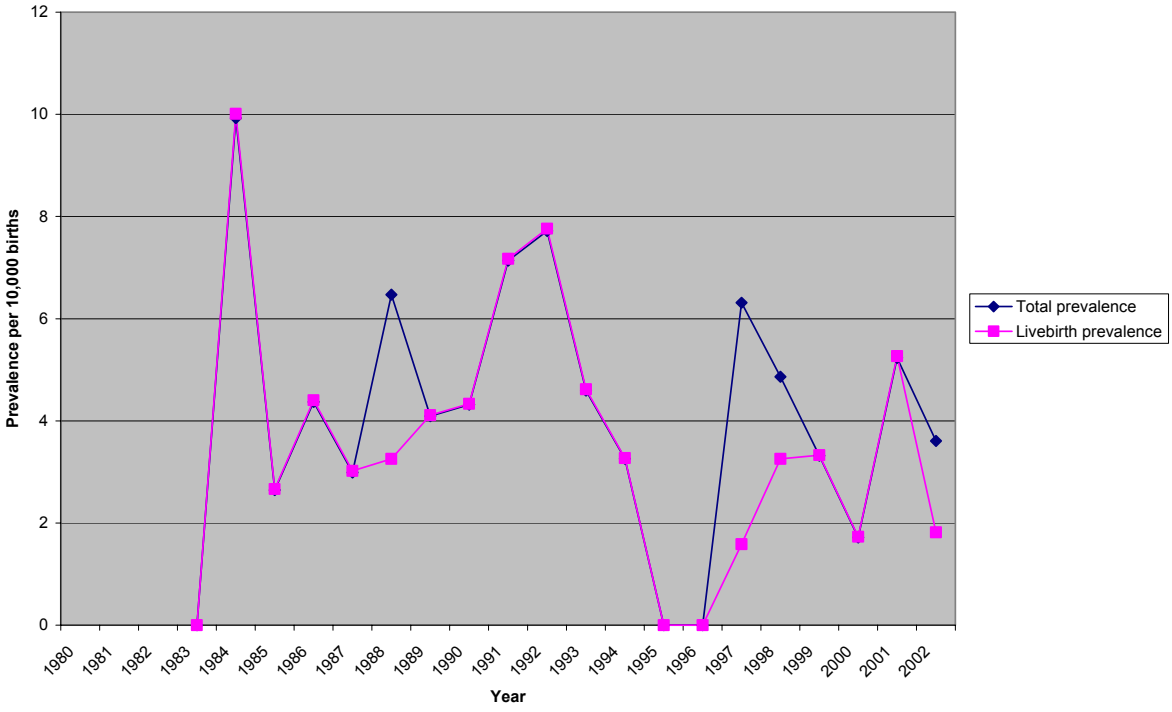
Laws Regarding Termination of Pregnancy

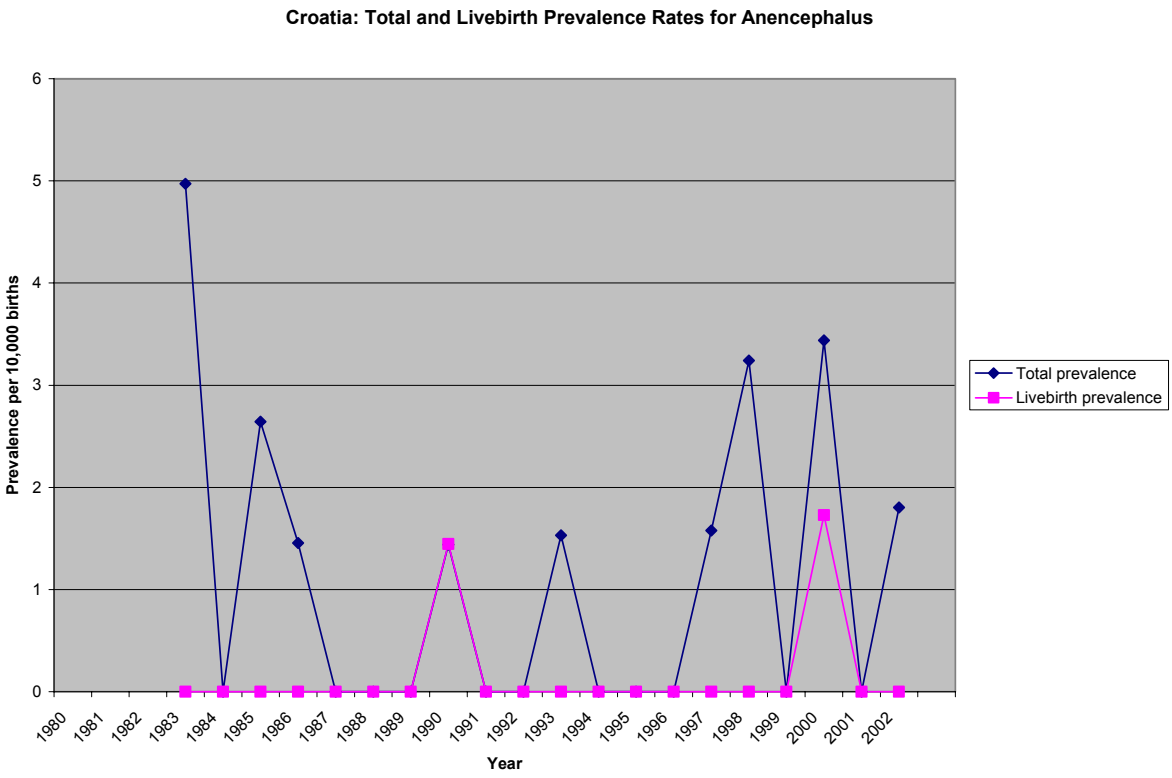
Termination of pregnancy for fetal abnormality is legal up to 24 weeks of gestation in Croatia. After 24 weeks gestation it is not legal, but if a life-threatening anomaly is found on ultrasound scan after 24 weeks, there is some possibility of termination of pregnancy if it is approved by the Hospital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

Croatia: Total and Livebirth Prevalence Rates for Neural Tube Defects



Croatia: Total and Livebirth Prevalence Rates for Spina Bifida




Croatia: Total and Livebirth Prevalence Rates for Anencephalus
Prevalence per 10,000 births
0
1
2
3
4
5
6
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Year
Total prevalence
Livebirth prevalence

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 initiative is still ongoing.

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 periconceptional 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 congenital anomaly is diagnosed, the upper gestational age for termination is usually 24 weeks. Termination may be permitted up to 28 weeks if survival is impossible.

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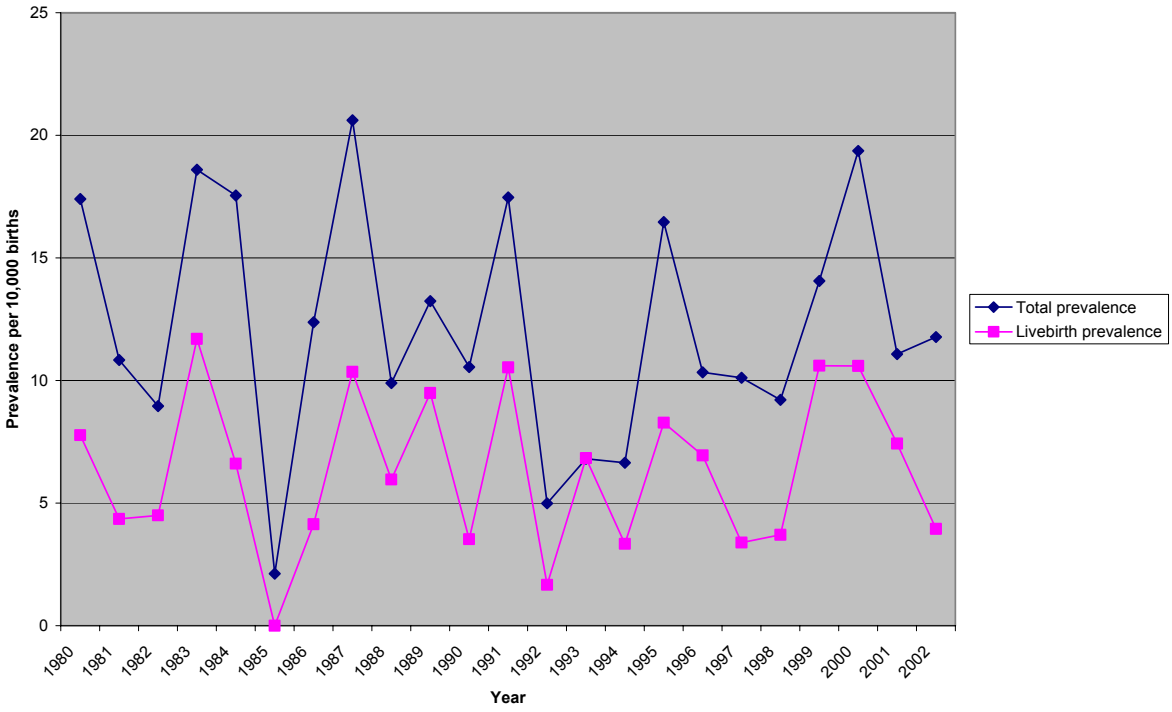
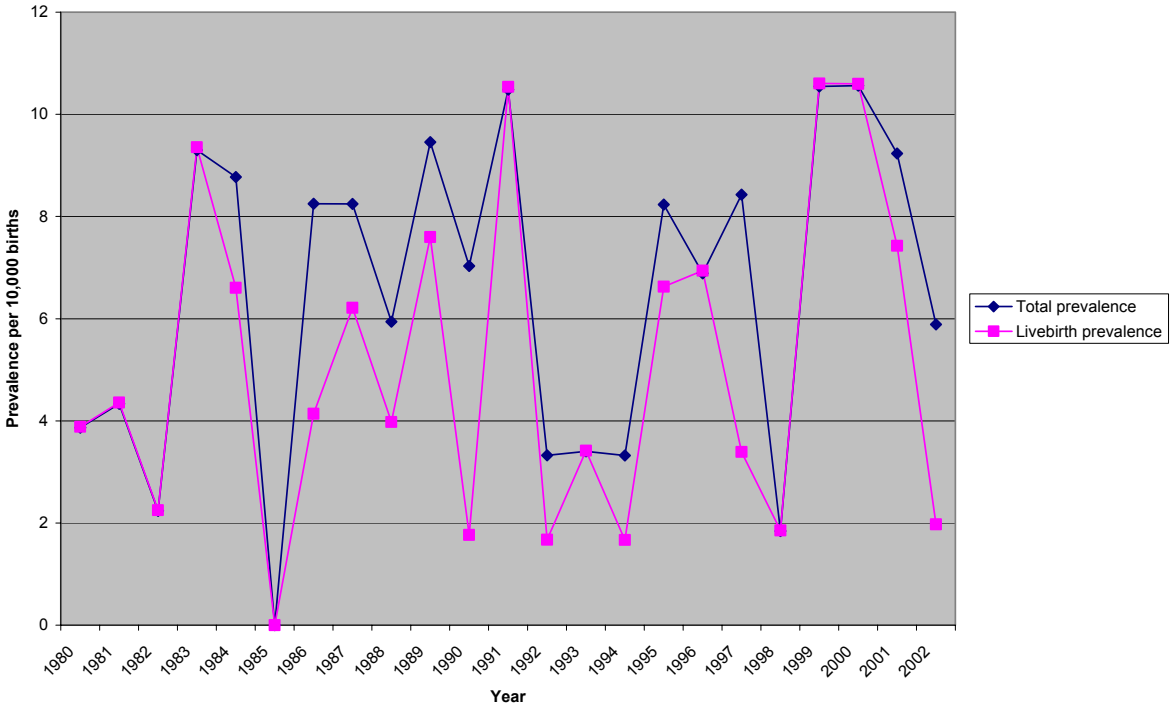
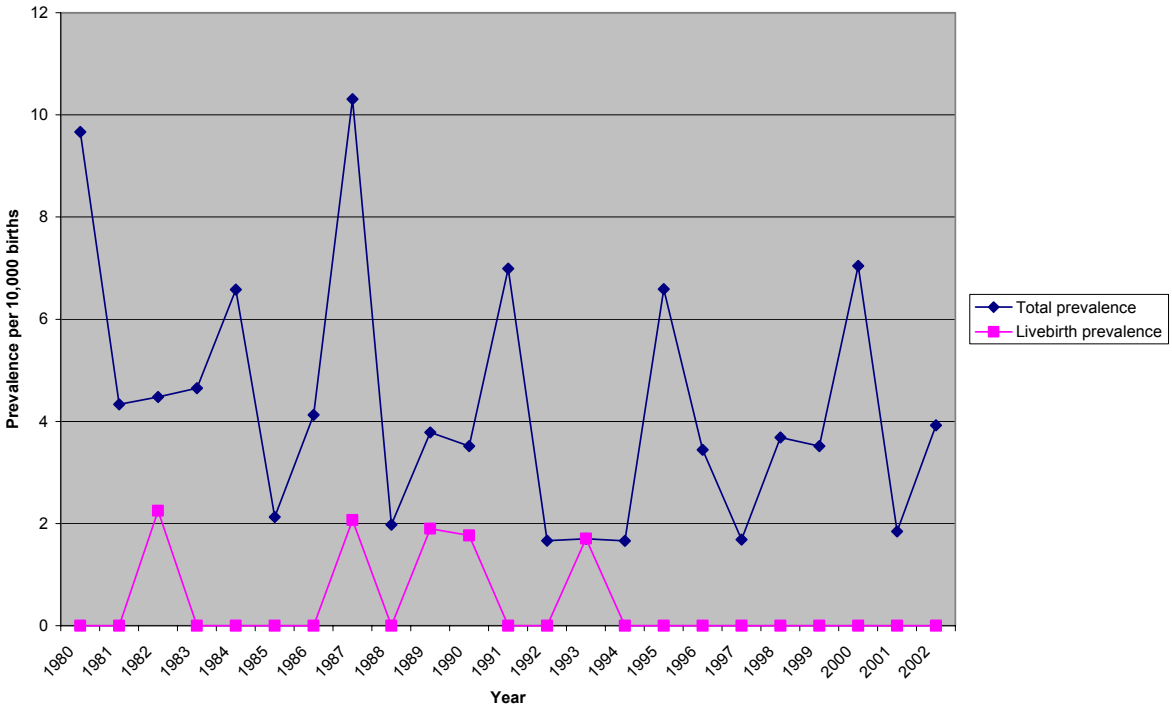
Denmark (Odense): Total and Livebirth Prevalence Rates for Neural Tube Defects



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



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



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR FINLAND

Dr Annukka Ritvanen

Folic Acid Supplementation Policy

The randomised, international study published by the UK Medical Research Council (MRC) in 1991 confirmed the results of the previous non-randomised studies carried out in the UK in the 1980's that folic acid prevented the majority of recurrences of neural tube defects (NTD).[1] The Hungarian randomised intervention study of Czeizel and Dúdas in 1992 showed that periconceptional use of a folic acid supplement significantly reduced the occurrence of NTD.[2]

In light of these studies, 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. [3] The recommendations were also published in the leading Finnish scientific medical paper in 1996.[4] 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 new official recommendation on folic acid supplementation has three sections:

1. <u>Prevention of first occurrence of NTD in ordinary pregnancies:</u>

   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 or 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 or 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, coeliac 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:
  - the parents have had a common child or fetus with NTD.
  - either parent has had a child or fetus with NTD with another partner
  - 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 B_{12} level should be checked in order to make sure that there is no deficiency of vitamin B_{12}. The reason for this is that an amount of 1mg folic acid can conceal megaloblastic anaemia, associated with deficiency of vitamin B_{12}, 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.[5]

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.[6]

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 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.[7]

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 women asked 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). [8]

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 Spring 2000. 6 % of the women asked 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 the changes were made only after the woman found out about her pregnancy. [9]

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 didn't 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

Laws Regarding Termination of Pregnancy

Termination of pregnancy is allowed up to 12 weeks gestation for many indications by permission of one or two doctors and up to 20 weeks by special permission of the National Authority for Medicolegal Affairs. If the mother's life is in danger, the pregnancy can be terminated at any gestational age.

Termination for fetal abnormality can be done up to 24 weeks only by special permission of the National Authority for Medicolegal Affairs.

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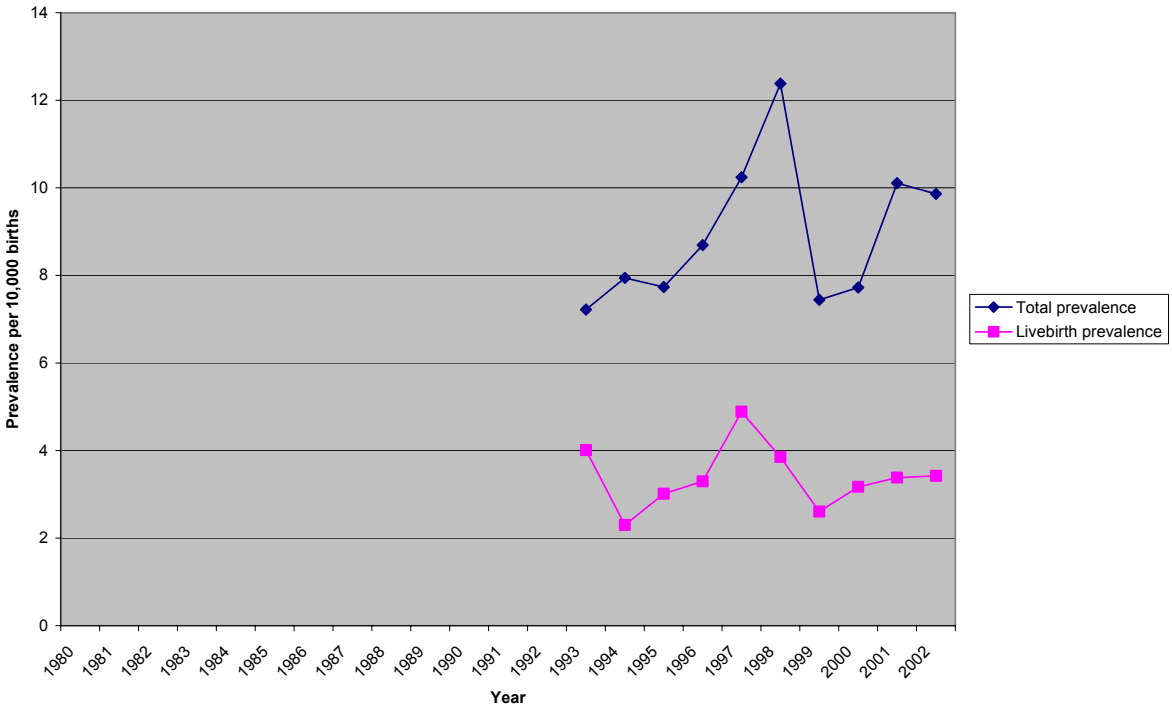
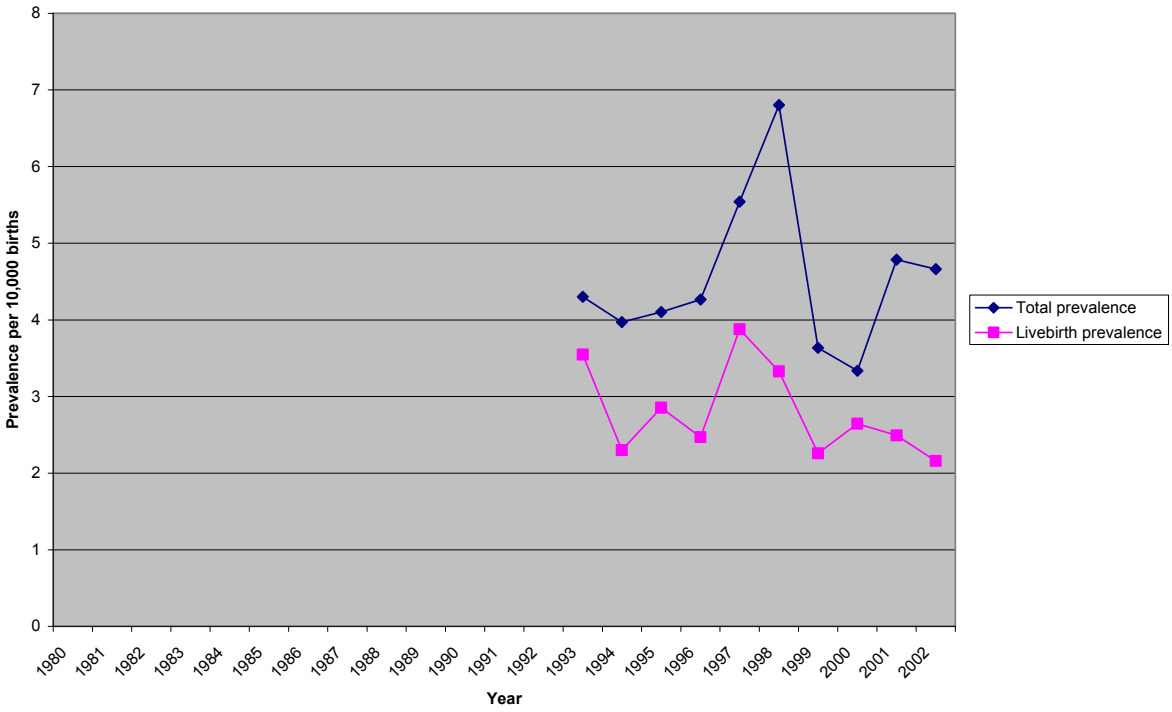
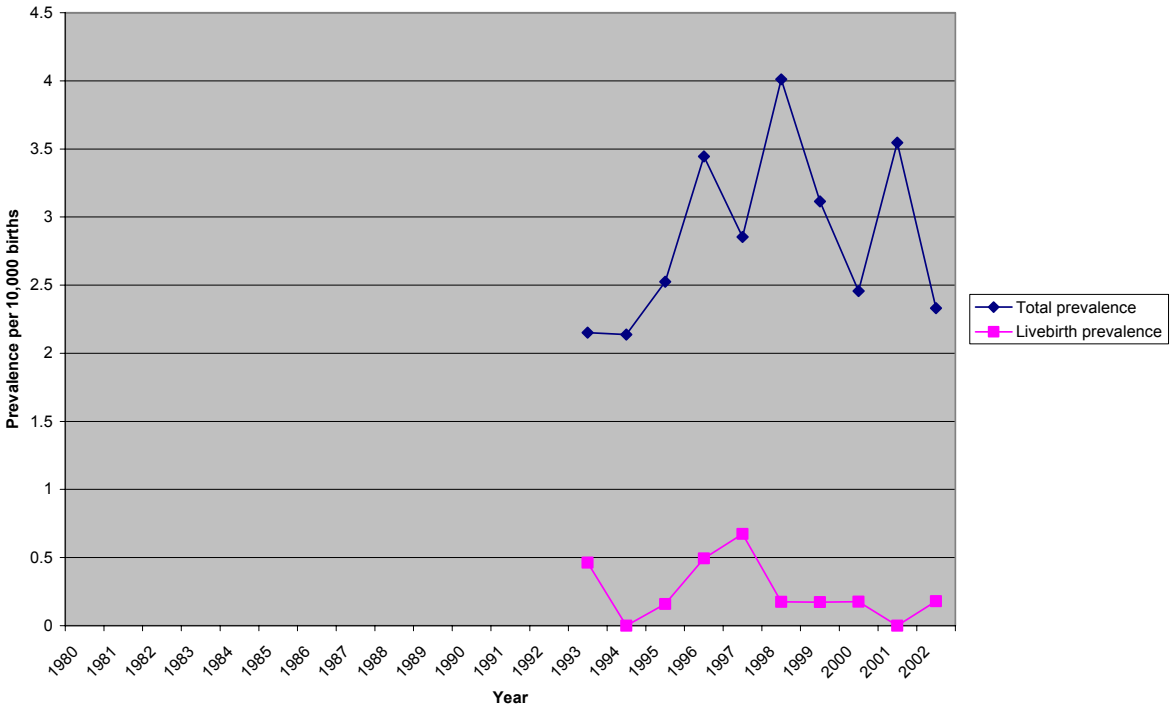
Finland: Total and Livebirth Prevalence Rates for Neural Tube Defects



Finland: Total and Livebirth Prevalence Rates for Spina Bifida



Finland: Total and Livebirth Prevalence Rates for Anencephalus



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 are currently organizing conferences and training programmes for gynaecologists across the country in order to stimulate prescription of folic acid by physicians.

Advice about periconceptional folic acid is being 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. There have been no studies about awareness since 1997.

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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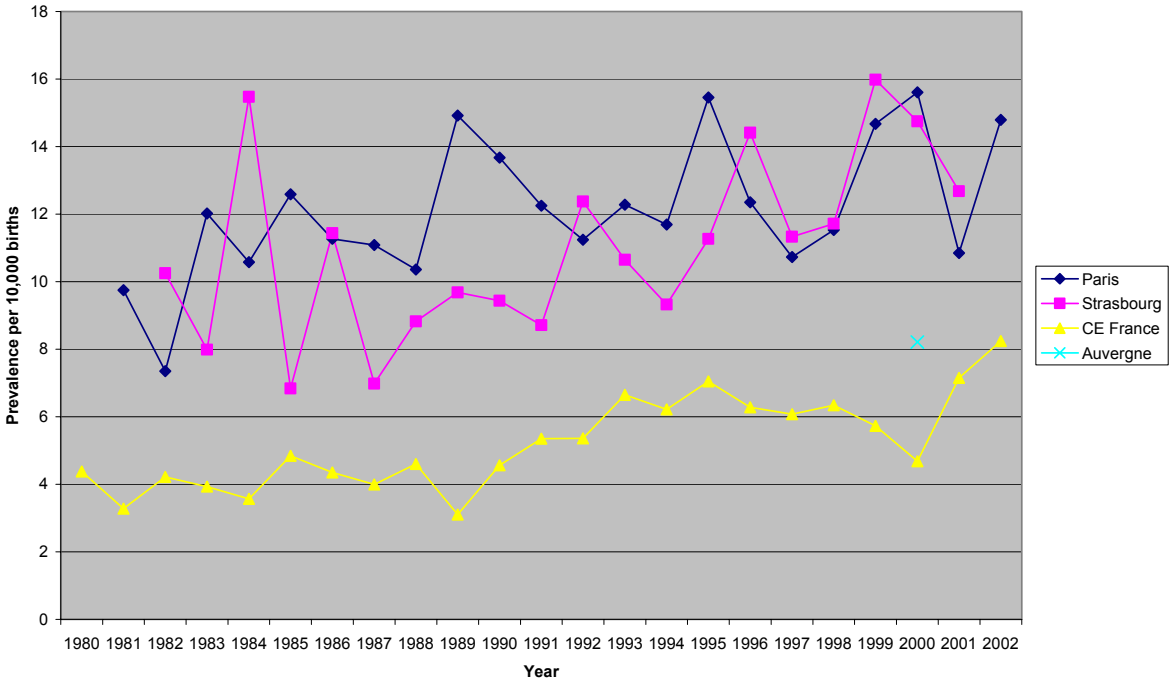
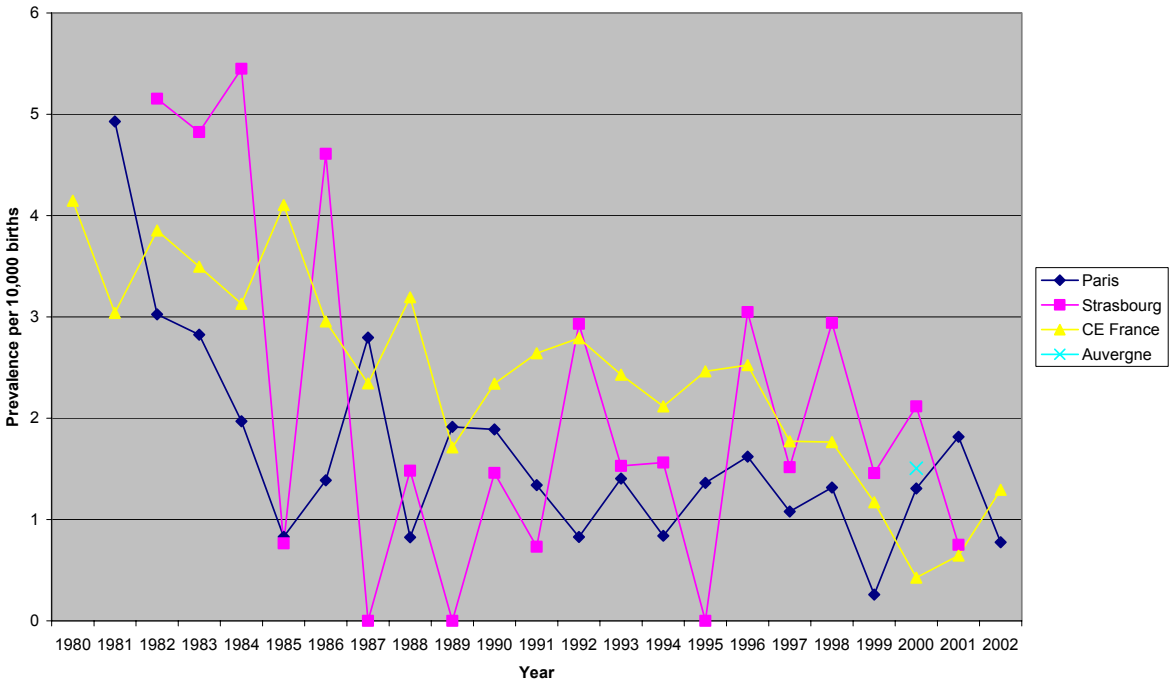
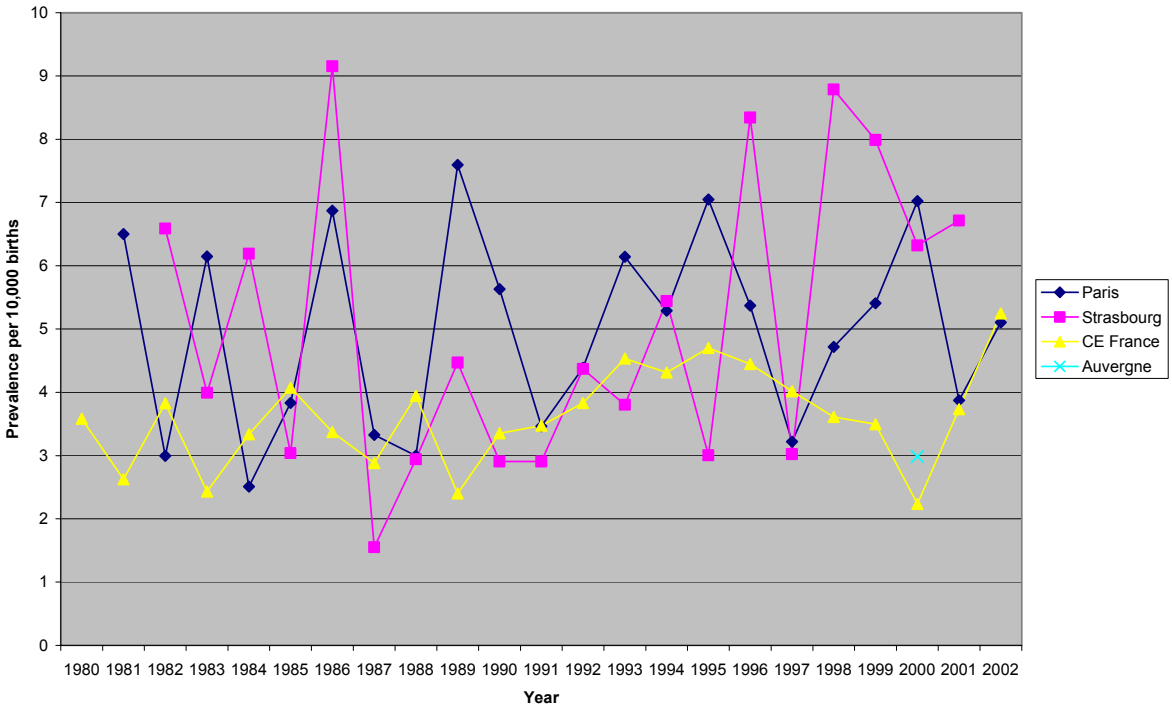
France (Auvergne, Central East France, Paris and Strasbourg): Total Prevalence Rates for Neural Tube Defects



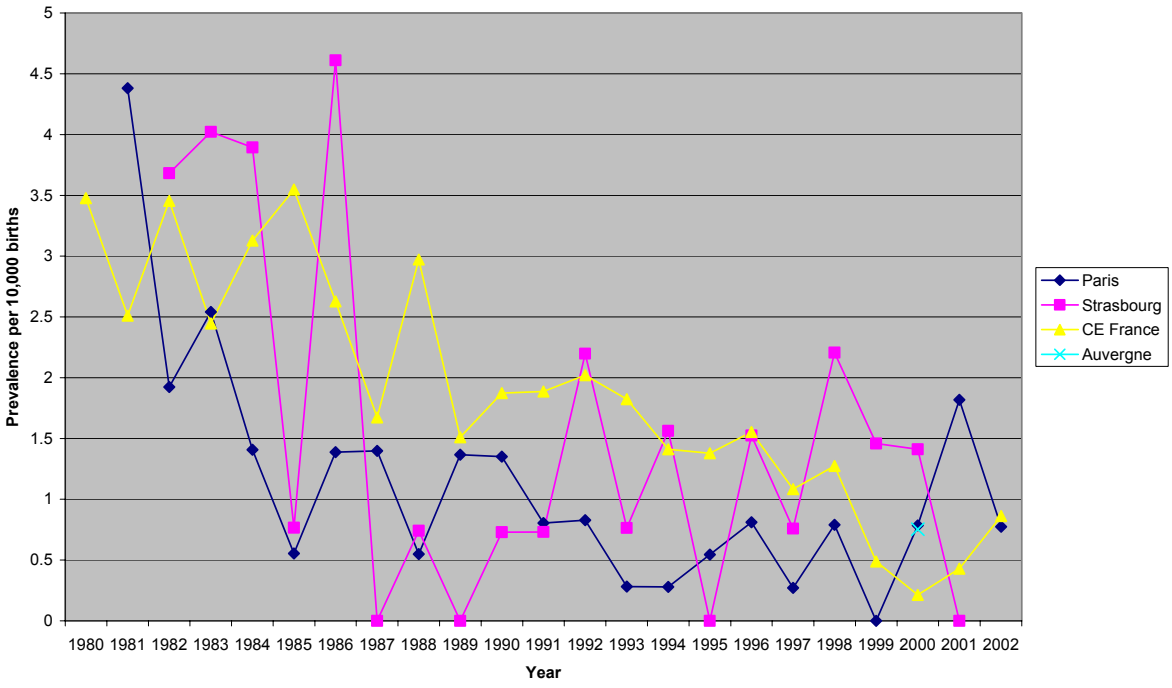
France (Auvergne, Central East France, Paris and Strasbourg: Livebirth Prevalence Rates for Neural Tube Defects



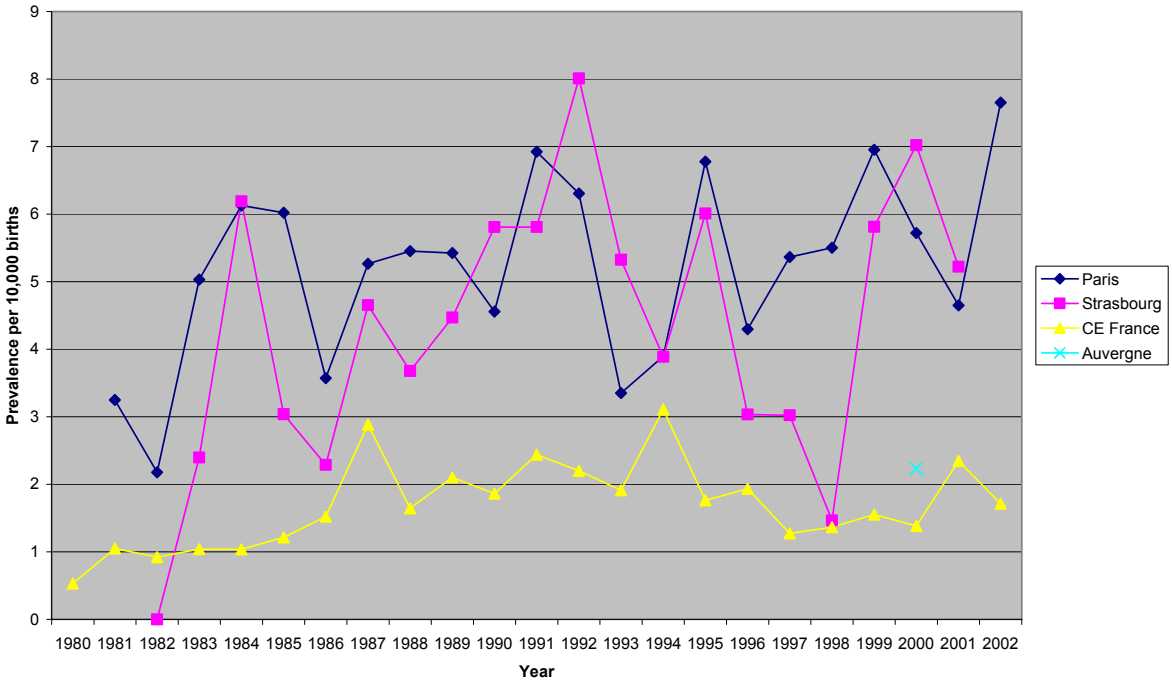
France (Auvergne, Central East France, Paris and Strasbourg): Total Prevalence Rates for Spina Bifida



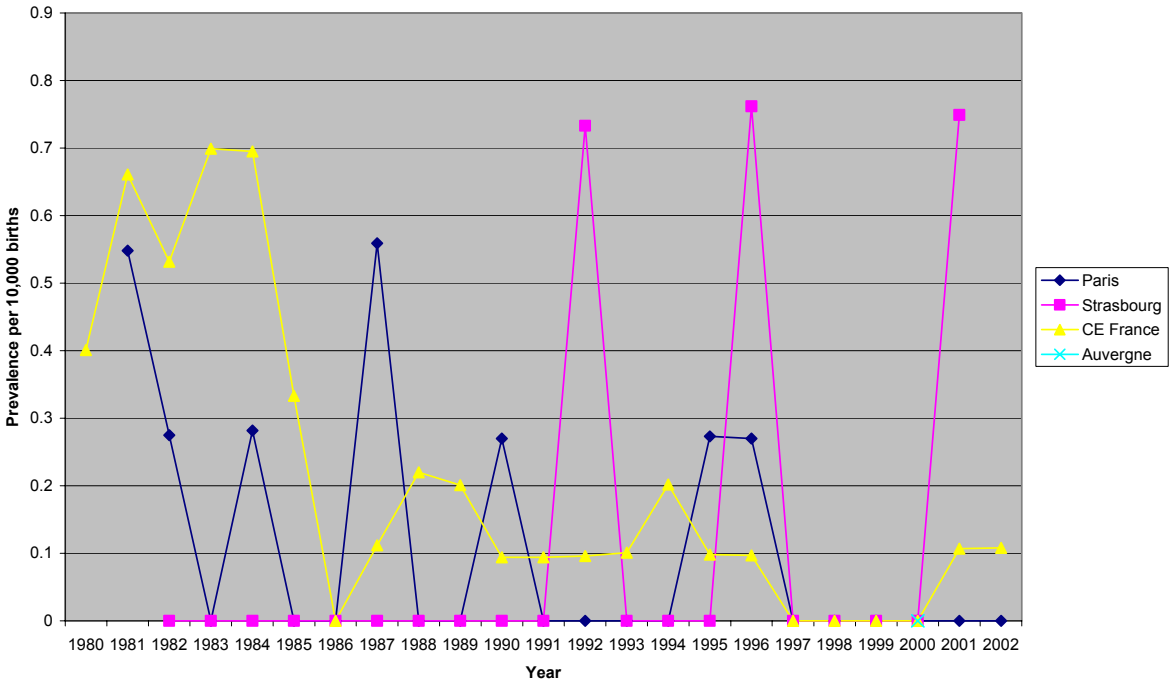
France (Auvergne, Central East France, Paris and Strasbourg): Livebirth Prevalence Rates for Spina Bifida



France (Auvergne, Central East France, Paris and Strasbourg): Total Prevalence rates for Anencephalus



France (Auvergne, Central East France, Paris and Strasbourg): Livebirth Prevalence Rates for Anencephalus



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR GERMANY

Prof Volker Steinbicker, Dr Christine Rösch, Dr Simone Poetzsch

Folic Acid Supplementation Policy

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

In 1991 the German Nutrition Society (Deutsche Gesellschaft für Ernährung) published "Recommendations for nutrient intake" which advised 150 μg of folate equivalent daily for adolescents and adults, and 300 μg daily for pregnant women (Deutsche Gesellschaft fur Ernahrung, 1991).

In 1994/95 recommendations published by the German Nutrition Society, the German Society of Obstetrics and Gynecology, the German Society of Human Genetics, the German Society of Pediatrics and Adolescent Medicine, and the German Society of Neuropediatrics advised 400 μg folic acid daily for women wishing a child, and 4000 μg 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 (B Koletzko 1994, B Koletzko 1995a and 1995b).

In 2000 the Societies of Nutrition in Germany (DGE), Austria (ÖGE) and Switzerland (SVE, SGE) published "Reference values for nutrient intake" for the German-speaking countries (Deutsche Gesellschaft fur Ernahrung 2000).

Table 1: Reference values for folic acid intake (Deutsche Gesellschaft fur Ernahrung 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 19 – under 25 years 25 – under 51 years 51 – under 65 years 65 years and elder	 400 400 400 400 400
Pregnant women	600
Nursing women	600

Food Fortification Policy

In Germany folic acid is classified as a supplementary food, and hence does not fall under drug approval requirements. The *Nährwertkennzeichnungsverordnung* (Nutritive Declaration Regulation) (Thamm 1999) stipulates that 100 g of grain may be fortified with up to 15 per cent of the recommended daily dose of 200 μg of folic acid. However, the maximum daily intake must not exceed three times the recommended daily dose (i.e. 600 μg folic acid).

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

Among the medical societies in Germany, only the Society of Pediatrics and Adolescent Medicine has published a recommendation for cereal grains enriched with folate (B Koletzko 2000). Some foodstuffs are fortified with folic acid, such as bread, cereal grains and fruit juice. 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 firms, 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” 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 body. The work of the group focuses on introducing folic acid fortification of basic food in Germany. As a first step to this end, a consensus paper was published in "Deutsches Ärzteblatt", the organ of the German medical profession, in 2004 (Koletzko 2004). The consensus paper is highly appreciated among German physicians.

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 at improving health knowledge and awareness of the population. Although they have all studied 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 was performed by Mrs Egen from Munich, comprising two inquiries: (i) during the first inquiry 346 newly delivered women were interviewed 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 periconceptional 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 held 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 newly delivered women. 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

A inquiry into 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 a and b; Seelig, Potzsch, Steinbicker 2005)

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

Gynecologists

- In 1998 Malformation-Monitoring Saxony Anhalt performed an anonymous inquiry among 234 gynecologists regarding pre- and post conceptional administration of folic acid. The questionnaire was returned by 104 gynecologists (44.4%). 76.9% of them said they would administer folic acid after confirmation of conception, whereas 87.5% would recommend preconceptional intake.
- In 1996 a total of 27 gynecologists in Munich were interviewed about their attitude to prophylactic folic acid. Nine gynecologists (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 with a family history of NTD, whereas nine (37%) did not give any recommendation at all.
- Following an intervention campaign in 1998, 20 (74%) recommended taking preconceptional folic acid, four gynecologists (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 Mrs 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

pharmacists (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 pharmacists (79%) recommended both a pre- and post-conceptional folic acid intake. Twelve pharmacists (11.5%) recommended taking folic acid preconceptionally, and eight pharmacists (7.7%) recommended it only in the post-conceptional phase. Two pharmacists (1.8%) did not give any recommendation at all (Kastner 2001).

Nutritional Habits and Other Supplementary Vitamins

- The German Food Consumer Study (Nationale Verzehrstudie 1991) found that the average daily folic acid intake for women was 90 μg folic acid equivalent while for men it was 110 μg folic acid equivalent. The recommended reference value was 150 μg (Heseker 1992).
- The Bavarian Food Consumer Study (Bayerische Verzehrstudie 1995) found that the average daily folic acid intake for women was 80 μg folic acid equivalent (Bayerisches Staatsministerium fur Ernahrung, Landwirtschaft und Forsten1997).
- In the German National Health Interview and Examination Survey (Bundesgesundheitssurvey 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 equivalent. The daily intake of 80.6 % of all women was less than 150 μg folic acid. 8.1 % of women in the western federal states (N = 1,231) and 5.5% women in the eastern federal states (N=601) between 18 and 45 years of age were taking multivitamin tablets. 0.6 % were taking folic acid tablets (Heinz 2001).
- The German Nutrition Report 2000 (Ernährungsbericht 2000) (Ernahrungsbericht 2000) stated that the daily intake of folic acid among women was 102.5 μg equivalent. About 70 to 80 % of all people in Germany take less folic acid than recommended.

Women's Sources of Information about Folic Acid

The German National Health Interview and Examination Survey (n = 562) (Bundesgesundheitssurvey 1999, Mensink 1999) found that women heard from the following sources:

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

Egen (1999) interviewed 35 women and found they heard from the following sources:

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

Investigations in Saxony-Anhalt (2000) (Heinz 2001) found that women heard from the following sources:

Sources of information	Prior to pregnancy		During pregnancy	
	N = 227	Rate In percent	N = 1,057	Rate in percent
Physicians	137	60.4	784	74.2
Radio/ TV/ journals	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

- Mrs Egen conducted a study comprising 131 newly delivered women, of which 94 women (72%) confirmed that they had planned their pregnancy. In 1998 Mrs Egen interviewed 118 newly delivered women. Out of them 80 women (68%) had planned their pregnancy (Egen 1999).
- In 1998 a study was performed in Saxony-Anhalt, comprising 567 newly delivered women 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.
- From October 1997 to March 1999 the first German Health Survey was carried out (German National Health Interview and Examination Survey) (Bundesgesundheitssurvey 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).

Molecular-Genetic Investigations

Under the German National Health Interview and Examination Survey (Bundesgesundheitssurvey 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 poses a serious threat to the pregnant woman’s physical or mental health, or if the fetus is affected by malformations.

