



Prevalence of Neural Tube Defects in Europe

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Subjects

1. Prevalence of Neural Tube Defects in European countries
2. Rate of pregnant women using folic acid periconceptionally in European countries
3. Conclusions of the presented data
4. Recommendations of the Eurocat study group



EUROCAT: European registration of congenital anomalies and twins

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Neural Tube Defects (NTD)

develop during the first days of pregnancy
(22nd – 28th day post conception)

- Anencephaly
- Encephalocele
- Spina bifida



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Prevalence of NTD



/ 1,000 births

World-wide	1 - 2
Canada, USA	1 - 2
Europe	1 - 2
Germany	1 - 2

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Periconceptional Folic Acid Supplementation

was shown to be an effective method of potentially preventing two thirds of cases with NTD

Cochrane Meta-Analysis:
OR 0,28 (KI 0.15-0.53)



MRC Vitamin Study Research Group: Lancet 1991; 338: 131-137;
Czeizel AE, Dudás I: N Engl J Med 1992; 327:1832-1835 ;
Werler MM, Shapiro S, Mitchel AA: JAMA 1993; 269:1257-1261

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Health expenses of children with NTD calculations for Europe

* about 300.000 US \$*

About 4.500 affected infants in Europe per year

Costs per year 1,500 000 000 €

Primary prevention 70% of NTD
Savings 1,000 000 000 €

and significant human suffering

Folic acid supplementation 12 €/woman and year

* Botto L, Moore C, Khoury M, Erickson JD: Neural-Tube Defects. N Engl J Med 1999; 341: 1509 - 1519
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Current Folic Acid Supplementation Policy in Europe

Country	Status	Year policy introduced	Health education campaign
UK	official	1992	2001
Netherlands	official	1993	1995
Ireland	official	1993	1993/2001
Malta	official	1994	1999
Denmark	official	1997	2000
France	official	2000	1999
...			
Germany	unofficial	1995	no
Austria	unofficial	1998	no
Belgium	unofficial	no	no
...			

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Prevalence of NTD in Europe /10.000

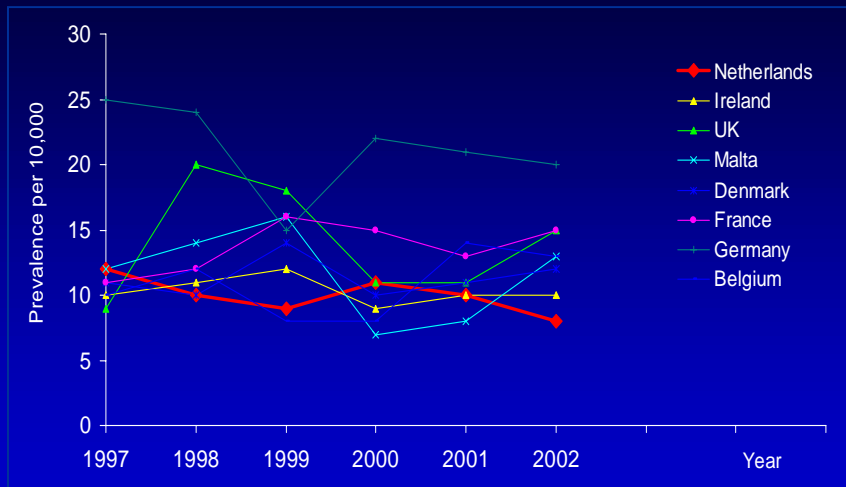
Registry	1992 – 1995	1996 – 1999	2000 – 2002
<u>Europe with policy</u>			
Ireland (Dublin)	14	10	10
UK (North-Thames)	13	12	11
Denmark	9	11	15
Netherlands	10	9	6
Norway	8	8	10
Portugal	5	6	6
Switzerland	10	10	13
Malta	13	13	9
Finland	7	8	7
...			
Total	10	10	9

