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Prevalence of neural tube defects in 20 regions of Europe and the impact of prenatal diagnosis, 1980–1986

EUROCAT Working Group

Abstract

***Study objective*—The aims were (1) to determine whether in Europe, 1980–86, geographical differences in total prevalence of neural tube defects persist; (2) to examine the stability of total prevalence rates over time; (3) to evaluate the impact of prenatal diagnosis in terms of frequency and timing of termination of pregnancy.**

***Design*—Prevalence rates of neural tube defects were determined from case registration data in 20 EUROCAT regional registers of congenital anomalies, 1980–86. The χ^2 test for homogeneity in proportions was used to test whether differences in total prevalence rates were significant between regions or over time.**

***Setting*—Geographically defined populations were used in the Republic of Ireland, United Kingdom, Belgium, The Netherlands, Luxemburg, Denmark, France, Italy, Yugoslavia, and Malta.**

***Patients*—The patients were 3113 cases of anencephaly, spina bifida, encephalocele, and iniencephaly. Total cases (livebirths, stillbirths and induced abortions following prenatal diagnosis) were registered in 14 regions. Induced abortions were excluded from registration in six regions.**

***Measurements and main results*—Total prevalence rates (including livebirths, stillbirths and induced abortions) were 24 to 38 per 10 000 in six areas of Ireland and United Kingdom. Average total prevalence rate in eight continental European areas was 11·5 per 10 000. There was a secular decline in total prevalence in Dublin (Republic of Ireland) and Northern Ireland (United Kingdom) and a fluctuation in Glasgow, Liverpool, and South Glamorgan (United Kingdom). Total prevalence in continental Europe was stable over time. There was no significant geographical or secular variation in the spina bifida to anencephaly ratio (1·3). The ratio of encephalocele to other neural tube defects was lower in the British Isles (0·09) than in continental Europe (0·18). The impact of prenatal diagnosis and termination of pregnancy is increasing over time. Terminations were performed 1984–86 in at least 80% of total cases of anencephaly in 6/11 centres registering induced abortions, and in at least 40% of total cases of spina bifida in four centres. Serum α fetoprotein screening in British centres was associated with earlier prenatal diagnosis of spina bifida than ultrasound screening in other centres.**

***Conclusions*—Geographical and secular variation in total prevalence of neural tube defects persists in Europe 1980–86, independent of the practice of prenatal diagnosis. There is considerable regional variation in the impact of prenatal diagnosis in terms of frequency and timing of diagnosis and pregnancy termination linked to different policies and practices of prenatal screening.**

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The EUROCAT network of congenital anomaly registers provided registration data on neural tube defects from 1980 to 1986 in 20 regions of Europe in 10 countries (United Kingdom, Republic of Ireland, France, Belgium, The Netherlands, Denmark, Italy, Luxemburg, Yugoslavia, and Malta), a total coverage of nearly two million births.[1]

Many published studies have been concerned with the high prevalence rate of neural tube defects in the British Isles, and the downward secular trend observed in neural tube defect prevalence both in the British Isles and in some Continental European countries.[2–11] Here we aim to assess in Europe of the 1980s whether geographical differences persist, and whether total prevalence rates are continuing to fall.

Secondly we aim to evaluate the impact of prenatal diagnosis on the prevalence at birth of neural tube defects, with reference to the different screening policies existing in the various areas. In recognition of the desirability of diagnosing neural tube defects as early as possible in pregnancy, we have also considered the impact of prenatal diagnosis with reference to gestational age at diagnosis.

Methods

The study population consists of a total of 1 734 262 live and stillbirths surveyed by 20 registries during the period 1980 to 1986, as shown in table I. The populations covered and the registration system in each of the EUROCAT registries have been described in previous publications.[12 13] In 11 centres (Odense, Florence, Dublin, Galway, Groningen, Glasgow, Northern Ireland, Liverpool, South Glamorgan, Marseille, and Malta), the registration system covers all births to mothers resident in a geographically defined area. In six centres (Hainaut, Strasbourg, West Flanders, Umbria, Emilia Romagna, and Zagreb), the reference population consists of all births occurring in all the maternity units of a geographically defined area. In Paris the reference population consists of all births to residents of Greater Paris taking place

within the City of Paris. The North-East Italy registry covers births in selected hospitals. The Luxemburg registry covers all births in the country with the exception of deliveries in one maternity unit where 45% of all births take place.