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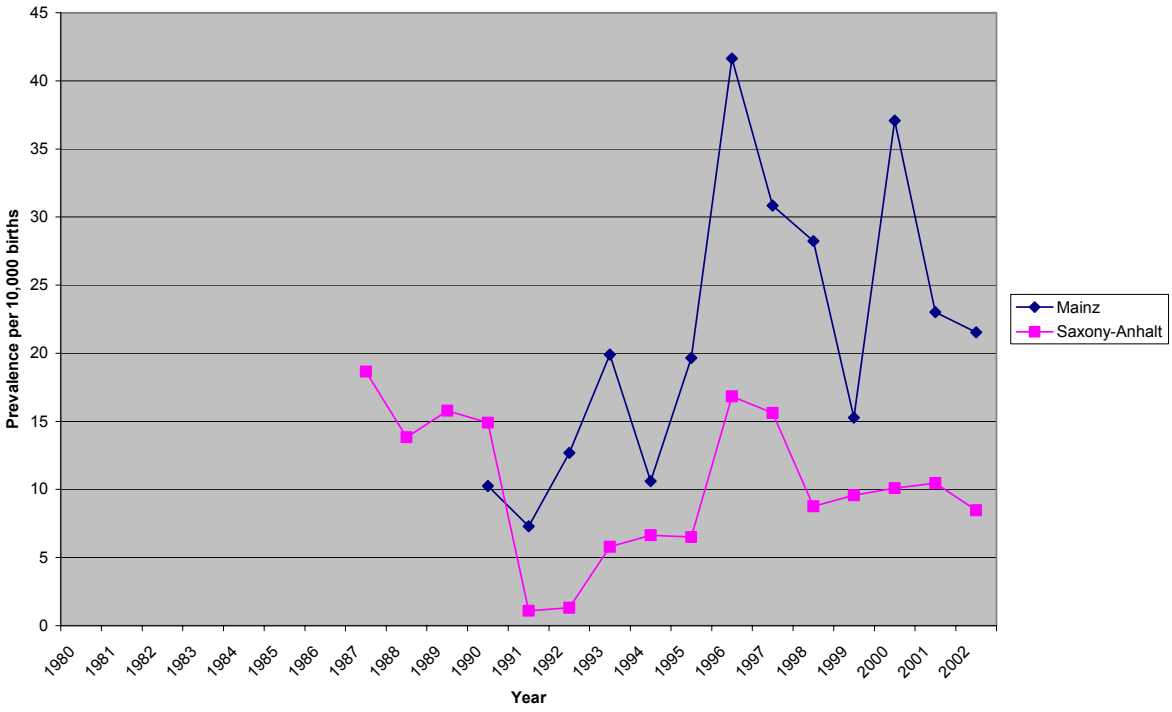
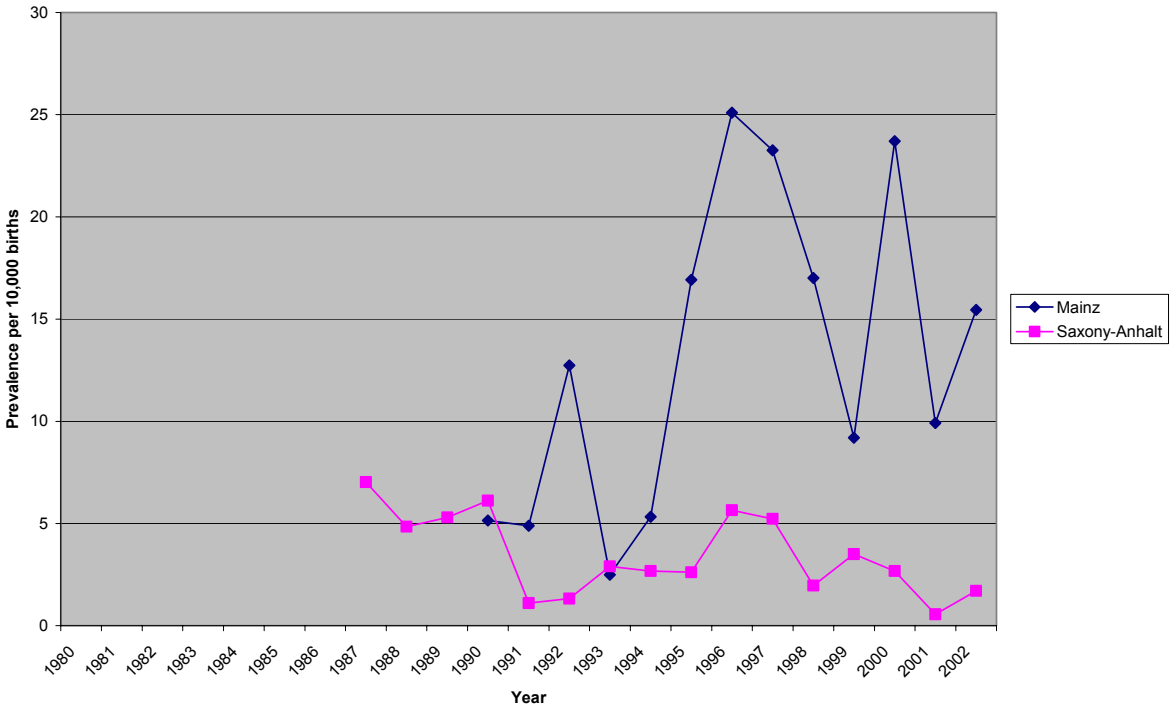
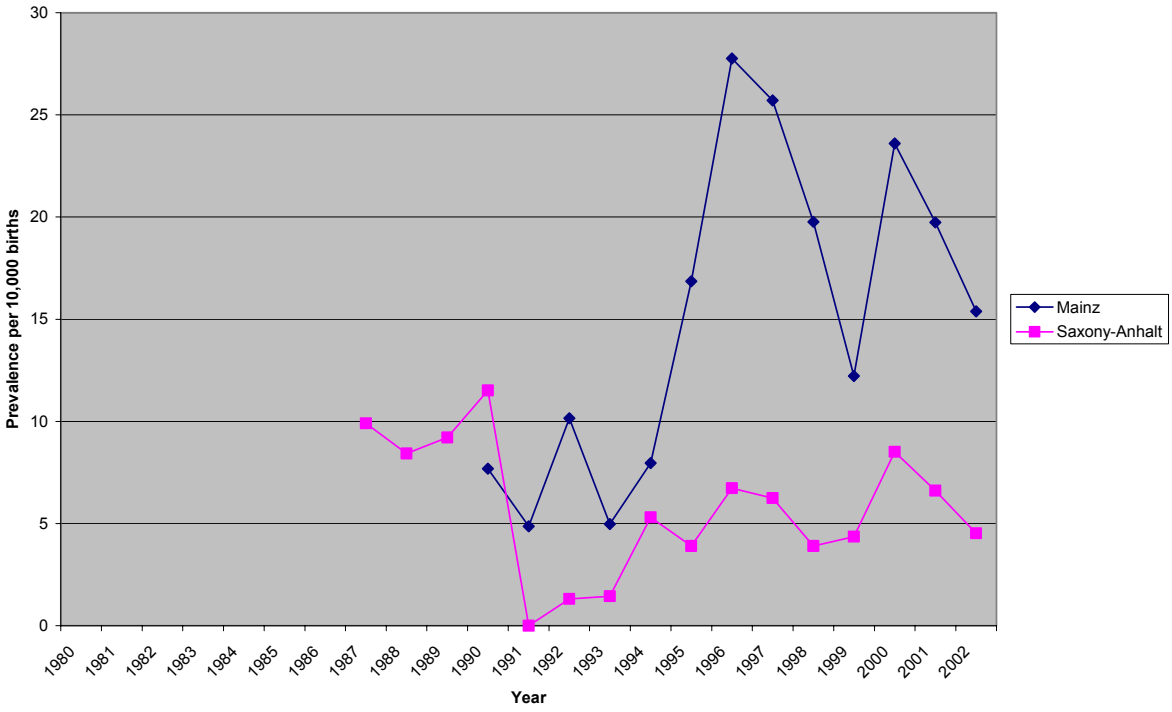
Germany (Mainz and Saxony-Anhalt): Total Prevalence Rates for Neural Tube Defects



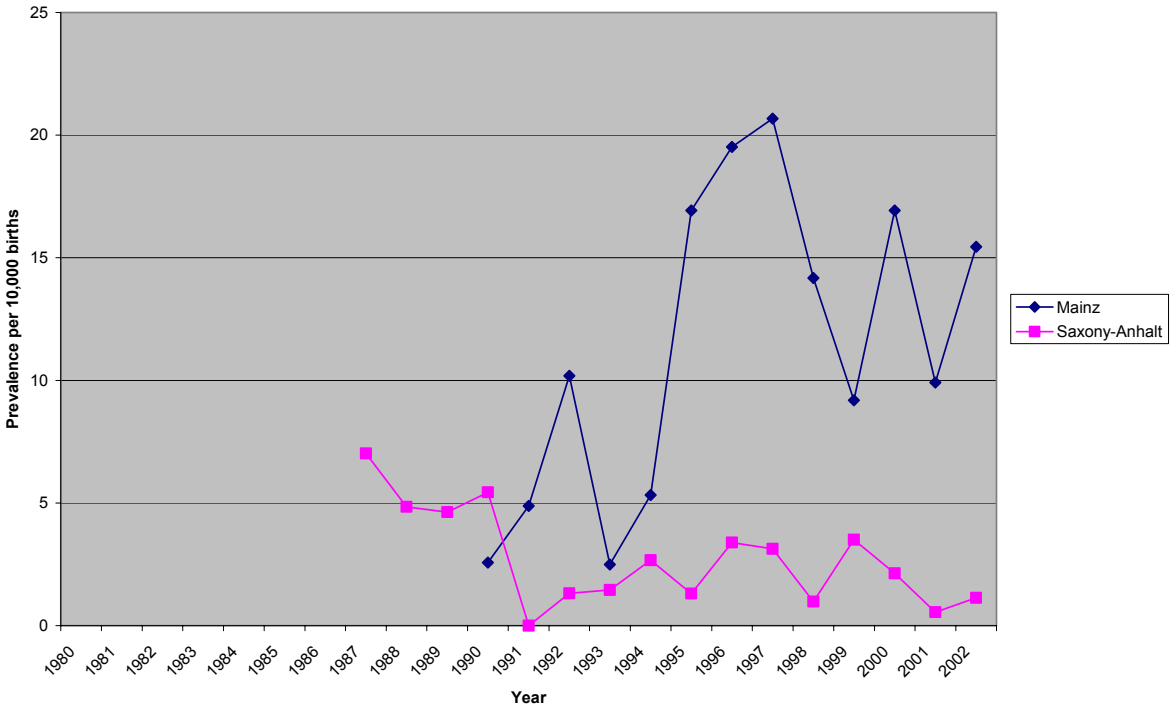
Germany (Mainz and Saxony-Anhalt): Livebirth Prevalence Rates for Neural Tube Defects



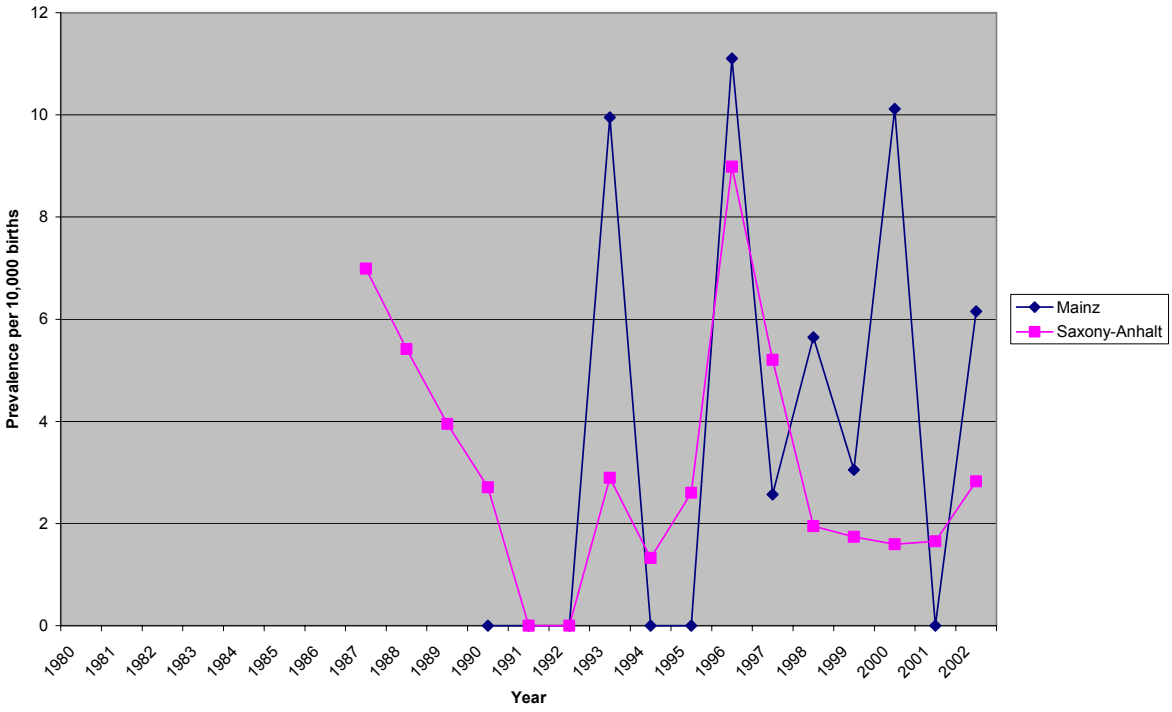
Germany (Mainz and saxony-Anhalt): Total Prevalence Rates for Spina Bifida



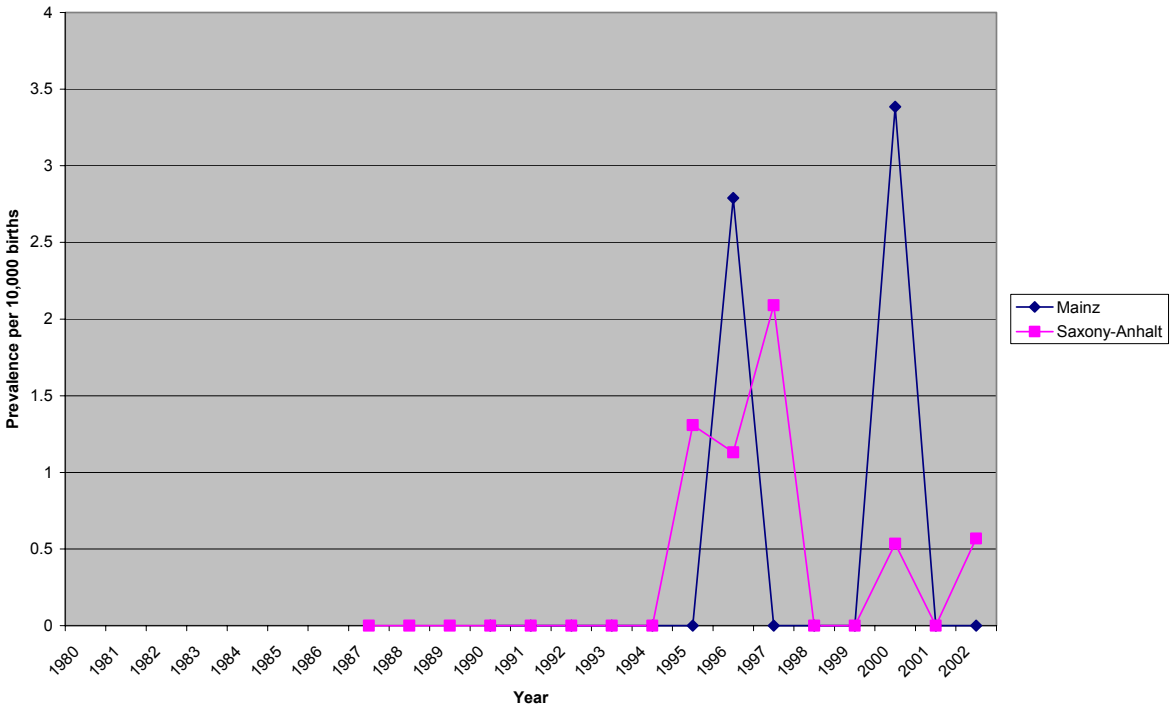
Germany (Mainz and Saxony-Anhalt): Livebirth Prevalence Rates for Spina Bifida



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



Germany (Mainz and Saxony-Anhalt): Livebirth Prevalence Rates for Anencephalus



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. Although there is no mandatory food fortification of staple foods at present, the Food Safety Advisory Board of Ireland (an official body) in a 1998 report[1] to the Minister for Health recommended that food fortification should be considered as a complimentary measure to supplementation (rather than an alternative).

However, recent and ongoing controversy on the fluoridation of water supplies and the absence of mandatory fortification of staple foodstuffs elsewhere in the European Union have not provided an ideal climate for the introduction of mandatory fortification in Ireland. 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); a report is due soon.

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. The most recent high profile promotion of folic acid consisted of a joint cross-border initiative between the Departments of Health in the Republic of Ireland and Northern Ireland in late 2000 and early 2001. This was a media campaign lasting some months with prime-time television and radio advertisements, and also involved daily newspapers. At a more local level, health promotion units and public health departments in the regional health boards undertake promotion of folic acid through a variety of channels, generally on an on-going basis. The Health Promotion Unit of the Irish Department of Health has undertaken much of this work at a national level.

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. [2-8] 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%

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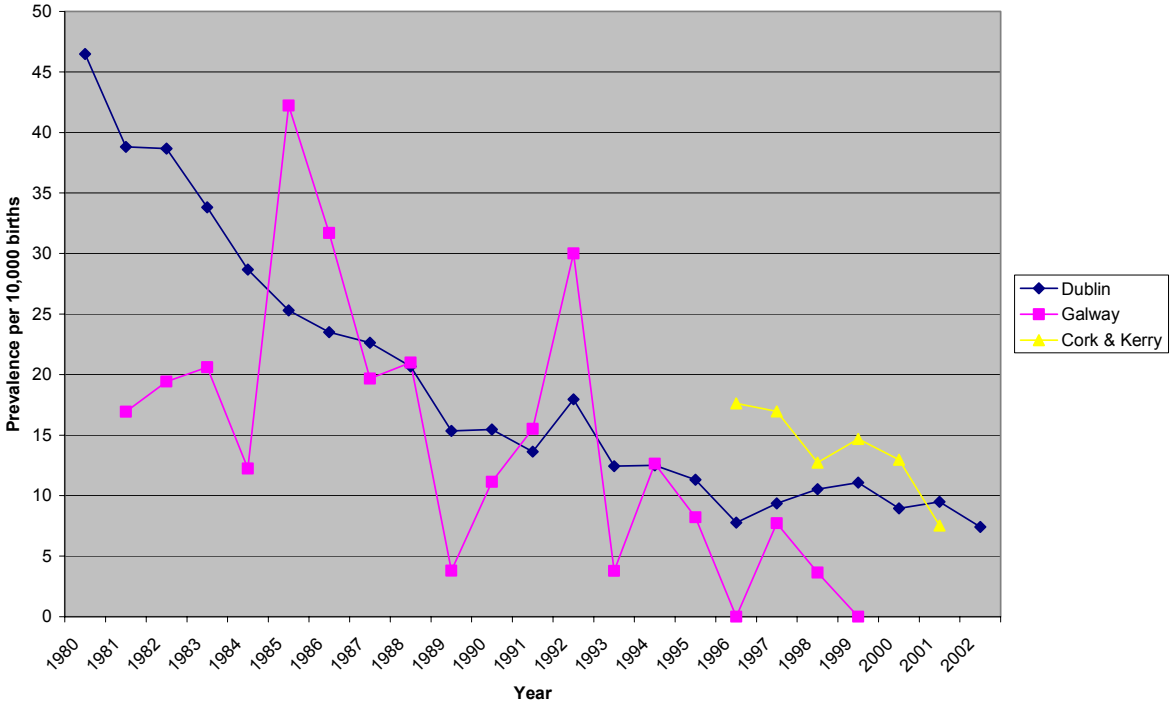
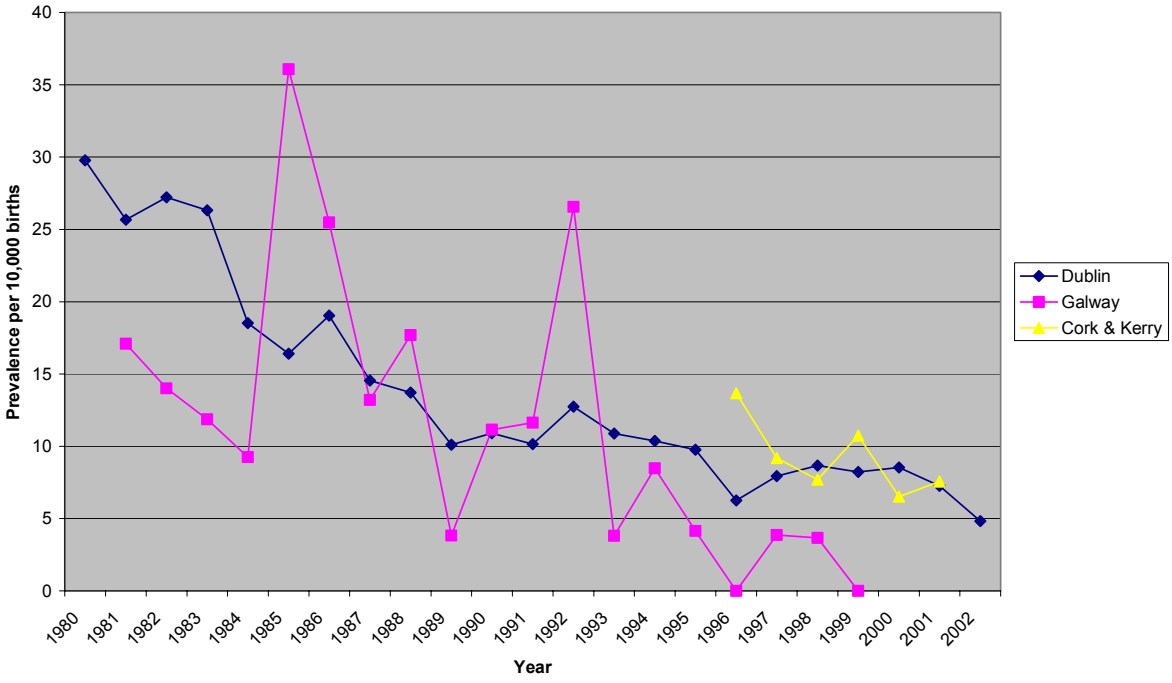
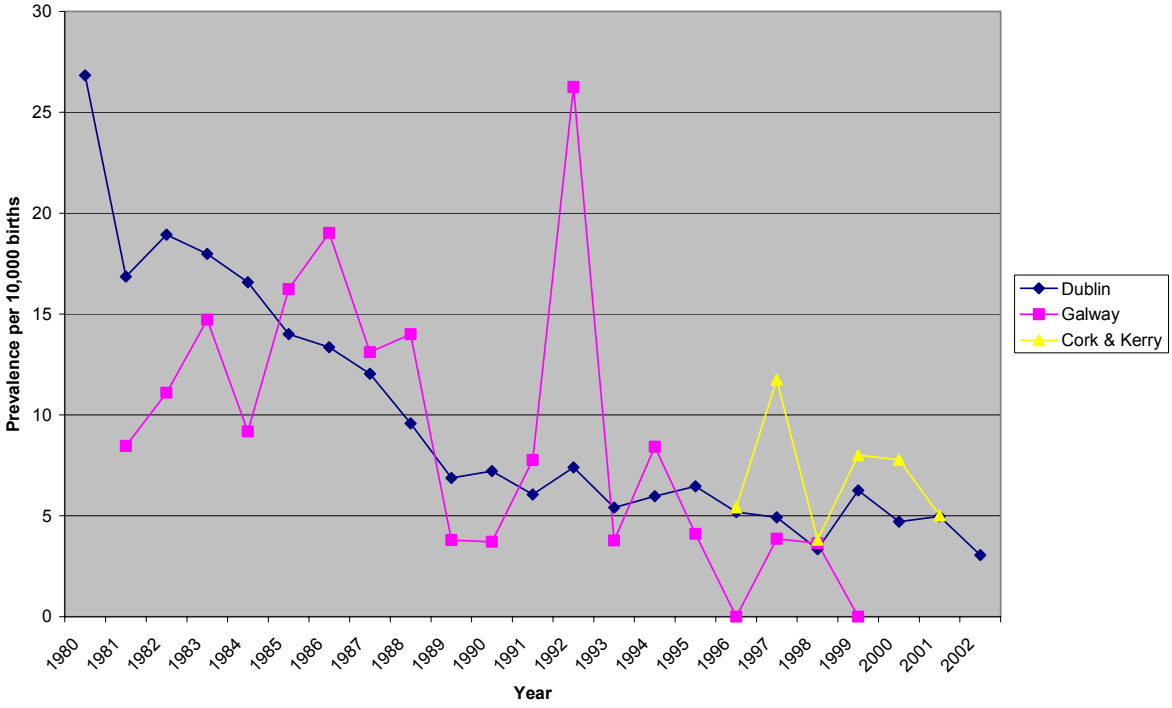
Ireland (Cork & Kerry, Dublin and Galway): Total Prevalence Rates for Neural Tube Defects



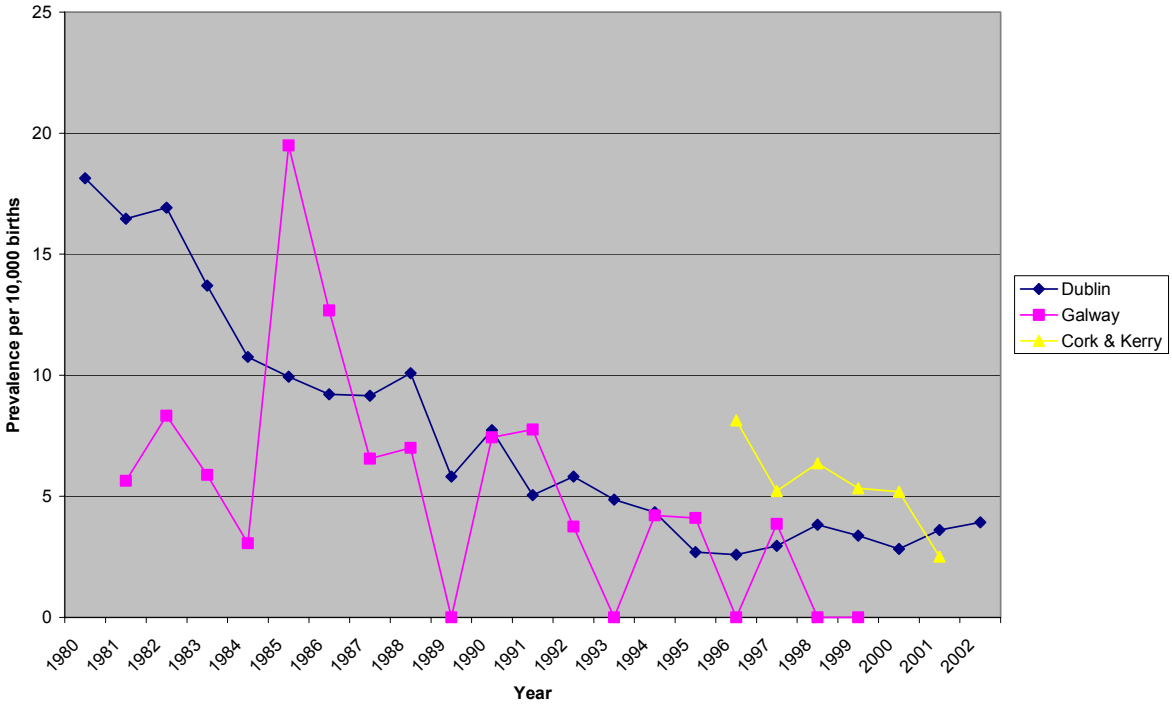
Ireland (Cork & Kerry, Dublin and Galway): Livebirth Prevalence Rates for Neural Tube Defects



Ireland (Cork & Kerry, Dublin and Galway): Total Prevalence Rates for Spina Bifida



Ireland (Cork & Kerry, Dublin and Galway): Total Prevalence Rates for Anencephalus



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR ITALY

A J Neville, E Calzolari, S Bianca and G Scarrano and F Bianchi.

Folic Acid Supplementation Policy

An Italian Network for the Promotion of Folic Acid for the Prevention of Congenital Defects has been formed. It is hosted by the Superior Health Institute (ISS) and held its first national conference in April 2004. 55 different organisations including registries, nutritionalists, the federation of general practitioners, researchers and spina bifida parents' associations met together to propose and agree recommendations regarding folic acid supplementation. 120 organisations are now part of the Network.

The recommendation, directed at the medical profession, has received formal support from 70 organisations. The summary recommendation was approved in November 2004 and is as follows:

It is 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 now freely accessible at http://www.cnmr.iss.it/

The recommendation will now be formally sent to the Minister of Health, President of the Superior Health Institute, President of the Medicines agency etc**.**

Implementation

At the April meeting, 31 project abstracts in support of the folic acid supplementation policy were presented and published [1]: Fourteen projects were classed as promotion and information to the population, five projects were on surveillance, eleven were research and one was on training. Details can be found at **http://www.cnmr.iss.it/**

The Italian Ministry of Health in the Drugs Bulletin [2] directed both to family practitioners and specialists has published the draft recommendation and distributed 360,000 copies. The first “Prevention of Spina Bifida” week organised by the spina bifida parents’ association, with the support of the Ministry of Health was held (2-10 October 2004) to promote the recommendation. There were also four scientific conventions on spina bifida. A leaflet on primary prevention was distributed to women at family clinics and through supermarkets. A television advertisement on primary prevention was shown on both national and local TV stations and a freephone helpline set up to provide information to interested women. A second Spina Bifida week is planned for next year.

The Network has identified issues to be addressed in the implementation phase.

- Given the numerous implementation initiatives launched by different organisations, many at a local level, the Network has a role to play in avoiding overlap and using financial resources most effectively.
- The effectiveness of different communication campaigns must be evaluated and the learning shared through the Network.
- Projects for training and widespread communications require a business plan to present the costs and benefits foreseen.
- The introduction of preventative medicine inside the health system is a new and difficult ground in Italy
- Whilst the Network provides a national forum, representation from the south of the country is less. Attention to advocacy and coverage is necessary.

Folic acid supplements on sale

Many of the preparations on sale in Italy are at high doses (5 to 15mg tablets), and for this reason the recommendation has a fall back position of 5mg per week, despite concerns regarding compliance. A 0.4mg tablet has now been registered and declared refundable (Class A) and once price negotiations have been concluded, it will be 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. An estimate has been made that a total 5 million packs of folic acid tablets are sold each year, but the use is unclear.

Food Fortification Policy

The 'Common statement of representatives of national food safety agencies and institutions involved in nutrition in the European countries and Norway (13 January 2004)' presented to the Italian Folic Acid Network in April 2004, advocates voluntary rather than mandatory fortification. This is in line with Italian law regarding addition of vitamins to foods.

Health Education Initiatives

Many health education initiatives have been started at the regional level. Regional strategies and information packs have been produced and information regarding the initiatives being taken is exchanged through the Network newsletter. At the Network meeting in April 2004, a total of 14 projects on Promotion and Information to the population were presented. Many different organisations have web pages dedicated to folic acid e.g http://www.ceveas.it/SaPeRiDoc

At the national level FIMMG, the Italian Federation of General Practitioners is planning a training cascade regarding the correct use of folic acid and a dynamic web site and forum. A publicity spot on folic acid will be included in all other residential courses organised in the next 12 months.

Knowledge and Uptake about Folic Acid

To our knowledge no national epidemiological studies have been conducted. A summary of the Italian Birth defects and Folate Situation was published in 2003 [3]

At a regional level the following studies have been reported:

FOLIC ACID IN TUSCANY, ITALY: WHAT DO WOMEN KNOW, THINK, AND DO? [4]

The effectiveness of periconceptional folic acid supplementation to prevent neural tube defects is well established, and some protection against other adverse pregnancy outcomes have been suggested. Italian families, because of their low

fertility, could substantially benefit from such prevention opportunity. Although data on use and knowledge are critically needed for planning and evaluating public health action, few are available.
Methods: We conducted a survey of knowledge, attitude, and use of folic acid among women who had recently given birth to a healthy newborn in Tuscany. This group was targeted because it would have been a premiere target for folic acid campaigns. We focused on one region to maximize the coverage of maternity wards. The questionnaire was based on questionnaires used in the United States, further modified and pilot tested in Tuscany. Trained interviewers (AC, SCGB, MS) visited maternity wards in and around Florence, Pisa and Siena (Tuscany, Italy). Eligible women were mothers present in maternity wards, within three days of delivery of an unaffected child. We categorized use in three groups: 1) Appropriate folic acid (AFA), defined as daily use of 400 mg or more of FA from before pregnancy through the first month of pregnancy (periconceptional period); 2) other folic acid use (OFA), defined as use during pregnancy but not during the periconceptional period; 3) No folic acid (NFA), defined as no use during pregnancy. We contrast AFA with the other two groups separately or combined (ONFA).
Results: We present findings on 1,066 respondents who were interviewed between February and April 2002.
Use: 5.7% of women (n=61) used folic acid as recommended (AFA). 52% (n=546) took folic acid but not in the periconceptional period (OFA), and 43% (n=452) did not use folic acid (NFA)(for 7 subjects information was not sufficient to classify folic acid use). AFA was more frequent among women who were older, better educated, and had seen a doctor before conception. Common reasons for not taking vitamins included “not specifically recommended by doctor” (37%) and “no perceived need (I eat well)” (20%).
Knowledge and attitudes: more women in the AFA group reported knowing that folic acid could prevent birth defects (43% vs. 17% among ONFA), and that it should be taken from before conception (31% vs. 9%, respectively). Most women (91%) who did not use folic acid appropriately (ONFA) reported that they would be willing to use folic acid daily to improve pregnancy outcomes. All women, regardless of FA use, regarded the physician as the most authoritative source of health information and counseling (67%).

Comments and conclusions: We found that approximately 1 in 17 women (5.7%) who had just given birth to a baby had used folic acid periconceptionally. This percentage is low but similar to that found in some other European countries. The survey also suggests that information campaigns, directly to women but also through the primary physician and specialist, could lead to substantial increases in knowledge and possibly periconceptional use of folic acid supplements.

PRIMARY PREVENTION OF NEURAL TUBE DEFECTS: LACK OF INFORMATION ABOUT FOLIC ACID SUPPLEMENTATION IN ITALY: EMILIA-ROMAGNA REGION[5]

A study was conducted at the Obstetric Clinic of Bologna on the percentage of women who had correctly consumed folic acid in the periconceptional period. In the early part of the study, 3.5% of women took folic acid correctly; a year later 5% did so.

Objective: To detect the level of knowledge of women of childbearing age about the ability of folic acid (FA) supplementation to reduce the risk of having a pregnancy affected by neural tube defects (NTD). To administer an ad hoc questionnaire prepared in relation to the goals of the BIOMED Project and conduct a survey in Bologna (one of the centres of the IMER Registry, Italy) on the policy of consuming FA before conception (at least 2 months) and in the first quarter after conception. Design: An educational campaign about the health benefits of periconceptional consumption of FA and reduction of the risk of NTD. Participants: A sample of women in hospital for delivery during November and December 1999. Methods: The questionnaire, in Italian, was administered to 302 women with healthy babies who were randomly selected in the 2-month period. The same doctor interviewed all the women. The information collected included data about maternal age, parity, education, smoking use, knowledge of the effect of FA and of food intake, changes in diet during pregnancy, and consumption of FA or a FA-containing multivitamin, with details about the period of consumption. Main outcome measures: Number of women who were aware of the FA recommendations, number who were aware of what FA is, who advised them about the benefits of FA, and when FA should be taken. Results: Only 9 women (2.9%) took FA correctly, in the perinatal period. These 9 women were mainly informed by their gynaecologist about FA preventive effect for NTD, tended to have a higher educational level (university) (χ^2=8.920; 2 gdl; p=0.0012) and tended to be older (> 30 years) (χ^2=9.364; 2 gdl; p=0.009).

Conclusions: These results demonstrate the lack of medical information in Italy about the preventive effect of FA and the necessity of carrying out information campaigns addressed to gynaecologists, general practitioners and to all women in childbearing age.

PERICONCEPTIONAL FOLIC ACID INTAKE BY SICILIAN COUPLES AT A RISK OF RECURRENCE OF NTD[6]

In Sicily a study was carried out on periconceptional folic acid intake by Sicilian couples at increased risk of NTD. The authors conclude that pregnant Sicilian women at risk for recurring NTD interviewed by the authors were not aware of the possible prevention of NTD using folic acid supplements during the periconceptional phase. In the study period, January 1997 until December 1998, 18 couples were identified as being at risk for recurring NTD. A further 15 couples showed a positive family history for NTD. Of 11 planned pregnancies, none of the pregnant women took folic acid during the periconceptional phase. Details of the study, "Periconceptional folic acid intake by Sicilian couples at a risk of recurrence of NTD": AIMS: The authors aimed to evaluate the frequency with which pregnant Sicilian women with a high risk of recurring neural tube defects (NTD) attending the Ultrasonography and Prenatal Diagnosis Clinic in the Department of Diagnosis and Treatment at Ospedale S. Bambino in Catania were aware of the preventive effect of folic acid supplements during the periconceptional period and whether they therefore took folic acid supplements before the next pregnancy. METHODS: All pregnant women undergoing ultrasonography between January 1997 and December 1998 were interviewed. It was noted whether any earlier offspring had suffered from NTD or whether relatives (sisters, brothers, parents) had suffered from a NTD. They were also asked whether they knew about the preventive effect of periconceptional folic acid supplements on the development of NTD, whether their pregnancy was planned and whether they had taken periconceptional folic acid supplements and, if so, at what dose. RESULTS: Eighteen couples were identified as being at risk for recurring NTD: 3 cases had an earlier pregnancy resulting in NTD (2 cases of spina bifida and 1 case of anencephaly) with a negative family history for NTD; a further 15 couples showed a positive family history for NTD. None of the women were aware of the preventive effect of folic acid supplements during the periconceptional period on the development of NTD. Out of 11 planned pregnancies, none of the pregnant

women took folic acid during the periconceptional phase. CONCLUSIONS: Pregnant Sicilian women at risk for recurring NTD interviewed by the authors were not aware of the possible prevention of NTD using folic acid supplements during the periconceptional phase.

A similar level of ignorance was found in a study conducted by the Emilia Romagna region (2)

Proportion of pregnancies which are planned

No information available.

Laws Regarding Termination of Pregnancy

Voluntary termination of pregnancy became legal in Italy in 1984. Termination due to a congenital anomaly can be 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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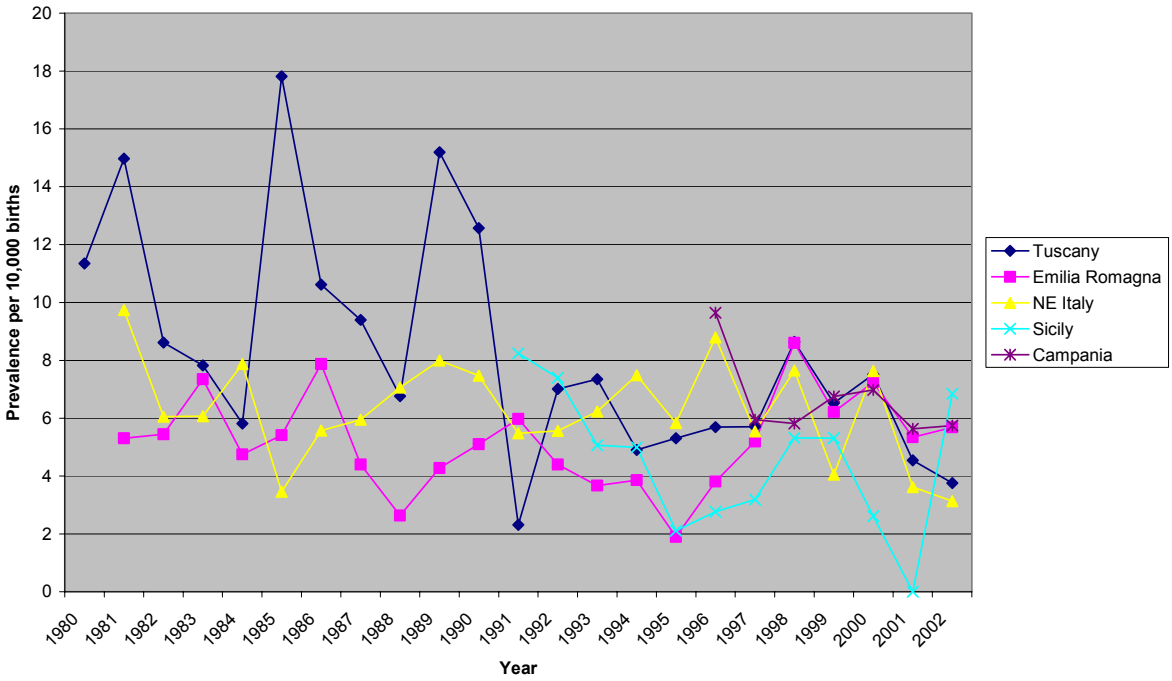
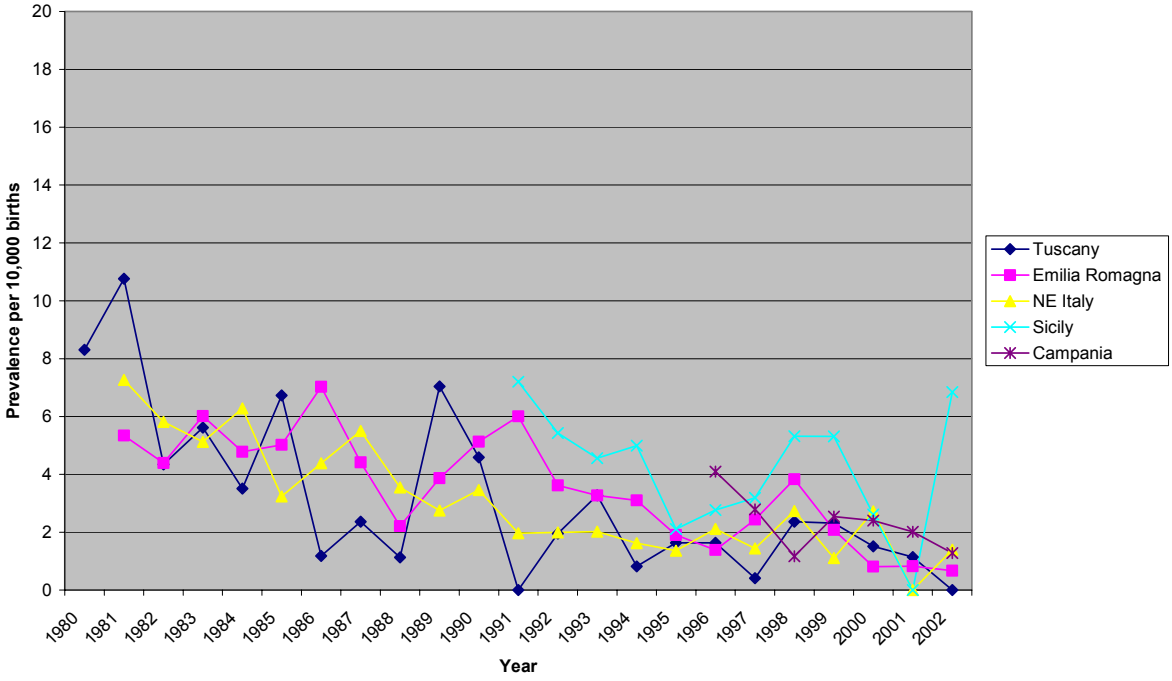
Acknowledgement

Data regarding the sales of folic acid preparations was provided courtesy of ITALFARMACO. Our thanks to FIMMG and the Italian Folic Acid Network for their contribution to this chapter.

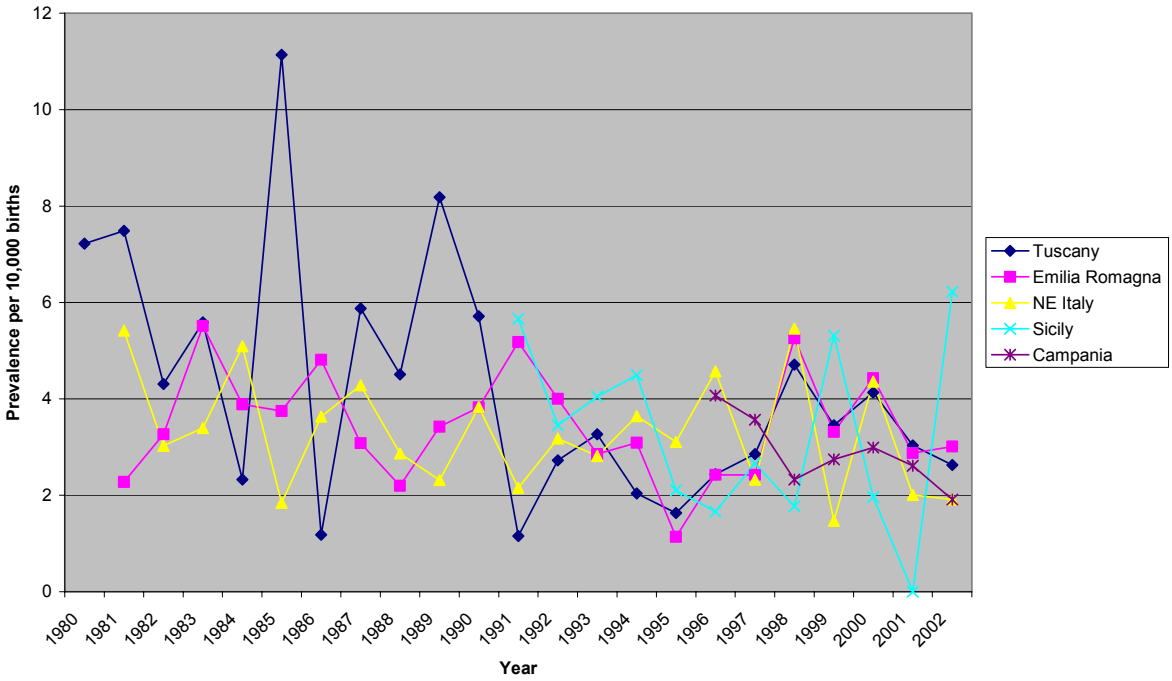
Italy (Campania, Emilia Romagna, North East Italy, South East Sicily and Tuscany): Total Prevalence Rates for Neural Tube Defects



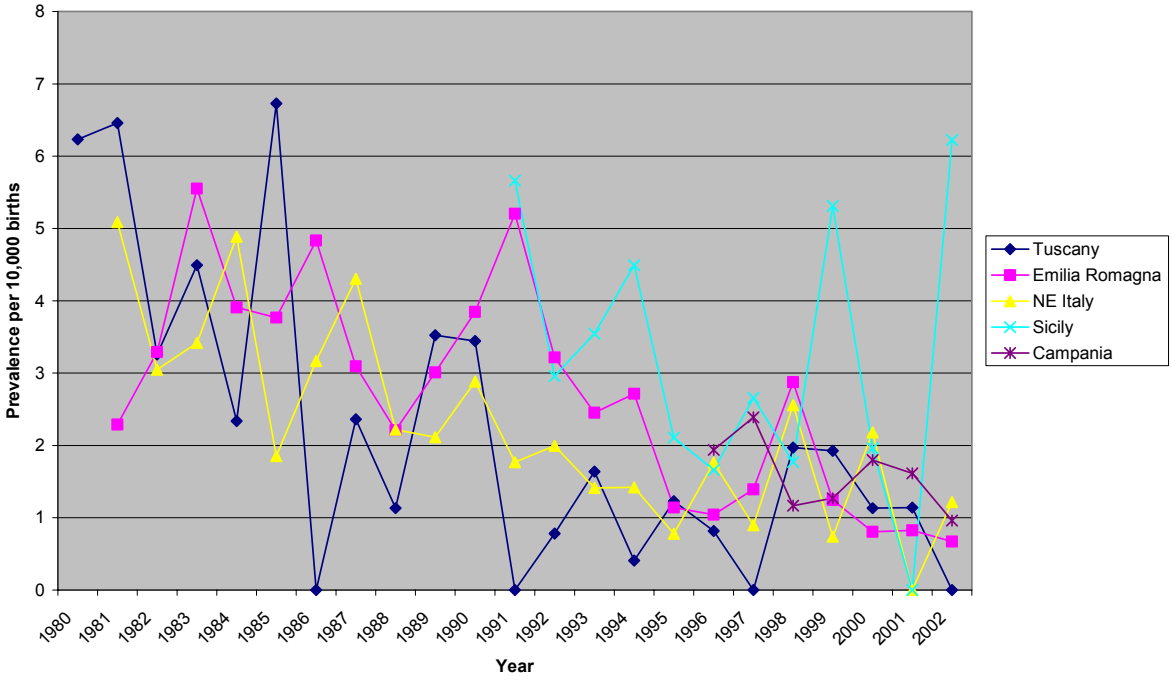
Italy (Campania, Emilia Romagna, North Easy Italy, South East Sicily and Tuscany): Livebirth Prevalence Rates for Neural Tube Defects



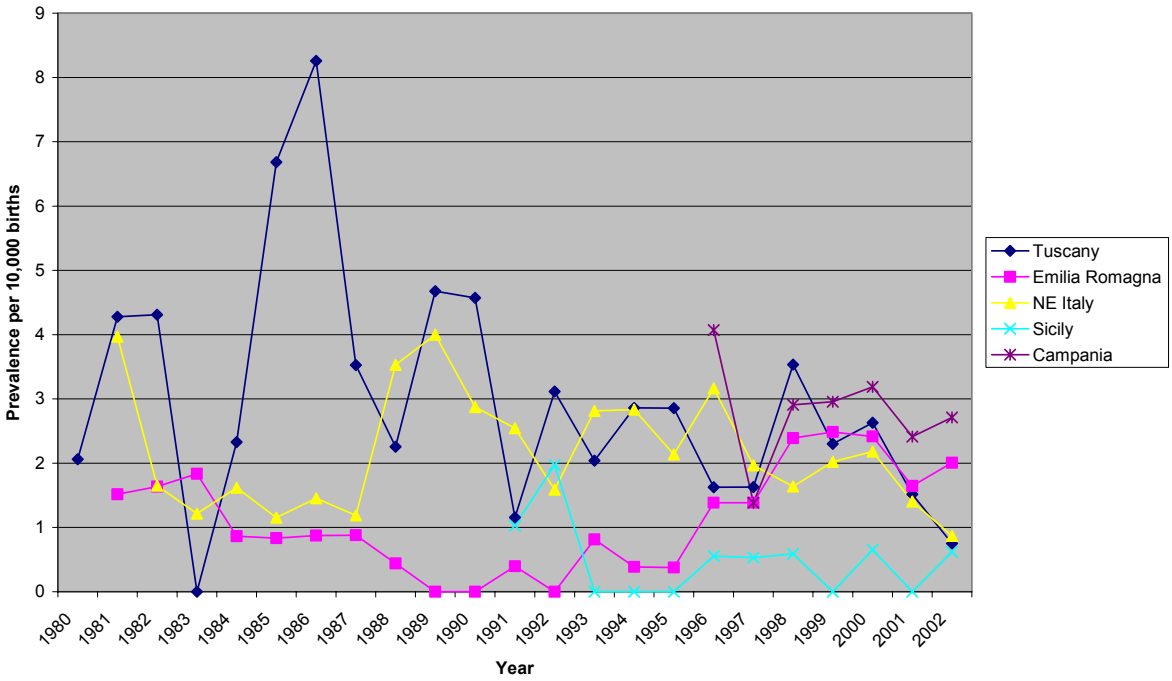
Italy (Campania, Emilia Romagna, North East Italy, South East Sicily and Tuscany): Total Prevalence Rates for Spina Bifida



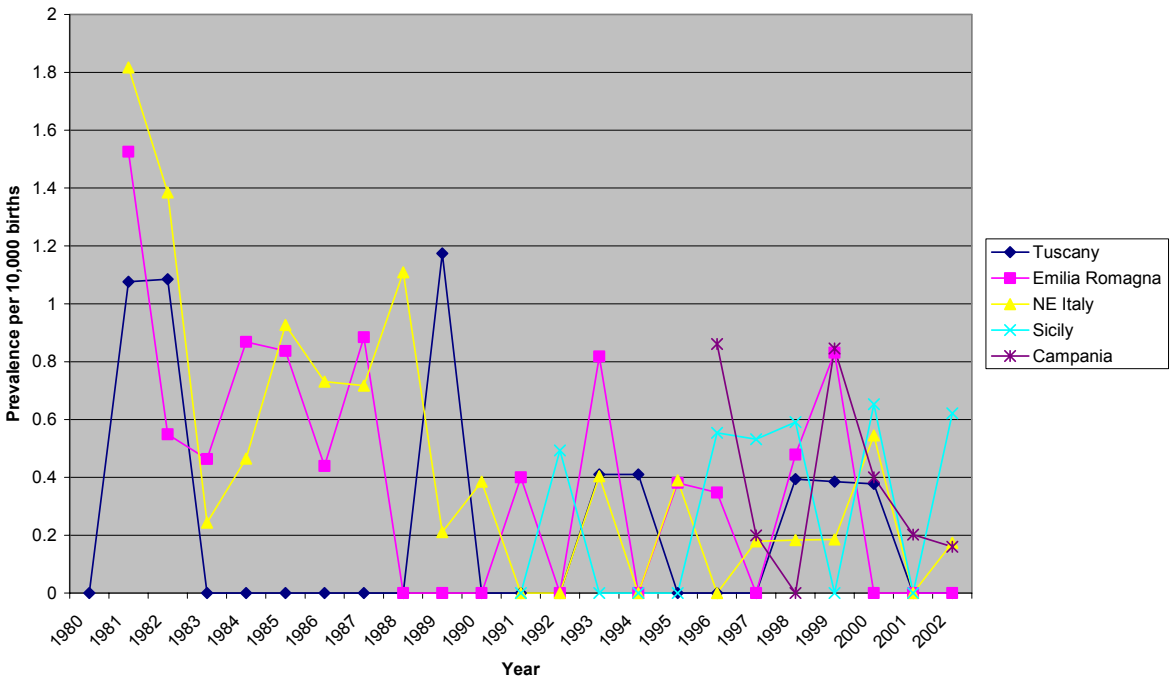
Italy (Campania, Emilia Romagna, North East Italy, South East Sicily and Tuscany): Livebirth Prevalence Rates for Spina Bifida



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



Italy (Campania, Emilia Romagna, North East Italy, South East Sicily and Tuscany): Livebirth Prevalence Rates for Anencephalus



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 being planned. However, a wide variety of imported fortified cereals and malted drinks are available. Cereals are relatively expensive locally and may not be accessible to people of all income brackets. Fortified breads are not readily available.