Prevalence of NTD in Europe /10.000

Registry	1992 – 1995	1996 – 1999	2000 – 2002
<u>Europe without policy</u>			
Austria	8	7	7
Belgium (Hainaut)	10	11	10
Croatia	6	6	7
France (Paris)	13	13	14
Germany (Saxony)	5	13	10
Italy (Tuscany)	6	7	5
Spain (Asturia)	13	13	10
...			
Total	8	8	8

Busby A, Abramsky L, Dolk H, Armstrong B, Eurocat Folic Acid Working Group: Eurocat special report annex 2005 ; Busby et al.: Preventing NTD in Europe; Reproductive Toxicology 2005; 20: 393-402.

Prevalence of NTDs in Europe 1997-2002



Data from the Eurocat report (2005)

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Changes in prevalence rates of NTDs over time

- Since the 1980s periconceptional folic acid supplementation is a well known instrument for primary prevention of NTDs
- No progress in Europe towards the prevention of NTDs over the last decade
- Only the Northern Netherlands show a significant decline in the prevalence of NTDs

(policy and education interventions were introduced very early; periconceptional folic acid uptake rose to 43%)

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Prevalence of NTD in Europe* and part of induced abortions

Registry	1992 – 1995		1996 – 1999		2000 – 2002	
	/10.000	%	/10.000	%	/10.000	%
Netherlands	10	44	9	53	6	36
Ireland (Dublin)	14	23	10	22	10	24
UK (North-Thames)	13	81	12	87	11	80
Denmark (Odense)	9	28	11	28	15	30
France (Paris)	13	89	13	88	14	88
Total (Eurocat)	10	30	10	29	10	28

Busby A, Abramsky L, Dolk H, Armstrong B, Eurocat Folic Acid Working Group: Eurocat special report annex 2005 ; Busby et al.: Preventing NTD in Europe; Reproductive Toxicology 2005; 20: 393-402.

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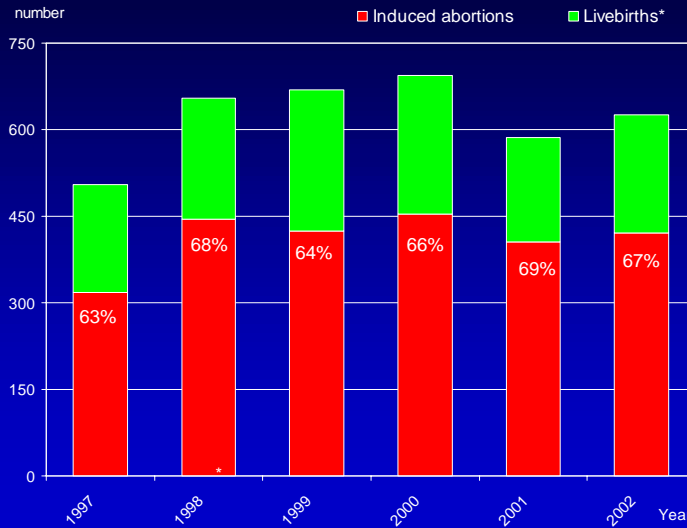
Prevalence of NTD in Europe* and part of induced abortions

Registry	1992 – 1995		1996 – 1999		2000 – 2002	
	/10.000	%	/10.000	%	/10.000	%
Germany (Saxony-Anhalt)	6	40	13	68	10	81
Germany (Mainz)	16	33	29	28	27	36
Italy (Tuscany)	6	67	7	72	6	83
Italy (Sicily)	5	14	5	2	5	2
Total (Eurocat)	10	30	10	29	10	28

Busby A, Abramsky L, Dolk H, Armstrong B, Eurocat Folic Acid Working Group: Eurocat special report annex 2005 ; Busby et al.: Preventing NTD in Europe; Reproductive Toxicology 2005; 20: 393-402.