Most registries covered a population of stable size. However some major changes in registry size occurred. Groningen expanded its area in 1986 from an annual 7800 births to nearly 12 000. Emilia Romagna expanded its coverage progressively from 12 500 annual births in 1980 to 23 000 in 1984 and thereafter. Zagreb expanded from 4000 annual births in 1983–85 to nearly 7000 in 1986. North-East Italy increased its population coverage from 27 500 annual births in 1981 to 41 000 by 1983 by extending the geographical area covered and the number of maternity clinics participating in the registration system.

Ascertainment of congenital anomalies is based on the use of multiple sources of information such as birth and death certificates, maternity and hospital records, and cytogenetic and pathology service reports. The use of these various sources differs from registry to registry.

Livebirths, fetal deaths, and induced abortions for congenital anomaly are registered. Stillbirths here include all fetal deaths of 20 weeks gestational age or more, but registries may have better systematic access to information on fetal deaths classified as stillbirths in their region according to other gestational or birthweight criteria (180 days, 28 weeks, 500 g, etc). There are generally upper gestational age limits on induced abortions (usually 27 weeks, but 24 weeks in Odense) but these may not apply where the fetus is not viable (eg, in cases of anencephaly). In France, induced abortions for fetal malformation do not have an upper gestational age limit.

Induced abortions are illegal in Ireland and Malta. They are illegal but tolerated in cases of severe fetal malformation in Northern Ireland and Belgium. In six centres (West Flanders, Umbria, Luxemburg, North-East Italy, Emilia Romagna, and Zagreb) there was little or no information on cases of congenital anomaly which had been prenatally diagnosed and aborted but would otherwise have formed part of their study populations.

Congenital anomalies are coded according to the ICD9/British Paediatric Association system.[14 15] Neural tube defects include anencephaly, iniencephaly, encephalocele, and spina bifida (codes 740−, 741− and 7420). Cases with multiple neural tube defects were assigned to only one of these four categories of defects. Anencephaly includes complete and incomplete anencephaly, craniorachischisis, and anencephaly associated with iniencephaly or spina bifida. Spina bifida excludes spina bifida occulta and cases associated with anencephaly, iniencephaly, or encephalocele. Encephalocele includes cases associated with spina bifida. Iniencephaly represented very few cases and as the diagnostic criteria are not well defined its prevalence is not analysed separately. All cases of neural tube defect were included, irrespective of whether the neural tube defect was isolated, associated with other anomalies, or part of a syndrome.

Total prevalence rates are calculated by dividing the total number of livebirths, stillbirths, and induced abortions with congenital anomaly by the total number of live and stillbirths in the population. Total prevalence rates are calculated only for the 14 centres which cover all types of birth/abortion in their study population. Prevalence rates at birth concern only livebirths and stillbirths in both numerator and denominator.

The χ^2 test for homogeneity in proportions was used to test whether differences in total prevalence rates were significant between regions or over time. To test for secular trend the χ^2 test for homogeneity was subdivided into a component that tests for a linear trend and a component that tests for departures from linearity.[16] Where geographical or temporal variation was found, the χ^2 test for homogeneity was used to test whether the anencephaly to spina bifida ratio varied, in order to see whether the variation in total neural tube defects could be equally attributed to both these anomalies. Values of χ^2 were considered significant where the probability of a Type I error was less than 5%.

Table I Birth populations surveyed by EUROCAT registries 1980–1986. (Total No of births = 1 734 262).