Health Education Initiatives

No official Department of Health Promotion campaigns have been undertaken but one is being planned for the near future. 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.

No official Department of Health Promotion campaigns 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. In 2002, a health promotion officer presented his postgraduate research investigating the needs of a national health promotion campaign to raise awareness of the benefits of periconceptional folic acid supplementation among sexually active Maltese women of childbearing age. This research utilized the data collected during a folic acid survey conducted in 1999-2000 as part of the needs assessment [1]. The results of this research will influence the health promotion campaign regarding periconceptional folic acid will be launched officially in Malta.

Folic Acid Awareness and Uptake

A study regarding folic acid awareness in Maltese mothers was undertaken between October 1999 and February 2000 (Gatt 1999). 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. It is hoped that a similar study will be carried out before any Health Promotion Campaigns are initiated and a repeat study will be done some time after the campaign.

Proportion of pregnancies which are planned

No information available

Laws Regarding Termination of Pregnancy

In Malta, termination of pregnancy is not legal.

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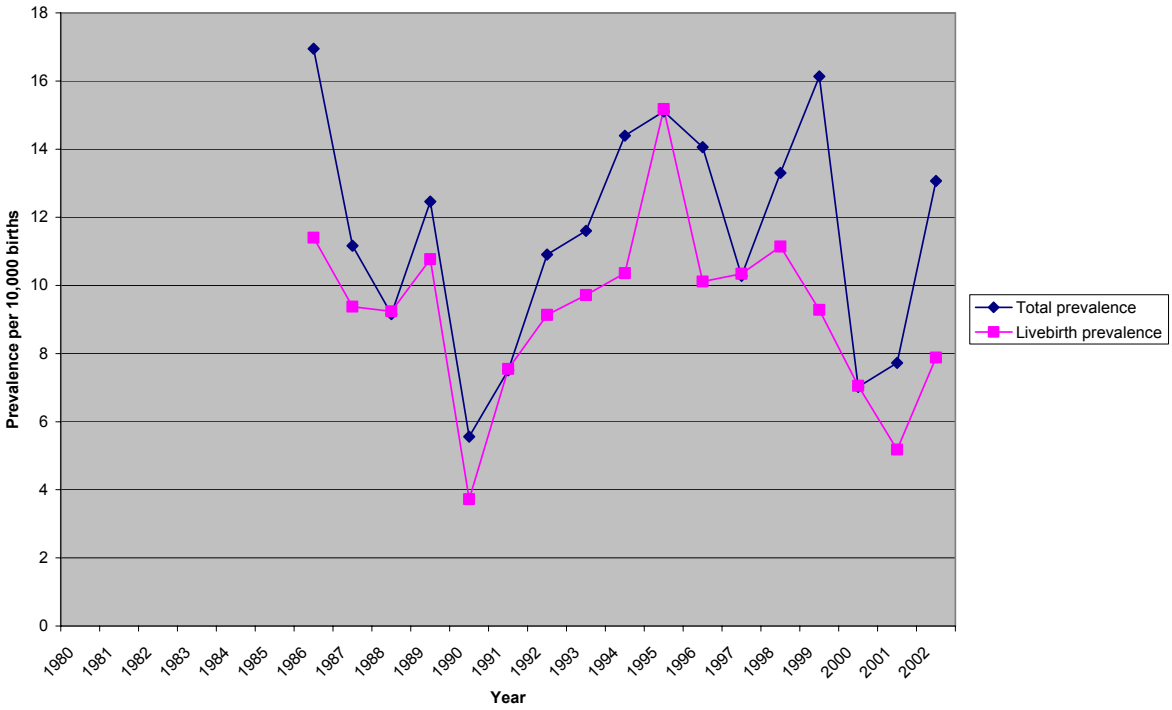
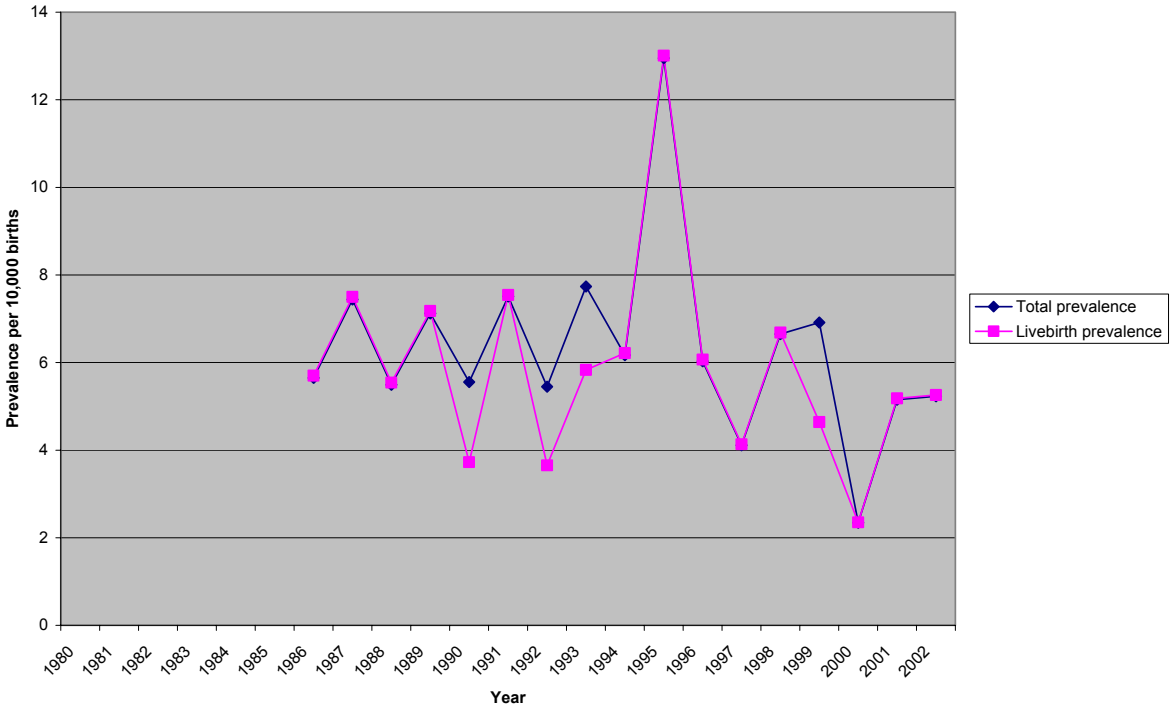
Gatt M **(1999)** Periconceptional Folic Acid Supplementation in Malta, in 'Half Yearly Report of Malta Congenital Anomalies Register, Malta Congenital Anomalies Registry, Department of Health Information.

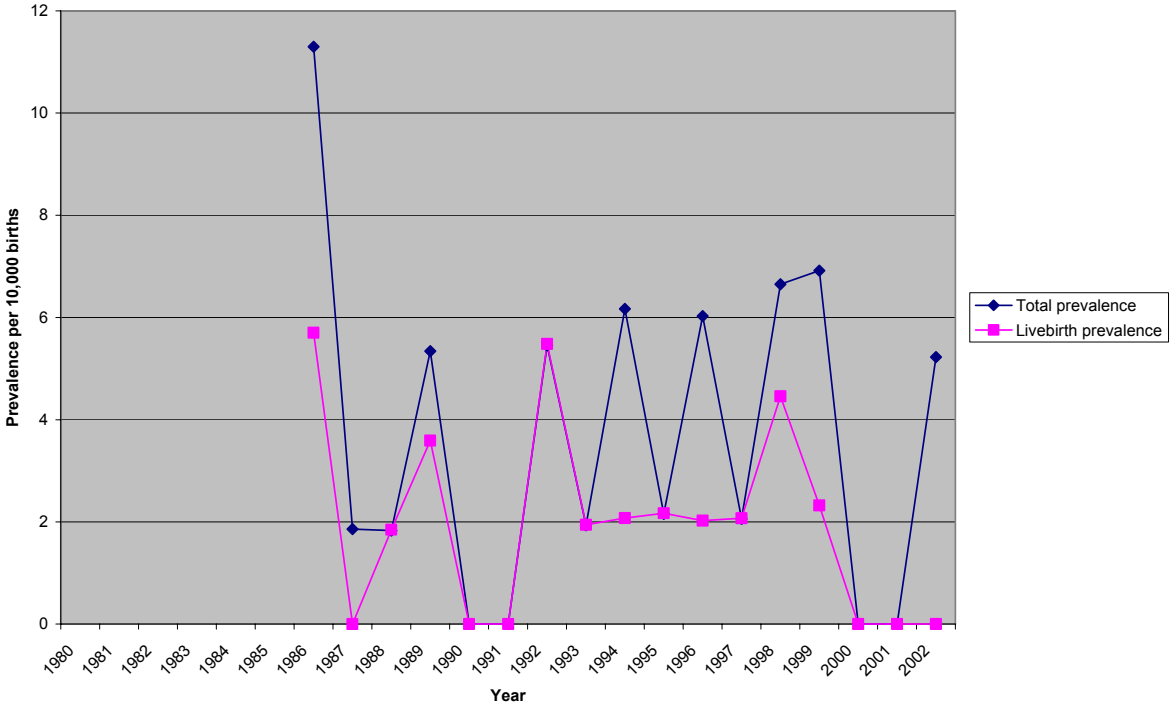
Malta: Total and Livebirth Prevalence Rates for Neural Tube Defects



Malta: Total and Livebirth Prevalence Rates for Spina Bifida



Malta: Total and Livebirth Prevalence Rates for Anencephalus



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 Sports[1].

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 vitamins are added to (expensive brands of) marmalade. Folic acid was not on the list of vitamins because of the risk of masking a vitamin B_{12} deficiency; only restoration was possible.

The likelihood of appropriate fortification of food with folic acid in the Netherlands is further decreased after the publication of a recent report of the Dutch Health Council.[2] They did not advise fortification of staple foods such as flour, but only products that can be specifically aimed at the target-population: women who want to become pregnant. No suggestions were made as to what these products could be or what the recommended amount of folic acid to be added to these products would be. For now, fortification with folic acid is officially not allowed for any product. However, for the past two years Kellogg's has put cornflakes with extra folic acid on the Dutch market. Very recently the advocate-general of the European Court of Justice decided that fortification of special foods must be allowed in the Netherlands.

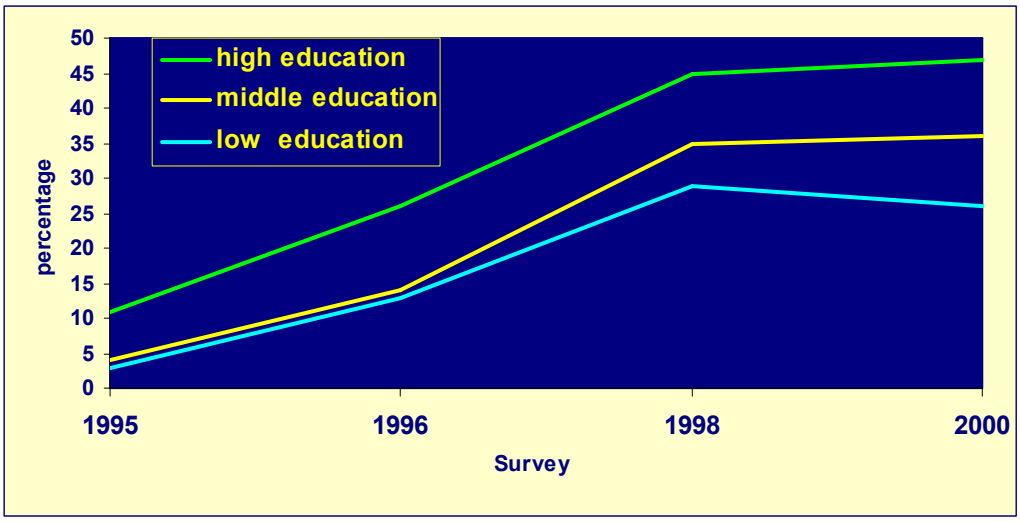
Health Education Initiatives

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

period [3]. This campaign was carried out in 1995.

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 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 surveys [4-8]. 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. We recently did another survey in the Northern Netherlands, and the results will be published soon.

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 education [9] . 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 pregnancy [10] The pilot study is currently being reproduced on a regional scale and will be reproduced in the whole country.

Proportion of Pregnancies which are Planned

The Netherlands has a high percentage of planned pregnancies[11]. 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 periconceptional 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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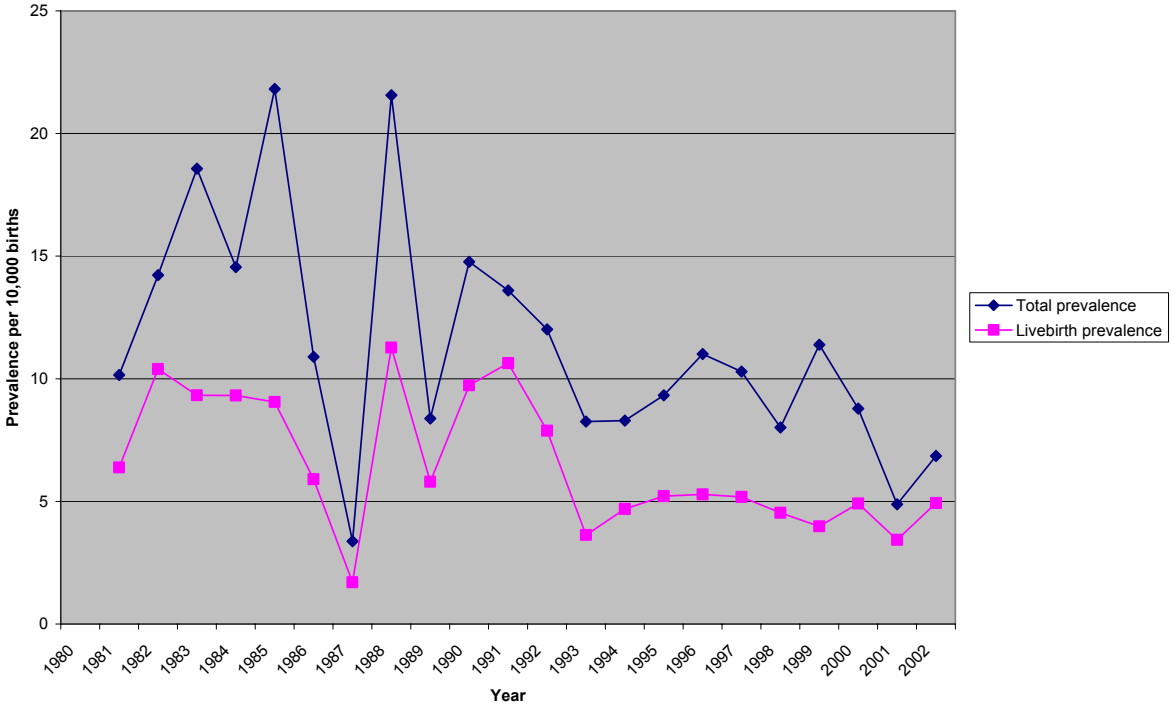
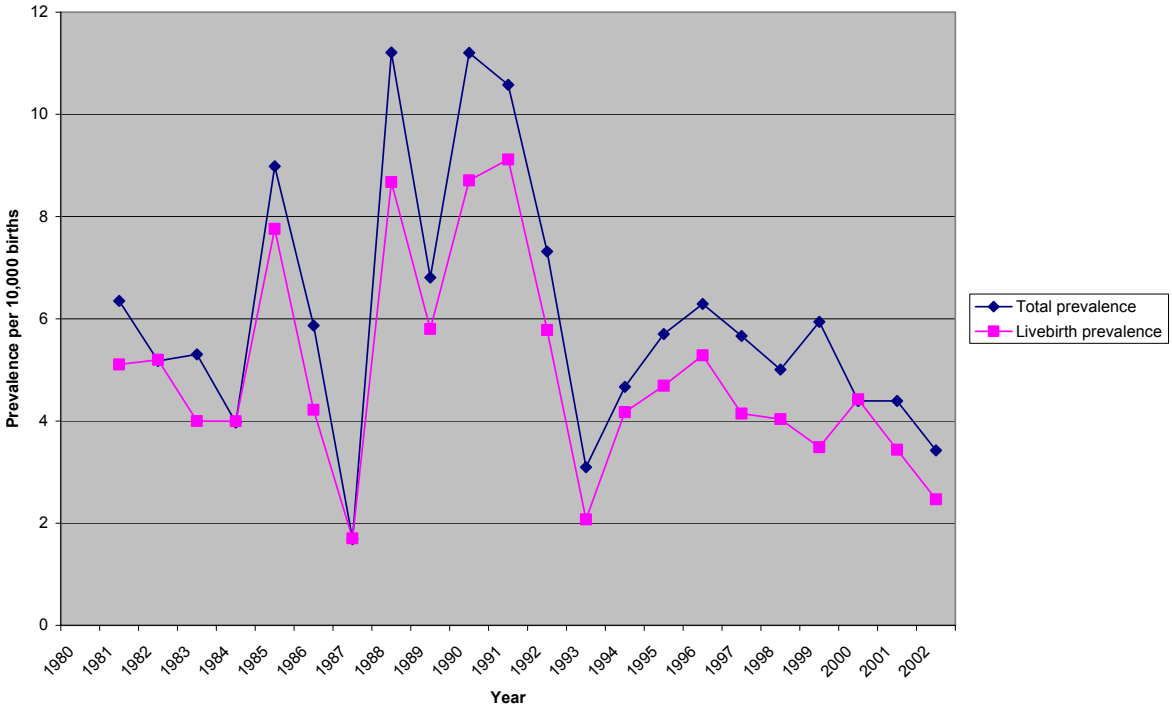
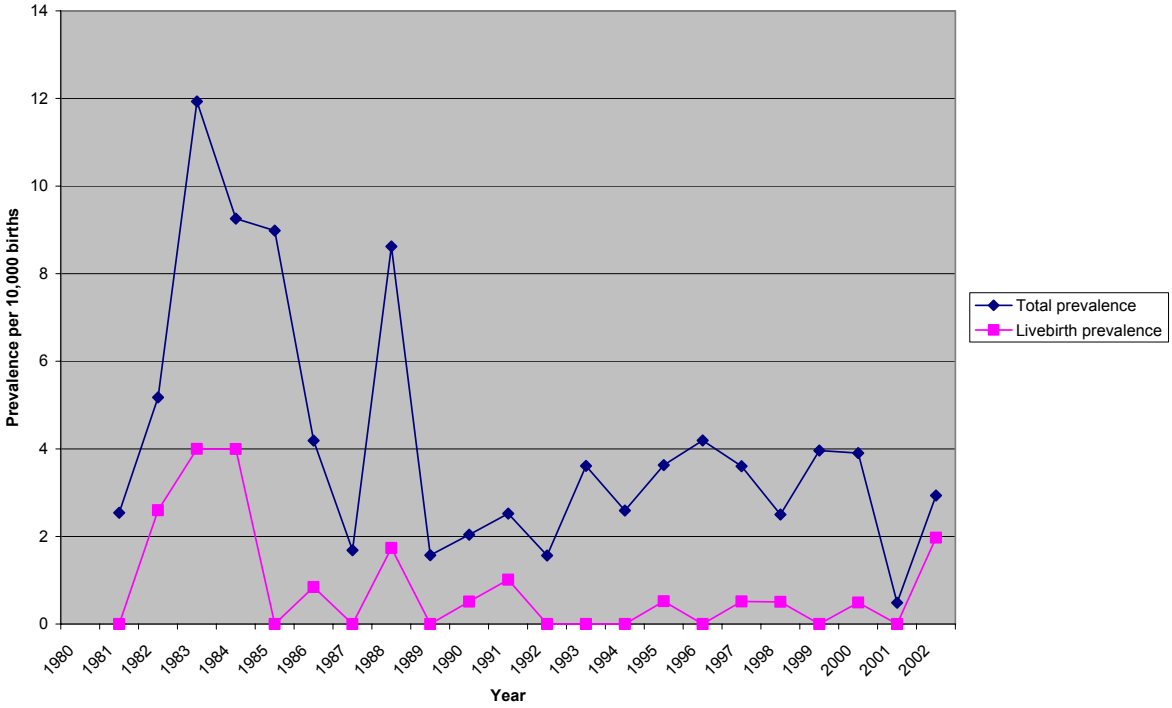
The Netherlands (Northern): Total and Livebirth Prevalence Rates for Neural Tube Defects



The Netherlands (Northern): Total and Livebirth Prevalence Rates for Spina Bifida



The Netherlands (Northern): Total and Livebirth Prevalence Rates for Anencephalus



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 the 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, child-bearing women 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 periconceptional 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 periconceptional 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, contents of folic acid 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 gynecology 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.

Folic Acid Awareness and Uptake

One paper was published in Norway concerning the awareness in the child bearing population of recommendations regarding folic acid supplementation and the uptake of advice regarding folic acid supplementation (Vollset & Lande 2000). After the recommendations were issued in the Spring of 1998, a random sample of 1500 Norwegian women of reproductive age was selected for study during the autumn 1998. Among the 1500 women, telephone interviews were carried out with 1146 women (Vollset & Lande 2000). A repeat study was done in 2000, in which telephone interviews were carried out with 1218 women. Results from this repeat study are not yet published, but some results are referred to here.

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 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.

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 to18 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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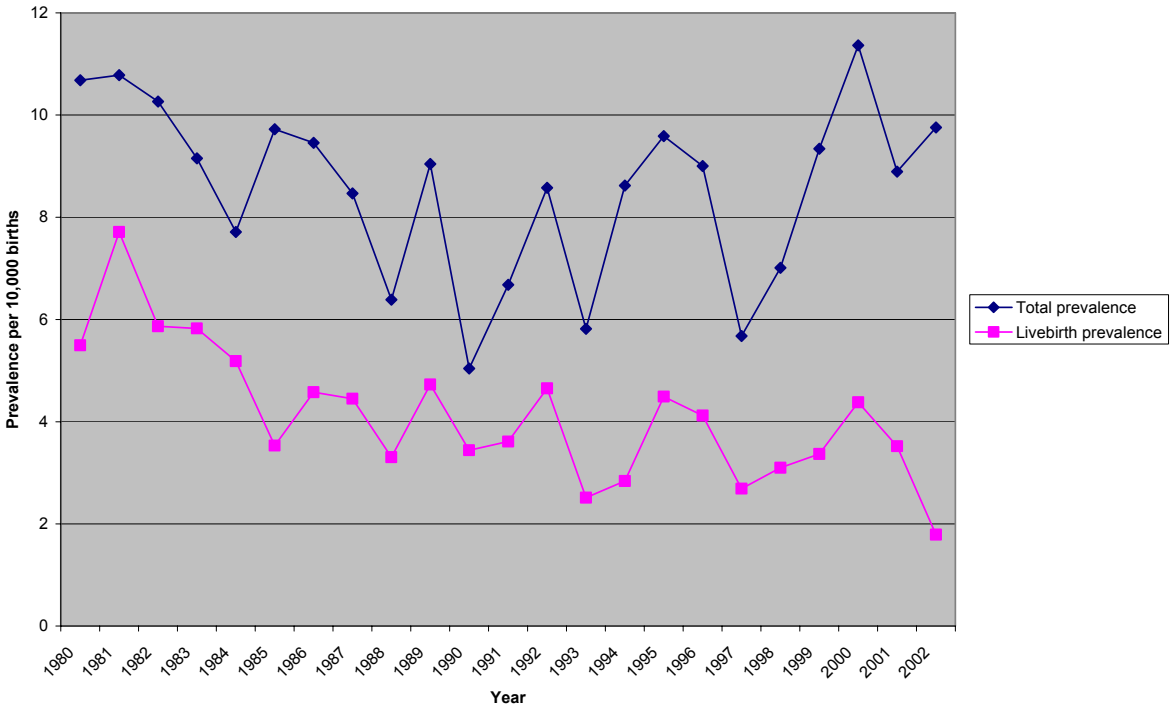
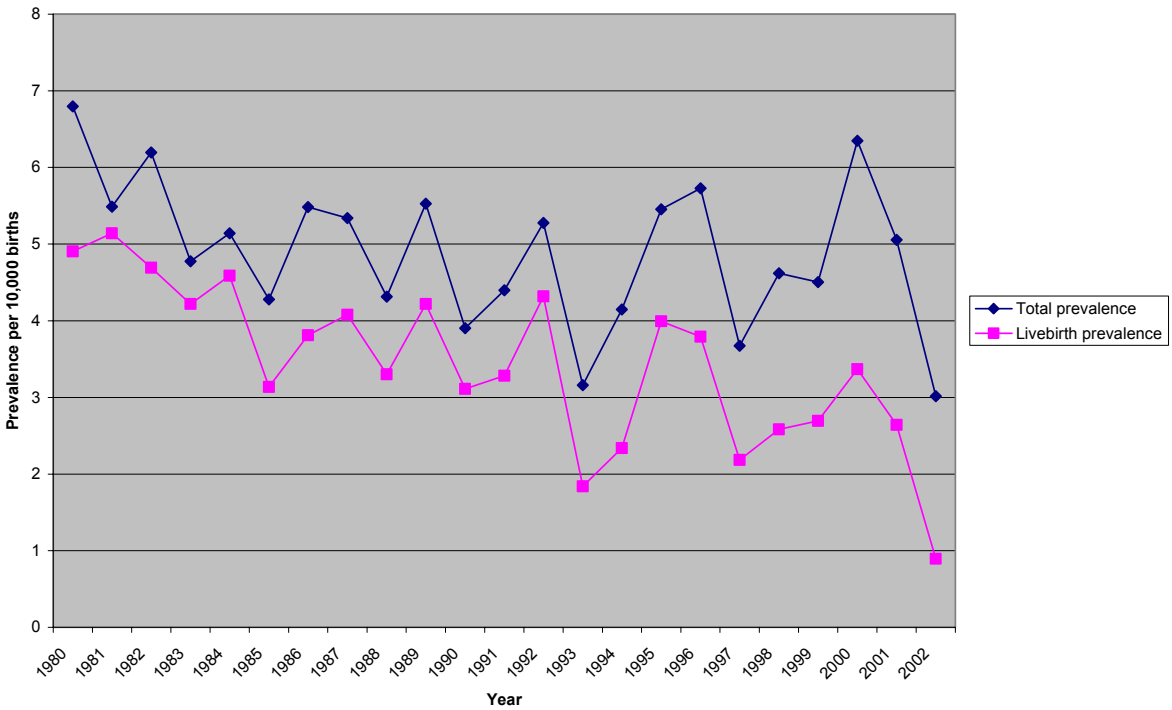
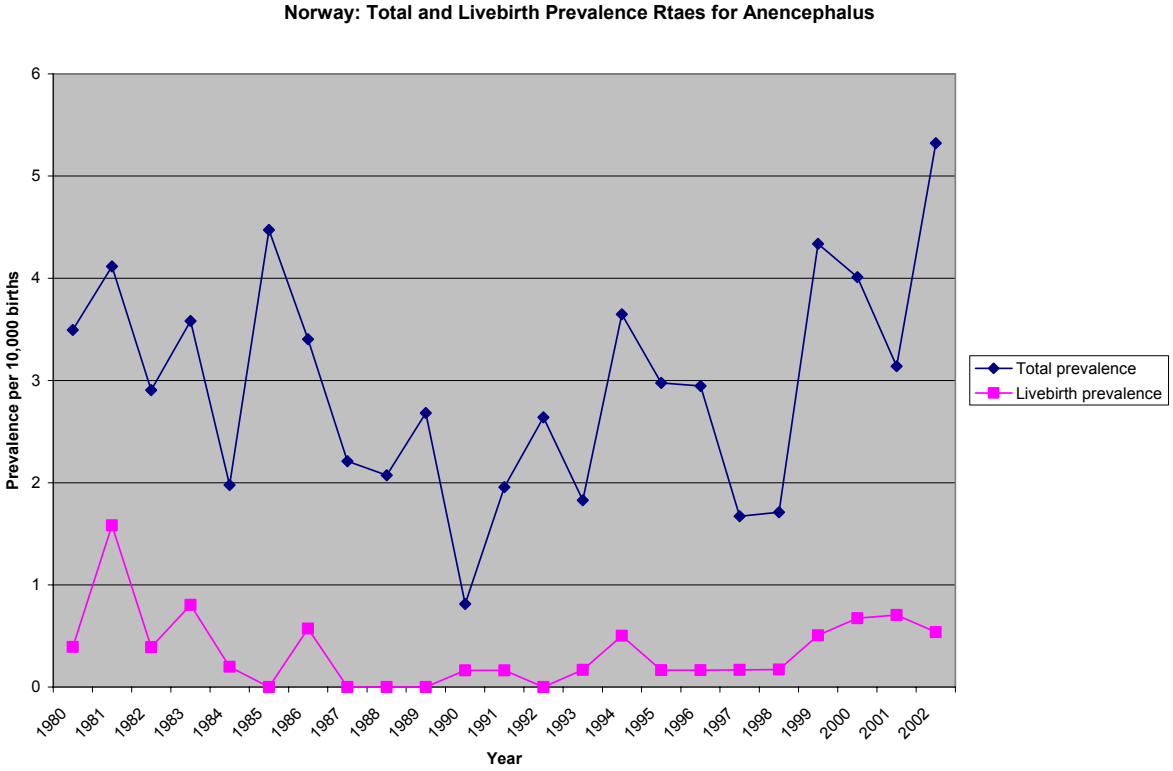
Norway: Total and Livebirth Prevalence Rates for Neural Tube Defects



Norway: Total and Livebirth Prevalence Rates for Spina Bifida




Norway: Total and Livebirth Prevalence Rtaes for Anencephalus
Prevalence per 10,000 births
0
1
2
3
4
5
6
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Year
Total prevalence
Livebirth prevalence

REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR POLAND

Dr Anna Latos-Bielenska

Folic Acid Supplementation Policy

Since 1997 there has been a nation wide government program regarding periconceptional folic acid supplementation. The program "Primary Prophylaxis of Neural Tube Defects", is headed by Professor Zbigniew Brzezinski, from the Department of Epidemiology, Institute of Mother and Child, Warsaw.

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.

Knowledge and Uptake of Folic Acid

In 1999, folic acid supplementation was taken by 15% of women aged 18-45; by 11% of non-pregnant women between those ages; and by 9% of women under 20 years of age.

In 2001, folic acid supplementation was taken by 19% of women aged18-45; by 13% of non-pregnant women between those ages, and by 16% of women under 20 years of age. Thus, folic acid supplementation rates had gone up for all three categories within the space of two years. (Report on realization of program of primary prophylaxis of neural tube defects in 1997-2001, Institute of Mother and Child, Warsaw 2000). 57% of women took other vitamin supplements.

Proportion of Pregnancies which are Planned

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

Laws regarding termination of pregnancy

Termination of pregnancy for fetal abnormality is permitted until viability. In the case of a lethal anomaly, there is no gestational age limit.

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Zbigniew Brzezinski, Report on realization of program of primary prophylaxis of neural tube defects in 1997-2001.

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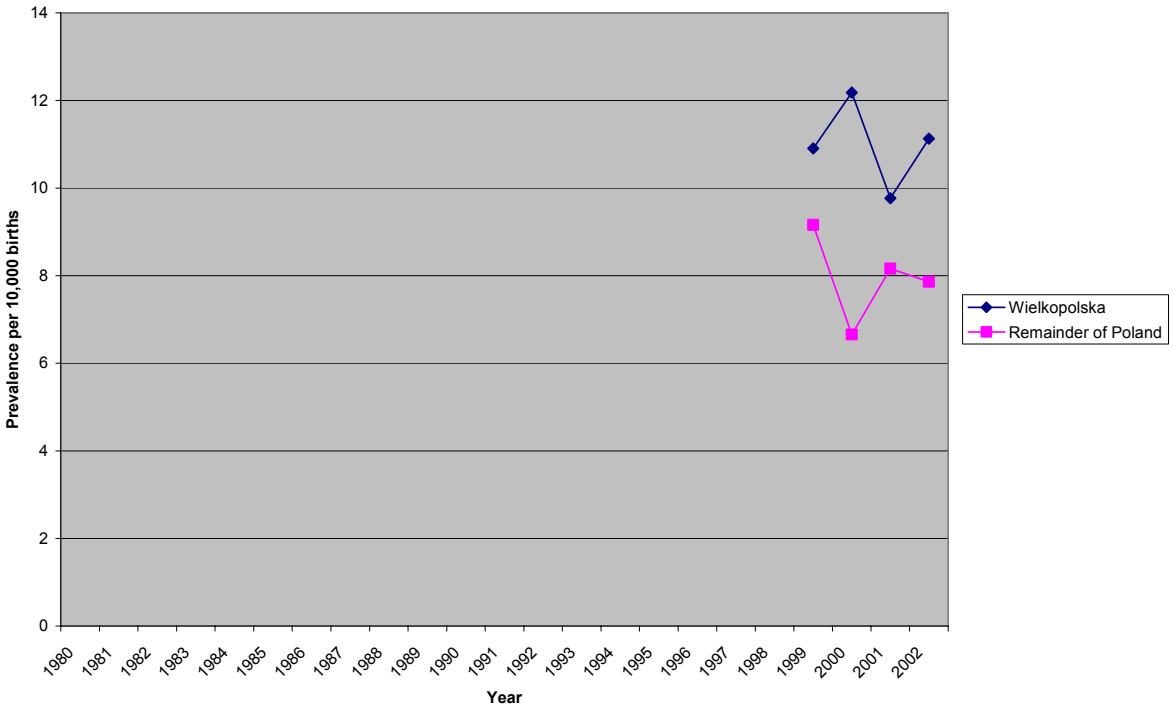
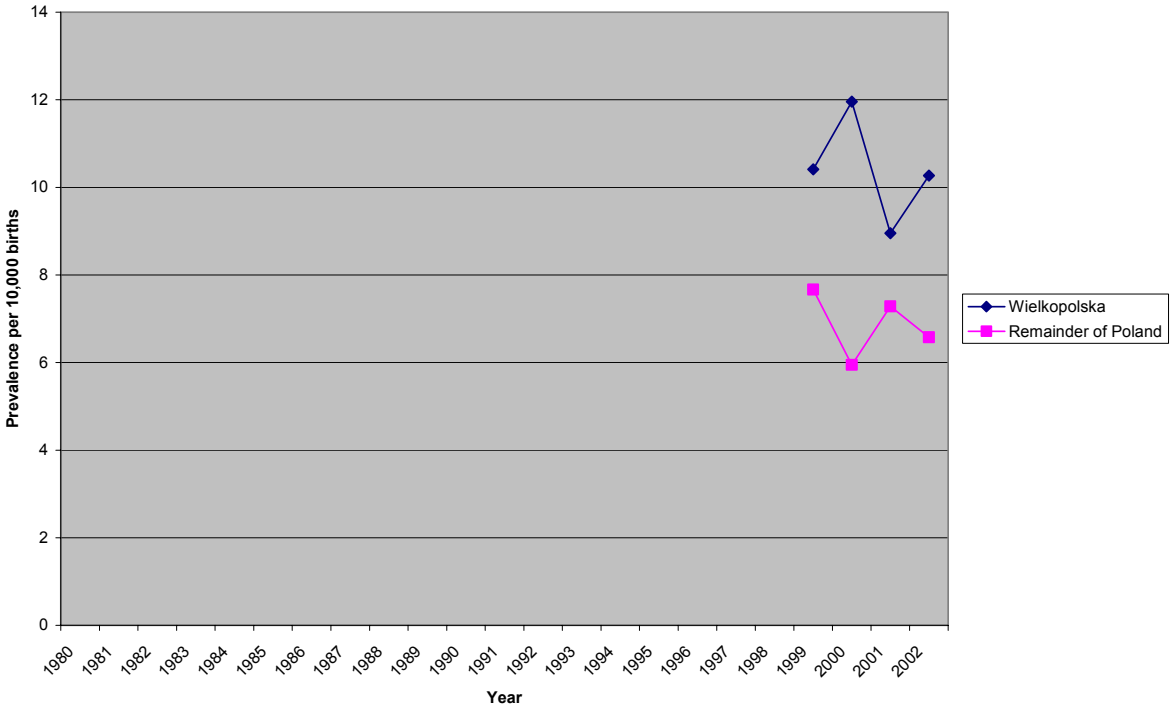
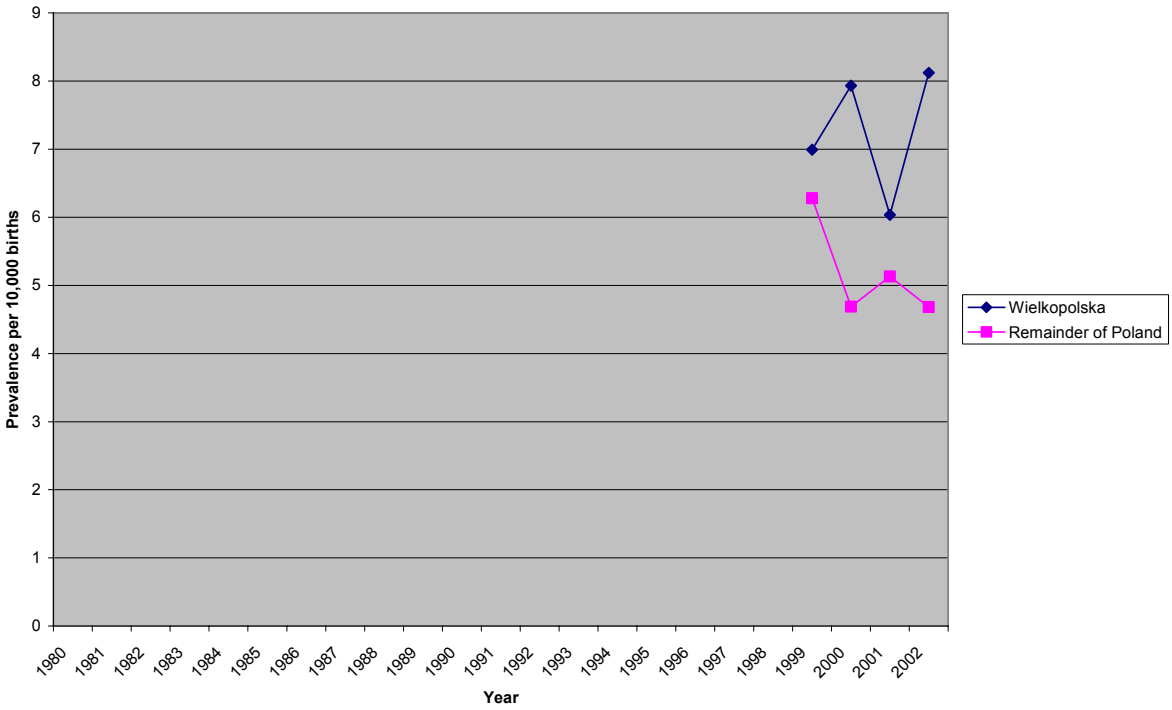
Poland (Wielkopolska and remainder of Poland): Total Prevalence Rates for Neural Tube Defects



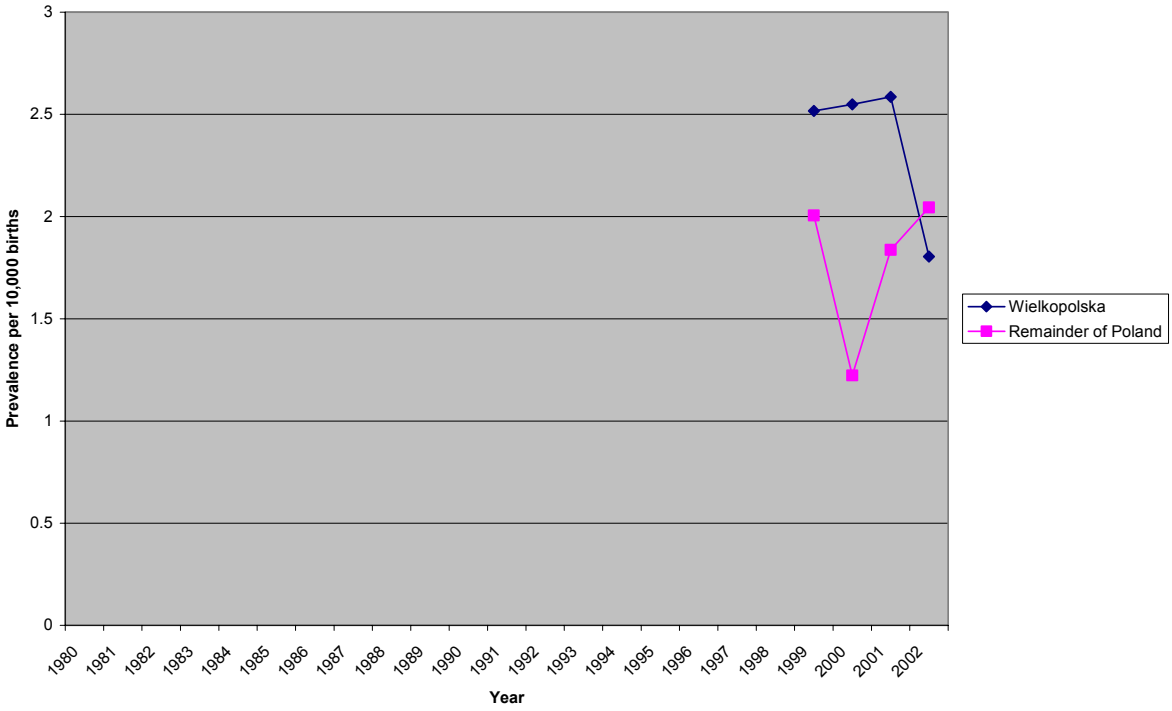
Poland (Wielkopolska and remainder of Poland): Livebirth Prevalence Rates for Neural Tube Defects



Poland (Wielkopolska and remainder of Poland): Total Prevalence Rates for Spina Bifida



Poland (Wielkopolska and remainder of Poland): Total Prevalence Rates for Anencephalus



REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR PORTUGAL

Dr Paula Braz

Folic Acid Supplementation Policy

There is a recommendation from the Directory of Health "Directory of Health guideline number 2/DSMIA" to all health care professionals, to inform the childbearing population about the importance of folic acid. There is no information about dosage. This policy was introduced in March 1998

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 three years ago to fortify milk with 50µg/100ml of folic acid.

Health Education Initiatives

There is no official health education initiative, but the recommendation from the Directory of Health in March 1998, suggested that general practitioners should inform their female patients about the importance of folic acid supplementation.

Knowledge and Uptake of Folic Acid

To our knowledge there are no studies in the Portuguese population.

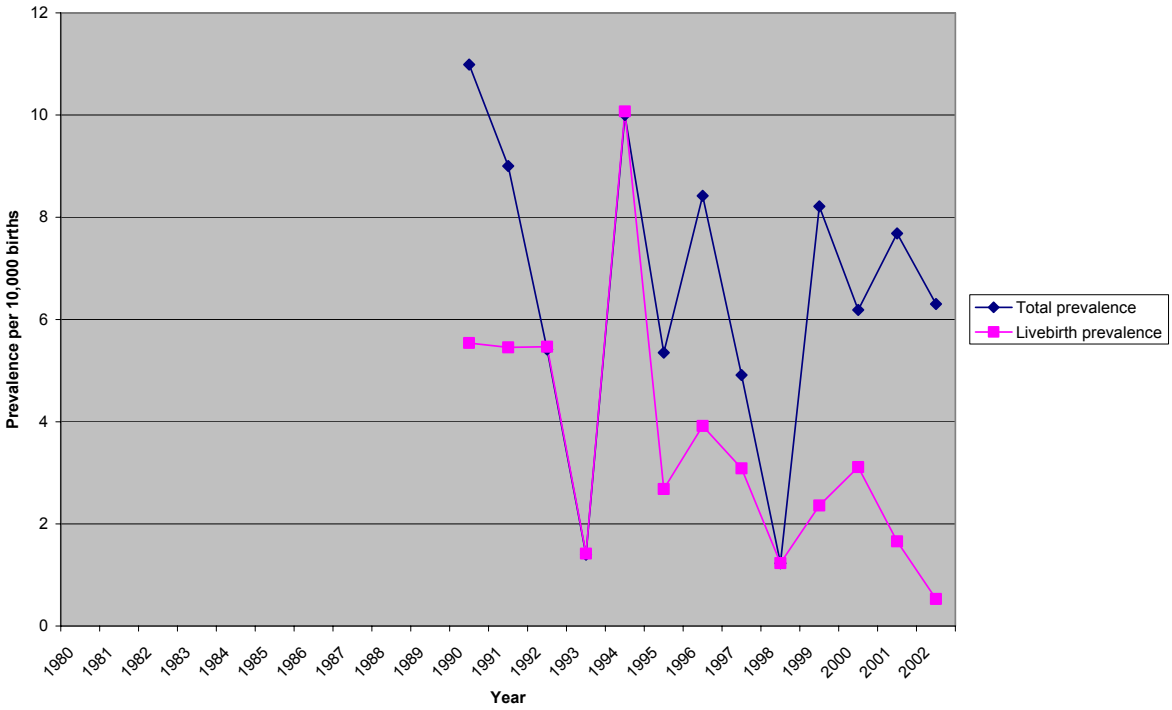
Proportion of Pregnancies which are Planned

No information is available.

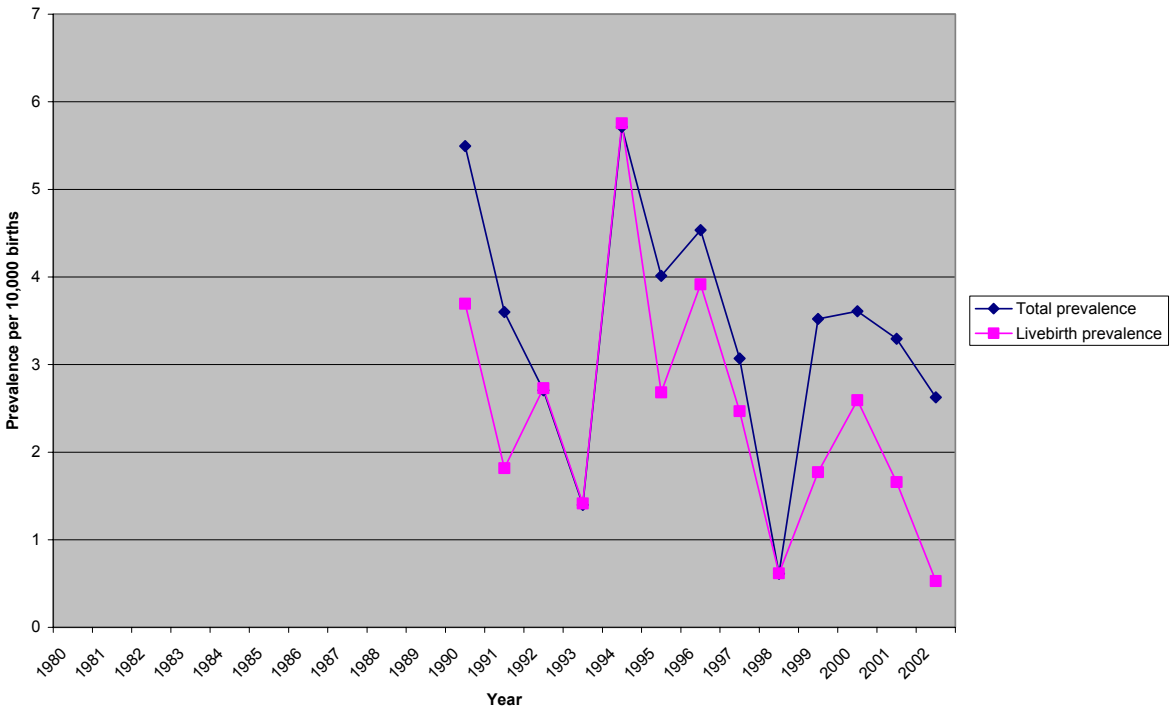
Laws Regarding Termination of Pregnancy

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.