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Neural tube defects in Europe - livebirths and induced abortions -

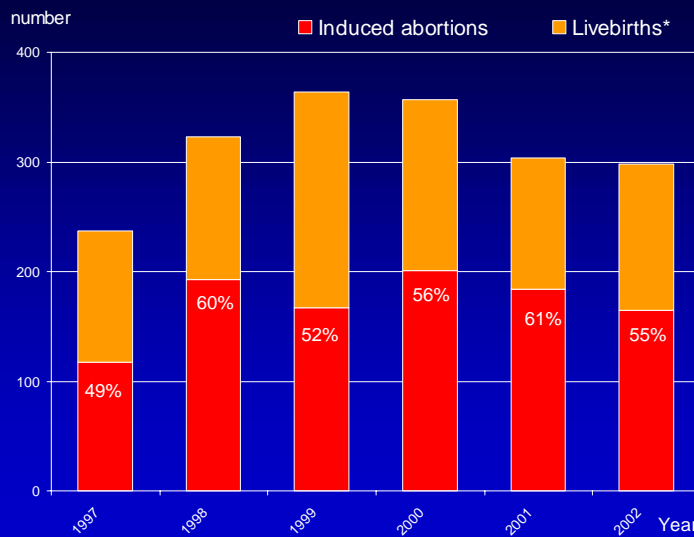


* including fetal death

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EUROCAT: 18 countries, 24 registries

Spina bifida in Europe - livebirths and induced abortions -

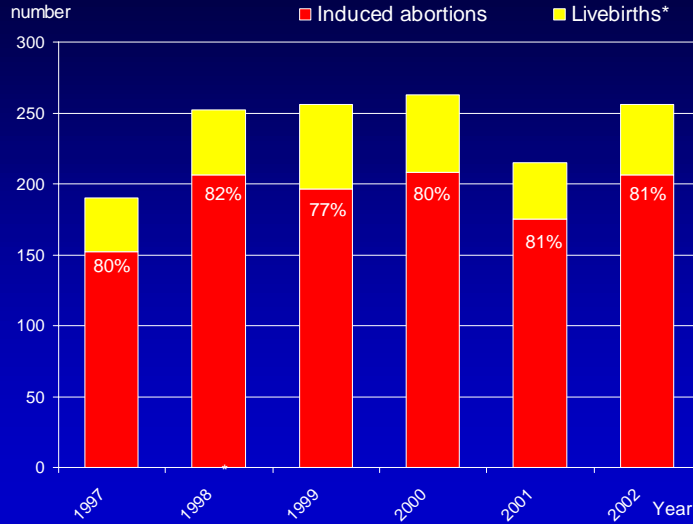


* including fetal death

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EUROCAT: 18 countries, 24 registries

Anencephalus in Europe - livebirths and induced abortions -

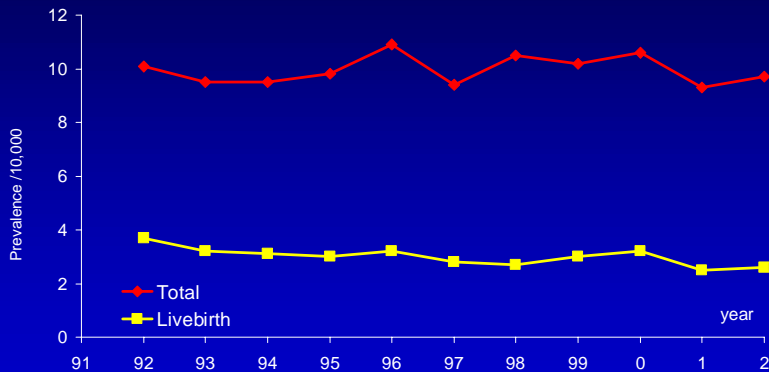


* including fetal death

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EUROCAT: 18 countries, 24 registries

Prevalence rates of NTDs in Europe



R. E. Stevenson et al. Pediatrics 2000; 106: 677-683

International Clearinghouse for birth defects monitoring systems, 2002

Livebirth prevalence of infants with NTDs

- In about two thirds of all NTD-cases termination of pregnancy was performed
- Number and rate of induced abortions have not declined during the past decade
- Induced abortions depend on the religious, ethnic, and socio-economic background
- Prenatal screening and termination strategies reduce the number of livebirths with NTDs
(instrument of secondary prevention ?)