Registry	*Country*	*Years*	*Total number of births*
Dublin	Republic of Ireland	1980–1986	163 985
Galway	Republic of Ireland	1981–1986	19 293
Glasgow	United Kingdom	1980–1986	91 359
Liverpool	United Kingdom	1980–1986	143 080
Northern Ireland	United Kingdom	1980–1986	195 012
South Glamorgan	United Kingdom	1980–1986	37 986
West Flanders	Belgium	1980–1986	50 386
Hainaut	Belgium	1980–1986	57 352
Luxembourg	Luxemburg	1980–1986	16 628
Groningen	Netherlands	1981–1986	50 437
Odense	Denmark	1980–1986	32 648
Paris	France	1981–1986	213 090
Strasbourg	France	1982–1986	65 383
Marseille	France	1984–1986	71 264
Florence	Italy	1980–1986	63 261
Umbria	Italy	1980–1986	52 279
Emilia Romagna	Italy	1980–1986	136 961
North east Italy	Italy	1981–1986	232 988
Zagreb	Yugoslavia	1983–1986	18 703
Malta	Malta	1983–1986	22 225

Results

A total of 3113 cases of neural tube defect were registered in 20 regions.

GEOGRAPHICAL VARIATION IN TOTAL PREVALENCE

The total prevalence rates of neural tube defect including livebirths, stillbirths and induced abortions are shown in table II. The six centres with insufficient access to information on induced abortions have been excluded from this table.

In the registries within the British Isles, over 30 cases per 10 000 were recorded in Glasgow, Dublin, Northern Ireland, and South Glamorgan, with lower rates of 26 per 10 000 in Liverpool and 24 per 10 000 in Galway. This heterogeneity in total prevalence rates among the six centres is highly significant ($p < 0.001$).

In the eight other European centres, total neural tube defect prevalence rates lie between 10·7 per 10 000 (Paris) and 14·3 per 10 000 (Groningen). These prevalence rates were not significantly heterogeneous and average 11·5 per 10 000.

The total prevalence rates of anencephaly, spina bifida, and encephalocele separately are

Table II Total reported prevalence (number and rate per 10 000 births) of neural tube defects (including livebirths, stillbirths, and induced abortions) in 14 EUROCAT registries 1980–1986.

Registry	All neural tube defects		Anencephaly		Spina bifida		Encephalocele	
	No	Rate per 10 000	No	Rate per 10 000	No	Rate per 10 000	No	Rate per 10 000
Dublin	565	34·5	224	13·7	299	18·2	33	2·0
Galway	47	24·4	18	9·3	26	13·5	3	1·6
Glasgow	342	37·4	133	14·6	162	17·7	39	4·3
Liverpool	366	25·6	135	9·4	196	13·7	32	2·2
Northern Ireland	670	34·4	281	14·4	322	16·5	48	2·5
South Glamorgan	119	31·3	48	12·6	58	15·3	13	3·4
Hainaut	64	11·2	31	5·4	24	4·2	9	1·6
Groningen	72	14·3	33	6·6	29	5·8	9	1·8
Odense	41	12·6	17	5·2	17	5·2	7	2·1
Paris	229	10·7	88	4·1	103	4·8	38	1·8
Strasbourg	79	12·1	22	3·4	44	6·7	12	1·8
Marseille	79	11·1	33	4·6	30	4·2	16	2·2
Florence	71	11·2	28	4·4	35	5·5	8	1·3
Malta	25	11·2	13	5·8	11	4·9	1	0·4

given in table II. Neither the ratio of spina bifida to anencephaly nor the ratio of encephalocele to all other neural tube defects showed significant heterogeneity within the two geographical areas (British Isles, and Continental Europe and Malta). The average spina bifida to anencephaly ratio of 1·3 in the British Isles did not differ significantly from the corresponding ratio of 1·1 outside the British Isles. The ratio of encephalocele to other neural tube defects of 0·09 in the British Isles was half the corresponding ratio of 0·18 outside the British Isles, a highly significant difference ($p < 0·001$).