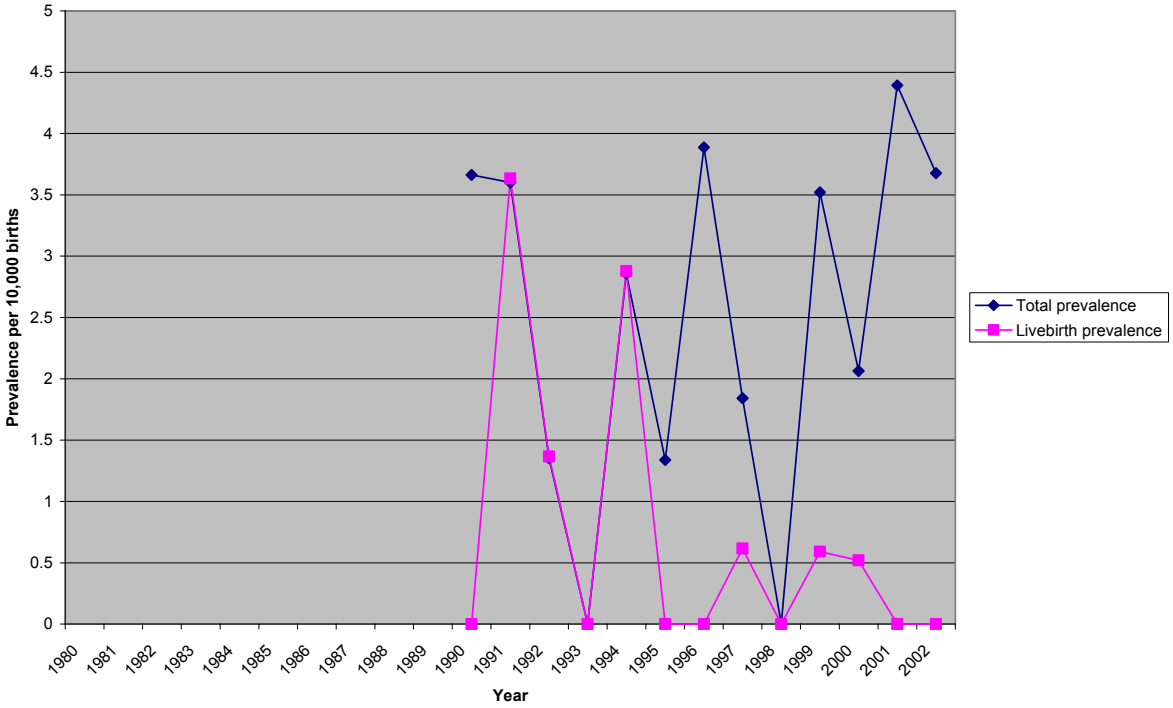
Portugal (Southern): Total and Livebirth Prevalence Rates for Neural Tube Defects



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



Portugal (Southern): Total and Livebirth Prevalence Rates for Anencephalus



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 web-page 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 is 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.

Studies of prophylaxis assessment

In addition to the study published in 2000 by Gilbert et al[8], six studies by Spanish authors were published in 2003 and 2004. Results of these studies are given below.

Study	Design	Intake of periconceptional folic acid supplements	Knowledge of benefits of folic acid	Recommendations
Gilbert et al (2000)[8]	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 midwifes 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[9] (2003)	Retrospective Mothers of controls ECEM 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[10] (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[11] (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 (400ц) supplement with sufficient B12 to prevent deficit of B12
Perez-Vázquez et al[12] (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)[13]	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

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. Three references should be mentioned: Madueño and Muñoz (2001)[14], Capitán and Carrera (2001)[15] and Carrera (2003)[16]. All of them stress the need to improve information to care providers and the general population.

Aranceta et al (2001)[17] and Ortega et al (2001)[18] 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 Congenitas). Some pamphlets for the general population about prevention of NTDs with folic acid are available from the web[19].

Proportion of pregnancies that are planned

There are no reliable figures about the number that are 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 4 compounds with Acid Folic: ACFOL (5 Mg); Acido Folico ASPOL (10 mg), ZOLICO (400Цg) and FOLI DOCE (400 цg + 2цg B12). The price per day ranges from 0.04 to 0.13 € and is 60% subsidized by Health System.

Some Levofolinic Acid compounds are licensed for sale but are not recommended for pregnant women. The price for these is 9 times more than for folic acid and is subsidized by more than 60% by the Health System. In 1999 the Basque Society of Gynaecology with the Health Department issued recommendations about periconceptional intake of folic acid and also discouraged gynaecologists from prescribing Levofolinic acid. Nevertheless, it would be advisable to monitor the use of Levofolinic Acid for periconceptional care.

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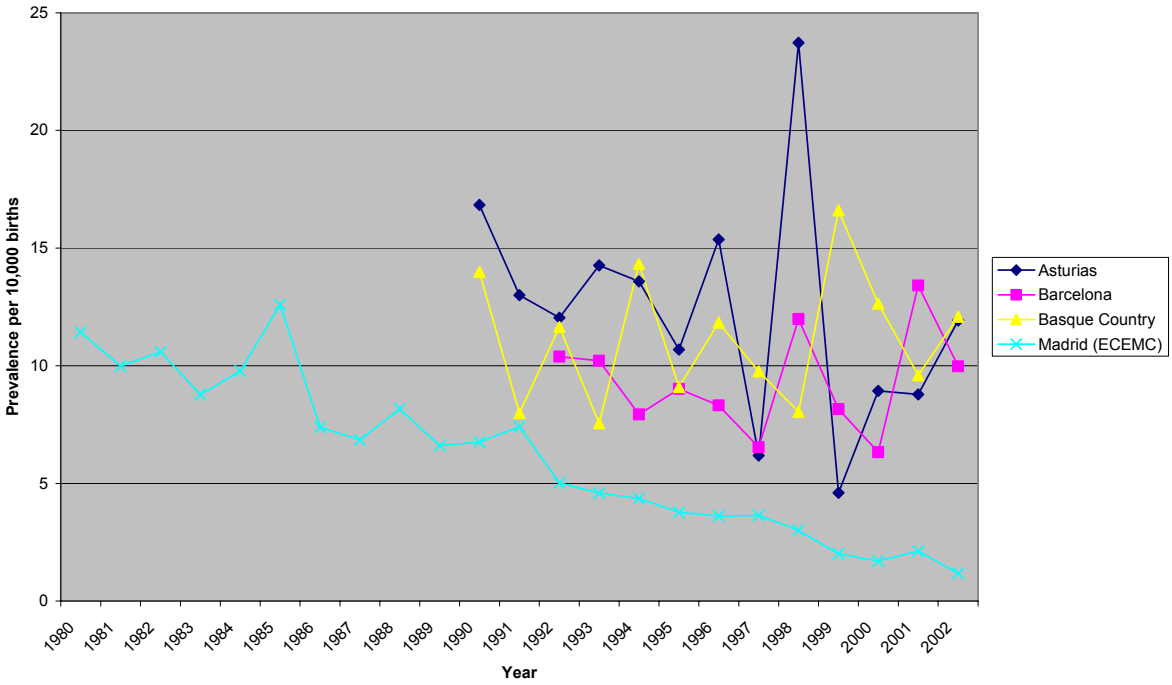
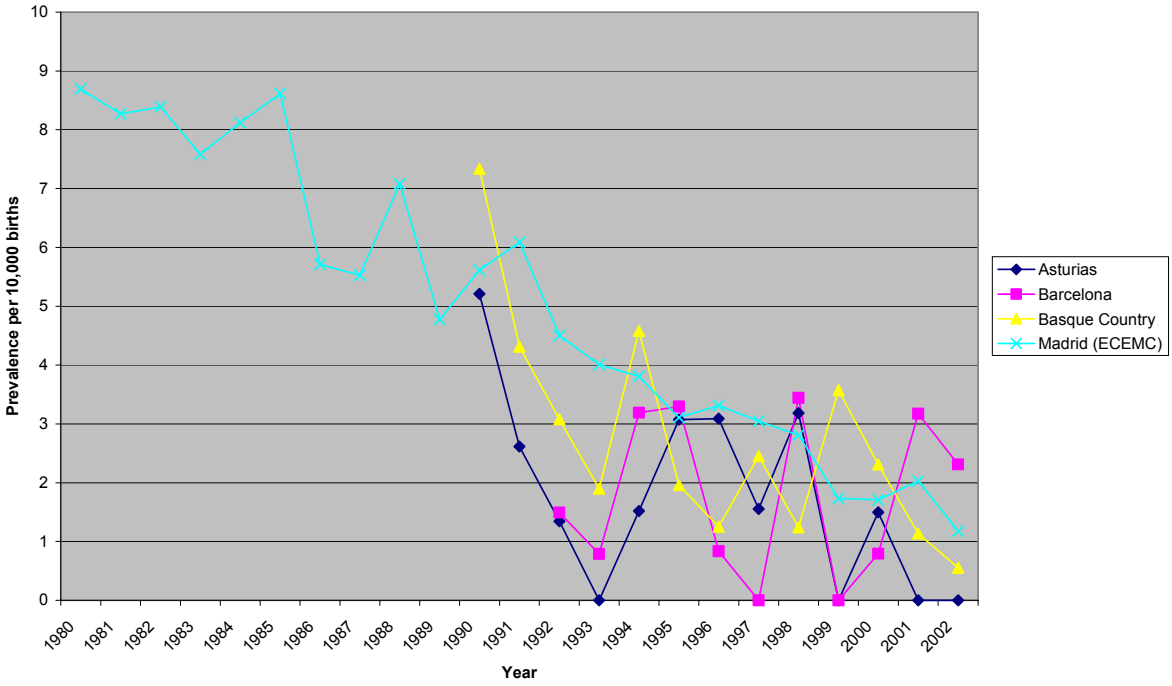
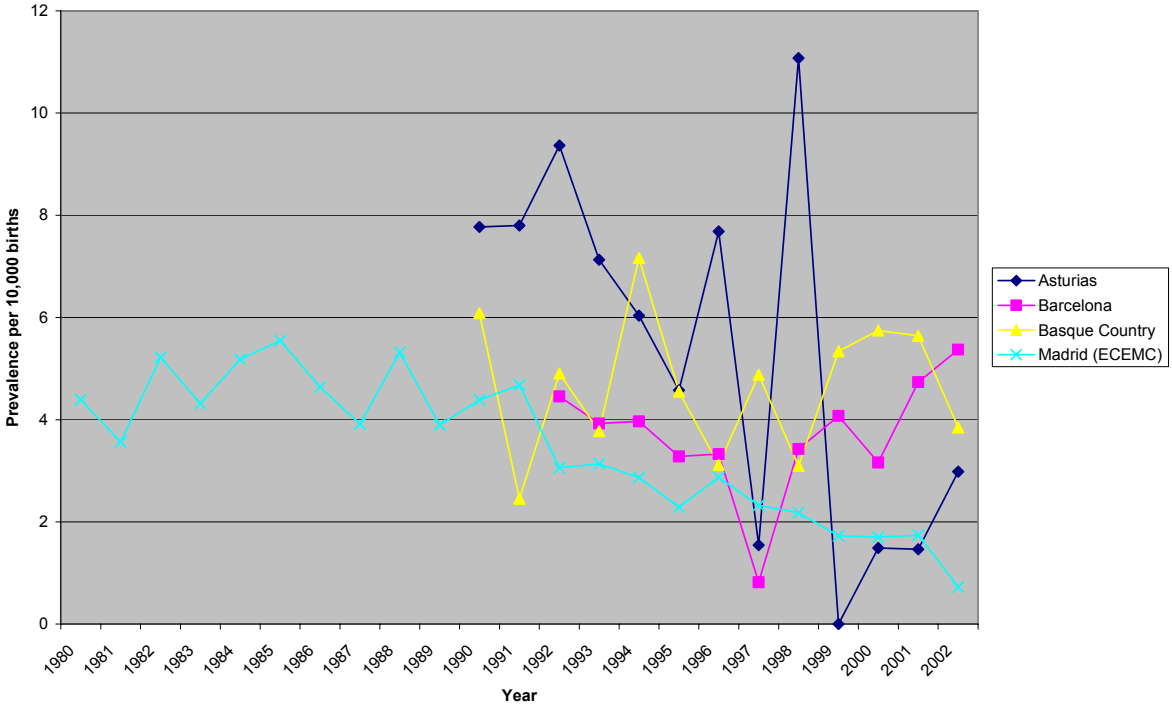
Spain (Asturias, Barcelona, Basque Country and Madrid): Total Prevalence Rates for Neural Tube Defects



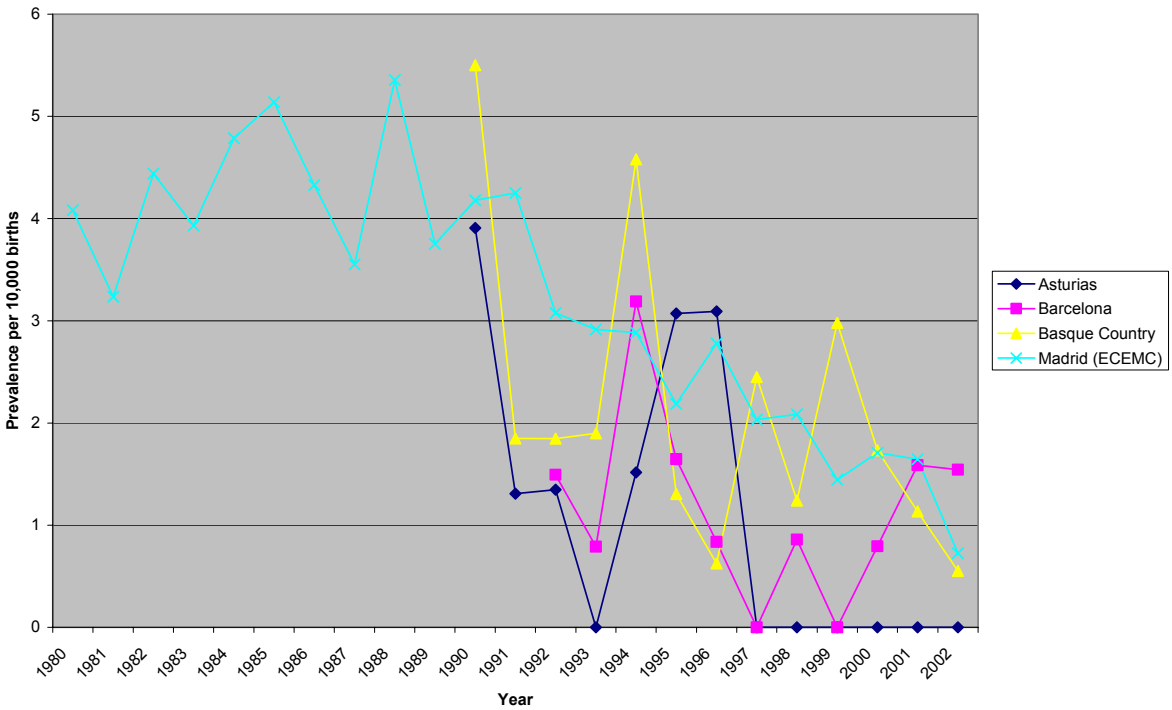
Spain (Asturias, Barcelona, Basque Country and Madrid): Livebirth Prevalence Rates for Neural Tube Defects



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



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



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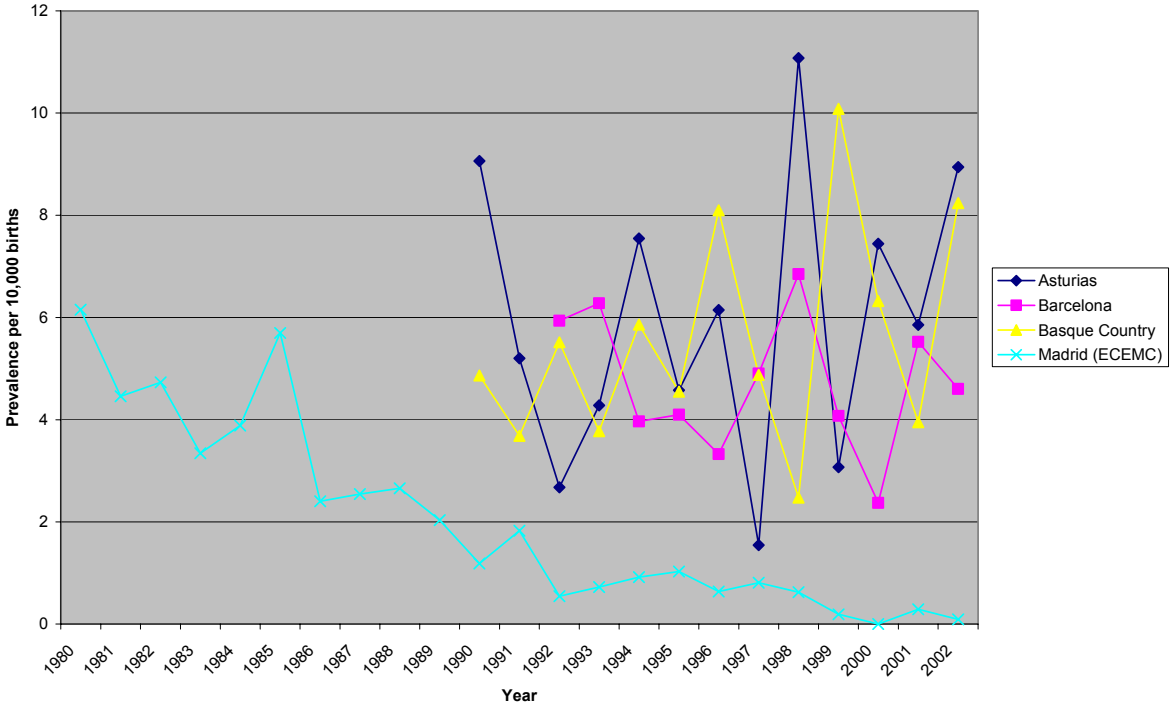
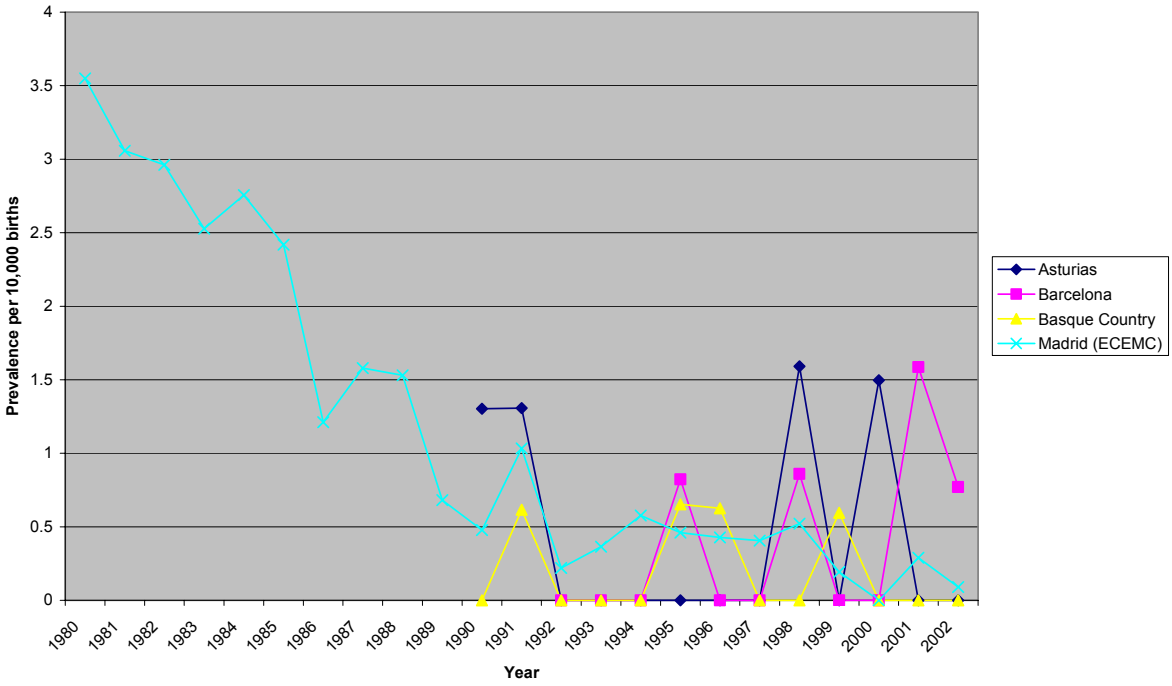


Spain (Asturias, Barcelona, Basque Country and Madrid): Livebirth Prevalence Rates for Anencephalus



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 1996[1] 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]

Food Fortification Policy

There is no policy in Sweden to fortify food with folic acid. A working group was established in 1996 by the Medical Products Agency to suggest recommendations and means of increasing the intake of folic acid among women of childbearing age.

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.

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]

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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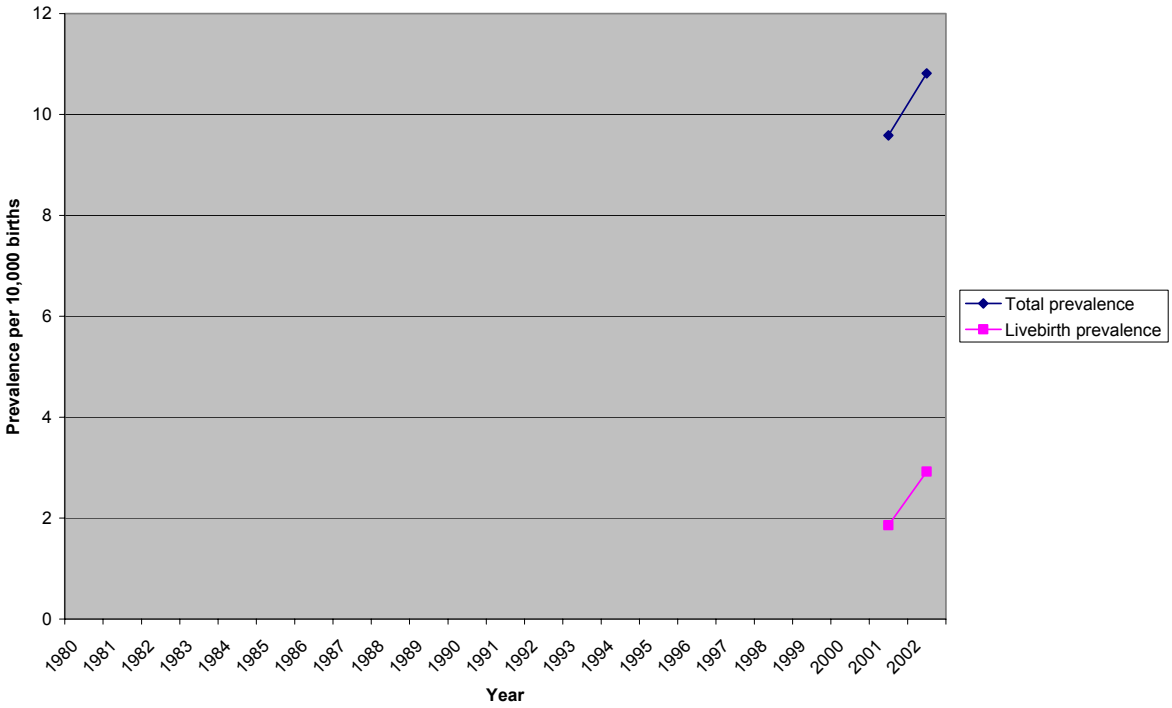
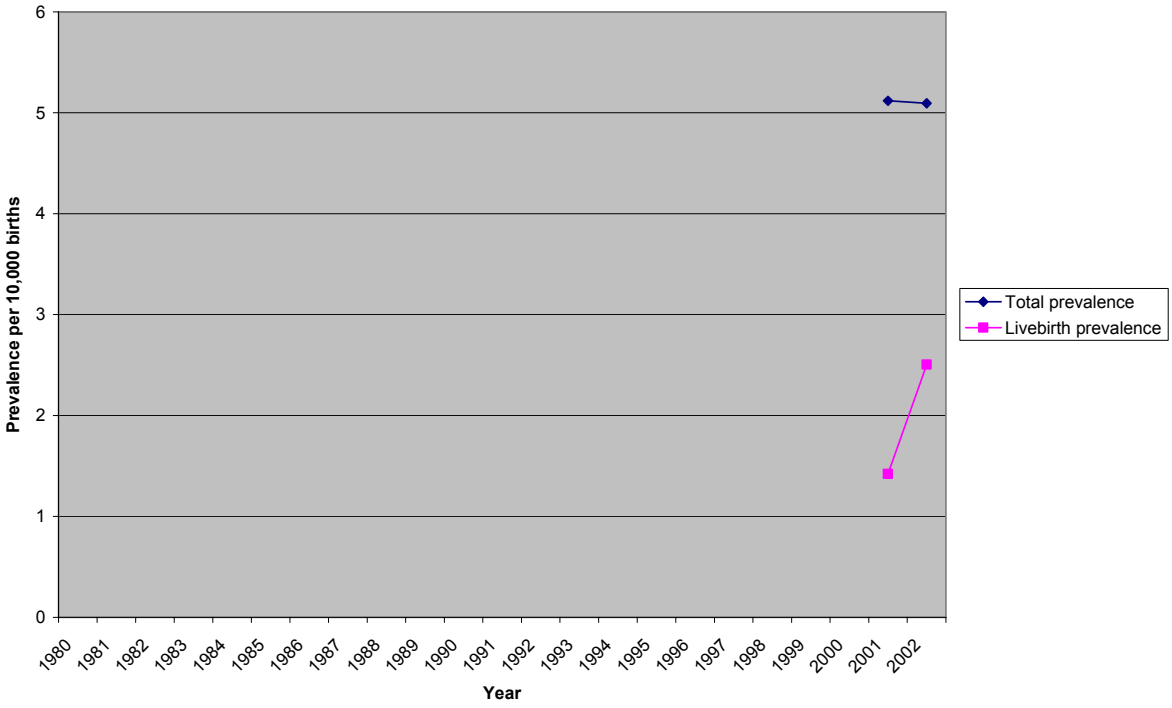
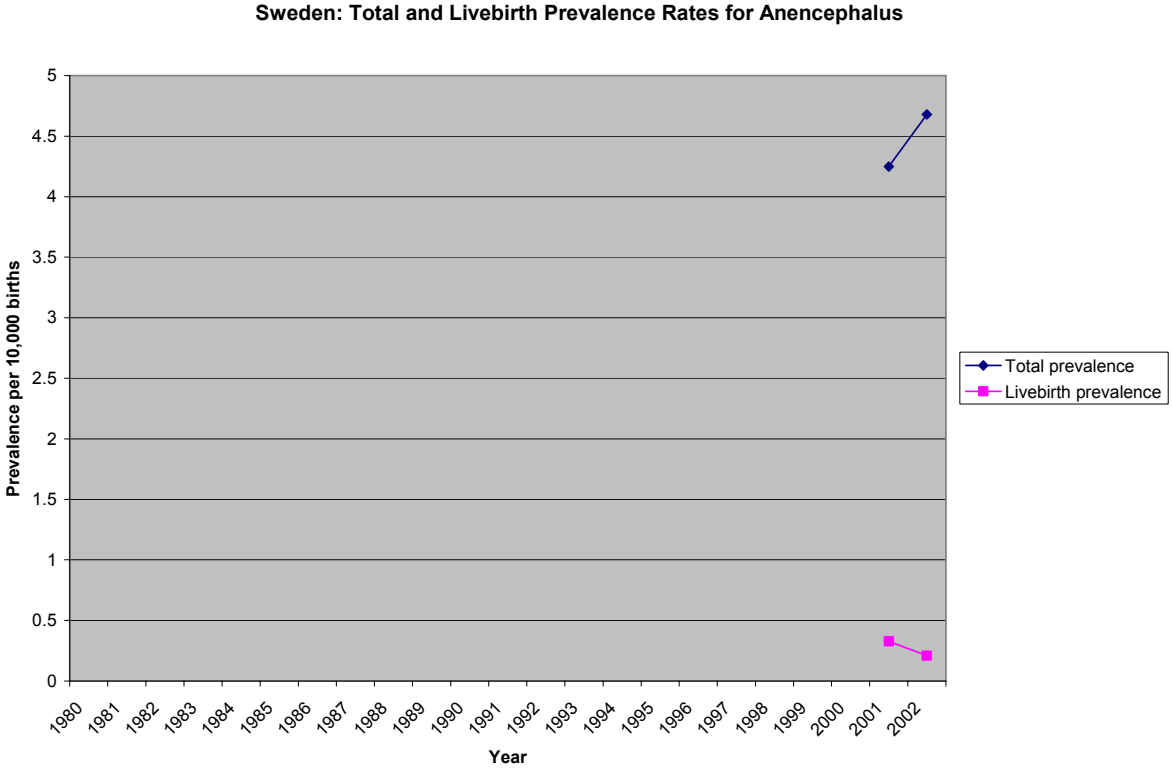
Sweden: Total and Livebirth Prevalence Rates for Neural Tube Defects



Sweden: Total and Livebirth Prevalence Rates for Spina Bifida




Sweden: Total and Livebirth Prevalence Rates for Anencephalus
Prevalence per 10,000 births
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Year
Total prevalence
Livebirth prevalence

REPORT ON PERICONCEPTIONAL FOLIC ACID SUPPLEMENTATION FOR SWITZERLAND

Dr Marie-Claude Addor

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 current 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 $\leq$ 8000 UI)

Food Fortification Policy

Voluntary fortification of food with folic acid is legal now, but mandatory fortification is still under consideration. 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.
Since 2000, the Federal Office of Public Health has been studying the folate situation in Switzerland (3) and a working group of the Swiss Nutrition Council has submitted a report for the Federal Government with scientific recommendations, published in 2002(4).
The current recommendation regarding fortification is 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. This is the most efficacious, sure and economic way to prevent NTD. This recommendation is supported by the Swiss Nutrition Council but not yet by the Federal Office of Public Health.

The fortification with folic acid of other foods is under re-evaluation. The potential benefits of folic acid in the Swiss population have now been evaluated and this knowledge will influence the official federal policy for folic acid fortification in Switzerland. At the moment the Federal Office of Public Health is considering the next steps to be taken.

Health Education Initiatives

A working group of the Federal Office of Public Health is preparing a booklet and a leaflet for women in childbearing age. Some booklets, edited by pharmacists "vitamin info" are available in waiting rooms of gynaecologists.

Uptake and Knowledge of Folic Acid.

According to recent market research, awareness of folic acid in the population has increased from 38% in 1999 to 58% in 2003.
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 very low, and there are very few “preconceptional consultations”.

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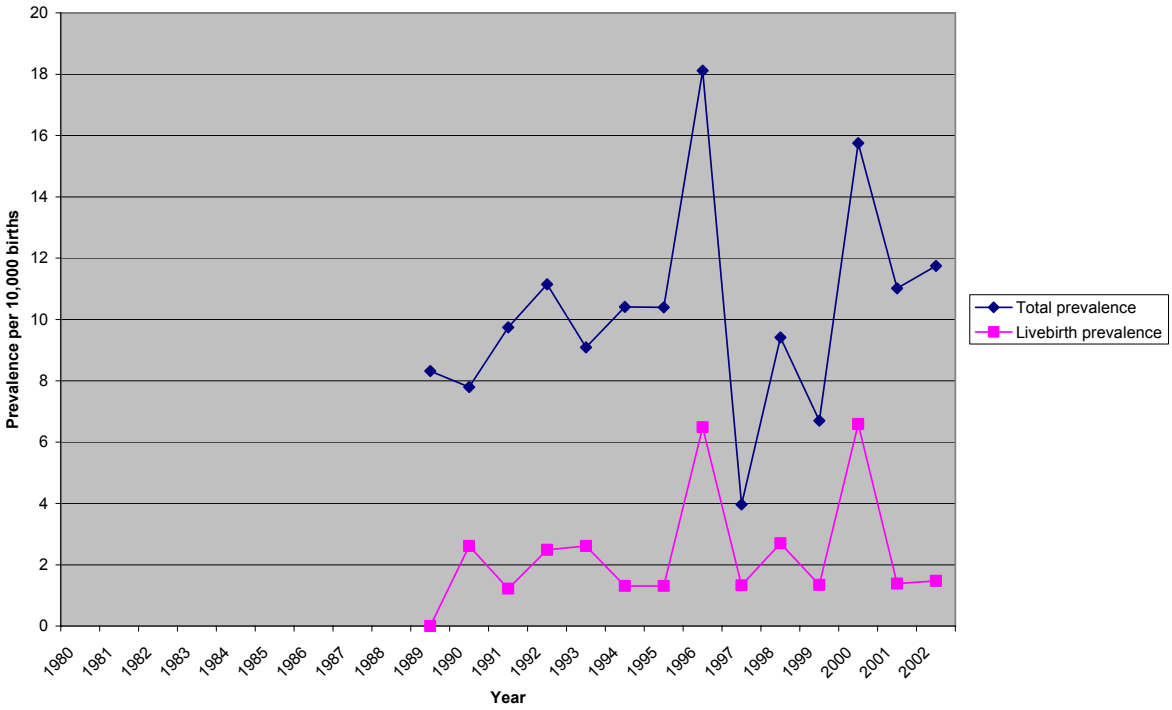
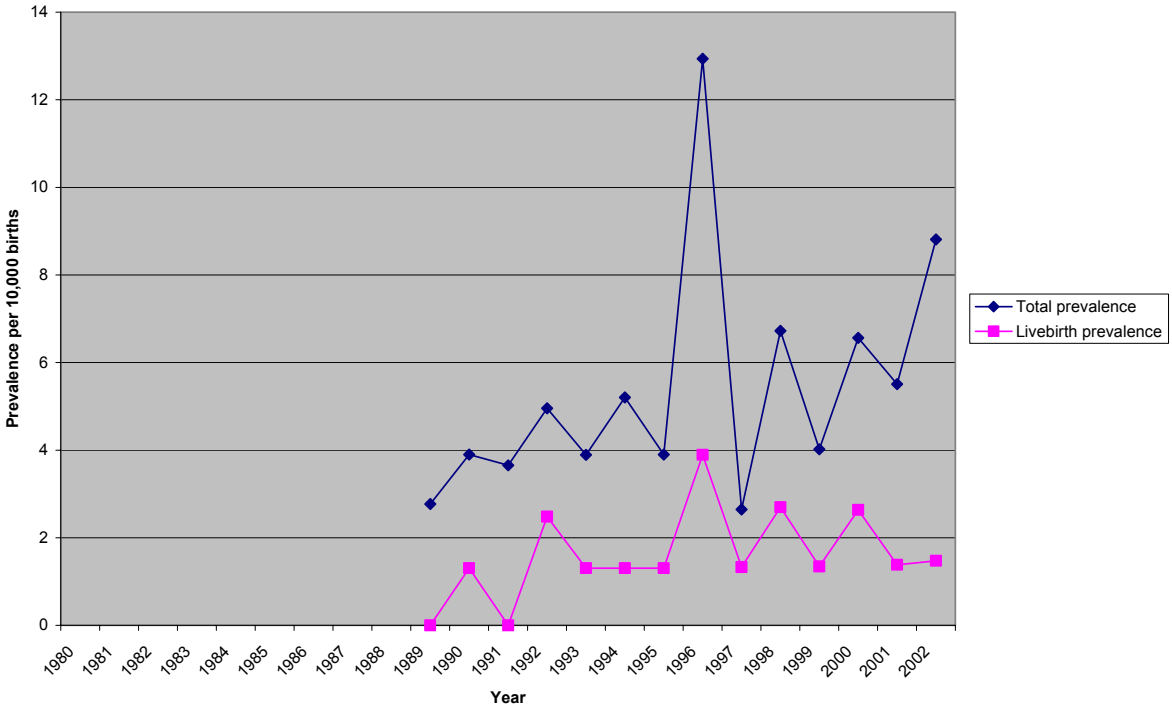
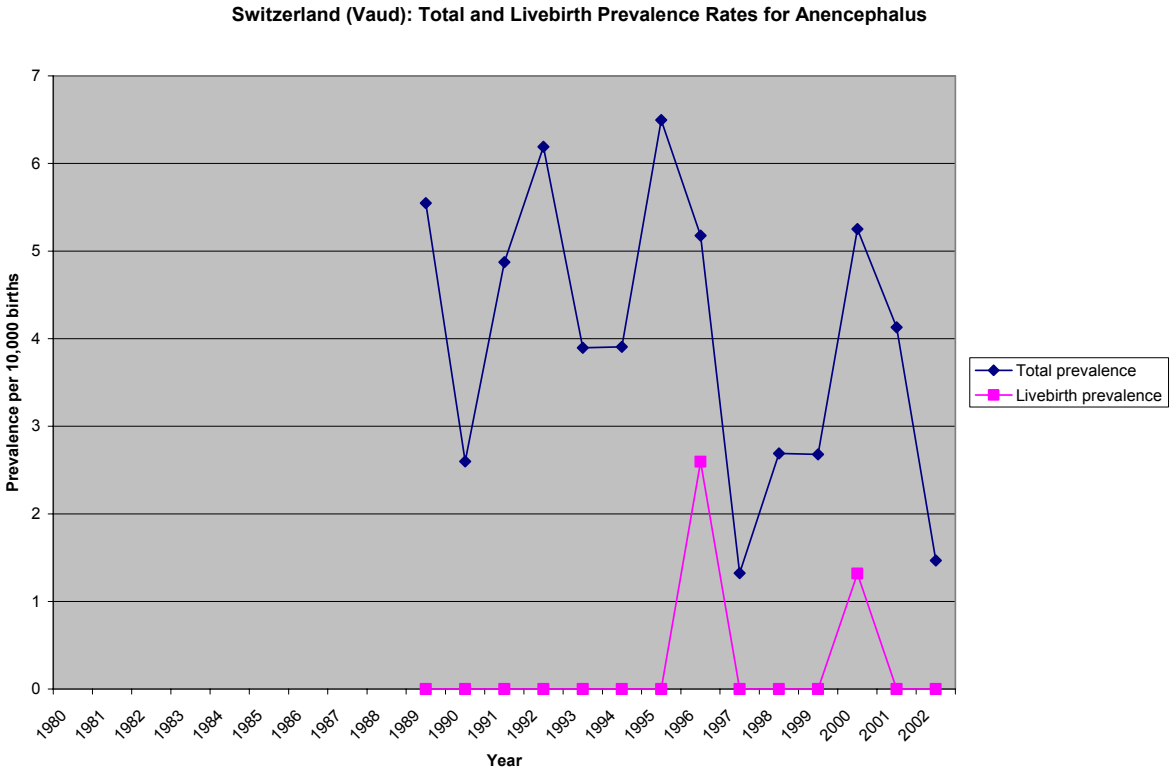
Switzerland (Vaud): Total Prevalence Rates for Neural Tube Defects



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




Switzerland (Vaud): Total and Livebirth Prevalence Rates for Anencephalus
Prevalence per 10,000 births
0
1
2
3
4
5
6
7
1980
1981
1982
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Year
Total prevalence
Livebirth prevalence

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

There is no mandatory fortification of food in the United Kingdom. However, 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.

The Committee on Medical Aspects of Food and Nutrition (COMA) report in 2000 concluded that by fortifying flour with folic acid, a significant proportion of neural tube defect affected births could be prevented. [3] The report looked at both the benefits and possible risks of folic acid intake and concluded that:

- Universal fortification of flour with folic acid at 240 μg per 100 grams in food products as consumed would reduce the risk of a neural tube defect in unborn babies and children by 41% without resulting in unacceptably high intakes in any group of the population.
- Women who could become pregnant should continue to be advised to take a diet rich in folate and take folic acid supplementation.

A public consultation was undertaken in the United Kingdom and the issue was considered by the Food Standards Agency (FSA). There was no consensus on the introduction of a food fortification programme without a controlled field trial, as there were concerns about the possibility of adverse effects. The main concern of the FSA was that fortification might mask megaloblastic anaemia in people with vitamin B12 deficiency .[4] In May 2002, the Food Standards Agency (FSA) recommended that mandatory fortification should not be implemented. To date, the FSA decision stands.

Health Education Initiatives

In 1995 a 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. [5]

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. [6-11]

Some work has been undertaken in the United Kingdom to measure the changes in dietary folate consumption. [12,13] 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. [14] These findings were supported by research in Merseyside, England where forty percent of women reported that their pregnancies were unplanned [15] and by research in other parts of Britain [6]

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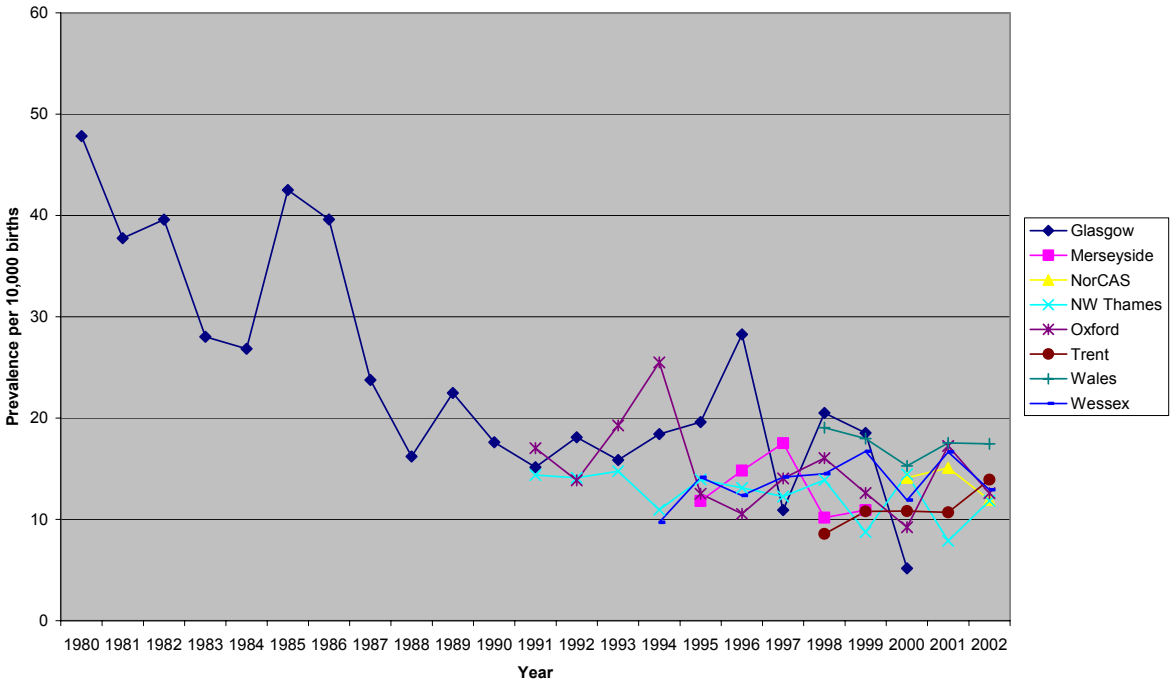
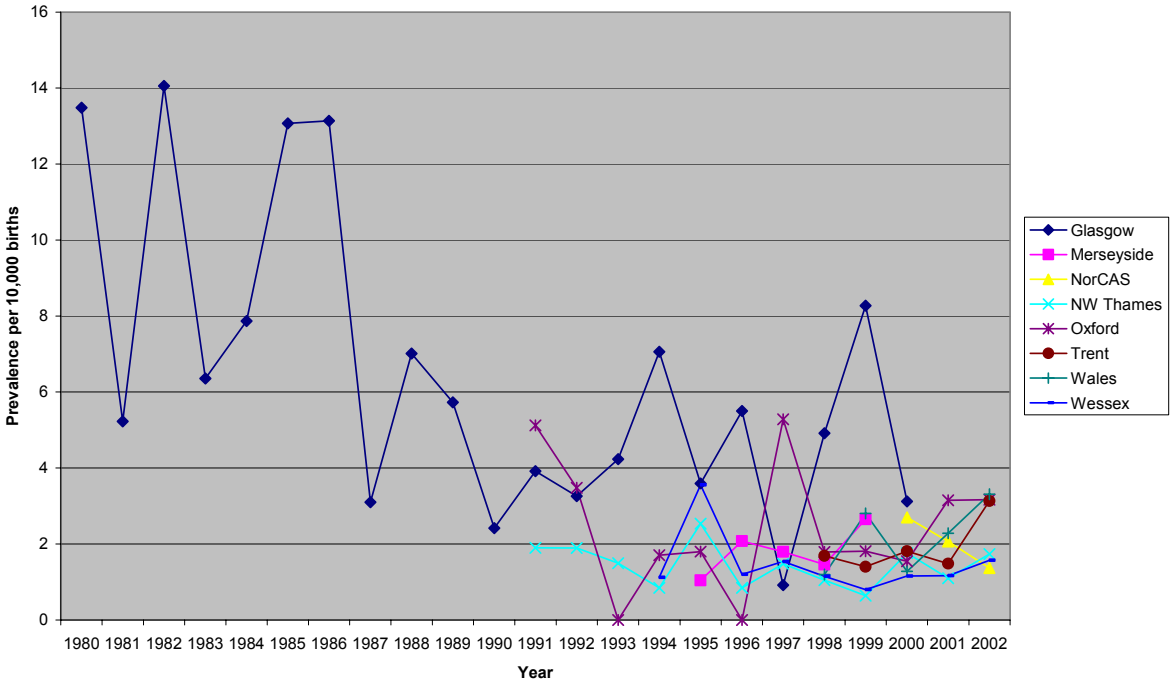
Thanks to Margaret Slane of the Health Promotion Agency in Northern Ireland and Margaret Boyle, Senior Medical Officer, Department of Health, Social Services and Personal Safety Northern Ireland for their input about the situation in Northern Ireland.