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Stern 36, 2004

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Current Folic Acid Supplementation Policy

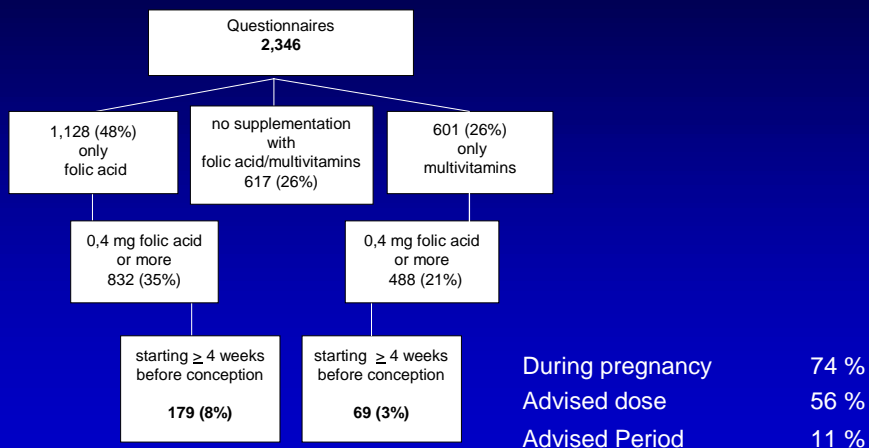
Country	Status	Women using folic acid periconceptionally
Netherlands	official	43 %
UK	official	38 %
Ireland	official	24 %
Denmark	official	22 %
Malta	official	15 %
France	official	1 % (data from 1999)
Germany	unofficial	11 %
Austria	unofficial	10 % (at GA < 12 weeks)
Belgium	unofficial	no data available

Low risk women: 0.4 mg /day (Netherlands 0.5mg)

Women with previously affected pregnancy: 4mg or 5mg /day

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Folic acid supplementation in pregnant women Mainz Model, Rhineland-Palatinate (2005)



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Folic acid supplementation in pregnant women

(Rhineland-Palatinate 2005)

- About two thirds of the pregnancies are reported to be planned
- In only 11% an adequate prophylaxis is performed
- An adequate prophylaxis is performed by 4% of mothers of non-German origin
- Periconceptional folic acid intake (advised period and dose)
28% women of higher, 5% women of lower social status

These results are comparable to published data for other European countries.

Folic acid supplementation in pregnant women with previously affected pregnancy

(Rhineland-Palatinate 2005)

- 80% of the mothers were of German origin
- 80% of the pregnancies were planned
- Effectiveness of periconceptional intake of folic acid was known for about 25% of these mothers
- An adequate prophylaxis was performed by 5% of these mothers

Conclusion I

- Preventing NTDs by periconceptional folic acid supplementation is still far from being satisfactory in Europe
- Termination of pregnancy has made NTD a relatively masked problem in many European countries
- It is unacceptable to ignore the option of primary prevention by continuing the use of prenatal screening and termination strategies

Conclusion II

- Only a European-wide public health policy
 - including folic acid fortification -is likely to result in large-scale prevention of NTDs and to reduce socio-economic inequalities
- Growing evidence exists that fortification may have additional health benefits (e.g.)
 - prevention of other congenital malformations
 - prevention of cardiovascular diseases

Eurocat Recommendations I

- 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 on 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 is aware of the benefits of supplementation and the importance of starting supplementation **before** conception.

Eurocat Recommendations II

- 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.

Eurocat Recommendations III

- 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



Busby et al.: Preventing NTD in Europe; Reproductive Toxicology 2005; 20: 393-402.

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Folsäure für ein gesundes Leben - von Anfang an -



Regional folic acid supplementation campaign
Rhineland-Palatinate