In the eight centres of Continental Europe and Malta, where significant regional variation in the total prevalence of neural tube defect could not be detected, the average total prevalence rates were 4·6 per 10 000 for anencephaly, 5·1 for spina bifida, and 1·7 for encephalocele.

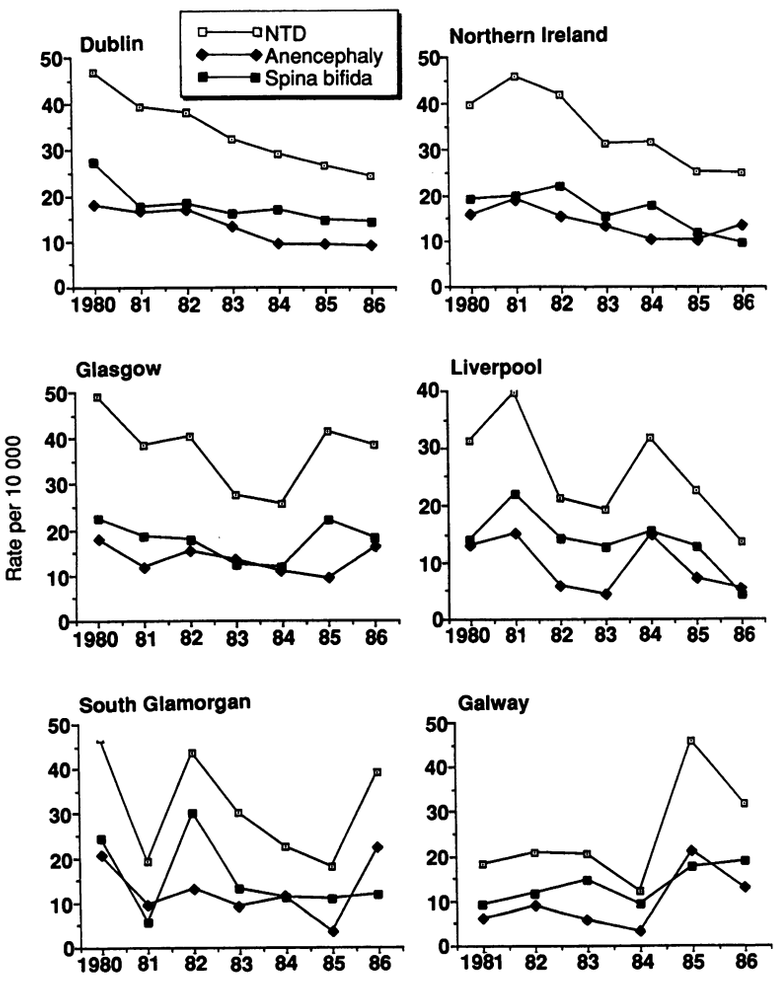

Figure 1 Secular change in total prevalence of neural tube defects in the United Kingdom and Ireland, 1980–86.

SECULAR TREND IN TOTAL PREVALENCE

Within the United Kingdom and Ireland, statistically significant variation in total neural tube defect prevalence rate over time was found in five of the centres (figure 1). In Dublin and Northern Ireland there was a highly significant downward secular trend ($p < 0·001$). In Liverpool there was a downward but non-linear change in prevalence over time ($p < 0·001$ for both linear and non-linear change). In Glasgow an apparent fall up to 1984 was followed by an upturn in 1985 and 1986, indicating significant yearly fluctuation ($p < 0·05$) but no overall trend. The South Glamorgan neural tube defect prevalence peaked in 1980, 1982, and 1986, giving significant fluctuation ($p < 0·05$) but no overall trend. In Galway four to seven cases (average 6·0) were recorded per year in 1981–84 rising to 13 in 1985 and 10 in 1986 in a population of stable size. This pattern of prevalence over time was not a statistically significant departure from homogeneity of yearly prevalence over time.

Analysis of the spina bifida to anencephaly ratio revealed no significant differences between the pattern of spina bifida prevalence and anencephaly prevalence over time in the British Isles centres.