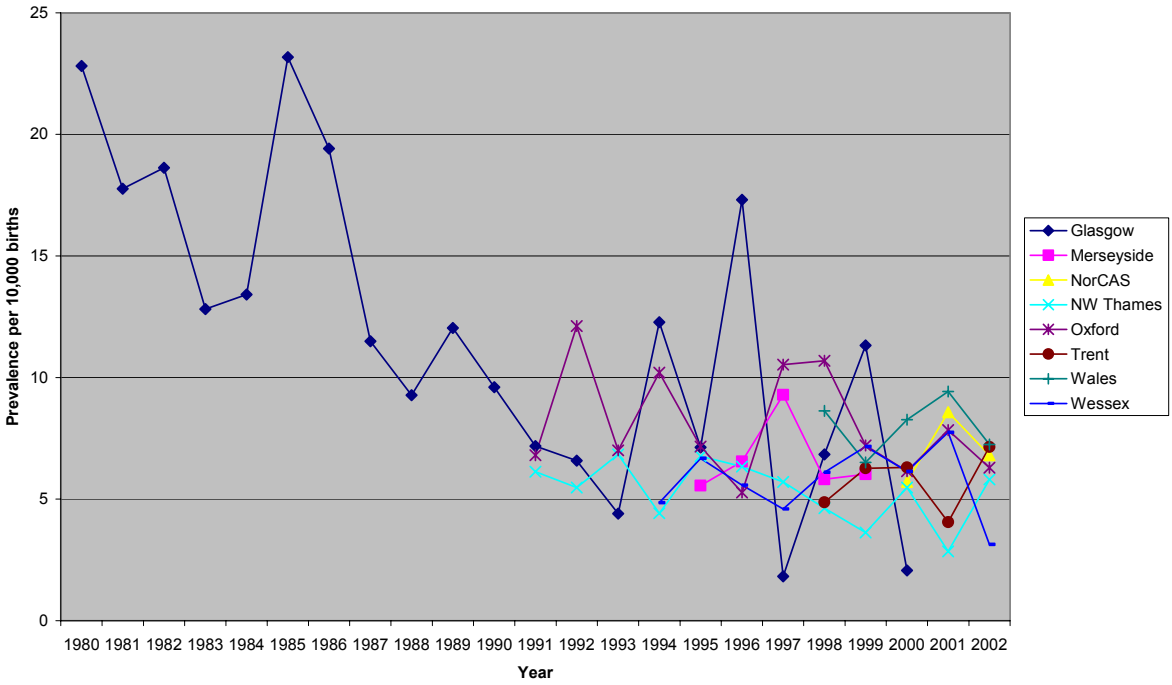
UK (Glasgow, Merseyside, NW Thames, Northerrn Regions, Oxford, Trent, Wales and Wessex): Total Prevalence Rates for Neural Tube Defects



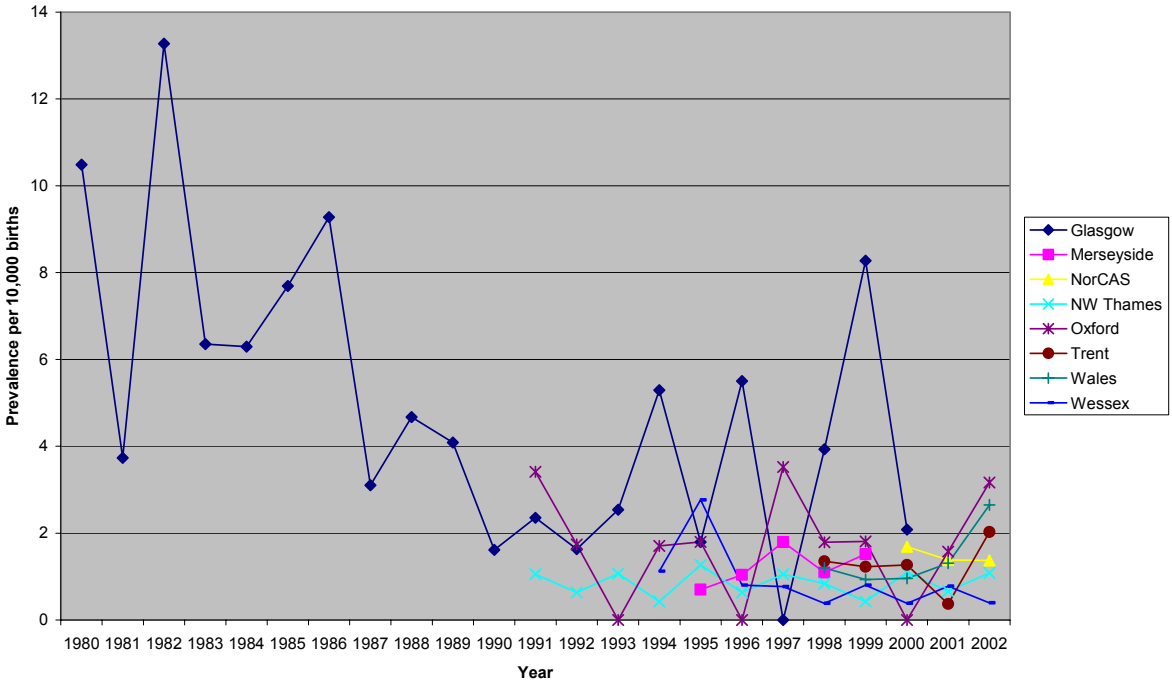
UK (Glasgow, Merseyside, NW Thames, Northern Regions, Oxford, Trent, Wales and Wessex): Livebirth Prevalence Rates for Neural Tube Defects



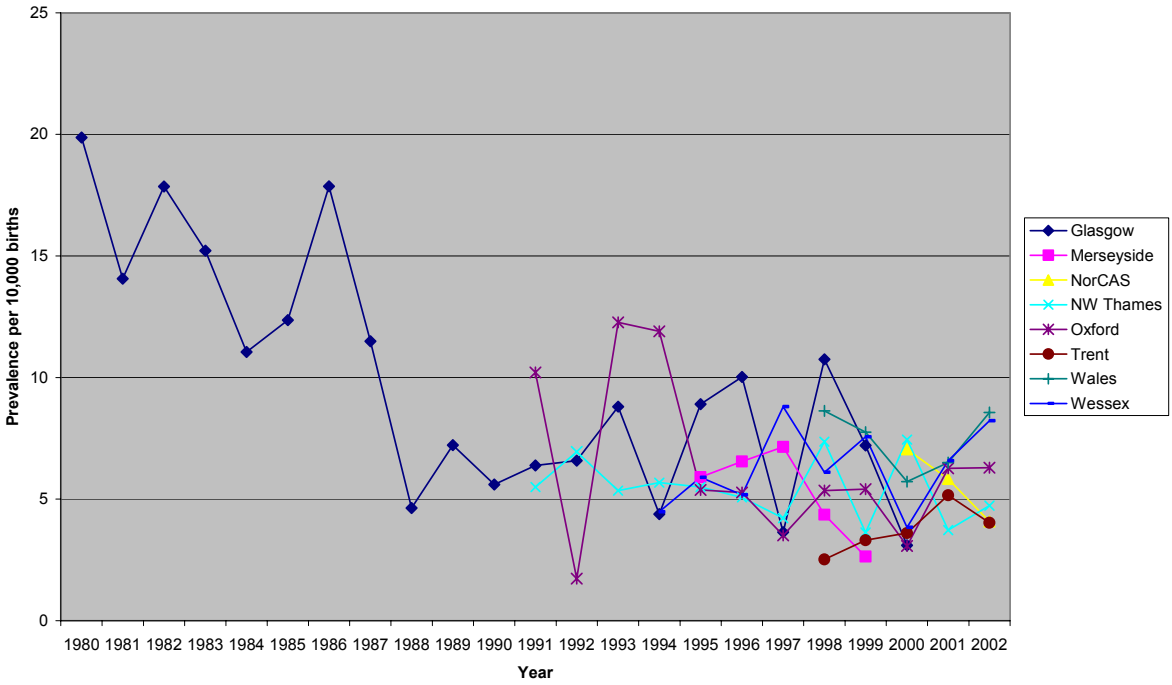
UK (Glasgow, Merseyside, NW Thames, Northern Regions, Oxford, Trent, Wales and Wessex): Total Prevalence Rates for Spina Bifida



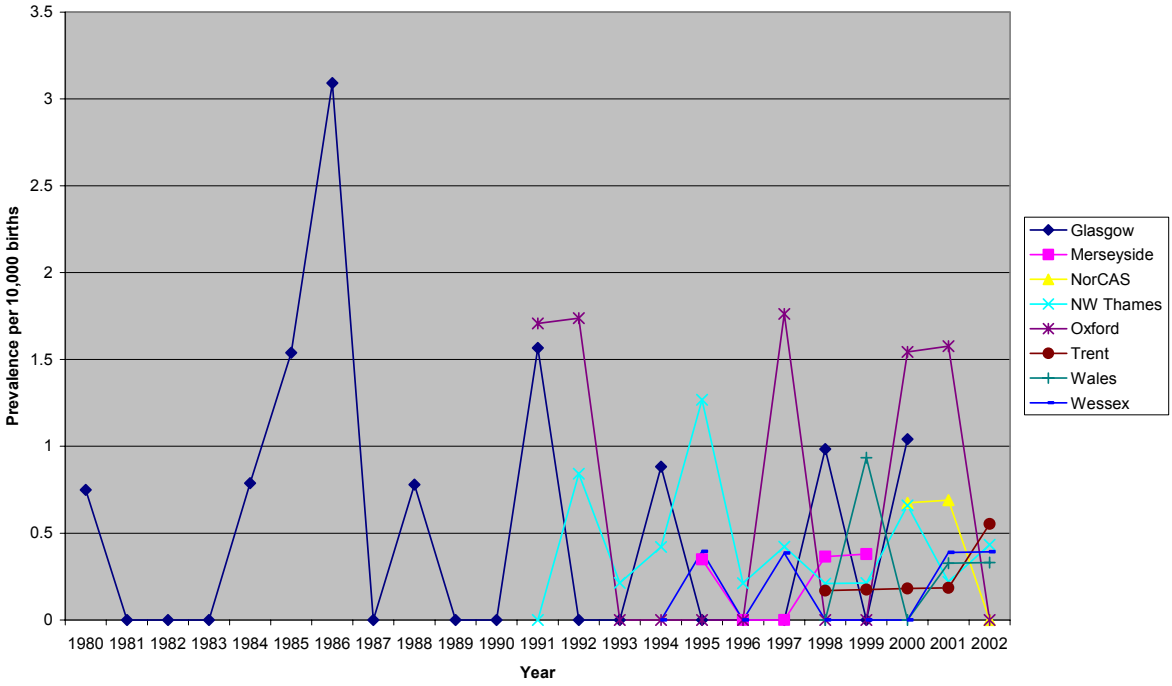
UK (Glasgow, Merseyside, NW Thames, Northern Regions, Oxford, Trent, Wales and Wessex): Livebirth Prevalence Rates for Spina Bifida



UK (Glasgow, Merseyside, NW Thames, Northern Regions, Oxford, Trent, Wales and Wessex): Total Prevalence Rates for Anencephalus



UK (Glasgow, Merseyside, NW Thames, Northern Regions, Oxford, Trent, Wales and Wessex): Livebirth Prevalence Rates for Anencephalus



Part III

Appendices

Appendix 1

Definition and ICD codes of Neural Tube Defects, Anencephaly and Spina Bifida

(Extract from EUROCAT Guide 1.2)

Subgroup	**ICD9-BPA**	**ICD10-BPA**	**Exclusions**
Neural Tube Defects: Neural tube defects include Anencephalus, encephalocele, spina bifida and iniencephaly	7400-7420	Q00,Q01, Q05, Q070	
Anencephalus and similar: Absence or deficiency of a major portion of the cranial vault, the covering skin and the brain tissue	7400-7401	Q000 and Q001	
Spina Bifida: Midline defect of the osseous spine usually affecting the posterior arches resulting in a herniation or exposure of the spinal cord and/or meninges	7410, 7419	Q050-Q059, Q070	Exclude association with Anencephalus

Appendix 2

NTD, Anencephaly and Spina Bifida:

Number of cases by type of birth[1], population (births), total prevalence rate and livebirth prevalence rate (per 10,000 births) by year and registry: 41 EUROCAT registries, 1980-2002

Table A2.1: Neural Tube Defects: Number of cases by type of birth[1], population (births), total prevalence rate and livebirth prevalence rate (per 10,000 births) by year and registry: 41 EUROCAT registries, 1980-2002

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Styria (Austria)																								
total cases						10	12	9	8	11	14	10	12	10	12	11	7	10	8	9	9	5		167
livebirths						7	8	4	1	5	6	6	5	4	5	8	4	6	2	4	5	2		82
fetal deaths						0	0	1	0	1	2	1	4	1	0	1	0	0	0	1	1	0		13
induced abortions						3	4	4	7	5	6	3	3	5	7	2	3	4	6	4	3	3		72
population:						13663	13303	13276	13340	13161	13349	13794	13744	13395	12988	12276	12465	11768	11026	10800	10719	10050		213117
Total Prevalence						7.32	9.02	6.78	6.00	8.36	10.49	7.25	8.73	7.47	9.24	8.96	5.62	8.50	7.26	8.33	8.40	4.98		7.84
Livebirth Prevalence						5.15	6.04	3.02	0.75	3.81	4.51	4.36	3.65	2.99	3.86	6.54	3.22	5.12	1.82	3.72	4.68	2.00		3.86
Antwerp (Belgium)																								
total cases											9	8	2	9	12	8	9	15	17	12	19	16	14	150
livebirths											4	2	0	7	6	4	2	2	6	1	4	5	5	48
fetal deaths											2	1	0	0	1	0	1	0	0	0	1	3	0	9
induced abortions											3	5	2	2	5	4	6	13	11	11	14	8	9	93
population:											3740	4688	6180	7555	10964	10899	10796	18282	17930	17968	17717	17318	17409	161446
Total Prevalence											24.06	17.06	3.24	11.91	10.94	7.34	8.34	8.20	9.48	6.68	10.72	9.24	8.04	9.29
Livebirth Prevalence											10.70	4.27	0.00	9.27	5.47	3.67	1.85	1.09	3.35	0.56	2.26	2.89	2.87	2.97
Hainaut (Belgium)																								
total cases	10	11	4	7	10	9	12	14	4	14	18	17	17	11	10	11	17	12	14	10	6	17	15	270
livebirths	6	4	2	2	5	2	4	3	0	7	6	6	6	5	5	5	7	1	3	3	0	8	4	94
fetal deaths	0	5	0	2	0	2	2	1	0	2	5	2	1	0	2	0	0	0	1	0	0	0	1	26
induced abortions	4	2	2	3	5	5	6	10	4	5	7	9	10	6	3	6	10	11	10	7	6	9	10	150
population:	8449	8204	8209	7862	8066	8182	8380	8518	8805	13579	13503	13595	13328	12583	12273	11933	12416	12314	12044	12097	12823	12405	12102	251670
Total Prevalence	11.84	13.41	4.87	8.90	12.40	11.00	14.32	16.44	4.54	10.31	13.33	12.50	12.76	8.74	8.15	9.22	13.69	9.75	11.62	8.27	4.68	13.70	12.39	10.73
Livebirth Prevalence	7.16	4.91	2.45	2.56	6.24	2.46	4.80	3.54	0.00	5.18	4.47	4.43	4.52	3.99	4.09	4.21	5.67	0.82	2.51	2.49	0.00	6.47	3.32	3.76
Sofia (Bulgaria)																								
total cases																	16	17	23	16				72
livebirths																	9	9	6	8				32
fetal deaths																	5	2	7	4				18
induced abortions																	2	6	10	4				22
population:																	9908	9004	9177	10168				38257
Total Prevalence																	16.15	18.88	25.06	15.74				18.82
Livebirth Prevalence																	9.16	10.07	6.59	7.92				8.43

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Zagreb (Croatia)																								
total cases				2	4	2	4	3	4	4	5	5	5	5	2	0	0	5	5	2	4	3	3	67
livebirths				0	4	1	3	3	2	4	5	5	5	4	2	0	0	1	2	2	2	3	1	49
fetal deaths				2	0	1	1	0	2	0	0	0	0	0	0	0	0	2	0	0	0	0	0	8
induced abortions				0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	3	0	2	0	2	10
population:				4023	4029	3784	6867	6686	6183	7329	6948	7003	6481	6532	6135	6280	6435	6337	6170	6033	5815	5731	5544	120345
Total Prevalence				4.97	9.93	5.29	5.82	4.49	6.47	5.46	7.20	7.14	7.71	7.65	3.26	0.00	0.00	7.89	8.10	3.32	6.88	5.23	5.41	5.57
Livebirth Prevalence				0.00	10.01	2.67	4.40	4.53	3.26	5.48	7.22	7.17	7.76	6.16	3.27	0.00	0.00	1.59	3.26	3.33	3.46	5.27	1.82	4.10
Odense (Denmark)																								
total cases	9	5	4	8	8	1	6	10	5	7	6	10	3	4	4	10	6	6	5	8	11	6	6	148
livebirths	4	2	2	5	3	0	2	5	3	5	2	6	1	4	2	5	4	2	2	6	6	4	2	77
fetal deaths	4	3	1	1	1	0	3	2	0	1	1	2	1	0	1	1	1	2	1	0	4	0	0	30
induced abortions	1	0	1	2	4	1	1	3	2	1	3	2	1	0	1	4	1	2	2	2	1	2	4	41
population:	5173	4614	4467	4301	4559	4698	4849	4852	5050	5287	5689	5723	6015	5876	6018	6073	5807	5933	5430	5689	5680	5415	5096	122294
Total Prevalence	17.40	10.84	8.95	18.60	17.55	2.13	12.37	20.61	9.90	13.24	10.55	17.47	4.99	6.81	6.65	16.47	10.33	10.11	9.21	14.06	19.37	11.08	11.77	12.10
Livebirth Prevalence	7.77	4.36	4.50	11.70	6.61	0.00	4.14	10.35	5.97	9.49	3.53	10.54	1.67	6.83	3.34	8.28	6.94	3.39	3.71	10.60	10.60	7.43	3.95	6.33
Auvergne (France)																								
total cases																							11	11
livebirths																							2	2
fetal deaths																							0	0
induced abortions																							9	9
population:																							13397	13397
Total Prevalence																							8.21	8.21
Livebirth Prevalence																							1.51	1.51
Paris (France)																								
total cases		36	27	43	38	46	41	40	38	55	51	46	41	44	42	57	46	40	44	57	60	42	58	992
livebirths		18	11	10	7	3	5	10	3	7	7	5	3	5	3	5	6	4	5	1	5	7	3	133
fetal deaths		10	7	11	5	7	12	3	4	6	4	2	2	2	1	0	0	0	2	4	2	0	3	87
induced abortions		8	9	22	26	36	24	27	31	42	40	39	36	37	38	52	40	36	37	52	53	35	52	772
population:		36917	36741	35783	35902	36536	36384	36080	36672	36866	37302	37541	36469	35819	35918	36884	37237	37272	38160	38835	38446	38716	39202	815682
Total Prevalence		9.75	7.35	12.02	10.58	12.59	11.27	11.09	10.36	14.92	13.67	12.25	11.24	12.28	11.69	15.45	12.35	10.73	11.53	14.68	15.61	10.85	14.80	12.16
Livebirth Prevalence		4.93	3.02	2.82	1.97	0.83	1.39	2.80	0.82	1.91	1.89	1.34	0.83	1.40	0.84	1.36	1.62	1.08	1.32	0.26	1.31	1.82	0.77	1.64

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Strasbourg (France)																								
total cases			14	10	20	9	15	9	12	13	13	12	17	14	12	15	19	15	16	22	21	17		295
livebirths			7	6	7	1	6	0	2	0	2	1	4	2	2	0	4	2	4	2	3	1		56
fetal deaths			2	2	2	1	2	3	2	0	2	0	1	0	1	0	1	2	2	0	0	0		23
induced abortions			5	2	11	7	7	6	8	13	9	11	12	12	9	15	14	11	10	20	18	16		216
population:			13662	12519	12924	13166	13112	12895	13595	13425	13775	13770	13736	13148	12865	13313	13185	13237	13656	13767	14238	13406		267394
Total Prevalence			10.25	7.99	15.48	6.84	11.44	6.98	8.83	9.68	9.44	8.71	12.38	10.65	9.33	11.27	14.41	11.33	11.72	15.98	14.75	12.68		11.03
Livebirth Prevalence			5.15	4.83	5.45	0.76	4.61	0.00	1.48	0.00	1.46	0.73	2.93	1.53	1.56	0.00	3.05	1.52	2.94	1.46	2.12	0.75		2.11
Mainz (Germany)																								
total cases											4	3	5	8	4	7	15	12	10	5	11	7	7	98
livebirths											2	2	5	1	2	6	9	9	6	3	7	3	5	60
fetal deaths											1	0	0	0	1	1	1	1	1	0	0	1	0	7
induced abortions											1	1	0	7	1	0	5	2	3	2	4	3	2	31
population:											3903	4113	3941	4020	3769	3560	3603	3890	3542	3275	2966	3040	3250	46872
Total Prevalence											10.25	7.29	12.69	19.90	10.61	19.66	41.63	30.85	28.23	15.27	37.09	23.03	21.54	20.91
Livebirth Prevalence											5.15	4.88	12.74	2.49	5.32	16.93	25.10	23.26	17.01	9.19	23.70	9.92	15.45	12.85
Saxony-Anhalt (Germany)																								
total cases								32	23	24	22	1	1	4	5	5	15	15	9	11	19	19	15	220
livebirths								12	8	8	9	1	1	2	2	2	5	5	2	4	5	1	3	70
fetal deaths								6	2	1	3	0	0	1	1	0	0	0	0	0	0	1	0	15
induced abortions								14	13	15	10	0	0	1	2	3	10	10	7	7	14	17	12	135
population:								17165	16623	15201	14764	9124	7633	6911	7529	7684	8906	9606	10257	11485	18799	18148	17688	197523
Total Prevalence								18.64	13.84	15.79	14.90	1.10	1.31	5.79	6.64	6.51	16.84	15.62	8.77	9.58	10.11	10.47	8.48	11.14
Livebirth Prevalence								7.03	4.84	5.29	6.12	1.10	1.32	2.90	2.67	2.62	5.65	5.22	1.96	3.50	2.67	0.55	1.70	3.56
Cork & Kerry (Ireland)																								
total cases																	13	13	10	11	10	7		64
livebirths																	10	7	6	8	5	7		43
fetal deaths																	3	6	4	3	5	0		21
induced abortions																	0	0	0	0	0	0		0
population:																	7377	7664	7854	7495	7714	7969		46073
Total Prevalence																	17.62	16.96	12.73	14.68	12.96	8.78		13.89
Livebirth Prevalence																	13.67	9.20	7.69	10.74	6.53	8.82		9.39

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Dublin (Ireland)																								
total cases	123	99	96	79	64	56	51	47	41	29	30	27	34	23	23	23	15	19	22	25	20	21	20	987
livebirths	78	65	67	61	41	36	41	30	27	19	21	20	24	20	19	18	12	16	17	18	17	16	13	696
fetal deaths	45	34	29	18	23	20	10	17	14	10	9	7	10	3	4	5	3	3	5	7	3	5	7	291
induced abortions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:	26460	25510	24822	23352	22312	22131	21708	20766	19830	18914	19393	19800	18933	18491	18412	18550	19288	20285	20899	20767	21236	22152	22936	486947
Total Prevalence	46.49	38.81	38.68	33.83	28.68	25.30	23.49	22.63	20.68	15.33	15.47	13.64	17.96	12.44	12.49	12.40	7.78	9.37	10.53	12.04	9.42	9.48	8.72	20.27
Livebirth Prevalence	29.77	25.67	27.22	26.33	18.53	16.41	19.04	14.55	13.72	10.11	10.90	10.16	12.73	10.88	10.32	9.76	6.25	7.94	8.18	8.72	8.06	7.27	5.71	14.39
Galway (Ireland)																								
total cases		6	7	7	4	13	10	6	6	1	3	4	8	1	3	2	0	2	1	0				84
livebirths		6	5	4	3	11	8	4	5	1	3	3	7	1	2	1	0	1	1	0				66
fetal deaths		0	2	3	1	2	2	2	1	0	0	1	1	0	1	1	0	1	0	0				18
induced abortions		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0
population:		3546	3604	3397	3268	3079	3155	3051	2858	2636	2691	2578	2666	2645	2375	2436	2534	2588	2747	2655				54509
Total Prevalence		16.92	19.42	20.61	12.24	42.22	31.70	19.67	20.99	3.79	11.15	15.52	30.01	3.78	12.63	8.21	0.00	7.73	3.64	0.00				15.41
Livebirth Prevalence		17.08	14.01	11.86	9.26	36.08	25.48	13.21	17.68	3.82	11.15	11.64	26.56	3.81	8.47	4.14	0.00	3.86	3.66	0.00				12.19
Campania (Italy)																	45	30	30	32	35	28	36	236
total cases																	19	14	6	12	12	10	8	81
livebirths																	1	1	3	2	0	0	0	7
fetal deaths																	25	15	21	18	23	18	28	148
induced abortions																	46658	50458	51568	47397	50171	49714	62708	358674
population:																	9.64	5.95	5.82	6.75	6.98	5.63	5.74	6.58
Total Prevalence																	4.09	2.78	1.17	2.54	2.40	2.02	1.28	2.26
Livebirth Prevalence																								
Emilia Romagna (Italy)																								
total cases		7	10	16	11	13	18	10	6	10	12	15	11	9	10	5	11	15	18	15	18	13	17	270
livebirths		7	8	13	11	12	16	10	5	9	12	15	9	8	8	5	4	7	8	5	2	2	2	178
fetal deaths		0	2	3	0	1	2	0	1	1	0	0	0	1	1	0	0	0	0	2	1	0	1	16
induced abortions		0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	7	8	10	8	15	11	14	76
population:		13189	18364	21769	23155	24016	22868	22726	22760	23380	23524	25095	25002	24533	25886	26359	28873	28859	20928	24130	24839	24330	29900	524485
Total Prevalence		5.31	5.45	7.35	4.75	5.41	7.87	4.40	2.64	4.28	5.10	5.98	4.40	3.67	3.86	1.90	3.81	5.20	8.60	6.22	7.25	5.34	5.69	5.15
Livebirth Prevalence		5.34	4.39	6.01	4.78	5.02	7.03	4.42	2.21	3.87	5.13	6.00	3.62	3.27	3.10	1.90	1.39	2.43	3.83	2.08	0.81	0.83	0.67	3.41

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
North East Italy																								
total cases		27	22	25	34	15	23	25	32	38	39	28	28	31	37	30	50	31	42	22	42	18	18	657
livebirths		20	21	21	27	14	18	23	16	13	18	10	10	10	8	7	12	8	15	6	15	0	8	300
fetal deaths		7	1	4	7	1	5	0	3	6	2	1	2	0	1	1	1	1	1	0	0	0	1	45
induced abortions		0	0	0	0	0	0	2	13	19	19	17	16	21	28	22	37	22	26	16	27	18	9	312
population:		27708	36321	41195	43202	43401	41265	42048	45307	47515	52205	51093	50340	49735	49443	51486	56869	55908	54939	54364	55052	49781	57495	1056672
Total Prevalence		9.74	6.06	6.07	7.87	3.46	5.57	5.95	7.06	8.00	7.47	5.48	5.56	6.23	7.48	5.83	8.79	5.54	7.64	4.05	7.63	3.62	3.13	6.22
Livebirth Prevalence		7.27	5.82	5.13	6.28	3.24	4.39	5.50	3.55	2.75	3.46	1.97	1.99	2.02	1.62	1.36	2.12	1.44	2.74	1.11	2.72	0.00	1.39	3.16
South East Sicily (Italy)																								
total cases												15	15	10	10	4	5	6	9	9	4	0	11	98
livebirths												14	11	9	10	4	5	6	9	9	4	0	11	92
fetal deaths												1	4	1	0	0	0	0	0	0	0	0	0	6
induced abortions												-	-	-	-	-	-	-	-	-	-	-	-	-
population:												19430	20273	19746	20031	18986	18054	18795	16922	16942	15304	16049	16073	216605
Total Prevalence												7.72	7.40	5.06	4.99	2.11	2.77	3.19	5.32	5.31	2.61	0.00	6.84	4.52
Livebirth Prevalence												7.21	5.43	4.56	4.99	2.11	2.77	3.19	5.32	5.31	2.61	0.00	6.84	4.25
Tuscany (Italy)																								
total cases	11	14	8	7	5	16	9	8	6	13	11	2	18	18	12	13	14	14	22	17	20	12	10	280
livebirths	8	10	4	5	3	6	1	2	1	6	4	0	5	8	2	4	4	1	6	6	3	3	0	92
fetal deaths	3	4	1	0	0	1	0	0	0	2	0	0	1	0	0	0	1	0	1	0	1	0	0	15
induced abortions	0	0	3	2	2	9	8	6	5	5	7	2	12	10	10	9	9	13	15	11	16	9	10	173
population:	9696	9350	9281	8948	8592	8980	8477	8511	8869	8556	8751	8657	25670	24687	24487	24288	24606	25216	25468	26060	26618	26381	26593	386742
Total Prevalence	11.34	14.97	8.62	7.82	5.82	17.82	10.62	9.40	6.77	15.19	12.57	2.31	7.01	7.29	4.90	5.35	5.69	5.55	8.64	6.52	7.51	4.55	3.76	7.24
Livebirth Prevalence	8.31	10.76	4.34	5.62	3.51	6.73	1.18	2.36	1.13	7.04	4.59	0.00	1.95	3.26	0.82	1.66	1.63	0.40	2.36	2.31	1.13	1.14	0.00	2.39
Malta																								
total cases							9	6	5	7	3	4	6	6	7	7	7	5	6	7	3	3	5	96
livebirths							6	5	5	6	2	4	5	5	5	7	5	5	5	4	3	2	3	77
fetal deaths							3	1	0	1	1	0	1	1	2	0	2	0	1	3	0	1	2	19
induced abortions							0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:							5310	5375	5461	5617	5400	5328	5503	5172	4863	4633	4978	4864	4511	4339	4272	3883	3826	83335
Total Prevalence							16.95	11.16	9.16	12.46	5.56	7.51	10.90	11.60	14.39	15.11	14.06	10.28	13.30	16.13	7.02	7.73	13.07	11.52
Livebirth Prevalence							11.40	9.38	9.24	10.77	3.73	7.54	9.13	9.71	10.36	15.17	10.11	10.34	11.14	9.29	7.05	5.18	7.88	9.30

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Northern Netherlands																								
total cases		8	11	14	11	17	13	4	25	16	29	27	23	16	16	18	21	20	16	23	18	10	14	370
livebirths		5	8	7	7	7	7	2	13	11	19	21	15	7	9	10	10	10	9	8	10	7	10	212
fetal deaths		2	2	3	3	4	2	1	5	2	5	3	1	6	1	1	3	2	3	5	4	2	3	63
induced abortions		1	1	4	1	6	4	1	7	3	5	3	7	3	6	7	8	8	4	10	4	1	1	95
population:		7877	7731	7542	7559	7792	11936	11847	11595	19093	19635	19853	19140	19387	19283	19296	19072	19427	19976	20198	20495	20487	20432	349653
Total Prevalence		10.16	14.23	18.56	14.55	21.82	10.89	3.38	21.56	8.38	14.77	13.60	12.02	8.25	8.30	9.33	11.01	10.29	8.01	11.39	8.78	4.88	6.85	10.58
Livebirth Prevalence		6.38	10.40	9.33	9.32	9.05	5.90	1.70	11.28	5.80	9.73	10.64	7.88	3.63	4.69	5.21	5.29	5.18	4.54	3.98	4.92	3.43	4.93	6.10
Wielkopolska (Poland)																								
total cases																				39	43	34	38	154
livebirths																				37	42	31	35	145
fetal deaths																				2	1	3	3	9
induced abortions																				-	-	-	-	-
population:																				35756	35309	34805	33253	139123
Total Prevalence																				10.91	12.18	9.77	11.43	11.07
Livebirth Prevalence																				10.41	11.96	8.95	10.57	10.48
Southern Portugal																								
total cases											6	5	4	1	7	8	13	8	2	14	13	14	17	112
livebirths											3	3	4	1	7	4	6	5	2	4	6	3	1	49
fetal deaths											0	2	0	0	0	2	1	0	0	0	1	1	1	8
induced abortions											3	0	0	0	0	2	6	3	0	10	6	10	15	55
population:											5461	5554	7391	7152	7000	14959	15439	16293	16312	17047	19390	18217	19041	169256
Total Prevalence											10.99	9.00	5.41	1.40	10.00	5.35	8.42	4.91	1.23	8.21	6.70	7.69	8.93	6.62
Livebirth Prevalence											5.54	5.45	5.46	1.42	10.07	2.68	3.92	3.08	1.23	2.36	3.11	1.66	0.53	2.91
Asturias (Spain)																								
total cases											13	10	9	10	9	7	10	4	15	3	6	6	8	110
livebirths											4	2	1	0	1	2	2	1	2	0	1	0	0	16
fetal deaths											0	0	1	0	0	0	0	0	0	0	0	0	0	1
induced abortions											9	8	7	10	8	5	8	3	13	3	5	6	8	93
population:											7722	7693	7474	7012	6626	6553	6507	6473	6321	6516	6719	6833	6709	89158
Total Prevalence											16.84	13.00	12.04	14.26	13.58	10.68	15.37	6.18	23.73	4.60	8.93	8.78	11.92	12.34
Livebirth Prevalence											5.21	2.61	1.35	0.00	1.52	3.07	3.09	1.55	3.18	0.00	1.50	0.00	0.00	1.80

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Barcelona (Spain)																								
total cases													14	13	10	11	10	8	14	10	8	17	13	128
livebirths													2	1	4	4	1	0	4	0	1	4	3	24
fetal deaths													1	1	0	1	1	1	1	2	0	2	1	11
induced abortions													11	11	6	6	8	7	9	8	7	11	9	93
population:													13477	12738	12609	12199	12031	12240	11684	12270	12655	12678	13034	137615
Total Prevalence													10.39	10.21	7.93	9.02	8.31	6.54	11.98	8.15	6.32	13.41	9.97	9.30
Livebirth Prevalence													1.49	0.79	3.19	3.29	0.84	0.00	3.44	0.00	0.79	3.17	2.31	1.75
Basque Country (Spain)																								
total cases											23	13	19	12	22	14	19	16	13	28	22	17	22	240
livebirths											12	7	5	3	7	3	2	4	2	6	4	2	1	58
fetal deaths											1	0	0	0	1	1	0	1	0	0	1	0	0	5
induced abortions											10	6	14	9	14	10	17	11	11	22	17	15	21	177
population:											16438	16291	16316	15891	15357	15397	16060	16397	16169	16859	17408	17718	18210	214511
Total Prevalence											13.99	7.98	11.65	7.55	14.33	9.09	11.83	9.76	8.04	16.61	12.64	9.59	12.08	11.19
Livebirth Prevalence											7.33	4.31	3.08	1.90	4.58	1.96	1.25	2.45	1.24	3.57	2.31	1.13	0.55	2.72
Vaud (Switzerland)																								
total cases										6	6	8	9	7	8	8	14	3	7	5	12	8	7	108
livebirths										0	2	1	2	2	1	1	5	1	2	1	5	1	1	25
fetal deaths										0	0	0	0	1	0	1	0	0	0	0	0	0	1	3
induced abortions										6	4	7	7	4	7	6	9	2	5	4	7	7	5	80
population:										7212	7697	8211	8076	7700	7683	7697	7730	7562	7438	7465	7618	7263	6810	106162
Total Prevalence										8.32	7.80	9.74	11.14	9.09	10.41	10.39	18.11	3.97	9.41	6.70	15.75	11.01	10.28	10.17
Livebirth Prevalence										0.00	2.61	1.22	2.48	2.61	1.31	1.30	6.49	1.33	2.70	1.34	6.59	1.38	1.47	2.36
Glasgow (UK)																								
total cases	65	51	51	35	34	55	51	31	21	28	22	19	22	18	21	22	31	12	21	18	5			633
livebirths	18	7	18	8	10	17	17	4	9	7	3	5	4	5	8	4	6	1	5	8	3			167
fetal deaths	13	9	3	1	0	3	2	2	0	1	2	1	2	2	0	5	1	3	1	1	0			52
induced abortions	34	35	30	26	24	35	32	25	12	20	17	13	16	11	13	13	24	8	15	9	2			414
population:	13590	13511	12884	12488	12673	12944	12875	13047	12949	12461	12494	12543	12157	11360	11407	11227	10976	10997	10239	9721	9682			252225
Total Prevalence	47.83	37.75	39.58	28.03	26.83	42.49	39.61	23.76	16.22	22.47	17.61	15.15	18.10	15.85	18.41	19.60	28.24	10.91	20.51	18.52	5.16			25.10
Livebirth Prevalence	13.48	5.23	14.05	6.35	7.87	13.07	13.14	3.10	7.01	5.73	2.42	3.92	3.26	4.23	7.06	3.59	5.50	0.91	4.92	8.27	3.12			6.63

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Merseyside & Cheshire (UK)																								
total cases																34	43	49	28	29				183
livebirths																3	6	5	4	7				25
fetal deaths																1	0	3	3	1				8
induced abortions																30	37	41	21	21				150
population:																28786	29031	27983	27514	26553				139867
Total Prevalence																11.81	14.81	17.51	10.18	10.92				13.08
Livebirth Prevalence																1.05	2.08	1.80	1.46	2.65				1.80
Northern Regions (UK)																								
total cases																					42	44	35	121
livebirths																					8	6	4	18
fetal deaths																					1	1	1	3
induced abortions																					33	37	30	100
population:																					29785	29159	29394	88338
Total Prevalence																					14.10	15.09	11.91	13.70
Livebirth Prevalence																					2.70	2.07	1.37	2.05
North West Thames (UK)																								
total cases												68	67	69	52	66	62	58	66	41	66	36	55	706
livebirths												9	9	7	4	12	4	7	5	3	8	5	8	81
fetal deaths												3	2	4	2	8	4	3	1	3	3	2	5	40
induced abortions												56	56	58	46	46	54	48	60	35	55	29	42	585
population:												47330	47493	46762	47526	47324	47324	47355	47549	46874	45652	45686	46518	563393
Total Prevalence												14.37	14.11	14.76	10.94	13.95	13.10	12.25	13.88	8.75	14.46	7.88	11.82	12.53
Livebirth Prevalence												1.90	1.90	1.50	0.84	2.54	0.85	1.48	1.05	0.64	1.76	1.10	1.73	5.91
Oxford (UK)																								
total cases												10	8	11	15	7	6	8	9	7	6	11	8	106
livebirths												3	2	0	1	1	0	3	1	1	1	2	2	17
fetal deaths												0	1	1	1	0	0	0	0	0	0	0	0	3
induced abortions												7	5	10	13	6	6	5	8	6	5	9	6	86
population:												5878	5778	5707	5882	5588	5693	5699	5613	5551	6504	6380	6355	70628
Total Prevalence												17.01	13.85	19.27	25.50	12.53	10.54	14.04	16.03	12.61	9.23	17.24	12.59	15.01
Livebirth Prevalence												5.12	3.48	0.00	1.71	1.80	0.00	5.29	1.79	1.81	1.54	3.15	3.16	2.42

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Trent (UK)																								
total cases																			51	62	60	58	76	307
livebirths																			10	8	10	8	17	53
fetal deaths																			6	3	3	3	6	21
induced abortions																			35	51	47	47	53	233
population:																			59509	57438	55541	54302	54601	281391
Total Prevalence																			8.57	10.79	10.80	10.68	13.92	10.91
Livebirth Prevalence																			1.69	1.40	1.81	1.48	3.13	1.89
Wales (UK)																								
total cases																			64	58	50	54	53	279
livebirths																			4	9	6	7	10	36
fetal deaths																			1	3	2	0	1	7
induced abortions																			59	46	42	47	42	236
population:																			33620	32266	31449	30771	30369	158475
Total Prevalence																			19.04	17.98	15.90	17.55	17.45	17.61
Livebirth Prevalence																			1.20	2.80	1.92	2.29	3.31	2.28
Wessex (UK)																								
total cases															26	36	31	37	38	42	31	43	33	317
livebirths															3	9	3	4	3	2	3	3	4	34
fetal deaths															2	0	0	6	1	2	0	2	1	14
induced abortions															21	27	28	27	34	38	28	38	28	269
population:															26806	25460	25110	26123	26213	25123	26080	25819	25548	232282
Total Prevalence															9.70	14.14	12.35	14.16	14.50	16.72	11.89	16.65	12.92	13.65
Livebirth Prevalence															1.13	3.55	1.20	1.54	1.15	0.80	1.16	1.17	1.57	1.47
Total (Full Member Registries)																								
total cases	218	264	254	253	243	262	274	254	236	276	339	367	398	364	391	439	570	505	655	669	694	586	625	**9136**
livebirths	114	144	153	142	128	117	142	117	100	108	146	151	145	121	128	134	166	147	164	196	206	153	166	**3288**
fetal deaths	65	74	50	50	42	43	46	39	34	34	40	27	36	25	24	30	30	40	46	48	34	27	38	**922**
induced abortions	39	46	51	61	73	102	86	98	102	134	153	189	217	218	239	275	374	318	445	425	454	406	421	**4926**
population:	63368	150426	176086	183179	186241	202372	210489	226843	229897	250232	294384	364685	393216	384557	414135	450126	524968	538829	621385	653903	656696	634606	643493	**8454116**
Total Prevalence	34.40	17.55	14.42	13.81	13.05	12.95	13.02	11.20	10.27	11.03	11.52	10.06	10.12	9.47	9.44	9.75	10.86	9.37	10.54	10.23	10.57	9.23	9.71	**10.81**
Livebirth Prevalence	18.18	9.65	8.75	7.80	6.92	5.82	6.79	5.19	4.38	4.34	4.99	4.15	3.70	3.15	3.10	2.99	3.18	2.74	2.65	3.01	3.15	2.42	2.59	4.17

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Associate Member Registries																								
Finland																								
total cases														47	52	49	54	61	71	44	44	57	55	534
livebirths														26	15	19	20	29	22	16	18	19	19	203
fetal deaths														1	2	2	4	5	2	1	1	3	1	22
induced abortions														20	35	28	30	27	47	27	25	35	35	309
population:														65098	65480	63368	60965	59569	57345	57782	56969	56397	55768	598741
Total Prevalence														7.22	7.94	7.73	8.86	10.24	12.38	7.61	7.72	10.11	9.86	8.92
Livebirth Prevalence														4.01	2.30	3.01	3.29	4.89	3.85	2.78	3.17	3.38	3.42	3.40
Central East France																								
total cases	33	25	32	34	31	44	40	36	42	31	49	57	56	66	62	72	65	62	65	59	44	67	77	1149
livebirths	31	23	29	30	27	37	27	21	29	17	25	28	29	24	21	25	26	18	18	12	4	6	12	519
fetal deaths	2	2	3	4	4	3	2	1	2	0	2	0	2	2	0	1	0	0	1	3	0	1	0	35
induced abortions	0	0	0	0	0	4	11	14	11	14	22	29	25	40	41	46	39	44	46	44	40	60	65	595
population:	75332	76220	75813	86433	86904	90825	91950	90191	91303	99858	107370	106607	104480	99249	99674	102153	103440	102090	102483	102982	93963	93721	93405	2176446
Total Prevalence	4.38	3.28	4.22	3.93	3.57	4.84	4.35	3.99	4.60	3.10	4.56	5.35	5.36	6.65	6.22	7.05	6.28	6.07	6.34	5.73	4.68	7.15	8.24	5.28
Livebirth Prevalence	4.15	3.04	3.85	3.49	3.13	4.10	2.96	2.34	3.19	1.71	2.34	2.64	2.79	2.43	2.12	2.46	2.52	1.77	1.76	1.17	0.43	0.64	1.29	2.40
Madrid (Spain)																								
total cases	65	56	65	63	68	84	43	35	43	39	57	65	46	38	38	33	34	36	29	21	18	22	13	1011
livebirths	49	46	51	54	56	57	33	28	37	28	47	53	41	33	33	27	31	30	27	18	18	21	13	831
fetal deaths	16	10	14	9	12	27	10	7	6	11	10	12	5	5	5	6	3	6	2	3	0	1	0	180
induced abortions	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
population:	56910	56102	61333	71812	69513	66720	58245	51051	52686	59046	84379	87708	91607	82925	87239	87372	94044	98945	96490	104336	105833	103404	110954	1838654
Total Prevalence	11.42	9.98	10.60	8.77	9.78	12.59	7.38	6.86	8.16	6.61	6.76	7.41	5.02	4.58	4.36	3.78	3.62	3.64	3.01	2.01	1.70	2.13	1.17	5.50
Livebirth Prevalence	8.69	8.27	8.39	7.58	8.12	8.62	5.71	5.53	7.08	4.78	5.61	6.09	4.50	4.01	3.81	3.11	3.31	3.05	2.81	1.73	1.71	2.03	1.18	4.82
Norway																								
total cases	55	55	53	46	39	50	50	46	37	54	31	41	52	35	52	58	55	34	41	61	77	53	56	1131
livebirths	28	39	30	29	26	18	24	24	19	28	21	22	28	15	17	27	25	16	18	20	25	20	10	529
fetal deaths	27	16	23	17	13	23	18	12	12	13	6	8	7	8	11	11	11	5	9	10	5	1	1	267
induced abortions	0	0	0	0	0	9	8	10	6	13	4	11	17	12	24	20	19	13	14	31	47	32	45	335
population:	51495	51021	51642	50258	50576	51416	52885	54313	57936	59712	61523	61386	60636	60166	60306	60488	61092	59896	58482	59967	59881	57475	56450	1309002
Total Prevalence	10.68	10.78	10.26	9.15	7.71	9.72	9.45	8.47	6.39	9.04	5.04	6.68	8.58	5.82	8.62	9.59	9.00	5.68	7.01	10.17	12.86	9.22	9.92	8.64
Livebirth Prevalence	5.49	7.71	5.87	5.83	5.18	3.53	4.57	4.45	3.30	4.72	3.44	3.61	4.65	2.51	2.84	4.49	4.12	2.69	3.10	3.37	4.21	3.51	1.78	4.07

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Neural Tube Defects (Contd)																								
Poland																								
total cases																				137	98	151	184	570
livebirths																				114	87	134	154	489
fetal deaths																				23	11	17	30	81
induced abortions																				-	-	-	-	-
population:																				149653	147228	185125	220040	702046
Total Prevalence																				9.15	6.66	8.16	8.36	8.12
Livebirth Prevalence																				7.67	5.95	7.28	7.04	7.01
Sweden																								
total cases																						88	104	192
livebirths																						17	28	45
fetal deaths																						1	0	1
induced abortions																						70	76	146
population:																						91815	96167	187982
Total Prevalence																						9.58	10.81	10.21
Livebirth Prevalence																						1.86	2.92	2.40
Total (Associate Member Registries)																								
total cases	153	136	150	143	138	178	133	117	122	124	137	163	154	186	204	212	208	193	206	322	281	438	489	**4587**
livebirths	108	108	110	113	109	112	84	73	85	73	93	103	98	98	86	98	102	93	85	180	152	217	236	**2616**
fetal deaths	45	28	40	30	29	53	30	20	20	24	18	20	14	16	18	20	18	16	14	40	17	24	32	**586**
induced abortions	0	0	0	0	0	13	19	24	17	27	26	40	42	72	100	94	88	84	107	102	112	197	221	**1385**
population:	183737	183343	188788	208503	206993	208961	203080	195555	201925	218616	253272	255701	256723	307438	312699	313381	319541	320500	314800	474720	463874	587937	632784	**6812871**
Total Prevalence	8.33	7.42	7.95	6.86	6.67	8.52	6.55	5.98	6.04	5.67	5.41	6.37	6.00	6.05	6.52	6.76	6.51	6.02	6.54	6.78	6.06	7.45	7.73	**6.73**
Livebirth Prevalence	5.93	5.94	5.88	5.46	5.31	5.40	4.17	3.76	4.24	3.36	3.70	4.06	3.84	3.21	2.77	3.15	3.21	2.92	2.71	3.81	3.29	3.71	3.75	3.92
Total (All registries)																								
total cases	371	400	404	396	381	440	407	371	358	400	476	530	552	550	595	651	778	698	861	991	975	1024	1114	**13723**
livebirths	222	252	263	255	237	229	226	190	185	181	239	254	243	219	214	232	268	240	249	376	358	370	402	**5904**
fetal deaths	110	102	90	80	71	96	76	59	54	58	58	47	50	41	42	50	48	56	60	88	51	51	70	**1508**
induced abortions	39	46	51	61	73	115	105	122	119	161	179	229	259	290	339	369	462	402	552	527	566	603	642	**6311**
population:	247105	333769	364874	391682	393234	411333	413569	422398	431822	468848	547656	620386	649939	691995	726834	763507	844509	859329	936185	1128623	1120570	1222543	1276277	**15266987**
Total Prevalence	15.01	11.98	11.07	10.11	9.69	10.70	9.84	8.78	8.29	8.53	8.69	8.54	8.49	7.95	8.19	8.53	9.21	8.12	9.20	8.78	8.70	8.38	8.73	**8.99**
Livebirth Prevalence	9.07	7.61	7.27	6.56	6.07	5.61	5.50	4.53	4.31	3.89	4.39	4.11	3.76	3.18	2.96	3.05	3.19	2.81	2.67	3.35	3.21	3.04	3.17	4.06

Table A2.2: Spina Bifida: Number of cases by type of birth[1], population (births), total prevalence rate and livebirth prevalence rate (per 10,000 births) by year and registry: 41 EUROCAT registries, 1980-2002

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Styria (Austria)																								
total cases						6	10	7	4	7	9	8	7	7	6	10	2	5	5	4	6	2		105
livebirths						6	8	3	1	5	5	6	4	4	5	8	2	5	1	2	4	1		70
fetal deaths						0	0	1	0	1	1	1	2	1	0	0	0	0	0	0	1	0		8
induced abortions						0	2	3	3	1	3	1	1	2	1	2	0	0	4	2	1	1		27
population:						13663	13303	13276	13340	13161	13349	13794	13744	13395	12988	12276	12465	11768	11026	10800	10719	10050		213117
Total Prevalence						4.39	7.52	5.27	3.00	5.32	6.74	5.80	5.09	5.23	4.62	8.15	1.60	4.25	4.53	3.70	5.60	1.99		4.93
Livebirth Prevalence						4.41	6.04	2.27	0.75	3.81	3.76	4.36	2.92	2.99	3.86	6.54	1.61	4.27	0.91	1.86	3.75	1.00		3.30
Antwerp (Belgium)																								
total cases											6	2	0	7	8	5	4	2	14	1	11	14	10	84
livebirths											4	0	0	6	6	4	2	2	6	0	4	4	5	43
fetal deaths											1	0	0	0	1	0	0	0	0	0	1	2	0	5
induced abortions											1	2	0	1	1	1	2	0	8	1	6	8	5	36
population:											3740	4688	6180	7555	10964	10899	10796	18282	17930	17968	17717	17318	17409	161446
Total Prevalence											16.04	4.27	0.00	9.27	7.30	4.59	3.71	1.09	7.81	0.56	6.21	8.08	5.74	5.20
Livebirth Prevalence											10.70	0.00	0.00	7.94	5.47	3.67	1.85	1.09	3.35	0.00	2.26	2.31	2.87	2.66
Hainaut (Belgium)																								
total cases	6	3	0	3	4	2	6	4	0	6	12	10	13	5	7	7	9	6	7	8	2	11	7	138
livebirths	6	2	0	1	4	0	4	3	0	5	4	6	6	4	4	5	5	1	2	3	0	7	4	76
fetal deaths	0	1	0	1	0	1	1	1	0	1	5	2	0	0	2	0	0	0	1	0	0	0	1	17
induced abortions	0	0	0	1	0	1	1	0	0	0	3	2	7	1	1	2	4	5	4	5	2	4	2	45
population:	8449	8204	8209	7862	8066	8182	8380	8518	8805	13579	13503	13595	13328	12583	12273	11933	12416	12314	12044	12097	12823	12405	12102	251670
Total Prevalence	7.10	3.66	0.00	3.82	4.96	2.44	7.16	4.70	0.00	4.42	8.89	7.36	9.75	3.97	5.70	5.87	7.25	4.87	5.81	6.61	1.56	8.87	5.78	5.48
Livebirth Prevalence	7.16	2.46	0.00	1.28	4.99	0.00	4.80	3.54	0.00	3.70	2.98	4.43	4.52	3.19	3.27	4.21	4.05	0.82	1.67	2.49	0.00	5.66	3.32	3.04
Sofia (Bulgaria)																								
total cases																	10	10	13	10				43
livebirths																	9	8	5	8				30
fetal deaths																	1	1	2	1				5
induced abortions																	0	1	6	1				8
population:																	9908	9004	9177	10168				38257
Total Prevalence																	10.09	11.11	14.17	9.83				11.24
Livebirth Prevalence																	9.16	8.95	5.49	7.92				7.90

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Zagreb (Croatia)																								
total cases				0	4	1	3	2	4	3	3	5	5	3	2	0	0	4	3	2	1	3	2	50
livebirths				0	4	1	3	2	2	3	3	5	5	3	2	0	0	1	2	2	1	3	1	43
fetal deaths				0	0	0	0	0	2	0	0	0	0	0	0	0	0	2	0	0	0	0	0	4
induced abortions				0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	3
population:				4023	4029	3784	6867	6686	6183	7329	6948	7003	6481	6532	6135	6280	6435	6337	6170	6033	5815	5731	5544	120345
Total Prevalence				0.00	9.93	2.64	4.37	2.99	6.47	4.09	4.32	7.14	7.71	4.59	3.26	0.00	0.00	6.31	4.86	3.32	1.72	5.23	3.61	4.15
Livebirth Prevalence				0.00	10.01	2.67	4.40	3.02	3.26	4.11	4.33	7.17	7.76	4.62	3.27	0.00	0.00	1.59	3.26	3.33	1.73	5.27	1.82	3.59
Odense (Denmark)																								
total cases	2	2	1	4	4	0	4	4	3	5	4	6	2	2	2	5	4	5	1	6	6	5	3	80
livebirths	2	2	1	4	3	0	2	3	2	4	1	6	1	2	1	4	4	2	1	6	6	4	1	62
fetal deaths	0	0	0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	2	0	0	0	0	0	5
induced abortions	0	0	0	0	1	0	0	1	1	1	3	0	1	0	0	1	0	1	0	0	0	1	2	13
population:	5173	4614	4467	4301	4559	4698	4849	4852	5050	5287	5689	5723	6015	5876	6018	6073	5807	5933	5430	5689	5680	5415	5096	122294
Total Prevalence	3.87	4.33	2.24	9.30	8.77	0.00	8.25	8.24	5.94	9.46	7.03	10.48	3.33	3.40	3.32	8.23	6.89	8.43	1.84	10.55	10.56	9.23	5.89	6.54
Livebirth Prevalence	3.88	4.36	2.25	9.36	6.61	0.00	4.14	6.21	3.98	7.60	1.77	10.54	1.67	3.42	1.67	6.62	6.94	3.39	1.85	10.60	10.60	7.43	1.97	5.09
Auvergne (France)																								
total cases																							4	4
livebirths																							1	1
fetal deaths																							0	0
induced abortions																							3	3
population:																							13397	13397
Total Prevalence																							2.99	2.99
Livebirth Prevalence																							0.75	0.75
Paris (France)																								
total cases		24	11	22	9	14	25	12	11	28	21	13	16	22	19	26	20	12	18	21	27	15	20	406
livebirths		16	7	9	5	2	5	5	2	5	5	3	3	1	1	2	3	1	3	0	3	7	3	91
fetal deaths		4	3	5	1	4	8	0	0	3	1	0	0	1	0	0	0	0	1	2	1	0	1	35
induced abortions		4	1	8	3	8	12	7	9	20	15	10	13	20	18	24	17	11	14	19	23	8	16	280
population:		36917	36741	35783	35902	36536	36384	36080	36672	36866	37302	37541	36469	35819	35918	36884	37237	37272	38160	38835	38446	38716	39202	815682
Total Prevalence		6.50	2.99	6.15	2.51	3.83	6.87	3.33	3.00	7.06	5.63	3.46	4.39	6.14	5.29	7.05	5.37	3.22	4.72	5.41	7.02	3.87	5.10	4.98
Livebirth Prevalence		4.38	1.92	2.54	1.41	0.55	1.39	1.40	0.55	1.37	1.35	0.80	0.83	0.28	0.28	0.55	0.81	0.27	0.79	0.00	0.78	1.82	0.77	1.12

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Strasbourg (France)																								
total cases			9	5	8	4	12	2	4	6	4	4	6	5	7	4	11	4	12	11	9	9		136
livebirths			5	5	5	1	6	0	1	0	1	1	3	1	2	0	2	1	3	2	2	0		41
fetal deaths			2	0	0	0	2	0	1	0	1	0	0	0	1	0	1	0	1	0	0	0		9
induced abortions			2	0	3	3	4	2	2	6	2	3	3	4	4	4	8	3	8	9	7	9		86
population:			13662	12519	12924	13166	13112	12895	13595	13425	13775	13770	13736	13148	12865	13313	13185	13237	13656	13767	14238	13406		267394
Total Prevalence			6.59	3.99	6.19	3.04	9.15	1.55	2.94	4.47	2.90	2.90	4.37	3.80	5.44	3.00	8.34	3.02	8.79	7.99	6.32	6.71		5.09
Livebirth Prevalence			3.68	4.02	3.89	0.76	4.61	0.00	0.74	0.00	0.73	0.73	2.20	0.76	1.56	0.00	1.52	0.76	2.21	1.46	1.41	0.00		1.54
Mainz (Germany)																								
total cases											3	2	4	2	3	6	10	10	7	4	7	6	5	69
livebirths											1	2	4	1	2	6	7	8	5	3	5	3	5	52
fetal deaths											1	0	0	0	0	0	1	1	1	0	0	1	0	5
induced abortions											1	0	0	1	1	0	2	1	1	1	2	2	0	12
population:											3903	4113	3941	4020	3769	3560	3603	3890	3542	3275	2966	3040	3250	46872
Total Prevalence											7.69	4.86	10.15	4.98	7.96	16.85	27.75	25.71	19.76	12.21	23.60	19.74	15.38	14.72
Livebirth Prevalence											2.57	4.88	10.19	2.49	5.32	16.93	19.52	20.67	14.18	9.19	16.93	9.92	15.45	11.14
Saxony-Anhalt (Germany)																								
total cases								17	14	14	17	0	1	1	4	3	6	6	4	5	16	12	8	128
livebirths								12	8	7	8	0	1	1	2	1	3	3	1	4	4	1	2	58
fetal deaths								2	2	1	2	0	0	0	1	0	0	0	0	0	0	0	0	8
induced abortions								3	4	6	7	0	0	0	1	2	3	3	3	1	12	11	6	62
population:								17165	16623	15201	14764	9124	7633	6911	7529	7684	8906	9606	10257	11485	18799	18148	17688	197523
Total Prevalence								9.90	8.42	9.21	11.51	0.00	1.31	1.45	5.31	3.90	6.74	6.25	3.90	4.35	8.51	6.61	4.52	6.48
Livebirth Prevalence								7.03	4.84	4.63	5.44	0.00	1.32	1.45	2.67	1.31	3.39	3.13	0.98	3.50	2.14	0.55	1.14	2.95
Cork & Kerry (Ireland)																								
total cases																	4	9	3	6	6	5		33
livebirths																	4	6	2	5	4	5		26
fetal deaths																	0	3	1	1	2	0		7
induced abortions																	0	0	0	0	0	0		0
population:																	7377	7664	7854	7495	7714	7969		46073
Total Prevalence																	5.42	11.74	3.82	8.01	7.78	6.27		7.16
Livebirth Prevalence																	5.47	7.89	2.56	6.71	5.22	6.30		5.68

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Dublin (Ireland)																								
total cases	71	43	47	42	37	31	29	25	19	13	14	12	14	10	11	13	10	10	7	15	11	11	8	503
livebirths	63	39	44	39	32	28	27	21	16	10	13	10	13	10	11	12	9	9	7	12	10	10	8	453
fetal deaths	8	4	3	3	5	3	2	4	3	3	1	2	1	0	0	1	1	1	0	3	1	1	0	50
induced abortions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:	26460	25510	24822	23352	22312	22131	21708	20766	19830	18914	19393	19800	18933	18491	18412	18550	19288	20285	20899	20767	21236	22152	22936	486947
Total Prevalence	26.83	16.86	18.93	17.99	16.58	14.01	13.36	12.04	9.58	6.87	7.22	6.06	7.39	5.41	5.97	7.01	5.18	4.93	3.35	7.22	5.18	4.97	3.49	10.33
Livebirth Prevalence	24.04	15.40	17.88	16.84	14.46	12.76	12.54	10.18	8.13	5.32	6.75	5.08	6.90	5.44	6.01	6.51	4.69	4.47	3.37	5.81	4.74	4.54	3.51	9.37
Galway (Ireland)																								
total cases		3	4	5	3	5	6	4	4	1	1	2	7	1	2	1	0	1	1	0				51
livebirths		3	4	4	3	5	6	3	4	1	1	2	6	1	2	0	0	1	1	0				47
fetal deaths		0	0	1	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0				4
induced abortions		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0
population:		3546	3604	3397	3268	3079	3155	3051	2858	2636	2691	2578	2666	2645	2375	2436	2534	2588	2747	2655				54509
Total Prevalence		8.46	11.10	14.72	9.18	16.24	19.02	13.11	14.00	3.79	3.72	7.76	26.26	3.78	8.42	4.11	0.00	3.86	3.64	0.00				9.36
Livebirth Prevalence		8.54	11.21	11.86	9.26	16.40	19.11	9.90	14.14	3.82	3.72	7.76	22.76	3.81	8.47	0.00	0.00	3.86	3.66	0.00				8.68
Campania (Italy)																	19	18	12	13	15	13	12	102
total cases																	9	12	6	6	9	8	6	56
livebirths																	0	0	1	0	0	0	0	1
fetal deaths																	10	6	5	7	6	5	6	45
induced abortions																	46658	50458	51568	47397	50171	49714	62708	358674
population:																	4.07	3.57	2.33	2.74	2.99	2.61	1.91	2.84
Total Prevalence																	1.94	2.39	1.17	1.27	1.80	1.61	0.96	1.57
Livebirth Prevalence																								
Emilia Romagna (Italy)																								
total cases		3	6	12	9	9	11	7	5	8	9	13	10	7	8	3	7	7	11	8	11	7	9	180
livebirths		3	6	12	9	9	11	7	5	7	9	13	8	6	7	3	3	4	6	3	2	2	2	137
fetal deaths		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	2
induced abortions		0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	4	3	5	5	9	5	7	41
population:		13189	18364	21769	23155	24016	22868	22726	22760	23380	23524	25095	25002	24533	25886	26359	28873	28859	20928	24130	24839	24330	29900	524485
Total Prevalence		2.27	3.27	5.51	3.89	3.75	4.81	3.08	2.20	3.42	3.83	5.18	4.00	2.85	3.09	1.14	2.42	2.43	5.26	3.32	4.43	2.88	3.01	3.43
Livebirth Prevalence		2.29	3.29	5.55	3.91	3.77	4.83	3.09	2.21	3.01	3.85	5.20	3.21	2.45	2.72	1.14	1.04	1.39	2.88	1.25	0.81	0.83	0.67	2.62

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
North East Italy																								
total cases		15	11	14	22	8	15	18	13	11	20	11	16	14	18	16	26	13	30	8	24	10	11	344
livebirths		14	11	14	21	8	13	18	10	10	15	9	10	7	7	4	10	5	14	4	12	0	7	223
fetal deaths		1	0	0	1	0	2	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	6
induced abortions		0	0	0	0	0	0	0	3	1	4	2	5	7	11	12	16	8	16	4	12	10	4	115
population:		27708	36321	41195	43202	43401	41265	42048	45307	47515	52205	51093	50340	49735	49443	51486	56869	55908	54939	54364	55052	49781	57495	1056672
Total Prevalence		5.41	3.03	3.40	5.09	1.84	3.64	4.28	2.87	2.32	3.83	2.15	3.18	2.81	3.64	3.11	4.57	2.33	5.46	1.47	4.36	2.01	1.91	3.26
Livebirth Prevalence		5.09	3.05	3.42	4.89	1.85	3.17	4.30	2.22	2.11	2.88	1.77	1.99	1.41	1.42	0.78	1.76	0.90	2.56	0.74	2.18	0.00	1.22	2.35
South East Sicily (Italy)																								
total cases												11	7	8	9	4	3	5	3	9	3	0	10	72
livebirths												11	6	7	9	4	3	5	3	9	3	0	10	70
fetal deaths												0	1	1	0	0	0	0	0	0	0	0	0	2
induced abortions												-	-	-	-	-	-	-	-	-	-	-	-	-
population:												19430	20273	19746	20031	18986	18054	18795	16922	16942	15304	16049	16073	216605
Total Prevalence												5.66	3.45	4.05	4.49	2.11	1.66	2.66	1.77	5.31	1.96	0.00	6.22	3.32
Livebirth Prevalence												5.66	2.96	3.55	4.49	2.11	1.66	2.66	1.77	5.31	1.96	0.00	6.22	3.23
Tuscany (Italy)																								
total cases	7	7	4	5	2	10	1	5	4	7	5	1	7	8	5	4	6	7	12	9	11	8	7	142
livebirths	6	6	3	4	2	6	0	2	1	3	3	0	2	4	1	3	2	0	5	5	3	3	0	64
fetal deaths	1	1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	4
induced abortions	0	0	1	1	0	4	1	3	3	2	2	1	5	4	4	1	4	7	7	4	8	5	7	74
population:	9696	9350	9281	8948	8592	8980	8477	8511	8869	8556	8751	8657	25670	24687	24487	24288	24606	25216	25468	26060	26618	26381	26593	386742
Total Prevalence	7.22	7.49	4.31	5.59	2.33	11.14	1.18	5.87	4.51	8.18	5.71	1.16	2.73	3.24	2.04	1.65	2.44	2.78	4.71	3.45	4.13	3.03	2.63	3.67
Livebirth Prevalence	6.23	6.46	3.26	4.49	2.34	6.73	0.00	2.36	1.13	3.52	3.44	0.00	0.78	1.63	0.41	1.24	0.82	0.00	1.97	1.93	1.13	1.14	0.00	1.66
Malta																								
total cases							3	4	3	4	3	4	3	4	3	6	3	2	3	3	1	2	2	53
livebirths							3	4	3	4	2	4	2	3	3	6	3	2	3	2	1	2	2	49
fetal deaths							0	0	0	0	1	0	1	1	0	0	0	0	0	1	0	0	0	4
induced abortions							0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:							5310	5375	5461	5617	5400	5328	5503	5172	4863	4633	4978	4864	4511	4339	4272	3883	3826	83335
Total Prevalence							5.65	7.44	5.49	7.12	5.56	7.51	5.45	7.73	6.17	12.95	6.03	4.11	6.65	6.91	2.34	5.15	5.23	6.36
Livebirth Prevalence							5.70	7.50	5.54	7.18	3.73	7.54	3.65	5.83	6.22	13.01	6.07	4.14	6.68	4.64	2.35	5.18	5.26	5.92

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Northern Netherlands																								
total cases		5	4	4	3	7	7	2	13	13	22	21	14	6	9	11	12	11	10	12	9	9	7	211
livebirths		4	4	3	3	6	5	2	10	11	17	18	11	4	8	9	10	8	8	7	9	7	5	169
fetal deaths		1	0	1	0	0	2	0	1	1	2	2	0	2	0	0	1	0	0	1	0	2	2	18
induced abortions		0	0	0	0	1	0	0	2	1	3	1	3	0	1	2	1	3	2	4	0	0	0	24
population:		7877	7731	7542	7559	7792	11936	11847	11595	19093	19635	19853	19140	19387	19283	19296	19072	19427	19976	20198	20495	20487	20432	349653
Total Prevalence		6.35	5.17	5.30	3.97	8.98	5.86	1.69	11.21	6.81	11.20	10.58	7.31	3.09	4.67	5.70	6.29	5.66	5.01	5.94	4.39	4.39	3.43	6.03
Livebirth Prevalence		5.11	5.20	4.00	3.99	7.76	4.22	1.70	8.67	5.80	8.71	9.12	5.78	2.08	4.17	4.69	5.29	4.14	4.03	3.49	4.42	3.43	2.47	4.86
Wielkopolska (Poland)																								
total cases																				25	28	21	27	101
livebirths																				24	28	21	27	100
fetal deaths																				1	0	0	0	1
induced abortions																				-	-	-	-	-
population:																				35756	35309	34805	33253	139123
Total Prevalence																				6.99	7.93	6.03	8.12	7.26
Livebirth Prevalence																				6.75	7.97	6.07	8.15	7.23
Southern Portugal																								
total cases											3	2	2	1	4	6	7	5	1	6	7	6	5	55
livebirths											2	1	2	1	4	4	6	4	1	3	5	3	1	37
fetal deaths											0	1	0	0	0	0	0	0	0	0	1	0	0	2
induced abortions											1	0	0	0	0	2	1	1	0	3	1	3	4	16
population:											5461	5554	7391	7152	7000	14959	15439	16293	16312	17047	19390	18217	19041	169256
Total Prevalence											5.49	3.60	2.71	1.40	5.71	4.01	4.53	3.07	0.61	3.52	3.61	3.29	2.63	3.25
Livebirth Prevalence											3.69	1.82	2.73	1.42	5.76	2.68	3.92	2.47	0.62	1.77	2.59	1.66	0.53	2.20
Asturias (Spain)																								
total cases											6	6	7	5	4	3	5	1	7	0	1	1	2	48
livebirths											3	1	1	0	1	2	2	0	0	0	0	0	0	10
fetal deaths											0	0	1	0	0	0	0	0	0	0	0	0	0	1
induced abortions											3	5	5	5	3	1	3	1	7	0	1	1	2	37
population:											7722	7693	7474	7012	6626	6553	6507	6473	6321	6516	6719	6833	6709	89158
Total Prevalence											7.77	7.80	9.37	7.13	6.04	4.58	7.68	1.54	11.07	0.00	1.49	1.46	2.98	5.38
Livebirth Prevalence											3.91	1.31	1.35	0.00	1.52	3.07	3.09	0.00	0.00	0.00	0.00	0.00	0.00	1.13

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Barcelona (Spain)																								
total cases													6	5	5	4	4	1	4	5	4	6	7	51
livebirths													2	1	4	2	1	0	1	0	1	2	2	16
fetal deaths													0	1	0	0	0	0	0	1	0	1	1	4
induced abortions													4	3	1	2	3	1	3	4	3	3	4	31
population:													13477	12738	12609	12199	12031	12240	11684	12270	12655	12678	13034	137615
Total Prevalence													4.45	3.93	3.97	3.28	3.32	0.82	3.42	4.07	3.16	4.73	5.37	3.71
Livebirth Prevalence													1.49	0.79	3.19	1.65	0.84	0.00	0.86	0.00	0.79	1.59	1.54	1.17
Basque Country (Spain)																								
total cases											10	4	8	6	11	7	5	8	5	9	10	10	7	100
livebirths											9	3	3	3	7	2	1	4	2	5	3	2	1	45
fetal deaths											0	0	0	0	0	1	0	1	0	0	0	0	0	2
induced abortions											1	1	5	3	4	4	4	3	3	4	7	8	6	53
population:											16438	16291	16316	15891	15357	15397	16060	16397	16169	16859	17408	17718	18210	214511
Total Prevalence											6.08	2.46	4.90	3.78	7.16	4.55	3.11	4.88	3.09	5.34	5.74	5.64	3.84	4.66
Livebirth Prevalence											5.50	1.85	1.85	1.90	4.58	1.31	0.63	2.45	1.24	2.98	1.73	1.13	0.55	2.11
Vaud (Switzerland)																								
total cases										2	3	3	4	3	4	3	10	2	5	3	5	4	5	56
livebirths										0	1	0	2	1	1	1	3	1	2	1	2	1	1	17
fetal deaths										0	0	0	0	1	0	0	0	0	0	0	0	0	1	2
induced abortions										2	2	3	2	1	3	2	7	1	3	2	3	3	3	37
population:										7212	7697	8211	8076	7700	7683	7697	7730	7562	7438	7465	7618	7263	6810	106162
Total Prevalence										2.77	3.90	3.65	4.95	3.90	5.21	3.90	12.94	2.64	6.72	4.02	6.56	5.51	7.34	5.27
Livebirth Prevalence										0.00	1.31	0.00	2.48	1.30	1.31	1.30	3.89	1.33	2.70	1.34	2.64	1.38	1.47	1.61
Glasgow (UK)																								
total cases	31	24	24	16	17	30	25	15	12	15	12	9	8	5	14	8	19	2	7	11	2	-	-	306
livebirths	14	5	17	8	8	10	12	4	6	5	2	3	2	3	6	2	6	0	4	8	2	-	-	127
fetal deaths	5	5	2	0	0	2	2	1	0	0	1	0	0	0	0	2	1	0	1	0	0	-	-	22
induced abortions	12	14	5	8	9	18	11	10	6	10	9	6	6	2	8	4	12	2	2	3	0	-	-	157
population:	13590	13511	12884	12488	12673	12944	12875	13047	12949	12461	12494	12543	12157	11360	11407	11227	10976	10997	10239	9721	9682	-	-	252225
Total Prevalence	22.81	17.76	18.63	12.81	13.41	23.18	19.42	11.50	9.27	12.04	9.60	7.18	6.58	4.40	12.27	7.13	17.31	1.82	6.84	11.32	2.07	-	-	12.13
Livebirth Prevalence	10.49	3.73	13.27	6.35	6.29	7.69	9.28	3.10	4.67	4.09	1.61	2.35	1.63	2.54	5.29	1.80	5.50	0.00	3.94	8.27	2.08			5.04

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Merseyside & Cheshire (UK)																								
total cases																16	19	26	16	16	-	-	-	93
livebirths																2	3	5	3	4	-	-	-	17
fetal deaths																1	0	1	2	1	-	-	-	5
induced abortions																13	16	20	11	11	-	-	-	71
population:																28786	29031	27983	27514	26553	-	-	-	139867
Total Prevalence																5.56	6.54	9.29	5.82	6.03	-	-	-	6.65
Livebirth Prevalence																0.70	1.04	1.80	1.10	1.51				1.22
Northern Regions (UK)																								
total cases																					17	25	20	62
livebirths																					5	4	4	13
fetal deaths																					0	0	0	0
induced abortions																					12	21	16	49
population:																					29785	29159	29394	88338
Total Prevalence																					5.71	8.57	6.80	7.02
Livebirth Prevalence																					1.69	1.38	1.37	1.48
North West Thames (UK)																								
total cases												29	26	32	21	32	30	27	22	17	25	13	27	301
livebirths												5	3	5	2	6	3	5	4	2	5	3	5	48
fetal deaths												2	0	1	1	2	1	1	0	1	0	0	0	9
induced abortions												22	23	26	18	24	26	21	18	14	20	10	22	244
population:												47330	47493	46762	47526	47324	47324	47355	47549	46874	45652	45686	46518	563393
Total Prevalence												6.13	5.47	6.84	4.42	6.76	6.34	5.70	4.63	3.63	5.48	2.85	5.80	5.34
Livebirth Prevalence												1.06	0.63	1.07	0.42	1.27	0.63	1.06	0.84	0.43	1.10	0.66	1.08	3.50
Oxford (UK)																								
total cases												4	7	4	6	4	3	6	6	4	4	5	4	57
livebirths												2	1	0	1	1	0	2	1	1	0	1	2	12
fetal deaths												0	1	0	0	0	0	0	0	0	0	0	0	1
induced abortions												2	5	4	5	3	3	4	5	3	4	4	2	44
population:												5878	5778	5707	5882	5588	5693	5699	5613	5551	6504	6380	6355	70628
Total Prevalence												6.81	12.11	7.01	10.20	7.16	5.27	10.53	10.69	7.21	6.15	7.84	6.29	8.07
Livebirth Prevalence												3.41	1.74	0.00	1.71	1.80	0.00	3.52	1.79	1.81	0.00	1.58	3.16	1.71

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Trent (UK)																								
total cases																			29	36	35	22	39	161
livebirths																			8	7	7	2	11	35
fetal deaths																			2	2	2	0	2	8
induced abortions																			19	27	26	20	26	118
population:																			59509	57438	55541	54302	54601	281391
Total Prevalence																			4.87	6.27	6.30	4.05	7.14	5.72
Livebirth Prevalence																			1.35	1.22	1.27	0.37	2.03	1.25
Wales (UK)																								
total cases																			29	21	27	29	22	128
livebirths																			4	3	4	4	8	23
fetal deaths																			1	1	2	0	0	4
induced abortions																			24	17	21	25	14	101
population:																			33620	32266	31449	30771	30369	158475
Total Prevalence																			8.63	6.51	8.59	9.42	7.24	8.08
Livebirth Prevalence																			1.20	0.93	1.28	1.31	2.65	1.46
Wessex (UK)																								
total cases															13	17	14	12	16	18	16	20	8	134
livebirths															3	7	2	2	1	2	1	2	1	21
fetal deaths															1	0	0	0	1	0	0	1	0	3
induced abortions															9	10	12	10	14	16	15	17	7	110
population:															26806	25460	25110	26123	26213	25123	26080	25819	25548	232282
Total Prevalence															4.85	6.68	5.58	4.59	6.10	7.16	6.13	7.75	3.13	5.77
Livebirth Prevalence															1.13	2.76	0.80	0.77	0.38	0.80	0.39	0.78	0.39	0.91
Total (Full Member Registries)																								
total cases	117	129	121	132	122	127	157	128	113	143	187	182	200	173	205	224	282	237	323	326	357	304	298	**4587**
livebirths	91	94	102	103	99	82	105	89	71	80	109	111	101	79	102	100	117	107	115	143	145	112	125	**2382**
fetal deaths	14	17	10	11	7	10	21	10	9	13	18	10	9	10	8	8	7	13	15	16	11	8	8	**263**
induced abortions	12	18	9	18	16	35	31	29	33	50	60	61	90	84	95	116	158	117	193	167	201	184	165	**1942**
population:	63368	150426	176086	183179	186241	202372	210489	226843	229897	250232	294384	364685	393216	384557	414135	450126	524968	538829	621385	653903	656696	634606	643493	**8454116**
Total Prevalence	18.46	8.58	6.87	7.21	6.55	6.28	7.46	5.64	4.92	5.71	6.35	4.99	5.09	4.50	4.95	4.98	5.37	4.40	5.20	4.99	5.44	4.79	4.63	**5.43**
Livebirth Prevalence	14.51	6.30	5.84	5.66	5.35	4.08	5.02	3.95	3.11	3.22	3.72	3.05	2.58	2.06	2.47	2.23	2.24	1.99	1.86	2.20	2.22	1.77	1.95	3.02

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Associate Member Registries																								
Finland																								
total cases														28	26	26	26	33	39	21	19	27	26	271
livebirths														23	15	18	15	23	19	13	15	14	12	167
fetal deaths														1	1	1	3	2	1	1	0	2	1	13
induced abortions														4	10	7	8	8	19	7	4	11	13	91
population:														65098	65480	63368	60965	59569	57345	57782	56969	56397	55768	598741
Total Prevalence														4.30	3.97	4.10	4.26	5.54	6.80	3.63	3.34	4.79	4.66	4.53
Livebirth Prevalence														3.55	2.30	2.85	2.47	3.88	3.33	2.26	2.64	2.49	2.16	2.80
Central East France																								
total cases	27	20	29	21	29	37	31	26	36	24	36	37	40	45	43	48	46	41	37	36	21	35	49	794
livebirths	26	19	26	21	27	32	24	15	27	15	20	20	21	18	14	14	16	11	13	5	2	4	8	398
fetal deaths	1	1	3	0	2	3	1	1	2	0	1	0	2	1	0	1	0	0	1	2	0	1	0	23
induced abortions	0	0	0	0	0	2	6	10	7	9	15	17	17	26	29	33	30	30	23	29	19	30	41	373
population:	75332	76220	75813	86433	86904	90825	91950	90191	91303	99858	107370	106607	104480	99249	99674	102153	103440	102090	102483	102982	93963	93721	93405	2176446
Total Prevalence	3.58	2.62	3.83	2.43	3.34	4.07	3.37	2.88	3.94	2.40	3.35	3.47	3.83	4.53	4.31	4.70	4.45	4.02	3.61	3.50	2.23	3.73	5.25	3.65
Livebirth Prevalence	3.48	2.51	3.46	2.45	3.13	3.55	2.63	1.67	2.97	1.51	1.87	1.89	2.02	1.82	1.41	1.38	1.55	1.08	1.27	0.49	0.21	0.43	0.86	1.84
Madrid (Spain)																								
total cases	25	20	32	31	36	37	27	20	28	23	37	41	28	26	25	20	27	23	21	18	18	18	8	589
livebirths	23	18	27	28	33	34	25	18	28	22	35	37	28	24	25	19	26	20	20	15	18	17	8	548
fetal deaths	2	2	5	3	3	3	2	2	0	1	2	4	0	2	0	1	1	3	1	3	0	1	0	41
induced abortions	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
population:	56910	56102	61333	71812	69513	66720	58245	51051	52686	59046	84379	87708	91607	82925	87239	87372	94044	98945	96490	104336	105833	103404	110954	1838654
Total Prevalence	4.39	3.56	5.22	4.32	5.18	5.55	4.64	3.92	5.31	3.90	4.38	4.67	3.06	3.14	2.87	2.29	2.87	2.32	2.18	1.73	1.70	1.74	0.72	3.20
Livebirth Prevalence	4.08	3.24	4.44	3.93	4.78	5.14	4.33	3.55	5.36	4.22	4.18	4.25	3.08	2.91	2.88	2.19	2.78	2.03	2.08	1.44	1.71	1.64	0.72	3.18
Norway																								
total cases	35	28	32	24	26	22	29	29	25	33	24	27	32	19	25	33	35	22	27	28	36	27	23	641
livebirths	25	26	24	21	23	16	20	22	19	25	19	20	26	11	14	24	23	13	15	16	19	15	6	442
fetal deaths	10	2	8	3	3	6	8	5	4	5	5	4	1	1	4	5	6	2	6	3	2	1	0	94
induced abortions	0	0	0	0	0	0	1	2	2	3	0	3	5	7	7	4	6	7	6	9	15	11	17	105
population:	51495	51021	51642	50258	50576	51416	52885	54313	57936	59712	61523	61386	60636	60166	60306	60488	61092	59896	58482	59967	59881	57475	56450	1309002
Total Prevalence	6.80	5.49	6.20	4.78	5.14	4.28	5.48	5.34	4.32	5.53	3.90	4.40	5.28	3.16	4.15	5.46	5.73	3.67	4.62	4.67	6.01	4.70	4.07	4.90
Livebirth Prevalence	4.91	5.14	4.69	4.22	4.59	3.14	3.81	4.08	3.30	3.75	3.11	3.28	4.32	1.84	2.34	3.99	3.79	2.18	2.58	2.69	3.20	2.63	1.07	3.40

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Spina Bifida (Contd)																								
Poland																								
total cases																				94	69	95	111	369
livebirths																				87	64	92	105	348
fetal deaths																				7	5	3	6	21
induced abortions																				-	-	-	-	-
population:																				149653	147228	185125	220040	702046
Total Prevalence																				6.28	4.69	5.13	5.04	5.26
Livebirth Prevalence																				5.85	4.37	5.00	4.80	4.99
Sweden																								
total cases																						47	49	96
livebirths																						13	24	37
fetal deaths																						0	0	0
induced abortions																						34	25	59
population:																						91815	96167	187982
Total Prevalence																						5.12	5.10	5.11
Livebirth Prevalence																						1.42	2.50	1.98
Total (Associate Member Registries)																								
total cases	87	68	93	76	91	96	87	75	89	80	97	105	100	118	119	127	134	119	124	197	163	249	266	**2760**
livebirths	74	63	77	70	83	82	69	55	74	62	74	77	75	76	68	75	80	67	67	136	118	155	163	**1940**
fetal deaths	13	5	16	6	8	12	11	8	6	6	8	8	3	5	5	8	10	7	9	16	7	8	7	**192**
induced abortions	0	0	0	0	0	2	7	12	9	12	15	20	22	37	46	44	44	45	48	45	38	86	96	**628**
population:	183737	183343	188788	208503	206993	208961	203080	195555	201925	218616	253272	255701	256723	307438	312699	313381	319541	320500	314800	474720	463874	587937	632784	**6812871**
Total Prevalence	4.74	3.71	4.93	3.65	4.40	4.59	4.28	3.84	4.41	3.66	3.83	4.11	3.90	3.84	3.81	4.05	4.19	3.71	3.94	4.15	3.51	4.24	4.20	**4.05**
Livebirth Prevalence	4.06	3.46	4.11	3.38	4.04	3.96	3.42	2.83	3.69	2.86	2.94	3.03	2.94	2.49	2.19	2.41	2.52	2.10	2.14	2.88	2.56	2.65	2.59	2.91
Total (All registries)																								
total cases	204	197	214	208	213	223	244	203	202	223	284	287	300	291	324	351	416	356	447	523	520	553	564	**7347**
livebirths	165	157	179	173	182	164	174	144	145	142	183	188	176	155	170	175	197	174	182	279	263	267	288	**4322**
fetal deaths	27	22	26	17	15	22	32	18	15	19	26	18	12	15	13	16	17	20	24	32	18	16	15	**455**
induced abortions	12	18	9	18	16	37	38	41	42	62	75	81	112	121	141	160	202	162	241	212	239	270	261	**2570**
population:	247105	333769	364874	391682	393234	411333	413569	422398	431822	468848	547656	620386	649939	691995	726834	763507	844509	859329	936185	1128623	1120570	1222543	1276277	**15266987**
Total Prevalence	8.26	5.90	5.87	5.31	5.42	5.42	5.90	4.81	4.68	4.76	5.19	4.63	4.62	4.21	4.46	4.60	4.93	4.14	4.77	4.63	4.64	4.52	4.42	**4.81**
Livebirth Prevalence	6.74	4.74	4.95	4.45	4.66	4.02	4.24	3.43	3.38	3.05	3.36	3.04	2.72	2.25	2.35	2.30	2.34	2.03	1.95	2.48	2.36	2.19	2.27	2.97

Table A2.3: Anencephalus: Number of cases by type of birth[1], population (births), total prevalence rate and livebirth prevalence rate (per 10,000 births) by year and registry: 41 EUROCAT registries, 1980-2002

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Styria (Austria)																								
total cases						4	1	1	3	3	3	1	3	3	4	0	4	4	2	2	2	2		42
livebirths						1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0		3
fetal deaths						0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0		2
induced abortions						3	1	1	3	3	3	1	1	3	4	0	3	4	2	1	2	2		37
population:						13663	13303	13276	13340	13161	13349	13794	13744	13395	12988	12276	12465	11768	11026	10800	10719	10050		213117
Total Prevalence						2.93	0.75	0.75	2.25	2.28	2.25	0.72	2.18	2.24	3.08	0.00	3.21	3.40	1.81	1.85	1.87	1.99		1.97
Livebirth Prevalence						0.74	0.00	0.00	0.00	0.00	0.00	0.00	0.73	0.00	0.00	0.00	0.80	0.00	0.00	0.00	0.00	0.00		0.14
Antwerp (Belgium)																								
total cases											3	5	2	2	4	2	4	10	1	9	8	1	4	55
livebirths											0	1	0	1	0	0	0	0	0	1	0	0	0	3
fetal deaths											1	1	0	0	0	0	1	0	0	0	0	1	0	4
induced abortions											2	3	2	1	4	2	3	10	1	8	8	0	4	48
population:											3740	4688	6180	7555	10964	10899	10796	18282	17930	17968	17717	17318	17409	161446
Total Prevalence											8.02	10.67	3.24	2.65	3.65	1.84	3.71	5.47	0.56	5.01	4.52	0.58	2.30	3.41
Livebirth Prevalence											0.00	2.13	0.00	1.32	0.00	0.00	0.00	0.00	0.00	0.56	0.00	0.00	0.00	0.19
Hainaut (Belgium)																								
total cases	4	6	2	3	5	5	5	8	4	6	5	5	3	4	1	4	3	5	6	2	4	4	7	101
livebirths	0	1	0	1	0	0	0	0	0	1	2	0	0	0	0	0	0	0	1	0	0	0	0	6
fetal deaths	0	3	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	5
induced abortions	4	2	2	2	5	4	5	8	4	4	3	5	3	4	1	4	3	5	5	2	4	4	7	90
population:	8449	8204	8209	7862	8066	8182	8380	8518	8805	13579	13503	13595	13328	12583	12273	11933	12416	12314	12044	12097	12823	12405	12102	251670
Total Prevalence	4.73	7.31	2.44	3.82	6.20	6.11	5.97	9.39	4.54	4.42	3.70	3.68	2.25	3.18	0.81	3.35	2.42	4.06	4.98	1.65	3.12	3.22	5.78	4.01
Livebirth Prevalence	0.00	1.23	0.00	1.28	0.00	0.00	0.00	0.00	0.00	0.74	1.49	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.84	0.00	0.00	0.00	0.00	0.24
Sofia (Bulgaria)																								
total cases																	6	5	10	6				27
livebirths																	0	0	1	0				1
fetal deaths																	4	0	5	3				12
induced abortions																	2	5	4	3				14
population:																	9908	9004	9177	10168				38257
Total Prevalence																	6.06	5.55	10.90	5.90				7.06
Livebirth Prevalence																	0.00	0.00	1.10	0.00				0.26

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Zagreb (Croatia)																								
total cases				2	0	1	1	0	0	0	1	0	0	1	0	0	0	1	2	0	2	0	1	12
livebirths				0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	2
fetal deaths				2	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
induced abortions				0	0	0	0	0	0	0	0	0	1	0	0	0	1	2	0	1	0	1	6
population:				4023	4029	3784	6867	6686	6183	7329	6948	7003	6481	6532	6135	6280	6435	6337	6170	6033	5815	5731	5544	120345
Total Prevalence				4.97	0.00	2.64	1.46	0.00	0.00	0.00	1.44	0.00	0.00	1.53	0.00	0.00	0.00	1.58	3.24	0.00	3.44	0.00	1.80	1.00
Livebirth Prevalence				0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.73	0.00	0.00	0.17
Odense (Denmark)																								
total cases	5	2	2	2	3	1	2	5	1	2	2	4	1	1	1	4	2	1	2	2	4	1	2	52
livebirths	0	0	1	0	0	0	0	1	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	5
fetal deaths	4	2	1	0	1	0	1	2	0	1	1	2	1	0	0	1	1	0	1	0	3	0	0	22
induced abortions	1	0	0	2	2	1	1	2	1	0	0	2	0	0	1	3	1	1	1	2	1	1	2	25
population:	5173	4614	4467	4301	4559	4698	4849	4852	5050	5287	5689	5723	6015	5876	6018	6073	5807	5933	5430	5689	5680	5415	5096	122294
Total Prevalence	9.67	4.33	4.48	4.65	6.58	2.13	4.12	10.31	1.98	3.78	3.52	6.99	1.66	1.70	1.66	6.59	3.44	1.69	3.68	3.52	7.04	1.85	3.92	4.25
Livebirth Prevalence	0.00	0.00	2.25	0.00	0.00	0.00	0.00	2.07	0.00	1.90	1.77	0.00	0.00	1.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.41
Auvergne (France)																								
total cases																							3	3
livebirths																							0	0
fetal deaths																							0	0
induced abortions																							3	3
population:																							13397	13397
Total Prevalence																							2.24	2.24
Livebirth Prevalence																							0.00	0.00
Paris (France)																								
total cases		12	8	18	22	22	13	19	20	20	17	26	23	12	14	25	16	20	21	27	22	18	30	425
livebirths		2	1	0	1	0	0	2	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	9
fetal deaths		6	3	5	3	0	3	3	2	2	0	2	1	1	1	0	0	0	0	1	1	0	2	36
induced abortions		4	4	13	18	22	10	14	18	18	16	24	22	11	13	24	15	20	21	26	21	18	28	380
population:		36917	36741	35783	35902	36536	36384	36080	36672	36866	37302	37541	36469	35819	35918	36884	37237	37272	38160	38835	38446	38716	39202	815682
Total Prevalence		3.25	2.18	5.03	6.13	6.02	3.57	5.27	5.45	5.43	4.56	6.93	6.31	3.35	3.90	6.78	4.30	5.37	5.50	6.95	5.72	4.65	7.65	5.21
Livebirth Prevalence		0.55	0.27	0.00	0.28	0.00	0.00	0.56	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.27	0.27	0.00	0.00	0.00	0.00	0.00	0.00	0.11

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Strasbourg (France)																								
total cases			0	3	8	4	3	6	5	6	8	8	11	7	5	8	4	4	2	8	10	7		117
livebirths			0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	1		3
fetal deaths			0	2	1	1	0	3	1	0	1	0	1	0	0	0	0	0	0	0	0	0		10
induced abortions			0	1	7	3	3	3	4	6	7	8	9	7	5	8	3	4	2	8	10	6		104
population:			13662	12519	12924	13166	13112	12895	13595	13425	13775	13770	13736	13148	12865	13313	13185	13237	13656	13767	14238	13406		267394
Total Prevalence			0.00	2.40	6.19	3.04	2.29	4.65	3.68	4.47	5.81	5.81	8.01	5.32	3.89	6.01	3.03	3.02	1.46	5.81	7.02	5.22		4.38
Livebirth Prevalence			0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.73	0.00	0.00	0.00	0.76	0.00	0.00	0.00	0.00	0.75		0.11
Mainz (Germany)																								
total cases											0	0	0	4	0	0	4	1	2	1	3	0	2	17
livebirths											0	0	0	0	0	0	1	0	0	0	1	0	0	2
fetal deaths											0	0	0	0	0	0	0	0	0	0	0	0	0	0
induced abortions											0	0	0	4	0	0	3	1	2	1	2	0	2	15
population:											3903	4113	3941	4020	3769	3560	3603	3890	3542	3275	2966	3040	3250	46872
Total Prevalence											0.00	0.00	0.00	9.95	0.00	0.00	11.10	2.57	5.65	3.05	10.11	0.00	6.15	3.63
Livebirth Prevalence											0.00	0.00	0.00	0.00	0.00	0.00	2.79	0.00	0.00	0.00	3.39	0.00	0.00	0.43
Saxony-Anhalt (Germany)																								
total cases								12	9	6	4	0	0	2	1	2	8	5	2	2	3	3	5	64
livebirths								0	0	0	0	0	0	0	0	1	1	2	0	0	1	0	1	6
fetal deaths								3	0	0	1	0	0	1	0	0	0	0	0	0	0	1	0	6
induced abortions								9	9	6	3	0	0	1	1	1	7	3	2	2	2	2	4	52
population:								17165	16623	15201	14764	9124	7633	6911	7529	7684	8906	9606	10257	11485	18799	18148	17688	197523
Total Prevalence								6.99	5.41	3.95	2.71	0.00	0.00	2.89	1.33	2.60	8.98	5.21	1.95	1.74	1.60	1.65	2.83	3.24
Livebirth Prevalence								0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.31	1.13	2.09	0.00	0.00	0.53	0.00	0.57	0.31
Cork & Kerry (Ireland)																								
total cases																	6	4	5	4	4	2		25
livebirths																	3	1	2	3	1	2		12
fetal deaths																	3	3	3	1	3	0		13
induced abortions																	0	0	0	0	0	0		0
population:																	7377	7664	7854	7495	7714	7969		46073
Total Prevalence																	8.13	5.22	6.37	5.34	5.19	2.51		5.43
Livebirth Prevalence																	4.10	1.31	2.56	4.03	1.31	2.52		2.62

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Dublin (Ireland)																								
total cases	48	42	42	32	24	22	20	19	20	11	15	10	11	9	8	6	5	6	8	7	7	8	10	390
livebirths	12	15	18	17	7	6	12	7	10	5	7	6	4	6	5	2	3	4	4	3	5	4	4	166
fetal deaths	36	27	24	15	17	16	8	12	10	6	8	4	7	3	3	4	2	2	4	4	2	4	6	224
induced abortions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:	26460	25510	24822	23352	22312	22131	21708	20766	19830	18914	19393	19800	18933	18491	18412	18550	19288	20285	20899	20767	21236	22152	22936	486947
Total Prevalence	18.14	16.46	16.92	13.70	10.76	9.94	9.21	9.15	10.09	5.82	7.73	5.05	5.81	4.87	4.34	3.23	2.59	2.96	3.83	3.37	3.30	3.61	4.36	8.01
Livebirth Prevalence	4.58	5.92	7.31	7.34	3.16	2.73	5.57	3.39	5.08	2.66	3.63	3.05	2.12	3.26	2.73	1.08	1.56	1.98	1.92	1.45	2.37	1.82	1.76	3.43
Galway (Ireland)																								
total cases		2	3	2	1	6	4	2	2	0	2	2	1	0	1	1	0	1	0	0				30
livebirths		2	1	0	0	4	2	1	1	0	2	1	1	0	0	1	0	0	0	0				16
fetal deaths		0	2	2	1	2	2	1	1	0	0	1	0	0	1	0	0	1	0	0				14
induced abortions		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0				0
population:		3546	3604	3397	3268	3079	3155	3051	2858	2636	2691	2578	2666	2645	2375	2436	2534	2588	2747	2655				54509
Total Prevalence		5.64	8.32	5.89	3.06	19.49	12.68	6.56	7.00	0.00	7.43	7.76	3.75	0.00	4.21	4.11	0.00	3.86	0.00	0.00				5.50
Livebirth Prevalence		5.69	2.80	0.00	0.00	13.12	6.37	3.30	3.54	0.00	7.43	3.88	3.79	0.00	0.00	4.14	0.00	0.00	0.00	0.00				2.95
Campania (Italy)																	19	7	15	14	16	12	17	100
total cases																	4	1	0	4	2	1	1	13
livebirths																	1	1	2	2	0	0	0	6
fetal deaths																	14	5	13	8	14	11	16	81
induced abortions																	46658	50458	51568	47397	50171	49714	62708	358674
population:																	4.07	1.39	2.91	2.95	3.19	2.41	2.71	2.79
Total Prevalence																	0.86	0.20	0.00	0.85	0.40	0.20	0.16	0.36
Livebirth Prevalence																								
Emilia Romagna (Italy)																								
total cases		2	3	4	2	2	2	2	1	0	0	1	0	2	1	1	4	4	5	6	6	4	6	58
livebirths		2	1	1	2	2	1	2	0	0	0	1	0	2	0	1	1	0	1	2	0	0	0	19
fetal deaths		0	2	3	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	2	1	0	1	12
induced abortions		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	4	4	2	5	4	5	27
population:		13189	18364	21769	23155	24016	22868	22726	22760	23380	23524	25095	25002	24533	25886	26359	28873	28859	20928	24130	24839	24330	29900	524485
Total Prevalence		1.52	1.63	1.84	0.86	0.83	0.87	0.88	0.44	0.00	0.00	0.40	0.00	0.82	0.39	0.38	1.39	1.39	2.39	2.49	2.42	1.64	2.01	1.11
Livebirth Prevalence		1.53	0.55	0.46	0.87	0.84	0.44	0.88	0.00	0.00	0.00	0.40	0.00	0.82	0.00	0.38	0.35	0.00	0.48	0.83	0.00	0.00	0.00	0.36

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
North East Italy																								
total cases		11	6	5	7	5	6	5	16	19	15	13	8	14	14	11	18	11	9	11	12	7	5	228
livebirths		5	5	1	2	4	3	3	5	1	2	0	0	2	0	2	0	1	1	1	3	0	1	42
fetal deaths		6	1	4	5	1	3	0	3	3	1	1	1	0	1	1	1	1	1	0	0	0	1	35
induced abortions		0	0	0	0	0	0	2	8	15	12	12	7	12	13	8	17	9	7	10	9	7	3	151
population:		27708	36321	41195	43202	43401	41265	42048	45307	47515	52205	51093	50340	49735	49443	51486	56869	55908	54939	54364	55052	49781	57495	1056672
Total Prevalence		3.97	1.65	1.21	1.62	1.15	1.45	1.19	3.53	4.00	2.87	2.54	1.59	2.81	2.83	2.14	3.17	1.97	1.64	2.02	2.18	1.41	0.87	2.16
Livebirth Prevalence		1.82	1.39	0.24	0.47	0.93	0.73	0.72	1.11	0.21	0.38	0.00	0.00	0.40	0.00	0.39	0.00	0.18	0.18	0.18	0.54	0.00	0.17	0.44
South East Sicily (Italy)																								
total cases												1	4	0	0	0	1	1	1	0	1	0	1	10
livebirths												0	1	0	0	0	1	1	1	0	1	0	1	6
fetal deaths												1	3	0	0	0	0	0	0	0	0	0	0	4
induced abortions												-	-	-	-	-	-	-	-	-	-	-	-	-
population:												19430	20273	19746	20031	18986	18054	18795	16922	16942	15304	16049	16073	216605
Total Prevalence												0.51	1.97	0.00	0.00	0.00	0.55	0.53	0.59	0.00	0.65	0.00	0.62	0.46
Livebirth Prevalence												0.00	0.49	0.00	0.00	0.00	0.55	0.53	0.59	0.00	0.65	0.00	0.62	0.28
Tuscany (Italy)																								
total cases	2	4	4	0	2	6	7	3	2	4	4	1	8	5	7	7	4	4	9	6	7	4	2	102
livebirths	0	1	1	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	1	1	0	0	0	7
fetal deaths	2	3	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	9
induced abortions	0	0	2	0	2	5	7	3	2	3	4	1	7	4	6	7	4	4	7	5	7	4	2	86
population:	9696	9350	9281	8948	8592	8980	8477	8511	8869	8556	8751	8657	25670	24687	24487	24288	24606	25216	25468	26060	26618	26381	26593	386742
Total Prevalence	2.06	4.28	4.31	0.00	2.33	6.68	8.26	3.52	2.26	4.68	4.57	1.16	3.12	2.03	2.86	2.88	1.63	1.59	3.53	2.30	2.63	1.52	0.75	2.64
Livebirth Prevalence	0.00	1.08	1.09	0.00	0.00	0.00	0.00	0.00	0.00	1.17	0.00	0.00	0.00	0.41	0.41	0.00	0.00	0.00	0.39	0.39	0.00	0.00	0.00	0.18
Malta																								
total cases							6	1	1	3	0	0	3	1	3	1	3	1	3	3	0	0	2	31
livebirths							3	0	1	2	0	0	3	1	1	1	1	1	2	1	0	0	0	17
fetal deaths							3	1	0	1	0	0	0	0	2	0	2	0	1	2	0	0	2	14
induced abortions							0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
population:							5310	5375	5461	5617	5400	5328	5503	5172	4863	4633	4978	4864	4511	4339	4272	3883	3826	83335
Total Prevalence							11.30	1.86	1.83	5.34	0.00	0.00	5.45	1.93	6.17	2.16	6.03	2.06	6.65	6.91	0.00	0.00	5.23	3.72
Livebirth Prevalence							5.70	0.00	1.85	3.59	0.00	0.00	5.48	1.94	2.07	2.17	2.02	2.07	4.46	2.32	0.00	0.00	0.00	2.05