In the other eight European centres (table II), total neural tube defect prevalence rates per year were stable both in individual centres and in all eight centres combined. However in Florence, while there was no significant change over time in the total neural tube defect rate, there was a significant upward linear secular trend for anencephaly ($p < 0·05$) with two to four cases per year (average 2·8) in 1980–1984 rising to seven cases per year in 1985 and 1986. The difference between the pattern of anencephaly and spina bifida over time in Florence was significant, there being a downward linear trend in the spina bifida to anencephaly ratio ($p < 0·05$).

PRENATAL DIAGNOSIS AND INDUCED ABORTIONS

Table III shows the 11 centres where the frequency of induced abortion can be directly assessed. In a further three centres (Dublin, Galway, and Malta) induced abortions are not performed.

A greater proportion of anencephaly than spina bifida cases were prenatally diagnosed, with subsequent termination of pregnancy (table III).

Table III Prenatal diagnosis (percentage of total cases) and induced abortion (number and percentage of total cases) for anencephaly and spina bifida in 11 EUROCAT centres 1980–1986.

	Anencephaly					*Spina bifida*				
	Induced Abortions				*Prenatally diagnosed**	*Induced abortions*				*Prenatally diagnosed**
	1980–83		*1984–86*		*1984–86*	*1980–83*		*1984–86*		*1984–86*
Registry	*No*	*%*	*No*	*%*	*%*	*No*	*%*	*No*	*%*	*%*
Glasgow	74	92·5	46	92·0	98·0	39	41·5	36	52·9	64·7
Liverpool	46	58·2	45	80·4	94·6	34	26·4	27	40·3	59·7[2]
Northern Ireland	32	18·0	57	57·0	90·0[1]	5	2·4	3	2·7	24·5[2]
South Glamorgan	14	50·0	15	71·4	76·2	5	12·8	7	36·8	42·1
Hainaut	9	60·0	15	93·8	100·0	1	8·3	1	8·3	41·7
Odense	4	36·4	4	66·7	83·3	0	0·0	1	12·5	25·0
Groningen	4	28·6	9	47·4	84·2	0	0·0	1	6·3	18·8
Paris	21	55·3	44	88·0	96·0	10	16·9	23	48·9	74·5
Strasbourg	3	60·0	16	94·1	100·0	6	31·6	10	40·0	64·0
Marseille	—	—	22	66·7	66·7	—	—	5	16·7	30·0
Florence	5	25·0	15	93·8	93·8	3	8·7	4	33·3	41·7

* ie, cases of livebirth, stillbirth, or induced abortion where prenatal diagnosis had been made at any gestational age.
[1] Not known whether prenatal diagnosis was made in 0·3% of cases in Northern Ireland.
[2] Not known whether prenatal diagnosis was made in 1% of cases in Liverpool and 2% in Northern Ireland.

A comparison of the years 1980–83 with 1984–86 shows an increase in induced abortions performed for anencephaly in all centres except Glasgow (where a very high detection rate had already been reached in the earlier period). There was a perceptible increase in the proportion of induced abortions performed for spina bifida in Paris, Florence, Glasgow, Liverpool, Strasbourg, and south Glamorgan. By 1984–1986 at least 80% of anencephaly cases were aborted in six centres, and at least 40% of spina bifida cases were aborted in four centres.

Figures 2 (anencephaly) and 3 (spina bifida) show the differences between centres regarding gestational age at abortion. Glasgow, Liverpool, and south Glamorgan reported earlier terminations of pregnancy than other centres, especially for spina bifida.