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Northern Netherlands																								
total cases		2	4	9	7	7	5	2	10	3	4	5	3	7	5	7	8	7	5	8	8	1	6	123
livebirths		0	2	3	3	0	1	0	2	0	1	2	0	0	0	1	0	1	1	0	1	0	4	22
fetal deaths		1	2	2	3	3	0	1	4	1	1	1	0	4	0	1	2	2	2	3	3	0	1	37
induced abortions		1	0	4	1	4	4	1	4	2	2	2	3	3	5	5	6	4	2	5	4	1	1	64
population:		7877	7731	7542	7559	7792	11936	11847	11595	19093	19635	19853	19140	19387	19283	19296	19072	19427	19976	20198	20495	20487	20432	349653
Total Prevalence		2.54	5.17	11.93	9.26	8.98	4.19	1.69	8.62	1.57	2.04	2.52	1.57	3.61	2.59	3.63	4.19	3.60	2.50	3.96	3.90	0.49	2.94	3.52
Livebirth Prevalence		0.00	2.60	4.00	3.99	0.00	0.84	0.00	1.73	0.00	0.51	1.01	0.00	0.00	0.00	0.52	0.00	0.52	0.50	0.00	0.49	0.00	1.97	0.63
Wielkopolska (Poland)																								
total cases																				9	9	9	6	33
livebirths																				9	9	6	4	28
fetal deaths																				0	0	3	2	5
induced abortions																				-	-	-	-	-
population:																				35756	35309	34805	33253	139123
Total Prevalence																				2.52	2.55	2.59	1.80	2.37
Livebirth Prevalence																				2.53	2.56	1.73	1.21	2.02
Southern Portugal																								
total cases											2	2	1	0	2	2	6	3	0	6	4	8	12	48
livebirths											0	2	1	0	2	0	0	1	0	1	1	0	0	8
fetal deaths											0	0	0	0	0	2	1	0	0	0	0	1	1	5
induced abortions											2	0	0	0	0	0	5	2	0	5	3	7	11	35
population:											5461	5554	7391	7152	7000	14959	15439	16293	16312	17047	19390	18217	19041	169256
Total Prevalence											3.66	3.60	1.35	0.00	2.86	1.34	3.89	1.84	0.00	3.52	2.06	4.39	6.30	2.84
Livebirth Prevalence											0.00	3.63	1.37	0.00	2.88	0.00	0.00	0.62	0.00	0.59	0.52	0.00	0.00	0.48
Asturias (Spain)																								
total cases											7	4	2	3	5	3	4	1	7	2	5	4	6	53
livebirths											1	1	0	0	0	0	0	0	1	0	1	0	0	4
fetal deaths											0	0	0	0	0	0	0	0	0	0	0	0	0	0
induced abortions											6	3	2	3	5	3	4	1	6	2	4	4	6	49
population:											7722	7693	7474	7012	6626	6553	6507	6473	6321	6516	6719	6833	6709	89158
Total Prevalence											9.07	5.20	2.68	4.28	7.55	4.58	6.15	1.54	11.07	3.07	7.44	5.85	8.94	5.94
Livebirth Prevalence											1.30	1.31	0.00	0.00	0.00	0.00	0.00	0.00	1.59	0.00	1.50	0.00	0.00	0.45

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Barcelona (Spain)																								
total cases													8	8	5	5	4	6	8	5	3	7	6	65
livebirths													0	0	0	1	0	0	1	0	0	2	1	5
fetal deaths													1	0	0	1	0	1	1	1	0	0	0	5
induced abortions													7	8	5	3	4	5	6	4	3	5	5	55
population:													13477	12738	12609	12199	12031	12240	11684	12270	12655	12678	13034	137615
Total Prevalence													5.94	6.28	3.97	4.10	3.32	4.90	6.85	4.07	2.37	5.52	4.60	4.72
Livebirth Prevalence													0.00	0.00	0.00	0.82	0.00	0.00	0.86	0.00	0.00	1.59	0.77	0.37
Basque Country (Spain)																								
total cases											8	6	9	6	9	7	13	8	4	17	11	7	15	120
livebirths											0	1	0	0	0	1	1	0	0	1	0	0	0	4
fetal deaths											0	0	0	0	1	0	0	0	0	0	1	0	0	2
induced abortions											8	5	9	6	8	6	12	8	4	16	10	7	15	114
population:											16438	16291	16316	15891	15357	15397	16060	16397	16169	16859	17408	17718	18210	214511
Total Prevalence											4.87	3.68	5.52	3.78	5.86	4.55	8.09	4.88	2.47	10.08	6.32	3.95	8.24	5.59
Livebirth Prevalence											0.00	0.62	0.00	0.00	0.00	0.65	0.63	0.00	0.00	0.60	0.00	0.00	0.00	0.19
Vaud (Switzerland)																								
total cases										4	2	4	5	3	3	5	4	1	2	2	4	3	1	43
livebirths										0	0	0	0	0	0	0	2	0	0	0	1	0	0	3
fetal deaths										0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
induced abortions										4	2	4	5	3	3	4	2	1	2	2	3	3	1	39
population:										7212	7697	8211	8076	7700	7683	7697	7730	7562	7438	7465	7618	7263	6810	106162
Total Prevalence										5.55	2.60	4.87	6.19	3.90	3.90	6.50	5.17	1.32	2.69	2.68	5.25	4.13	1.47	4.05
Livebirth Prevalence										0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.59	0.00	0.00	0.00	1.32	0.00	0.00	0.28
Wales (UK)																								
total cases																			29	25	18	20	26	118
livebirths																			0	3	0	1	1	5
fetal deaths																			0	1	0	0	1	2
induced abortions																			29	21	18	19	24	111
population:																			33620	32266	31449	30771	30369	158475
Total Prevalence																			8.63	7.75	5.72	6.50	8.56	7.45
Livebirth Prevalence																			0.00	0.93	0.00	0.33	0.33	0.32

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Glasgow (UK)																								
total cases	27	19	23	19	14	16	23	15	6	9	7	8	8	10	5	10	11	4	11	7	3			255
livebirths	1	0	0	0	1	2	4	0	1	0	0	2	0	0	1	0	0	0	1	0	1			14
fetal deaths	7	3	0	1	0	0	0	1	0	0	1	1	1	2	0	2	0	1	0	1	0			21
induced abortions	19	16	23	18	13	14	19	14	5	9	6	5	7	8	4	8	11	3	10	6	2			220
population:	13590	13511	12884	12488	12673	12944	12875	13047	12949	12461	12494	12543	12157	11360	11407	11227	10976	10997	10239	9721	9682			252225
Total Prevalence	19.87	14.06	17.85	15.21	11.05	12.36	17.86	11.50	4.63	7.22	5.60	6.38	6.58	8.80	4.38	8.91	10.02	3.64	10.74	7.20	3.10			10.11
Livebirth Prevalence	0.75	0.00	0.00	0.00	0.79	1.54	3.09	0.00	0.78	0.00	0.00	1.57	0.00	0.00	0.88	0.00	0.00	0.00	0.98	0.00	1.04			0.56
Merseyside & Cheshire (UK)																								
total cases																17	19	20	12	7				75
livebirths																1	0	0	1	1				3
fetal deaths																0	0	2	1	0				3
induced abortions																16	19	18	10	6				69
population:																28786	29031	27983	27514	26553				139867
Total Prevalence																5.91	6.54	7.15	4.36	2.64				5.36
Livebirth Prevalence																0.35	0.00	0.00	0.37	0.38				0.22
Northern Regions (UK)																								
total cases																					21	17	12	50
livebirths																					2	2	0	4
fetal deaths																					1	1	0	2
induced abortions																					18	14	12	44
population:																					29785	29159	29394	88338
Total Prevalence																					7.05	5.83	4.08	5.66
Livebirth Prevalence																					0.68	0.69	0.00	0.46
North West Thames (UK)																								
total cases												26	33	25	27	26	24	20	35	17	34	17	22	306
livebirths												0	4	1	2	6	1	2	1	1	3	1	2	24
fetal deaths												1	1	2	1	5	3	1	0	2	3	2	5	26
induced abortions												25	28	22	24	15	20	17	34	14	28	14	15	256
population:												47330	47493	46762	47526	47324	47324	47355	47549	46874	45652	45686	46518	563393
Total Prevalence												5.49	6.95	5.35	5.68	5.49	5.07	4.22	7.36	3.63	7.45	3.72	4.73	5.43
Livebirth Prevalence												0.00	0.84	0.21	0.42	1.27	0.21	0.42	0.21	0.21	0.66	0.22	0.43	1.75

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Oxford (UK)																								
total cases												6	1	7	7	3	3	2	3	3	2	4	4	45
livebirths												1	1	0	0	0	0	1	0	0	1	1	0	5
fetal deaths												0	0	1	1	0	0	0	0	0	0	0	0	2
induced abortions												5	0	6	6	3	3	1	3	3	1	3	4	38
population:												5878	5778	5707	5882	5588	5693	5699	5613	5551	6504	6380	6355	70628
Total Prevalence												10.21	1.73	12.27	11.90	5.37	5.27	3.51	5.34	5.40	3.08	6.27	6.29	6.37
Livebirth Prevalence												1.71	1.74	0.00	0.00	0.00	0.00	1.76	0.00	0.00	1.54	1.58	0.00	0.71
Trent (UK)																								
total cases																			15	19	20	28	22	104
livebirths																			1	1	1	1	3	7
fetal deaths																			3	1	1	3	3	11
induced abortions																			11	17	18	24	16	86
population:																			59509	57438	55541	54302	54601	281391
Total Prevalence																			2.52	3.31	3.60	5.16	4.03	3.70
Livebirth Prevalence																			0.17	0.17	0.18	0.19	0.55	0.25
Wessex (UK)																								
total cases															12	15	13	23	16	19	10	17	21	146
livebirths															0	1	0	1	0	0	0	1	1	4
fetal deaths															1	0	0	6	0	2	0	1	1	11
induced abortions															11	14	13	16	16	17	10	15	19	131
population:															26806	25460	25110	26123	26213	25123	26080	25819	25548	232282
Total Prevalence															4.48	5.89	5.18	8.80	6.10	7.56	3.83	6.58	8.22	6.29
Livebirth Prevalence															0.00	0.39	0.00	0.38	0.00	0.00	0.00	0.39	0.39	0.17
Total (Full Member Registries)																								
total cases	86	102	97	99	95	101	98	100	100	96	109	138	148	136	144	172	220	190	252	256	263	215	256	**3473**
livebirths	13	28	30	23	16	19	26	16	20	11	18	18	17	15	12	20	22	17	21	33	36	23	24	**478**
fetal deaths	49	51	36	36	31	26	22	27	22	15	15	15	19	14	13	18	21	21	25	27	19	17	26	**565**
induced abortions	24	23	31	40	48	56	50	57	58	70	76	105	112	107	119	134	177	152	206	196	208	175	206	**2430**
population:	63368	150426	176086	183179	186241	202372	210489	226843	229897	250232	294384	364685	393216	384557	414135	450126	524968	538829	621385	653903	656696	634606	643493	**8454116**
Total Prevalence	13.57	6.78	5.51	5.40	5.10	4.99	4.66	4.41	4.35	3.84	3.70	3.78	3.76	3.54	3.48	3.82	4.19	3.53	4.06	3.91	4.00	3.39	3.98	**4.11**
Livebirth Prevalence	2.07	1.88	1.72	1.26	0.86	0.94	1.24	0.71	0.88	0.44	0.61	0.50	0.43	0.39	0.29	0.45	0.42	0.32	0.34	0.51	0.55	0.36	0.37	0.61

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Associate Member Registries																								
Finland																								
total cases														14	14	16	21	17	23	19	14	20	13	171
livebirths														3	0	1	3	4	1	2	1	0	1	16
fetal deaths														0	0	0	1	1	1	0	1	1	0	5
induced abortions														11	14	15	17	12	21	17	12	19	12	150
population:														65098	65480	63368	60965	59569	57345	57782	56969	56397	55768	598741
Total Prevalence														2.15	2.14	2.52	3.44	2.85	4.01	3.29	2.46	3.55	2.33	2.86
Livebirth Prevalence														0.46	0.00	0.16	0.49	0.67	0.18	0.35	0.18	0.00	0.18	0.27
Central East France																								
total cases	4	8	7	9	9	11	14	26	15	21	20	26	23	19	31	18	20	13	14	16	13	22	16	375
livebirths	3	5	4	6	6	3	0	1	2	2	1	1	1	1	2	1	1	0	0	0	0	1	1	42
fetal deaths	1	3	3	3	3	3	1	3	3	2	0	0	0	0	0	0	1	0	0	0	0	0	0	26
induced abortions	0	0	0	0	0	5	13	22	10	17	19	25	22	18	29	17	18	13	14	16	13	21	15	307
population:	75332	76220	75813	86433	86904	90825	91950	90191	91303	99858	107370	106607	104480	99249	99674	102153	103440	102090	102483	102982	93963	93721	93405	2176446
Total Prevalence	0.53	1.05	0.92	1.04	1.04	1.21	1.52	2.88	1.64	2.10	1.86	2.44	2.20	1.91	3.11	1.76	1.93	1.27	1.37	1.55	1.38	2.35	1.71	1.72
Livebirth Prevalence	0.40	0.66	0.53	0.70	0.70	0.33	0.00	0.11	0.22	0.20	0.09	0.09	0.10	0.10	0.20	0.10	0.10	0.00	0.00	0.00	0.00	0.11	0.11	0.19
Madrid (Spain)																								
total cases	35	25	29	24	27	38	14	13	14	12	10	16	5	6	8	9	6	8	6	2	0	3	1	311
livebirths	20	17	18	18	19	16	7	8	8	4	4	9	2	3	5	4	4	4	5	2	0	3	1	181
fetal deaths	15	8	11	6	8	22	7	5	6	8	6	7	3	3	3	5	2	4	1	0	0	0	0	130
induced abortions	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
population:	56910	56102	61333	71812	69513	66720	58245	51051	52686	59046	84379	87708	91607	82925	87239	87372	94044	98945	96490	104336	105833	103404	110954	1838654
Total Prevalence	6.15	4.46	4.73	3.34	3.88	5.70	2.40	2.55	2.66	2.03	1.19	1.82	0.55	0.72	0.92	1.03	0.64	0.81	0.62	0.19	0.00	0.29	0.09	1.69
Livebirth Prevalence	3.55	3.06	2.96	2.53	2.75	2.42	1.21	1.58	1.53	0.68	0.48	1.03	0.22	0.36	0.58	0.46	0.43	0.41	0.52	0.19	0.00	0.29	0.09	1.05
Norway																								
total cases	18	21	15	18	10	23	18	12	12	16	5	12	16	11	22	18	18	10	10	31	35	18	27	396
livebirths	2	8	2	4	1	0	3	0	0	0	1	1	0	1	3	1	1	1	1	3	4	4	2	43
fetal deaths	16	13	13	14	9	15	9	5	8	7	1	3	5	7	6	5	5	3	2	6	3	0	1	156
induced abortions	0	0	0	0	0	8	6	7	4	9	3	8	11	3	13	12	12	6	7	22	28	14	24	197
population:	51495	51021	51642	50258	50576	51416	52885	54313	57936	59712	61523	61386	60636	60166	60306	60488	61092	59896	58482	59967	59881	57475	56450	1309002
Total Prevalence	3.50	4.12	2.90	3.58	1.98	4.47	3.40	2.21	2.07	2.68	0.81	1.95	2.64	1.83	3.65	2.98	2.95	1.67	1.71	5.17	5.84	3.13	4.78	3.03
Livebirth Prevalence	0.39	1.58	0.39	0.80	0.20	0.00	0.57	0.00	0.00	0.00	0.16	0.16	0.00	0.17	0.50	0.17	0.16	0.17	0.17	0.50	0.67	0.70	0.36	0.33

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	1980-2002
Anencephalus (Contd)																								
Poland																								
total cases																				30	18	34	44	126
livebirths																				15	13	21	25	74
fetal deaths																				15	5	13	19	52
induced abortions																				-	-	-	-	-
population:																				149653	147228	185125	220040	702046
Total Prevalence																				2.00	1.22	1.84	2.00	1.79
Livebirth Prevalence																				1.01	0.89	1.14	1.14	1.06
Sweden																								
total cases																						39	45	84
livebirths																						3	2	5
fetal deaths																						1	0	1
induced abortions																						35	43	78
population:																						91815	96167	187982
Total Prevalence																						4.25	4.68	4.47
Livebirth Prevalence																						0.33	0.21	0.27
Total (Associate Member Registries)																								
total cases	57	54	51	51	46	72	46	51	41	49	35	54	44	50	75	61	65	48	53	98	80	136	146	**1463**
livebirths	25	30	24	28	26	19	10	9	10	6	6	11	3	8	10	7	9	9	7	22	18	32	32	**361**
fetal deaths	32	24	27	23	20	40	17	13	17	17	7	10	8	10	9	10	9	8	4	21	9	15	20	**370**
induced abortions	0	0	0	0	0	13	19	29	14	26	22	33	33	32	56	44	47	31	42	55	53	89	94	**732**
population:	183737	183343	188788	208503	206993	208961	203080	195555	201925	218616	253272	255701	256723	307438	312699	313381	319541	320500	314800	474720	463874	587937	632784	**6812871**
Total Prevalence	3.10	2.95	2.70	2.45	2.22	3.45	2.27	2.61	2.03	2.24	1.38	2.11	1.71	1.63	2.40	1.95	2.03	1.50	1.68	2.06	1.72	2.31	2.31	**2.15**
Livebirth Prevalence	1.37	1.65	1.28	1.35	1.27	0.92	0.50	0.46	0.50	0.28	0.24	0.43	0.12	0.26	0.32	0.22	0.28	0.28	0.22	0.47	0.39	0.55	0.51	0.54
Total (All registries)																								
total cases	143	156	148	150	141	173	144	151	141	145	144	192	192	186	219	233	285	238	305	354	343	351	402	**4936**
livebirths	38	58	54	51	42	38	36	25	30	17	24	29	20	23	22	27	31	26	28	55	54	55	56	**839**
fetal deaths	81	75	63	59	51	66	39	40	39	32	22	25	27	24	22	28	30	29	29	48	28	32	46	**935**
induced abortions	24	23	31	40	48	69	69	86	72	96	98	138	145	139	175	178	224	183	248	251	261	264	300	**3162**
population:	247105	333769	364874	391682	393234	411333	413569	422398	431822	468848	547656	620386	649939	691995	726834	763507	844509	859329	936185	1128623	1120570	1222543	1276277	**15266987**
Total Prevalence	5.79	4.67	4.06	3.83	3.59	4.21	3.48	3.57	3.27	3.09	2.63	3.09	2.95	2.69	3.01	3.05	3.37	2.77	3.26	3.14	3.06	2.87	3.15	**3.23**
Livebirth Prevalence	1.55	1.75	1.49	1.31	1.08	0.93	0.88	0.60	0.70	0.36	0.44	0.47	0.31	0.33	0.30	0.36	0.37	0.30	0.30	0.49	0.48	0.45	0.44	0.58

Data Source: EUROCAT Website Database (http://www.eurocat.ulster.ac.uk/pubdata/tables.html)

Appendix 3

EUROCAT Registry Descriptions by:

Full Member Registry

Associate Registry

Styria (Austria) – Full Member Registry
Styrian Malformation Registry

History and funding: The registry was set up in 1986 following the Chernobyl disaster. It registers fetuses/babies with congenital anomalies born after January 1st 1985. The registry has been a member of EUROCAT since 1995. It is funded by research grants provided by the Styrian government on an annual basis.

Population coverage: The registry covers all births to residents of the province of Styria (Population-based I = All mothers resident in defined geographic area) which amounts to a total of approximately 11,000 births annually.

Sources of ascertainment: The registry operates as a research programme with voluntary participation of hospitals. Information is actively gathered from 49 sources and reports are requested once per year. Sources consist of 34 minor or major obstetric hospitals, 1 cytogenetic laboratory, 2 pathology services, 11 child health services, including specialised departments for diagnosis and treatment, and free practicing midwives. The main record forms are filled out by medical doctors at the reporting source and are sent to the registry. Six sources have to be visited for data collection by a member of the registry. 48% of cases are reported by more than one source. In the remaining 52% of cases, only one source provided data. Fetuses/babies with anomalies are registered if diagnosed before birth, at birth or during the first year of life.

Terminations of pregnancy: Terminations of pregnancy following prenatal diagnosis of congenital anomaly are registered. Termination of pregnancy is legal in all cases for Socioeconomic reasons up to 12 weeks and thereafter, if serious psychological or health problems for mother or the fetus were to be expected. If a non-lethal congenital anomaly is diagnosed, most obstetricians in Austria would follow the maternal wish for TOP only up to 24 WG+0. Non-viable forms of congenital anomalies may be terminated at any stage of gestation. The official policy regarding prenatal diagnosis is: pregnant women are offered 2 ultrasound scans (16-20 and 30-34 weeks' gestation) according to a booklet called 'Mother-child passport'. More scans are done in most cases.

Stillbirth and early fetal deaths: Stillbirths with congenital anomaly are registered. Stillbirth definition is: late fetal death from a Crown Foot Length>=35cm and from 01.01.95 a limit of >=500g has been introduced by law. There is no lower gestational age or weight limit for registration of congenital anomaly in early fetal deaths/spontaneous abortions. Autopsy rates in 1999 were are as follows: stillbirths 63, induced abortions 68%, early neonatal deaths (0-7 days) 70% (estimate), later deaths 1 week to 1 year 70% (estimate) and deaths with congenital anomaly 64%.

Exposure data availability: Exposure information (e.g. maternal occupation, intake of drugs or illnesses during pregnancy) is not available. Data about techniques of prenatal screening (ultrasound, serum markers) and prenatal diagnosis are not systematically collected. Maternal residency is recorded and can be used for evaluating the sub-regional pattern of birth defects.

Denominators and controls information: Information on all births is available from birth certificates, gathered by Statistics Austria.

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Antwerp (Belgium) – Full Member Registry

History and funding: The registry began with a pilot study on procedures for registration of congenital anomalies in 1989. In 1990 the registry formally started in a region in Antwerp. Since 1997, the whole province of Antwerp has been covered. The registry is developed in collaboration with the provincial government and the university of Antwerp. The program is funded by the provincial government of Antwerp. The Registry has been a member of EUROCAT since1990.

Population coverage: The registry covers about 18,000 births annually, these are all births in the province of Antwerp (about 15% of the births in Belgium, Population-based I = All mothers resident in defined geographic area).

Sources of ascertainment: Reports are actively collected from maternity, Pediatric, and neonatologic units by registry staff who visit each maternity and neonatal unit in the covered region. There are a total of 23 participating hospitals. The midwife gives the basic information of children born with congenital anomalies. Further information is gathered from the Gynecologist and Pediatrician. Information about the parents is obtained from the general practitioners. The Gynecologist also reports cases to the registry if an anomaly is prenatally detected. If an anomaly is detected after the stay in the maternity hospital the Pediatrician reports it to the head nurse of the Pediatric ward. A check is made to ascertain whether the case has already been notified. Clinical geneticists, surgeons, pathologists and the Pediatrician of the centre of metabolic diseases are also contacted for more information. In 1996, the Child Welfare centres, an important notifier underwent re-organisation and computerisation, leading to a deficit of notifications that year. All cases of congenital anomaly diagnosed prenatally or in the first year of birth are registered. Reporting by hospitals and health workers is voluntary.

Termination of pregnancy: Termination of pregnancy is registered. Termination of pregnancy is legal under 13 weeks. If congenital anomaly is diagnosed, the upper gestational age for termination is 23 to 24 weeks.

Stillbirth definition and early fetal deaths: The stillbirth definition for denominators is: a baby which is not viable with a gestational age of >180 days. Stillbirths are registered. Early fetal deaths/spontaneous abortions are registered. Autopsy rates are as follows: stillbirths 75% (estimate), induced abortions 61%, neonatal deaths (0-7 days) unknown, later deaths 1 week to 1 year unknown and deaths with congenital anomaly 48%.

Exposure data availability: Exposure information: includes: maternal drug use maternal smoking and alcohol abuse, maternal and paternal diseases and family history, parental occupation.

Denominators and controls information: Background data on births are retrieved from the population databases of the local authorities and from the study centre for perinatal epidemiology in the Flanders region. Controls are not included in the registry, but data can be ascertained for specific studies.

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Hainaut (Belgium) – Full Member Registry

History and funding: The registry of Hainaut-Namur was initiated in 1978 and it started in 1979. It has been a member of EUROCAT since the beginning. From 1979 to 1990, it was located at the School of Public Health of the Catholic University of Louvain (Brussels). Since 1990, it was integrated into the Centre of Human Genetics of the Institute of Pathology and Genetics of the Institute of Pathology and Genetics (Loverval – Belgium). As a part of the Institute of Pathology and Genetics of Loverval, it is supported by an annual grant front the Institute of Research in Pathology and Genetics of Loverval. From 2001 it is also partly supported by the Ministry of Public Health of Wallonia.

Population coverage: The registry annually covers approximately 12,000 births in the provinces of Hainaut (south) and Namur (Population-based II = All mothers delivering within defined geographic area, irrespective of place of residence), which represents about 11% of all births in Belgium.

Sources of ascertainment: Delivery units, neonatal and Pediatric departments divided into 13 hospitals. All cytogenetic, genetic and pathological data including the examination of aborted fetuses are regionally concentrated in the Institute of Pathology and Genetics of Loverval. Children with malformations are registered up to one year of age.

Termination of pregnancy: Termination of pregnancy is legal up to 12 weeks of gestation. If a congenital anomaly is diagnosed, the upper gestational age limit for termination is approximately 24 weeks. Theoretical access to information is available on all cases of termination of pregnancy as they are registered, however, in practice ascertainment is slow to process.

Stillbirth definition and early fetal deaths: Stillbirth definition is: 28 weeks (or 180 days). Stillbirths are registered. Early fetal deaths/spontaneous abortions are included if the gestational age is greater than or equal to 20 weeks (weight is not a factor). Early fetal deaths/spontaneous abortions are registered. Autopsy rates are as follows: stillbirths 52% for all cases (95% of cases of malformations), induced abortions virtually 100%, early neonatal deaths (0-7 days) 52% for all cases (95% of cases of malformations), later deaths 1 week to 1 year unknown and deaths with congenital anomaly 48% in 1992-94 compared with 25% in 1982.

Exposure data availability: Exposure information: All that concerns information of maternal diseases during pregnancy, maternal drugs, occupations and genetic data is available.

Denominators and controls information: Background data on births are available from national and regional institutes of statistics. It is also based on our own statistics in collaboration with the ONE (Office de la Naissance et de l'Enfance).

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Bulgaria – Full Member Registry
Sofia Registry of Congenital Anomalies (SORCA)

History and funding: The registry started in 1995 when it became a member of EUROCAT in 1996. The registry is organised by the Bulgarian Society of Human Genetics and Sofia Municipality, and was supported by the State and private sponsors until 2001. The registry is not currently funded.

Population coverage: The registry covers all mothers resident in the region of Sofia (Population-based III = All mothers delivering in defined geographic area excluding non-residents of that area) and covers approximately 10,000 births annually.

Sources of ascertainment: The registry covers livebirths up to 1-year life, stillbirths and terminations of pregnancy. In practice, cases are notified by: obstetricians, neonatologists, Pediatricians, and pathologists. However, according to the Ministry of Health Act, every physician is allowed to notify by telephone or special form. Birth certificates do not include notification of congenital anomaly whereas death certificates do and are used as a source. Developmental screening clinics and child health centres are used as a source of notification of congenital anomaly.

Terminations of pregnancy: Termination of pregnancy is legal, with an upper gestational age limit of 12 weeks without special permission and up to 20 weeks with permission. If a congenital anomaly is diagnosed, the upper gestational age limit for termination is 27 weeks. The timing of termination depends on the severity of the defect. The Information Group (registry leader, two Pediatricians and a midwife) has full access to the data relating to invasive prenatal diagnosis carried out in the Genetic Centre in Sofia.

Stillbirth definition and early fetal deaths: Stillbirth definition is death at 20 or more weeks of gestation with no evidence of life after delivery. Stillbirths are registered. Early fetal deaths/spontaneous abortions are registered and included if the gestational age is less than 20 weeks.

Exposure data availability: Exposure information: Information about maternal drug use, maternal diseases, maternal occupation, and obstetric history is available for cases.

Denominators and controls information: Denominators are available from the Statistics unit of the regional health centre of Sofia municipality, the Ministry of Health and the statistics units of Sofia maternity clinics.

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Croatia – Full Member Registry

History and funding: The project started as a pilot investigation in 1982 and began formally as a registry in 1983 when it also joined EUROCAT. Until the end of 2000 we did not have any local funding, collection and transmission of data were on voluntary basis. From the year 2000 we have received funding from Ministry of Science and Technology and as a public health project we are in process of applying for funding from the Ministry of Health.

Population coverage: The registry is population based (Population-based I: All mothers resident in defined geographic area) and covers approximately 6000 annual births, up to 12% of births in Croatia (cities Rijeka, Varazdin, Koprivnica and region Pula).

Sources of ascertainment: Data are actively collected from four Delivery Units in the cities of Rijeka, Varazdin, Koprivnica and region Pula by neonatologists and Gynecologists. Birth certificates include notification of congenital anomaly and are used as a source. Death certificates also allow for notification of congenital anomaly and are used as a source. Children can be registered up to the first week of life.

Termination of pregnancy: Termination of pregnancy is legal and the upper gestational age limit set for termination is 24 weeks for all reasons. Terminations of pregnancy with congenital anomaly are not completely ascertained, but ascertainment has improved since 1996.

Stillbirth definition and early fetal deaths: Stillbirth definition is: 22 completed gestational weeks/500g weight. Stillbirths and early fetal deaths/spontaneous abortions are registered. Autopsy rates are as follows: stillbirths 90-100%, induced abortions 100%, early neonatal deaths (0-7) days 90-100%, later deaths 1 week to 1 year 90-100% and deaths with congenital anomaly 100%.

Exposure data availability: Exposure information: information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies is available for almost all malformed cases.

Denominators and controls information: Information on all births is available from the birth certificates.

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Odense (Denmark) – Full Member Registry
Registry of Funen County

History and funding: The registry started in 1979 and joined the EUROCAT network from the beginning of EUROCAT. The registry has been approved by the "Data Tilsynet" as a private registry for the purpose of research. There is no specific funding except private funding for computer equipment.

Population coverage: The registry covers Funen County (island of Funen with surrounding small islands) situated in the middle of Denmark (Population-based I = All mothers resident in defined geographic area). The total number of births per year in Funen County is around 6,000.

Sources of ascertainment: The registry is based on active case finding. Data for the registry includes hospital records from obstetric and Pediatric departments, birth notifications, deaths certificates, post-mortem examinations and data from the cytogenetic laboratory. For livebirths, late diagnosed cases are included up to the age of seven years.

Terminations of pregnancy: Termination of pregnancy is legal and the upper gestational age limit is 12 weeks without special permission. After 12 weeks of gestation induced abortion can be performed after permission from a local committee. If a congenital anomaly is diagnosed, the upper gestational age for termination is usually 24 weeks (24 to 28 weeks possible if survival is impossible). Terminations of pregnancy for fetal malformations are registered.

Stillbirth definition and early fetal deaths: Stillbirths include fetal deaths with gestational age ≥ 28 weeks. Stillbirths and fetal deaths/spontaneous abortions from 20 weeks are registered. The autopsy rate in stillbirths is 70% but is declining over the years.

Exposure data availability: Exposure information: Parental occupation, maternal smoking and medication during first trimester, maternal illness before and during pregnancy.

Denominators and controls information: Data on births per year and maternal age distribution covering Funen county is available from National Danish Statistics.

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Paris (France) – Full Member Registry

History and funding: The programme was initiated in 1975, but the registry began formally in 1981. It has also been a member of EUROCAT since 1982. The registry is part of a research unit of INSERM (National Institute of Health and Medical Research). The registry has been officially recognised by the French National Committee of Registries, and is renewed for four years (2001-2004) and partially supported by an annual grant from INSERM and Institut de la Veille Sanitaire (Institute for Health Surveillance).

Population coverage: The registry is population-based III (includes all mothers delivering in defined geographic area excluding non-residents of that area) and covers 38,000 annual births (about 5% of all births in France), that is, all births (live and stillbirths of 22 weeks or more) and terminations of pregnancy in the population of Greater Paris delivering in Paris maternity units. The estimation of the coverage of the registry is around 95%. The percentage of non-residents delivering within the registry area was 9.5% in 1998.

Sources of ascertainment: Notification to the registry is voluntary. Reports are actively collected from delivery units, Pediatric departments, cytogenetic laboratories, and pathology departments. Terminations of pregnancy are included. Case information is also received from the health certificates of the first week of life and this is the maximum age at diagnosis. Birth certificates include notification of congenital anomaly and are used as a source of notification.

Termination of pregnancy: Termination of pregnancy is legal and there is no upper gestational age limit for termination after diagnosis of congenital anomaly.

Stillbirth definition and early fetal deaths: Stillbirths of 22 weeks after the last menstrual period or more are registered. Early fetal deaths/spontaneous abortions are registered and included when the gestational age is 16 weeks. Autopsy rates in 1998 were as follows: 86% in stillbirths, 90% in induced abortions, 70% in early neonatal deaths (0-7 days) and no data are available for later deaths except from specific studies. All autopsies are carried out by fetopathologists.

Exposure data availability: Information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies, is available for the malformed cases.

Denominators and controls information: Background data on births are available from the National Institute of Statistics (INSEE).

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Strasbourg (France) – Full Member Registry
Strasbourg Prospective Study of Congenital Malformations.

History and funding: The registry was started in 1979 and became a member of EUROCAT in 1982. The programme is a research program, recognised by the local health authorities and funded by Social Security, Ministry of Health and INSERM.

Population coverage: The registry is population-based III and includes all mothers delivering in the covering area excluding non-residents. 3.5% of non-residents gave birth in the covered hospitals and 2% of the residents delivery outside the area. The geographic area covered by the Registry is the "departement du Bas-Rhin", Northeastern France, including Strasbourg, an urban area, and rural areas around Strasbourg. The registry covers about 13,500 births which represents approximately 2% of all births in France.

Sources of ascertainment: Registration is active. Sources of information are multiple including reports obtained from Pediatricians examining the newborn infants, hospital discharge records, maternity records, fetal ultrasound screening, laboratory records (cytogenetic, molecular, pathology) and specialised departments. Birth certificates include notification of congenital anomaly and are also used as a source of notification. The maximum age at diagnosis is between 2 and 5 years of age.

Termination of pregnancy: Termination of pregnancy is legal and there is no upper gestational age limit set for either social terminations or terminations as a result of diagnosis of a congenital anomaly. Terminations of pregnancy are registered.

Stillbirth definition and early fetal deaths:
Before 1993 stillbirths were defined as 180 days and since 1993 the definition has been set at 22 weeks of gestation. There is no limit, with regard to either gestational age or weight which impedes notification of a fetal death/spontaneous abortion to the register. Both stillbirths and fetal death/spontaneous abortions are registered. Autopsy is refused by about 10% of parents in cases not involving a congenital anomaly. Rates were as follows in 1994: in stillbirths 94%, in induced abortions 94%, in early neonatal deaths (0-7 days) 94%, in later deaths 1 week to 1 year 94% and 80% in deaths with congenital anomaly.

Exposure data availability: Detailed information on various exposures is obtained by interview of the mothers of the malformed infants and their controls. The children are followed to the age of one year.

Denominators and controls information: General demographic information is obtained from the National Institute of Statistics. Further information is obtained from Social Security Records and Health Sheets. A control infant is selected for each malformed one: the next infant of the same sex as the proband born at that hospital.

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Mainz (Germany) – Full Member Registry

History and funding: The Mainz Model was launched in 1990. The aim of this screening project was to determine prevalences and etiological causes of congenital birth defects. The registry and its associated research is funded by the Ministry of Health of the Federal Republic of Germany from 1990-1995 and by the Ministry of Labour, Social Affairs and Health of Rhineland-Palatine from 1990 until now. The Registry joined EUROCAT in 1992.

Population coverage: The registry covers births in three maternity hospitals which serve the Mainz district of Rhineland-Palatinate in SW Germany with approximately 3,300 births per year. Births to non-residents of the area are excluded (population-based III).

Sources of ascertainment: The registry employs three Pediatricians specially trained in clinical genetics, neonatalology and pediatric ultrasonography who examine each baby born in the participating hospitals twice within the first week of life. Routine sonography of hips and kidneys are performed. For particular indications (e.g. microcephaly or heart murmur) further ultrasound examinations of heart, brain and other investigations are made. Both major and minor anomalies are recorded according to a standard examination protocol, but only major anomalies are transmitted to the EUROCAT Central Registry. Information concerning stillbirths is obtained from pathology reports. Information concerning terminations of pregnancy is obtained from pathology reports and from the one centre in the district doing the final prenatal diagnosis. Cases of Microcephaly are not transmitted to EUROCAT Central Registry.

Termination of pregnancy: Terminations of pregnancy following prenatal diagnosis are registered. Induced abortion for social reasons is legal but not done in the Mainz region. Terminations of pregnancy for fetal malformation are performed in one of the hospitals. It is relatively common for prenatal diagnosis of major malformation not to result in a decision to terminate the pregnancy. 60% of terminations have an autopsy examination.

Stillbirth definition and early fetal deaths: The official stillbirth definition in Germany is a baby born with no signs of life weighing >=500g. The registry records information on all fetal deaths (including both stillbirths and spontaneous abortions) from 16 weeks gestation. Autopsy rates were as follows in 1995: in stillbirths 70%, in induced abortions 70%, in early neonatal deaths (0-7 days) 55%, in later deaths 1 week to 1 year - not applicable and in deaths with congenital anomaly – not known.

Exposure data availability: Exposure information on the EUROCAT form is obtained for both malformed and non-malformed babies from the pregnancy pass filled out throughout pregnancy and data collected by midwives 6-8 weeks before birth. Additional exposure data is held which is not transmitted to EUROCAT. Drugs are ATC coded.

Denominators and controls information: There is comparable information on all non-malformed babies in the population from the same process of Pediatric examination and information gathering. The number of births is taken from this database. Information on the total number of fetal deaths from 16 weeks is available and included in “stillbirth” statistics.

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Saxony-Anhalt (Germany) – Full Member Registry

History and Funding: The registry started in 1980. The years 1980-89 were funded by Ministry of Health of former German Democratic Republic. The years 1990-92 were funded by the Academy of Medicine, Magdeburg whereas the period between 1993 and 1995 was sponsored by the Ministry of Health, Federal Republic of Germany. Since 1995, the registry has been funded by the Ministry of Labour, Women, Health and Social Security of the Federal State of Saxony-Anhalt. The registry joined EUROCAT in 1992.

Population Coverage: The registry started in 1980 in the city of Magdeburg with about 4,000 annual births. After it there was a successive enlargement of the registry from 1981 to 1986. In 1981 we expanded to include some counties around the city of Magdeburg and this process continued until 1987 when we registered the whole district (about 17,000 births per year). Then we had a stable system from 1987 to 1989 and in 1990 there was a dramatic political change. Since the reunification there has been a two-third decrease in the number of births in the so-called new federal states. After the reunification, a similar process of territorial enlargement took place. In year 2000, registration expanded to the entire Federal State of Saxony-Anhalt, with about 18,000 annual births, 21 counties and three major cities.

By comparison to 1987, we currently survey a much larger area in our registry with approximately twice as many inhabitants (2.65 million) but the births rate is the same as the 1980s. Registration concerns deliveries within surveyed region excluding non-residents (Population-based III).

Sources of Ascertainment: Multiple sources, such as delivery units, paediatric departments, laboratories, prenatal diagnostic centres, departments of pathology and other specialities report children/fetuses with malformations and healthy children as a control group in the first week of life.

The registration of a child requires the informed consent of the parents. The registration sheet does not include much personal identifiable data, thus making follow-up investigations almost impossible. Exposure information of the mother (including drug intake before and in pregnancy, including periconceptional folic acid intake) and the father is documented on a standardized documentation sheet.
Until 1990, registration extended to diagnoses made in the first year of life.

Termination of Pregnancy: Terminations of pregnancy ("medical indication") have no time limitation by law in Germany. We have had complete information about terminations of pregnancy after prenatal diagnosis of fetal malformations since 1987.

Stillbirth Definition and Early Fetal Deaths: Stillbirths and spontaneous abortions with malformations from 16 weeks gestation are registered. The stillbirth definition has been >=500 g from 1.4.94 and >= 1000g before 1994.

Exposure Data Availability: Maternal and paternal occupation, drugs in pregnancy (ATC coded), alcohol, nicotine, drug abuse.

Denominators and Controls Information: Statistics on the total number of births comes from Statistical Office Saxony-Anhalt. There is the opportunity to exclude non-resident mothers with assistance of the postal code. A woman who gives birth outside Saxony-Anhalt, but is a result here is included in the statistics. The denominators include only livebirths and stillbirths. Information about maternal age for all births is available at the level of the entire state of Saxony-Anhalt and also the single counties.

Information is also reported about two control infants per malformed child. The two control infants, theoretically, are those born directly before and directly after the malformed child. The information about the control children is the same as malformed because a standardised documentation sheet is used.

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Web site: http://www.med.uni-magdeburg.de/fme/zkh/mz/

Dublin (Ireland) – Full Member Registry
Dublin EUROCAT Registry

History and funding: Register began in September 1979 and joined EUROCAT in 1980. The Registry is located within the Public Health Department of HSE – Eastern Region. Staffing includes a full time nurse/researcher and a part time secretary plus a part-time public health specialist and a part-time epidemiologist. Funding is provided by the Department of Health through the HSE – Eastern Region. There is a Steering Committee comprising specialists from each of Maternity and Pediatric Hospitals in the catchment plus a representative from the Department of Health.

Population coverage: The Registry is population-based I which includes all mothers resident in the HSE – Eastern Region of Ireland covering the counties of Dublin, Wicklow and Kildare. In 1999, less than 3% of resident mothers delivered outside the registry area. About one third (21,000 births) of all births in Ireland occur in this area.

Sources of ascertainment: All live and stillbirths are covered. Information collected by developmental screening clinics, child health centres, social allowances and health visitors are used as sources of notification. Birth certificates and death certificates do not include notification of congenital anomaly. Children with congenital anomaly are included in the registry when diagnosed up to the age of 5 years.

Termination of pregnancy: Abortion is illegal in Ireland.

Stillbirth definition and early fetal deaths: Babies born without signs of life with a gestational age of >=24 weeks or a weight of >=500g are registered. Early fetal deaths/spontaneous abortions are not registered. *National* autopsy rates only were available for 1999 for the following: stillbirths 50-60% and early neonatal deaths (0-7 days) 50-60%. There has been a decrease in the proportions having an autopsy due to controversy arising from the issue of consent – from about 70-80% in 1997 to 50-60% in 1999.

Exposure data availability: For each malformed infant reported, limited information is given on certain exposures.

Denominators and controls information: Denominator data are supplied by the government body - the Central Statistics Office. No information is available on controls.

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Galway (Ireland) – Full Member Registry

History and funding: Funding for the registry is provided nationally by the Department of Health and the Western Health Board. The Registry joined EUROCAT in 1981.

Population coverage: The registry is population-based I and includes all mothers resident in the County of Galway. The registry covers a total of about 3,000 births per year which represents 5% of all births in the Republic of Ireland.

Sources of ascertainment: Death certificates allow for the notification of a congenital anomaly, however, birth certificates do not. Notifications of children who are diagnosed up to the age of 5 years are included in the registry database.

Termination of pregnancy: Termination of pregnancy is illegal in the Republic of Ireland.

Stillbirth definition and early fetal deaths: The official definition of stillbirth is: a baby who shows no sign of life with a gestational age of >=24 weeks or weight of >= 500g. All stillbirths are registered. Early fetal deaths/spontaneous abortions are considered as such at a gestational age of 24 weeks and are included in the register if the birthweight is 500g. Autopsy rates for 1994 were: 90% in stillbirths, 70% in early neonatal deaths (0-7 days), 70% in later deaths 1 week to 1 year, 70% in deaths with congenital anomaly.

Additional exclusions and exposure data availability: No information was supplied on this section for the report.

Denominators and controls information: No information was supplied on this section for the report.

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Campania (Italy) – Full Member Registry
Birth Defects Registry of Campania

History and funding: The registry started in 1991. The programme is a surveillance programme supported by grants from Regional Health Authorities. The Registry joined EUROCAT in 1997.

Population coverage: The registry is hospital-based with participating hospitals distributed in Campania, a region of southern Italy where Naples is the main city. Initially 38 hospitals reported and the annual number of births was 38,000. At the present time, 80 hospitals participate, covering just over 60,000 annual births, approximately 90% of all births in Campania region which is approximately 8% of all births in Italy.

Sources of ascertainment: Participation was voluntary up to 1995 but became mandatory from 1996 onwards. Report forms are obtained from delivery units, Pediatric clinics and all divisions that care for babies with birth defects at the participating hospitals. From 1994, a report form has been introduced to record anomalies diagnosed from induced abortions. From 2002 sonographers and pathologists send notification to the Registry. Birth certificates include notification of congenital anomaly (after 2000) as do death certificates and both are used as a source of notification. Formerly notification occurred up to 1 year of life, but in current practice there is no age limit for diagnosis.

Termination of pregnancy: Termination of pregnancy is legal with an upper gestational age limit of 180 days for all reasons including a diagnosis of congenital anomaly. Terminations of pregnancy are registered.

Stillbirth definition and early fetal deaths: Any baby born without signs of life after 180 gestational days may be classified as stillborn and is included in the register. Hence any baby born without signs of life at less than or equal to 180 days is classified as an early fetal death/spontaneous abortion. Autopsy rates are as follows: 100% in stillbirths, 100% in induced abortions and about 90% in deaths with congenital anomaly. There were no figures available for early neonatal deaths or deaths between 1 week and 1 year.

Exposure data availability: For each malformed infant reported, information is given on certain exposures, including maternal drug usage and parental occupation. From 2002 information on induced abortions and controls are available. Information on all births from birth certificates is available.

Denominators and controls information: The ISTAT – National Institute of Statistics – is the source of birth statistics. Only demographic information is available on controls.

Address for further information:
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Emilia Romagna (Italy) – Full Member Registry
Emilia-Romagna Registry of Congenital of Malformations

History and funding: The registry started in 1978 in a few hospitals, has increased in size, and now includes 35 delivery units (2001). The programme is recognised and financed by the Emilia Romagna region and the Ministry of Scientific Research. The Registry joined EUROCAT in 1980.

Population coverage: The programme is population-based II and includes all mothers delivering within the region of Emilia Romagna, irrespective of place of residence (about 95% of all births in the Emilia-Romagna region) and covers approximately 24,000 annual births per year. Approximately 10% of non resident mothers are thought to deliver within the defined geographic region.

Sources of ascertainment: Hospital participation is voluntary. Reporting is carried out by both neonatologists and Pediatricians during the first week of the infant's life. Notification of congenital anomaly is recorded up to 1 week (after 1 week for selected malformations e.g. Downs Syndrome, cardiovascular defects, cleft palate). Selected malformations are followed up. An information exchange between Cytogenetic Laboratories, Pathology Services and Health Services has been established.

Termination of pregnancy: Termination of pregnancy became legal in Italy in 1978. At present the usual upper gestational age limit is 12 weeks and 23-24 weeks if a congenital anomaly is diagnosed. A psychiatric report is required for termination in the latter category. Data on induced abortions was not available to the IMER Registry until 1989. Between 1989 and 1993, recording was very incomplete due to difficulties in obtaining the data from the centres. Since 1994, ascertainment of IA has improved, but the data were still under revision of closure of the database of this Report.

Stillbirth definition and early fetal deaths: Stillbirths of 28 weeks or more gestation are included. The lower gestational age limit for inclusion of fetal deaths/spontaneous abortions is: less than 28 weeks of gestation (with no lower weight limit exclusion criteria). The autopsy rates for 1999 were: <10% in stillbirths, <5% in induced abortions, ~90% in early neonatal deaths (0-7 days), ~90% in later deaths 1 week to 1 year and ~90% in deaths with congenital anomaly.

Exposure data availability: Detailed exposure information is obtained by interviews of the mothers of malformed infants.

Denominators and controls information: Some general demographic information is known for all births in the area (e.g. mean maternal and paternal ages, percentage of mothers 35 years or older). For each participating hospital, the number of livebirths and stillbirths are known. A good information exchange has been established with regional health services. For each malformed infant, a control is chosen (the baby born before or after the malformed case in the same hospital) and its mother is interviewed in a similar way to the mothers with a registered baby.

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North-East (Italy) – Full Member Registry
North East Italy Registry of Congenital Malformations

History and funding: The Registry was established in 1980 to include Veneto and Friuli Venezia Giulia regions. Trentino Alto Adige region was added in 1990. The Registry became a member of EUROCAT in 1985. The programme is partly run by privately funded research organisations and partly by Regional Health Authorities.

Population coverage: The registry is population-based II and so it includes all mothers delivering within the Veneto, Friui-Venezia, Giulia and Trentino-Alto Adige Regions, irrespective of place of residence. Reports are obtained from 78 participating hospitals, with a total of approximately 54,000 annual births. The estimated proportion of non-resident mothers giving birth in the covered hospitals is 1.8% (calculated using controls).

Sources of ascertainment: Reporting is voluntary and they are obtained on specific forms from delivery units, induced abortion units, Pediatric, cardiology, ophthalmology and pathology departments, regional induced abortion database and cytogenetic laboratories. Thirty-two selected malformations are recorded within 7 days from birth (as of 1st July 1991 postnatal registration up to 3 years of age is limited to cardiovascular and ophthalmologic anomalies only). In terminated fetuses all anomalies are recorded. From 1st January 2000 we are now registering all congenital anomalies adopting the EUROCAT list of exclusions (revised 1985). Up to 1999 we did not register cases of: microcephaly, arhinencephaly/ holoprosencephaly, cystic kidney disease, indeterminate sex, diaphraghmatic hernia, Patau syndrome (Trisomy 13), Edward syndrome (Trisomy 18). The following anomalies were not coded according to EUROCAT standard and therefore are included in total case counts but not tabulated separately: common arterial truncus, transposition of the great vesssels (complete), congenital absence, atresia and/or stenosis of duodenum, congenital absence, atresia and/or stenosis of other specified parts of the small intestine.

Termination of pregnancy: Termination of pregnancy is legal under normal circumstances up to 12 weeks of gestation and up to 26 weeks if a fetal anomaly is diagnosed. Most terminations in the latter category, however, are carried out before 22 weeks. The recording of induced abortions for embryo-fetal anomaly was established on 1st July 1988. A form is completed in the hospital where the pregnancy is terminated by a Gynecologist.

Stillbirth definition and early fetal deaths: The official stillbirth definition: is a gestational age of >=28 weeks. Death certificates do not always allow for notification of congenital anomaly as a cause of death and they are not used as a source of information for registration. Autopsy rates quoted for 1994 were: 44% in stillbirths, 74% in induced abortions, 60% in early neonatal deaths, (0-7 days) with congenital anomaly. If no information was found on the death certificate then it was assumed that an autopsy was not performed.

Exposure data availability: Detailed information on various exposures, including maternal or paternal occupation, diseases and drug use is obtained by interview of the mothers at the birth of the malformed infants and their controls.

Denominators and controls information: Some epidemiological background data of all births are available. For each participating hospital the number of livebirths and stillbirths by sex and number of twin pairs are known. Information on controls are available – two control infants are selected for each malformed one.

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South East Sicily (Italy) – Full Member Registry
Sicilian Registry of Congenital Malformations

History and funding: The Registry started in 1991 and became a member of EUROCAT in 1997. The registry collaborates with other Italian Registries under supervision of the Italian National Institute of Health in Rome. The programme is supported at local level by A.S.MA.C, the Sicilian association for congenital malformation prevention.

Population coverage: It is hospital based and includes all mothers delivering in selected hospitals, irrespective of place of residence. The registry collaborates with four southeast provinces of the nine Sicilian provinces, (with a covering rate higher than 75% per year) which represented about one third of all births in Sicily with approximately 17,000 births per year.

Sources of ascertainment: Reports are obtained from delivery units, Pediatric units and other specialist departments. Congenital anomaly is registered up to and after 1 year of birth. The following anomalies are not coded according to EUROCAT standard and therefore not tabulated separately: cleft lip with or without palate, cleft palate, bilateral renal agenesis.

Termination of pregnancy: Termination of pregnancy is legal and the upper limit is usually 12 weeks, rising to 24 weeks if a congenital anomaly is diagnosed. Terminations of pregnancy following prenatal diagnosis are registered when notified, but ascertainment is currently still very incomplete. Registered terminations have been excluded from this Report.

Stillbirth definition and early fetal deaths: Stillbirths are registered as such if the gestational age is >180 days. Early fetal deaths/spontaneous abortions are not included. Although deaths due to congenital anomaly can be recorded on a death certificate, this information is not used as a source of notification. Autopsy rates were not reported.

Exposure data availability: For each malformed reported (livebirth, stillbirth and voluntary abortion), information is given on certain exposures, including maternal drug usage and parental occupation.

Denominators and controls information: Up to now no information on controls is available.

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Tuscany (Italy) – Full Member Registry
Tuscany Registry of Congenital Defects

History and funding: The registry started in 1979 in the province of Florence and from 1992 in the whole Tuscany region. The Registry is a surveillance programme included in the Regional Statistics System; it is formally recognised and supported by the Tuscany Region Health Authority. The Registry joined EUROCAT in 1979.

Population coverage: The programme is population-based I which includes all mothers resident in the Region of Tuscany. It involves all the regional hospitals and the coverage is around 95% of all births in the Tuscany region (approximately 3.5 million inhabitants and 26,000 births per year). Exchanges between regional informative systems indicate that approximately 0.2% of resident mothers gave birth in a hospital outside Tuscany in 1999.

Sources and ascertainment: Multiple sources are used to ascertain malformed infants; records are obtained from all obstetrical and maternity units, Pediatric departments, neonatal and Pediatric surgery units, prenatal diagnostic centres and pathology services. Mothers are interviewed by using a standardised questionnaire. Malformed babies diagnosed within the first year of life are also registered.

Termination of pregnancy: Termination of pregnancy became legal in Italy in 1978. Termination of pregnancy is legal when there is no possibility of autonomous life for the fetus. The Italian law (L.N. 194/78) lays down that termination is allowed in the case of diagnosis of serious fetal pathology which may detrimentally affect the woman's physical or psychological health. Induced abortions after prenatal diagnosis of birth defects are systematically included. Data for induced abortions first became available in 1982. Early ascertainment, however, was incomplete.

Stillbirth definition and early fetal deaths: The official definition of stillbirth in this registry is: 180 gestational days. Fetal deaths of 20 weeks or more gestation are systematically included if the weight is >=500g. Autopsy rates in 1999 were: ~60% in stillbirths, ~30% in induced abortions, ~50% in early neonatal deaths (0-7 days), ~30% in later deaths 1 week to 1 year and ~50% in deaths with congenital anomaly.

Exposure data availability: Maternal and paternal occupation, life-style, and Socioeconomic characteristics are obtained by interviews of mothers of malformed infants.

Denominators and controls information: Vital statistics and other epidemiological information is obtained by the birth medical records collected by the Regional Bureau of Statistics. Selected information is obtained from the control material collected.

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Malta – Full Member Registry
Malta Congenital Anomalies Register

History and funding: The register started in 1985 as a research project of the University of Malta. It started as a hospital-based register collecting data regarding congenital anomalies diagnosed in babies born at the main general hospital. It became a member of EUROCAT in 1986. Funding for the research project was stopped in 1995 and in 1997 the Department of Health Information resumed the functions of the registry increasing coverage to all hospitals on the islands making it a population-based register. The registry is now run and funded by the Government Department of Health Information. The aim of the Registry is to provide accurate epidemiological information regarding the occurrence of congenital anomalies in Malta and Gozo.

Population coverage: The registry is population-based I: covering all resident mothers in Malta, Gozo and Comino and presently covers about 4,300 births per year. The number of resident mothers giving birth in a hospital outside the area is considered to be negligible as Malta is an island and population movement is limited. It is unlikely that mothers will go abroad to give birth. It is precisely for this reason that the registry is thought to cover close to 100% of births.

Sources of ascertainment: Reporting is voluntary. Several new sources of information have been used since 1997 and the registry has back-dated its information to include these sources of information from 1993. For this reason data since 1993 may be considered most complete and reliable. The registry now employs active data collection from multiple sources including: labour, postnatal and nursery wards, cardiac laboratory records, genetics clinic records, National Mortality Register, National Obstetric Systems database, Hospital Activity Analysis database, National Cancer Register and the hypothyroid screening programme. Voluntary reporting by doctors is also available. These sources cover the whole population of the Maltese Islands. Babies with a congenital anomaly may be diagnosed and registered up to 1 year of age. Minor anomalies (as defined by EUROCAT) are not registered unless occurring in combination with other major defects.

Termination of pregnancy: Termination of pregnancy is illegal in Malta.

Stillbirth definition and early fetal deaths: The official definition of stillbirth is: a baby born with no signs of life at gestational age of 22 weeks or more, of a birth weight equal to or greater than 500g. Stillbirths are registered. All early fetal deaths of 20 weeks gestation and over which have been diagnosed as having a congenital anomaly are included. Autopsy rates for 1999 were as follows: 55% in stillbirths, 6% in early neonatal deaths (0-7 days), 20% in later deaths 1 week to 1 year and 50% in deaths with a congenital anomaly aged 0-1 years of age.

Exposure data availability: Information regarding maternal disease and exposure to medicinal drugs, smoking, alcohol and drug abuse as well as parental occupation are collected for all malformed infants.

Denominators and controls information: Epidemiological background data on all births are available from the National Obstetric Information Systems (NOIS) database and the National Statistics Office (NSO).

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Northern Netherlands – Full Member Registry
EUROCAT Registration Northern Netherlands

History and funding: The programme started in 1981, and became a member of EUROCAT in that year. The programme is funded by the Dutch Ministry of Public Health, Welfare and Sports. The registry is carried out in the Department of Medical Genetics of the University of Groningen.

Population coverage: The registry is population-based I which includes all mothers resident in the Provinces of Groningen, Friesland and Drenthe. In the beginning the programme covered 7,500 births annually when it covered the province of Groningen and the northern part of the province of Drenthe. Coverage was gradually increased to 19,000 births annually in the provinces from 1989 onwards. Home deliveries (30% of births per year) are included and it is estimated that only a few percent of resident mothers would give birth outside the defined registry area.

Sources of ascertainment: Obstetricians, Pediatricians, clinical geneticists, surgeons, general practitioners, midwives, well-baby clinics, pathologists and the national obstetric registry send information to the registry on a voluntary basis. Registry personnel are actively involved in data collection. There are no age limits are applied regarding maximum age at diagnosis and if new information becomes available on infants born in 1981 or later, the files are updated.

Termination of pregnancy: Termination of pregnancy is legal. There is no specified upper gestational age limit for termination written in law –viability is the criterion. In practice 22 weeks is the usual upper limit unless a child has a lethal (or almost lethal) condition. In the case of diagnosis of congenital anomaly, there is no upper limit.

Stillbirth definition and early fetal deaths: Stillbirths are registered and the official stillbirth definition is: a gestational age of >=24 weeks. There are no age or weight limits for inclusion of early fetal deaths/spontaneous abortions. Autopsy rates in year were not given.

Exposure data availability: Since 1997 parents have been asked to fill out a questionnaire including questions on occupational activities, smoking, alcohol and drug use. In addition, data from community pharmacies are used to collect maternal drug exposure data.

Denominators and controls information: General statistics are available from the Dutch Central Bureau of Statistics (CBS).

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Poland – Full Member Registry
The Polish Registry of Congenital Malformations

History and Funding
The Polish Registry of Congenital Malformations has been in operation since 1997. It was founded as a scientific project ordered by the Polish Ministry of Health and financed by the State Committee for Scientific Research. Since July 1, 2000 it has been part of the Government Programme of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland. As part of this Programme the Registry provides the Polish Ministry of Health with important information needed in health care management.

Population Coverage
The PRCM is a population based registry of Type I (all mothers resident in defined geographic area). Until 2001 PRCM covered 9 provinces of Poland: Pomorskie, Zachodniopomorskie, Warmińsko-Mazurskie, Kujawsko-Pomorskie, Wielkopolskie, Lubuskie, Łódzkie, Dolnośląskie and Opolskie. In 2001 the Śląskie Province (Silesia) was added, and in 2002 the Lubelskie and Podkarpackie Regions joined the Registry. With these newly added regions the Registry covers 12 of 16 provinces of Poland: 73.6% of the area of Poland (230,091 km^2) with the population of 27,815,601 (72.0%), and about 267,300 births (life and stillbirths) per year (70.27%) (2002).

Sources of Ascertainment
Reporting is recommended by the Ministry of Health (as an official Government Programme) and consists of multi-source reporting. The sources include: delivery unit staff, ultrasound staff, postnatal ward staff, Pediatric intensive care unit staff, foetal medicine unit staff, Pediatricians, post-mortem reports, regional genetic and cytogenetic services, and Pediatric cardiology referral centres. The main source of information is a double sided notification form filled up by a physician responsible for diagnosing the malformation. The notification forms are sent immediately to the PRCM Central Working Group. Birth certificates do not record congenital anomaly. Death certificates allow for notification of congenital anomaly as a cause of death and they are therefore used as a source. The maximum age at diagnosis is 24 months.

Termination of Pregnancy
Although termination of pregnancy is legal, it can only be performed by a physician when: 1) a pregnancy poses danger to health or life of the pregnant woman; 2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or its untreatable life-threatening disease; 3) there is a plausible suspicion the pregnancy has arisen from a prohibited act. The upper gestational limit for termination of a congenital anomaly affected pregnancy is viability. Although the termination of pregnancy is legal, in Poland there is a public pressure not to perform such a procedure and that is why the availability of information on pregnancy terminations is rather low as there is no central registry for the IAs. Hence the registry currently does not register terminations of pregnancy following prenatal diagnosis

Stillbirth Definition and Early Fetal Deaths
The official stillbirth definition is as follows: foetal death (stillbirth) is a death prior to the complete expulsion or extraction of a product of conception from a mother, irrespective of pregnancy duration; the death is indicated by the fact that after separation the fetus does not breathe, or shows no other evidence of life, such as heart beating, pulsation of the umbilical cord or definite movement of voluntary muscles. For statistical purposes we include all fetuses weighing at least 500 grams at the moment of birth, having reached the 22nd week of gestational age, if the weight is unknown, or reaching 25cm of the body length (crown-heel).
We do not include early foetal deaths or spontaneous abortions. Autopsy rates vary between regions or even between health care units, the ranges for performance are as follows: stillbirths 10-30%, early neonatal deaths 20-30%, later deaths 1 week to 1 year 10-20% and deaths with congenital anomaly 30-40%.

Data Availability
The following data is gathered by way of registration forms, although its availability may be limited, depending on the source of registration: chronic illness in mother, pregnancy induced conditions in mother, acute maternal illness during pregnancy, therapeutic and recreational drugs taken during pregnancy, invasive tests in pregnancy, folic acid use in pregnancy, smoking habits, alcohol use, mother's obstetric history as well as the county of residence, family history of congenital malformations, and genetic conditions in family members, father's and mother's occupational and environmental hazards, father's and mother's education.

Denominators and Controls Information
Information on all births (live & stillbirths) is available from birth certificates, gathered by the Central Statistical Office of Poland. No information is available on controls.

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Southern Portugal – Full Member Registry

History and funding: The registry started in 1990 and became a member of EUROCAT then. The registry is funded by the National Institute of Health.

Population coverage: The registry is population-based and includes all mothers resident in Algarve, Alentejo, Setubal and part of Santaren. It covers approximately 18 000 births annually (representing 14% of total births in Portugal).

Sources and ascertainment: Pediatricians and obstetricians are responsible for case notification in each region up to the end of the neonatal period. Other sources of ascertainment are fetal pathology, pediatric cardiology, cytogenetic laboratories and clinical genetics services. Data are validated at central level in Lisbon.

Termination of pregnancy: Termination of pregnancy is legal up to 24 weeks gestation and requires the permission of a technical committee. There is no upper gestational age limit for terminations for non-viable anomalies.

Stillbirth definition: The definition of stillbirth in Southern Portugal is: a gestational age of 22 weeks or a birthweight of 500g. Stillbirths and terminations as a result of diagnosis of congenital anomaly are included in the registry. Most fetuses in the covered area have an autopsy performed.

Exposure data availability: Information about maternal drug use, maternal diseases, maternal occupation, and obstetric history is available for cases.

Denominators and controls information: Demographic information is available from the National Statistic Office.

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Asturias (Spain) – Full Member Registry

History and funding: The registry started in 1990 and became a member of EUROCAT in 1992. The registry is situated in the Epidemiology Unit of the Regional Public Health Department which provides accommodation and computer facilities.

Population coverage: The registry is population-based III which covers all mothers delivering in Asturias in Northern Spain excluding non-residents of that area. In 1999, 1.5 % of non-resident mothers gave birth in the covered hospitals of Asturias. The registry covers approximately 6,500 births annually.

Sources and ascertainment: Case forms are collected from pathology units, biochemical and cytogenic laboratories, neonatology and Pediatric units, obstetricians, geneticists, death certificates and hospital discharge forms. The registry covers livebirths up to five years of age.

Termination of pregnancy: Termination of pregnancy is legal up to 12 gestational weeks in the case of sexual assault and no upper limit for maternal illness. If a congenital anomaly is diagnosed, the upper gestational limit is 22 weeks with an additional stipulation that two specialised medical reports are completed. Terminations of pregnancy have been registered since the registry's inception.

Stillbirth definition and early fetal deaths: The official stillbirth definition is: a gestational age of 26 weeks and these are registered. The registry definition for denominators is 22 weeks or a birthweight >=500g. Early fetal deaths/spontaneous abortions are defined as a gestational age of 20 weeks or a birthweight of 500g but these are not registered. Autopsy rates in 1999 were as follows: 84% in stillbirths, <50% in induced abortions, 60% in early neonatal deaths (0-7days) % in later deaths 1 week to 1 year unknown and 92% deaths with congenital anomaly.

Exposure data availability: Information about maternal drug use, maternal diseases, and obstetric history is available for cases.

Denominators and controls information: Denominators are available from the Asturias Natural Population Movement Statistics.

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Barcelona (Spain) – Full Member Registry
Barcelona Birth Defects Registry (Registro de Defectos Congénitos de Barcelona: REDCB).

History and funding: The programme was initiated in 1990 and reached a population based status by 1992, when it became a member of EUROCAT. The registry is part of the Health Information Service in the Municipal Institute of Public Health of Barcelona. It is partially funded by national research grants.

Population coverage: The registry is population-based I which includes all mothers resident in the city of Barcelona, Catalonia. The registry covers about 12 500 births annually which represents about 3% of all births in Spain.

Sources of ascertainment: General information on cases and controls as well as clinical information on cases is collected using questionnaires specifically made for the registry. An interview of the mother is the main source of general information. Delivery units, Pediatric departments, cytogenetic laboratories, pathology departments, prenatal diagnosis units, etc. are the sources of clinical information. Since 1995, the register has incorporated most Pediatric cardiology services to its coverage.

Termination of pregnancy: Termination of pregnancy is legal with an upper gestational age limit of 22 weeks for all reasons including diagnosis of a congenital anomaly following prenatal screening. Data about techniques of prenatal screening and diagnosis are systematically collected

Stillbirth definition and early fetal deaths: The official definition of stillbirth is: a gestational age of 22 weeks or more. Earlier fetal deaths are not recorded. Autopsy rates in 1994 were as follows: 71% in stillbirths, unknown in induced abortions, 57% in early neonatal deaths, unknown in later deaths 1 week to 1 year and 78% in deaths with a congenital anomaly.

Exposure data availability: Information on maternal drug use, maternal and paternal diseases and occupations, is available for cases and controls.

Denominators and controls information: Background data on births are available from birth certificates and the Barcelona perinatal mortality registry. A random sample (not case-matched) of about 2% of the babies expected in each maternity unit is selected.

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Basque Country (Spain) – Full Member Registry
Registry of Congenital Anomalies of the Basque Country (RACAV)

History and funding: Registration of congenital anomalies in the Basque Country started on January 1st 1990. The Registry became a EUROCAT member in September 1990. The registry is financially supported by the Health Department of the Basque Government.

Population coverage: The registry is located in the Basque Country region, in northern Spain, covering a geographic area of 7260 Km^2, and a population of 2,250,000 inhabitants. It is a population-based III registry which therefore includes all mothers delivering in the Basque Country excluding any non-residents. The total number of annual births is about 16,000. It is estimated that 1-2% of outside resident mothers deliver in the covered hospitals.

Sources of ascertainment: Reporting is voluntary. There is an active search for cases (livebirths, stillbirths and induced abortions) through multiples sources of information: Neonatal Units, Specialist Pediatrics Departments, Cytogenetics and Pathology laboratories, Hospital discharge records and private maternity hospitals. The maximum age at diagnosis routinely reported to the registry is one year of age.

Termination of pregnancy: Termination of pregnancy is legal for certain indications, including prenatal diagnosis of severe anomaly with an official upper gestational age limit of 22 weeks. In practice there is no upper limit in the main public maternity hospitals, although in some the cases are officially registered as stillbirths. The private maternity hospitals send such mothers to the public hospitals or abroad (to the UK). Data about techniques of prenatal screening and diagnosis are systematically collected.

Stillbirth definition and early fetal deaths: The official definition of stillbirth in the Basque Country is: a gestational age of 22 weeks or a birthweight of 500g. Postmortem examination rates are highly variable in the region. About 90% of autopsies in stillbirths and neonatal deaths were performed in the public maternity hospitals (the remaining 10% of parents did not give permission). Autopsy following induced abortion usually depends upon the condition of the fetus.

Exposure data availability: Information on maternal drug use, maternal and paternal diseases, outcome of previous pregnancies and assisted conception is available.

Denominators and controls information: Statistics are provided by the Basque Statistics Institute (EUSTAT).

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Vaud (Switzerland) – Full Member Registry
Registry of Switzerland

History and funding: The registry of Switzerland was originally set up in 1988, and also became member of EUROCAT in 1988. Different cantonal registries sent their data to the central registry in Lausanne. The aim at the beginning was to cover the whole country (80,000 births/year). In the first years of activity, 30% - 81% of births were surveyed. For financial reasons, many cantons had to stop this activity and in 1993, the Swiss registry covered 50% of all births in Switzerland. In 1998, the following cantons were included in the programme: Zurich, Fribourg, Argovie, Tessin, Vaud, Valais, Neuchâtel and Jura. The registry is located in the Division of Medical Genetics of the University hospital in Lausanne. The registry has formerly been associated with members from the Swiss Academy of Medical Sciences and from the Swiss Society of Pediatrics. The system is financed by the Swiss Federal Agency for Statistics for the central registry and by the cantonal health department for some cantonal registries. As the level of ascertainment was quite heterogeneous between the local cantonal registries and their activities fluctuating according to the years (cf prevalence rate <200 per 10,000), it was decided in January 2002 to restrict the registration in canton of Vaud only and to change the name of the Registry: Registry of Vaud (Switzerland).

Population coverage: The registry is population-based I and as such it covers all mothers resident in the canton of Vaud. The percentage of mothers delivering in a hospital outside the registry area is not known precisely although it is thought to be very low. The registry covers about 9% of all births in Switzerland (approximately 7,500 births annually). The changing coverage is detailed above.

Sources of ascertainment: Reporting is voluntary. Active case finding and multiple sources of information are used: delivery units; Pediatric departments; cytogenetic and genetic counseling and pathology unit. Data about different methods of prenatal diagnosis are collected (ultrasound, serum markers, cytogenetic and molecular). There is no upper age limit for registration of a child with a malformation.

Termination of pregnancy: Termination of pregnancy is legal up to 12 weeks gestation under most circumstances but this limit is extended to 24 gestational weeks if a congenital anomaly is diagnosed. In the latter circumstance, additional permission must be granted by two further physicians. Induced abortions following prenatal diagnosis are included in the register.

Stillbirth definition and early fetal deaths: The official stillbirth definition is: a gestational age of >= 27 weeks or length >=30cm and these are included in the register. Early fetal deaths/spontaneous abortions are included if they are 20 gestational weeks or more with no weight restrictions. Autopsy statistics were not available.

Exposure data availability: Information on maternal occupations and diseases, maternal drug use, outcome of previous pregnancies is available for the malformed infants.

Denominators and controls information: Background data on births are available from the Swiss Federal Agency for Statistics and from Service Cantonal de Recherche et d'Information Statistique (SCRIS).

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Username: eurocat, password: tropic

Glasgow (UK: Scotland) – Full Member Registry
Greater Glasgow NHS Board Congenital Anomalies Register

History and funding: The Glasgow Register of Congenital Malformations was founded in 1972 under the auspices of the Social Pediatric and Obstetric Research Unit and jointly administered by the University of Glasgow and the Corporation of Glasgow. It became a member of EUROCAT in 1978. The first full year for which standardised notifications were made was 1979. Greater Glasgow NHS Board (formerly Greater Glasgow Health Board) funds the Register. The Register had three initial objectives: the detection of epidemics, the calculation of prevalence rates and the epidemiological investigation of selected malformations. The objectives were broadened after joining EUROCAT to include the evaluation of preventive and therapeutic measures.

Population coverage: Population based I: the reference population is defined as all births (live and still) to women resident in the Greater Glasgow NHS Board area irrespective of the place of birth. Livebirths, stillbirths of 24 weeks gestation or more, spontaneous and induced abortions are included. In 2000, 3% of Greater Glasgow NHS livebirths were delivered outwith the study area and 18% of Scottish births resided in Greater Glasgow NHS Board area (Source: General Register Office for Scotland). From 1972 to March 1974 the Registry population and geographic area was defined by the boundaries of the former City of Glasgow. Following the reorganisation of the National Health Service in 1974, the Greater Glasgow Health Board assumed responsibility for the Register. Consequently the population under observation was enlarged by 35% to accommodate those areas formerly outside the boundaries of the City of Glasgow which were included within the area of the newly created Greater Glasgow Health Board. Annual number of births within Greater Glasgow has dropped from 13,500 in 1979 to 9,500 in 2000.

Sources of ascertainment: Notification is voluntary. Sources available are: Hospital discharge data, Health visitor immunisation consent forms, Inborn errors of metabolism screening programme, Child health surveillance programme, Death & stillbirth registration, Regional medical genetics department, Regional pathology department. Maternal and Pediatric hospital case records are viewed to confirm each case. Two useful sources are no longer available: Pediatric discharge letters are no longer sent to registry staff due to the closure of participating Pediatric units and perinatal summaries - an important early source for terminations for fetal abnormality – were sent by one maternity hospital for a number of years but this has ceased. The time-delay in ascertainment is a growing problem. This is partly due to the above-mentioned loss of earlier notifications but also due to time constraints on medical records staff who pull hospital case records for the registry worker to view. Due to reorganization of medical records in some hospitals, a delay in obtaining 1998 and 1999 data was experienced, leading to deficits in the prevalence rates for those years in this Report. Around 20% of cases in 2000 were reported by more than one source of information. There is no time limit for registration or for updating diagnostic detail. Cases with antenatal false positive screening results that do not have a congenital anomaly are not recorded.

Terminations: Termination of pregnancy became legal in the United Kingdom in 1967 (Abortion Act). Termination for fetal malformation is legal up to 24 weeks gestation. Information on terminations is now mainly obtained by viewing post mortem reports in regional medical genetics department.

Stillbirth definition and early fetal deaths: The official stillbirth definition is: fetal death after 24 completed weeks. Stillbirths and infant deaths are routinely notified to the register where at least one cause of stillbirth/death is a congenital anomaly. There is no lower gestational age or weight limit. Autopsy rates are not known.

Exposure data availability: No information available.

Denominators and controls information: Data on births is available from the Registrar General for Scotland. Mid-year estimates are published by the middle of the year following. The number of births (live and still) is available by maternal age and by month of birth for the population from1983. These figures are produced by analysing birth and child record files from a quarterly download based on current status of residence and not initial status at birth. As a result the denominator data will therefore vary from quarter to quarter and will never correspond to the Registrar General's figures. Demographic/exposure information on controls is not collected.

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Mersey (UK: England) – Full Member Registry
Mersey Congenital Anomaly Survey

History and funding: In 1992 a fetal anomaly survey was initiated in the former Mersey region. Its aim was to assess the effectiveness of antenatal diagnosis. However, this survey proved difficult to establish and anomalies were under reported. In 1995 the survey linked to CESDI (Confidential Enquiry into Stillbirths and Deaths in Infancy), became the responsibility of the CESDI Regional Co-ordinator and was relaunched as the Congenital Anomalies Survey. Funding is obtained from various sources which is bid for annually. The registry joined EUROCAT in 1995.

Population coverage: The registry is population-based II All mothers delivery in a defined geographic area, irrespective of place of residence, the number of women from outside Mersey accounts for around 8-10% of all anomalies. The Survey covers Merseyside and Cheshire with about 27,000 annual births. Despite many national boundary changes, the survey has maintained its boundaries since 1995.

Sources of Ascertainment: Reporting is voluntary. The survey records all anomalies which: (a) are first detected antenatally, at birth or termination of pregnancy, or during the first year of life (b) involve a structural, metabolic, endocrine or genetic defect in the child/fetus. The survey relies on multi source ascertainment and has developed an extensive network of health professionals, obstetricians, Pediatricians, midwives, neonatal nurses, pathologists and ultrasonographers. There is also close collaboration with CESDI, the Regional Cytogenetic department, the Royal Liverpool Children's Hospital Alder Hey including the cleft lip and palate unit and birth and death district notification. This network has ensured our local ascertainment is better than national statistics. Birth certificates do not include notification of congenital anomaly.

Termination of pregnancy: Termination of pregnancy is legal and there is a statutory requirement for registration. The upper gestational age limit is 24 weeks, however, if a congenital anomaly is diagnosed this upper gestational age limit no longer applies.

Stillbirth definition and early fetal deaths: Stillbirth definition is: any baby born after 24 completed weeks of gestation that shows no sign of life. Stillbirths and fetal deaths/spontaneous abortions are registered. There is no lower gestational age limit for inclusion of early fetal deaths/spontaneous abortions although in practice the registry is notified of very few spontaneous abortions. Autopsy rates are as follows: stillbirths 32%, induced abortions 47%, early neonatal deaths (0-7 days) 23%, later deaths 1 week to 1 year 45% and deaths with congenital anomaly 37%.

Exposure data availability: Exposure Information: No information on exposure is collected other than self reported information on smoking, alcohol and drug intake during pregnancy.

Denominators and controls information: Denominator data is supplied in an aggregated format by each hospital within Mersey. No control cases are currently collected.

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North Thames (West) (UK: England) – Full Member Registry
North Thames (West) Congenital Malformation Register

History and Funding: Case registration began on 1 January 1990 and EUROCAT reporting began in 1996. Data transmission to ONS (the Office for National Statistics) began on 1 January 2000. The Registry is an active member of BINOCAR (British Isles Network of Congenital Anomaly Registers) and FOCAL (Follow-up of Congenital Anomalies Long Term). Registry data continue to be used in many collaborative research projects as well as for local audit of prenatal screening and diagnostic programs. The Registry is funded by the London Genetics Commissioning Consortium.

Population Coverage: This is a hospital based registry (all mothers delivering in selected hospitals, irrespective of place of residence). However, in utero transfers to contributing hospitals due to an anomaly are excluded, whereas in utero transfers away from contributing hospitals following prenatal diagnosis of a congenital anomaly are included. It covers 17 NHS obstetric units in the North West Thames area (North West London, Hertfordshire and Bedfordshire). These hospitals had about 48,000 births in 2003 representing about 8% of all births in England (98% of which occurred in hospital).

Sources of Ascertainment: Reporting is voluntary and multi-source.

Spontaneous reporting:
Midwives, obstetricians, paediatricians, and sonographers in contributing hospitals all complete forms when an anomaly is diagnosed pre or post natally. Each month, each contributing hospital downloads information about babies noted on the database to have anomalies and sends it to the registry. Each month, the regional cytogenetic laboratory downloads a list of all abnormal karyotypes for the registry. Information about deaths is provided by CEMACH (Confidential Enquiry on Maternity and Child Health) who share their forms and postmortem reports with the registry when the fetus/ baby had an anomaly. The regional fetal medicine unit sends copies of ultrasound reports. Information about postnatally diagnosed cardiac defects is provided by the unit that sees most such cases. ASCAL (Audit of Screening for Chromosome Anomalies in London) shares information with the registry. Notifications from contributing hospitals to the National Congenital Anomaly Surveillance System are sent to the registry.

When information about a case is thought to be incomplete or incorrect, staff contact the appropriate source and endeavour to ensure that the information is correct and complete.

Birth certificates do not include notification of congenital anomaly.

Registration covers fetuses with prenatally diagnosed anomalies, affected fetuses spontaneously lost from 16 weeks gestation, babies diagnosed before their first birthday in the case of structural anomalies, and babies diagnosed at any time in the case of chromosome anomalies.

- Cardiac defects that have not been prenatally diagnosed are under ascertained.
- Between 1993 and the end of 2004, the registry excluded babies in whom the main diagnosis was hypospadias, polydactyly and syndactyly.
- Between 1996 and the end of 2004, the registry did not register cases where the main diagnosis was talipes.
- The Registry does not register fetuses in which the only anomalies reported are soft markers on ultrasound (such as dilated renal pelves, choroid plexus cysts, ventriculomegaly, bright bowel, golf balls in heart).
- Prior to 1996, ano-rectal atresia was not coded in a way that allowed it to be distinguished from other intestinal anomalies; so prior to 1996 cases of ano-rectal atresia were only included in total case counts of intestinal anomalies and not in case count of ano-rectal atresia.
- The code for indeterminate sex is almost never used, since cytogenetic and pathology investigations almost always determine the sex, and the coding is then adjusted as appropriate (such as malformation of external male genitalia).
- Prune Belly syndrome is not coded if underlying anomaly is known.
- Ascertainment was generally low in 1999 and in 2002.

Termination of Pregnancy: Termination of pregnancy is legal up to 24 weeks of gestation but if a serious congenital anomaly is diagnosed there is no gestational age limit. If the termination is carried out after 22 weeks and the condition is not lethal, a fetocide is usually performed prior to induction of labour. Terminations performed due to a congenital anomaly are reported to the register by all the same sources which report term

deliveries. Information is collected on how and when anomalies were diagnosed, the indication for any invasive tests that were done and why prenatal karyotyping was not done.

Stillbirth Definition and Early Fetal Deaths: The official stillbirth definition is: a child born with no signs of life after complete expulsion from the mother after the 24th week of pregnancy (there is no weight limit). All stillbirths are registered. Early fetal deaths/spontaneous abortions are included with a lower limit of 16 weeks for chromosome anomalies unless they were prenatally diagnosed. Autopsy rates were as follows in 2000: 66% in stillbirths, 47% in induced abortions (some autopsies not done include early terminations of pregnancy with dilatation and curettage), 46% in early neonatal death (0-7 days), 59% in later deaths 1 week to 1 year and 66% in deaths with congenital anomaly.

Exposure Data Availability: Chronic illness in mother, pregnancy induced condition in mother, acute maternal illness during pregnancy, therapeutic and recreational drugs taken around conception and during pregnancy, invasive tests in pregnancy, smoking habits, alcohol abuse, consanguinity and post code of residence. Post code of residence is very well reported. Other exposures are thought to be under-reported.

Denominators and Controls Information: As the numerator is hospital based, the denominator is the births and terminations of pregnancies in the contributing hospitals. Hospitals have a computerized database in which information is stored on all births. This database holds much of the same information about babies as stored on the registry database and is one of the reporting sources to the register.

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Wales (UK) – Full Member Registry
Congenital Anomaly Register and Information Service (CARIS)

History and funding: Data collection commenced on 1st January 1998 and includes any baby where pregnancy ended after this date. CARIS joined EUROCAT in 1998. CARIS is based at Singleton Hospital, Swansea and is funded by the National Assembly for Wales. CARIS aims to collect data which can be used to describe the pattern of congenital anomalies across Wales. This should help:

- Build up and monitor the picture of congenital anomalies in Wales
- Assess interventions intended to help prevent or detect congenital anomalies
- Plan and co-ordinate provision of health services for affected babies and children
- Assess possible clusters of birth defects and their causes

Population coverage: The registry covers the entire country of Wales (Population-based I = All mothers resident in defined geographic area) with an annual number of births of around 32,000.

Sources of ascertainment: Reporting is voluntary. The Register relies upon multi-source reporting including: antenatal clinics, delivery units, pediatric departments, ophthalmology, cytogenetics, pathology and regional; centers of pediatric surgery. Each delivery unit has a nominated co-ordinator to help ensure good reporting and chase for further details. CARIS staff also visit units to help with data collection. Registration covers all fetuses with prenatally diagnosed anomalies. There is no lower age of cut off, so the fetal losses and early terminations with anomalies are registered. All live born babies with structural anomalies are registered if diagnosed before their 1st birthday, but all chromosomal anomalies are registered, even if diagnosed later. Data exchange with the Mersey Register is also important as babies needing specialist services in North Wales are referred to Liverpool.

Termination of pregnancy: Termination of pregnancy is legal up to 24 weeks of gestation. Terminations of pregnancy are registered. If congenital anomaly is diagnosed, there is no upper gestational age limit for termination in cases of major anomaly.

Stillbirth definition and early fetal deaths: Stillbirth definition: 24 weeks gestation (late fetal death after 23 completed weeks of gestation). Stillbirths of 24 weeks or more gestation are registered. Early fetal deaths/spontaneous abortions have no lower limit for inclusion on the register (earliest cases recorded go down to 8 weeks gestation. Autopsy rates were not given.

Exposure data availability: Exposure information: Information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies is available. Folic acid supplementation before and during pregnancy is also collected.

Denominators and controls information: Denominator data is obtained from the Office for National Statistics.

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Finland – Associate Registry

History and funding: The registry was established in 1963 and regular monitoring started in 1977. In 1998 the registry became an associate member of EUROCAT. The registry system (data collection etc) has been changed twice, in 1985 and in 1993. The activities of the Registry are regulated by specific laws and statutes affecting national healthcare registers which hold personal data. It is run and financed by STAKES, the governmental National Research and Development Centre for Welfare and Health (under the Ministry of Social Affairs and Health).

Population coverage: The registry is national and population-based I: all mothers resident in defined geographic area. All births in Finland are covered, representing approximately 58 000 births annually. As a research project selective terminations for fetal reasons and spontaneous abortions with malformations have also been included since 1993.

Sources and ascertainment: Notification to the registry is compulsory. Reports are obtained from delivery units, neonatal, Pediatric and pathology departments, death certificates and cytogenetic laboratories. Case information is also received from the national Medical Birth Register, Abortion Register and Hospital Discharge Register. The diagnoses of the malformation cases received from other sources are confirmed from the hospitals. Information on malformations is principally collected up to 1 year of age, but later information is also included. Aggregated data is transmitted to EUROCAT.

Termination of pregnancy: Termination of pregnancy is legal. Termination of pregnancy for fetal reasons (congenital anomaly, other birth defect or disease) can only be granted by a special permission from the National Authority for Medicolegal Affairs (TEO). At the gestational age of >20+0 to ≤24+0 weeks, termination can only be granted by TEO's permission when a severe fetal malformation or disease has been detected by reliable prenatal diagnostics.

Stillbirth definition and early fetal deaths: Prior to 1987, stillbirths of 28 weeks or more were registered. At present, stillbirths of at least 22 weeks of gestation or 500g of birth weight are registered. All notified early fetal deaths have been registered since 1993 but are only included for transmission to EUROCAT if > 20+0 gestational weeks.

Exposure data availability: Until 1986, extensive exposure information was obtained from maternity health centres and by personal interview for selected malformations and their controls. In 1987-1992 only parental occupation was reported. Exposure information, like maternal occupation, medication, X-rays and diseases, etc., has been obtained since 1993. Some exposure information on all births is also available in the Medical Birth Register since 1987.

Denominators and controls information: Epidemiological background data are available on all births in the Medical Birth Register and in the Statistics Finland.

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Central East France – Associate Registry
Central-East France Register of Congenital Malformations.

History and funding: The registry began in 1973 within the Rhone-Alps area -the Auvergne region was added in 1983, the Jura area in 1985, the Côte d'Or & Nièvre in 1989 and Saône-et-Loire in 1990. In 1998 the registry was split up and the Auvergne region, became financially independent, under the responsibility of Christine Francannet. The collaboration between Auvergne and the rest of the FCE-registry is maintained and common results are published. The Registry joined EUROCAT as an associate member in 1999. Until 1991, 90% of the funding was provided by an insurance company. The system currently has multiple sources of funding: 33% from an insurance company (GROUPMA), 13% from the Ministry of Health, 5% from local health authorities, 10% from specific epidemiological studies, 13% from the French National Electricity Agency, and 26% from contracts with drug companies for the surveillance of their products with respect to potential teratogenic effects. The registry was set up to monitor birth defects.

Population coverage: The registry is population-based II where all mothers delivering within defined geographic area, irrespective of place of residence. Approximately 1.5% of non-resident mothers deliver within the registry area. Mothers living in the defined area who are later transferred outside the area for delivery because of prenatal diagnosis of malformation made in the defined are included as well. The registry covers the Rhône-Alps region, Auvergne region, plus 4 departments: Côte d'Or, Jura, Nièvre, Saône-et-Loire with approximately 104,000 births annually (90,000 from 200), which represents about 14% of all births in France. The geographic regions have changed over time as follows: Rhône-Alps from 1976 onwards, Auvergne from 1983 to 1999 (from 2000, Auvergne still uses the same database, but the registry is separated from an administrative point of view), Jura from 1985 onwards, Côte d'Or and Nièvre from 1989 onwards and Saône-et-Loire from 1990 onwards.

Sources of ascertainment: Notification to the registry is voluntary. Reports are received from multiple sources: Pediatric records, cytogenetic laboratory,pathology laboratory, child health services, specialized departments for medical genetics, orthopaedics, cardiology, Pediatric surgeons, midwives, birth notifications, maternity unit records. Active registration is performed by midwives in the large units in which a lot of cases present. For small maternity or Pediatric units, registration relies on passive notification. Confirmatory sources: every year a list of abnormal karyotypes is sent by cytogenetics laboratories, and copies of pathology reports are systematically sent to the registry if malformations are present. Ascertainment is not complete because passive notification depends on the goodwill of collaborating doctors. The registry leader has a clinical activity of genetic counseling and stimulates colleagues to notify cases. Constant relationships are maintained with clinicians and also through the Teratology Information Service that is available to them, provided by the doctors working for the registry. Between the years 1980 to 1990 30% of cases are reported by more than one source. Infants up to the age of one are registered, as well as fetuses delivered after medical abortion. A cut-off for notification is applied: for children born in year x, notifications are taken into account until March x+2. There is no follow-up procedure. Children are notified whennoticed by the persons in charge of data collection in hospitals. There is a gap for hypospadias that are notified only by Pediatric surgeons because the children are scarcely operated before the age of 18 months. The following specific anomalies are excluded: balanced chromosomal anomalies, pyloric stenosis, metabolic disorders, minor malformations (small angiomas or naevi, hip subdislocation, small foot deformities, ill-defined facial anomalies, inguinal and umbilical hernias). Aggregated data transmitted to EUROCAT.

Termination of pregnancy: Termination of pregnancy is legal and there is no upper gestational age limit for any cause whatsoever. In the case of termination after diagnosis of a congenital anomaly, agreement is sought from a multidisciplinary committee. Terminations for fetal malformation have been registered since 1985. Notification of terminations of pregnancy is provided by: obstetric units, cytogenetic laboratories and pathology reports.

Stillbirth definition and early fetal deaths: Currently stillbirths of 22 weeks or more gestation are registered. Before 1997, stillbirths were registered at 28weeks or more after the last menstrual period. Stillbirth and infant death certificates are not routinely available as a source. Early fetal deaths/spontaneous abortions are included 22 weeks after the last menstrual period. Again, before 1997, this was 28 weeks or more. Autopsy rates for spontaneous abortions are not registered, stillbirths 90%, induced abortions 90% and early neonatal deaths (0-7 days) 80%. These numbers are only available to the registry as autopsy rates for malformed infants/fetuses. Most autopsies of stillborn babies are performed by a fetal pathologist.

Exposure data availability: Information on maternal and paternal occupation, drug use, diseases, etc. is collected by interviews of the mothers of the malformed infants. This is not transmitted to Central Registry. No controls are interviewed.

Denominators and controls information: Birth statistics are provided by the National Institute of Statistics. The same population definition is used for the birth statistics except for induced abortions. Some background information is also available from the general population statistics. No information on controls is collected.

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Norway – Associate Registry
Medical Birth Registry of Norway

History and funding: The programme was started in 1967. The programme is run and funded by the governmental National Institute of Public Health. The registry joined EUROCAT in 1998.

Population coverage: The programme is population-based and covers all mothers delivering within Norway, irrespective of place of residence, approximately 59 000 annual births. Non-resident mothers delivering within the registry area account for approximately 0.2% of all births.

Sources of ascertainment: Reporting is compulsory. The registry is based on the notification of births from the delivery units and since 1999 also from the neonatal units. Congenital anomaly is registered up to 1 year and there is no maximum age for registration of mortality.

Termination of pregnancy: Termination of pregnancy is legal and is the mother's decision up to 12 weeks gestation. After 12 weeks gestation permission is required from the commission and these have been recorded from 1999 onwards. If a congenital anomaly is diagnosed the upper gestational age limit is 18 weeks (with exemptions). On 1st December 1998, registration, by the MBRN, of all abortions induced on the indication of a prenatally diagnosed congenital anomaly was introduced.

Stillbirth definition and early fetal deaths: The official definition of a stillbirth for perinatal mortality purposes is: fetal death before or during labour with a gestational age of >=28 weeks or with a birthweight >=1000g. Early fetal deaths/spontaneous abortions of 16 weeks or more were included between the years 1967 to 2001 inclusive. This has been decreased to a gestational age of 12 weeks or more from 2002 onwards. Autopsy rates were reported as follows: 50% in stillbirths, 50% in induced abortions, 80% in early neonatal deaths (0-7 days), 90% in later deaths 1 week to 1 year and 80% in deaths with congenital anomaly.

Exposure data availability: Some basic information, such as maternal disease and since 1999:smoking and occupation, is collected on all infants, malformed or not.

Denominators and controls information:
All information available for the reported malformed infants is also available for the total population of births.

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ECEMC (Spain) – Associate Registry
Spanish Collaborative Study of Congenital Malformations

History and funding: The programme started in 1976 as a hospital-based case-control study and surveillance system. It is a research programme with voluntary participation of hospitals, and is financed mainly by the Spanish Administration and, partially, by non-governmental organisations. Since 2002, the ECEMC is integrated into the CIAC (Research Center on Congenital Anomalies). The main objectives are: active surveillance of congenital defects, investigation of causes, education and information to the population (through informative sessions and two teratology information services by telephone). The Registry joined EUROCAT as an associate member in 1998.

Population coverage: The registry is hospital based and includes all mothers delivering in selected hospitals, irrespective of place of residence. Reports are obtained from hospitals (84 at present) distributed all over Spain. The annual number of births now surpasses 100,000, representing more than 27% of all Spanish births. Almost 100% of births take place in hospitals in the registry region.

Sources of ascertainment: The detection period is the first 3 days of life, including major and/or minor/mild defects. In some special cases, a longer follow-up is performed. Reports come from delivery units and Pediatric departments of the participating hospitals. Mothers are interviewed directly to fill in the ECEMC standard protocols, which include more than 300 data items for each child (family history, demographic and obstetrical data, prenatal exposures, etc), whether case or control. In many instances, photographs, imaging studies, high-resolution bands karyotypes and molecular analysis when needed, and other complementary studies are available.

Termination of pregnancy: Up to 1985 termination of pregnancy was illegal in Madrid. From 1985 onwards, induced abortions have been legal but they are not registered by ECEMC. It should be noted that they *are* registered by the other Spanish registers, which results in a lower total prevalence rate for ECEMC compared with other Spanish registers. The upper gestational age limit for termination is 22 weeks in cases of congenital anomaly or 12 weeks in cases of violation.

Stillbirth definition and early fetal deaths: The official definition of stillbirth in Spain registry is: 24 weeks or later or weighing at least 500g. Stillbirths have been included since 1980. Autopsy rates in the year 2000 were: 31% for stillbirths and 38% for deaths with a congenital anomaly. Other autopsy rates were not available.

Exposure data availability: The mother of each reported infant (case or control) is interviewed on various exposures (parental occupation, maternal acute or chronic diseases, drug usage, exposure to other chemical or physical factors) within the first three days after delivery.

Denominators and controls information: Total number of births by sex and number of twin pairs in each participating hospital is gathered. Other background information (including maternal age) is obtained from the control material. Controls are defined as the next non-malformed infant born at the same hospital as the case with the same sex as the malformed infant.

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Sweden – Associate Registry

History and Funding: The Registry started in 1964 as a trial and was established in 1965. In 2003 the Registry became an associate member of EUROCAT. The Registry system (data collection etc) was changed in 1999. Specific laws and statutes on national health care registers, which hold personal data, regulate the activities of the Registry. It is run and financed by the National Board of Health and Welfare, the governmental National Research and Development Centre for Health and Welfare (under the Ministry of Social Affairs and Health).

Population Coverage: The Registry is national and population based I: All mothers resident in a defined geographic area. All births in Sweden are covered, representing approximately 100,000 births annually. Selective terminations of foetuses with malformations are included since 1999.

Sources of Ascertainment: Notification to the Registry is compulsory. Reports are obtained from departments of paediatrics, obstetrics and clinical genetics (cytogenetic aberrations). The diagnoses of the malformed cases are often received from more than one source. Information on malformations is principally reported before one month of age except for congenital heart malformations, which are reported up to 1 year of age. Aggregated data are transmitted to EUROCAT.

Termination of Pregnancy: Termination of pregnancy is legal. Termination of pregnancy for foetal reasons (congenital anomaly) can be granted after special permission after 18 weeks and up to 23 weeks of gestation from an ethical committee at the National Board of Health and Welfare.

Stillbirth Definition and Early Fetal Deaths: The definition of stillbirths in Sweden is birth after 28 weeks of gestation. Since 1999 all foetal deaths with congenital malformations greater than 22 weeks of gestation are registered at the Swedish Registry of Congenital Malformations.

Exposure Data Availability: Exposure information on all births is available in the Medical Birth Register since 1973.

Denominators and Controls Information: Epidemiological background data are available on all births in the Medical Birth Register and in the Statistics of Sweden.

Address for Further Information:

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