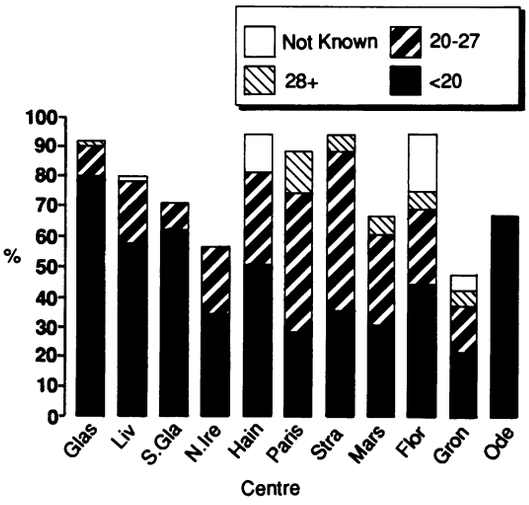

Figure 2 Gestational age (in weeks) of induced abortions for anencephaly, 1984–86 (expressed as proportion of total cases). Glas = Glasgow; Liv = Liverpool; S. Gla = South Glamorgan; N. Ire = Northern Ireland; Hain = Hainaut; Stra = Strasbourg; Mars = Marseille; Flor = Florence; Gron = Groningen; Ode = Odense.

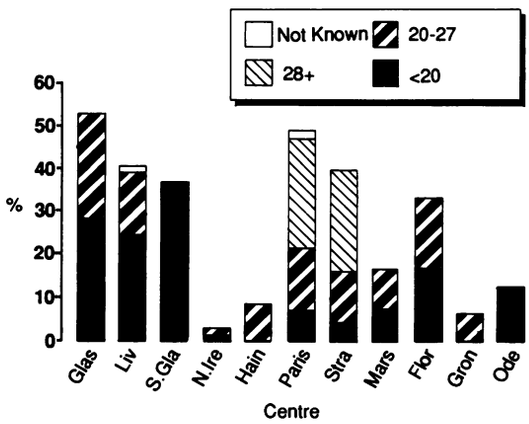

Figure 3 Gestational age (in weeks) of induced abortions for spina bifida, 1984–1986 (expressed as a proportion of total cases). For abbreviations see Fig 2.

In French centres, a substantial proportion of abortions were performed at 28 weeks gestation or later, particularly for spina bifida (figs 2 and 3). In other centres, late diagnosed pregnancies end mainly in livebirth or stillbirth and account for most of the difference seen in table III between the proportion of cases prenatally diagnosed and the proportion where an induced abortion was performed. Prenatal diagnosis before 28 weeks was almost invariably followed by induced abortion, except for a few cases where there was spontaneous delivery soon after diagnosis, or where a twin pregnancy was allowed to continue for the normal twin. Northern Ireland was an exception—in the period 1980–86 an induced abortion was performed in only 66% of anencephaly cases diagnosed before 28 weeks and in eight out of 14 cases of spina bifida diagnosed before 28 weeks.

An amniocentesis was more frequently recorded as one of the diagnostic methods leading to induced abortion for spina bifida than for anencephaly. In the latter half of the study period (1984–86) an amniocentesis had been performed in 26/36 (72%) spina bifida abortions in Glasgow, 10/27 (37%) in Liverpool, 1/3 in Northern Ireland, 6/7 in south Glamorgan, 3/5 in Marseille, 6/10 in Strasbourg, 1/1 in Odense, and 1/1 in Groningen. During the same period an aminocentesis had been performed in 3/46 (7%) of anencephaly abortions in Glasgow, 2/45 (4%) in Liverpool, 4/57 (7%) in Northern Ireland, 6/15 in south Glamorgan, 8/22 (36%) in Marseille, 3/16 in Strasbourg, 3/4 in Odense, and 2/13 in Groningen.

In Galway, where induced abortion is not performed, prenatal diagnosis had been made in 1984–86 in 76% of anencephaly cases and in 36% of spina bifida cases. No information was available about prenatal diagnosis in Dublin or Malta.

PREVALENCE IN LIVEBIRTHS AND STILLBIRTHS

Table IV gives the prevalence of anencephaly and spina bifida among live and stillbirths in the early (1980–83) and later (1984–86) part of the study period. The increasing practice of prenatal diagnosis and induced abortion has led to a decrease in the prevalence at birth of neural tube defects within the study period in many centres. In Northern Ireland this was combined with the "natural" decline in total prevalence. By 1984–86 the birth prevalence of anencephaly had dropped to below one per 10 000 in six of the 20 centres.

Table IV Prevalence at birth of anencephaly and spina bifida 1980–1986. (Number of cases and rate per 10 000 births).

	Anencephaly				*Spina bifida*				*Spina bifida LB:SB ratio 1980–1986*
	LB + SB 1980–1983		*LB + SB 1984–1986*		*LB + SB 1980–1983*		*LB + SB 1984–1986*		
	No	*Rate*	*No*	*Rate*	*No*	*Rate*	*No*	*Rate*	
Dublin	161	16·2	62	9·6	199	20·1	100	15·4	9·3
Galway	7	7·0	11	11·9	12	12·0	14	15·1	25·0
Glasgow	9	1·7	4	1·0	55	10·5	32	8·2	4·4
Liverpool	33	4·1	11	1·8	95	11·7	40	6·5	5·1
Northern Ireland	149	13·4	43	5·1	207	18·6	107	12·7	6·1
South Glamorgan	13	6·1	6	3·6	34	16·1	12	7·1	14·3
West Flanders	9	3·3	10	4·3	13	4·8	9	3·9	21·0
Hainaut	6	1·8	1	0·4	11	3·4	11	4·5	3·4
Luxembourg	3	3·3	0	—	3	3·3	3	4·0	LB only
Groningen	10	5·2	10	3·7	13	5·6	15	5·5	13·0
Odense	7	3·8	2	1·4	9	4·9	7	5·0	7·0
Paris	17	1·6	6	0·6	49	4·7	24	2·2	2·2
Strasbourg	2	0·8	1	0·3	13	5·0	15	3·8	4·6
Marseille	—	—	11	1·5	—	—	25	3·5	2·1
Florence	9	2·4	1	0·4	21	5·6	8	3·1	13·5
Umbria	5	1·6	4	1·9	12	3·8	8	3·9	LB only
Emilia Romagna	11	1·6	6	0·9	31	4·6	29	4·1	LB only
North-East Italy	22	2·1	18	1·4	40	3·8	45	3·5	20·3
Zagreb	2	5·0	2	1·4	0	0·0	8	5·4	LB only
Malta	2	3·5	11	6·7	2	3·5	9	5·5	LB only

LB = livebirths, SB = stillbirths.

In the six centres where a direct assessment of the impact of prenatal diagnosis is not possible due to the lack of information on induced abortions, an indirect assessment can be made according to the prevalence at birth of anencephaly and spina bifida, and the spina bifida to anencephaly ratio (higher ratios reflect the greater prenatal detection of anencephaly). In West Flanders, induced abortion would appear to be infrequent.

The overall ratio of liveborn to stillborn spina bifida in all centres together (1980–86) was 7:1. The ratio varies significantly between centres ($p < 0.001$).

There were 30 cases of live or stillborn spina bifida of less than 28 weeks gestation (seven in Liverpool, seven in Northern Ireland, three each in Paris and Glasgow, two each in Strasbourg and Marseille, and one each in west Flanders, Hainaut, Florence, Umbria, Galway, and Groningen), and 34 cases of live or stillborn anencephaly of less than 28 weeks gestation (12 in Northern Ireland, four in Dublin and Marseille, three in Liverpool, two each in west Flanders, Paris and Groningen, and one each in Florence, Umbria, Glasgow, Galway and north east Italy).

Discussion

There are several differences between the 20 EUROCAT registries in their methods of data collection which could potentially affect the reported total prevalence rates. The first of these concerns the potential for selection bias in case ascertainment. In six registries total prevalence rates could not be determined due to insufficient access to information on induced abortions following prenatal diagnosis. Of the remaining 14 registries, 11 are truly population based, ie, the population is defined by residence of the mother. There would nevertheless be a potential for selection bias in Ireland and Malta, where induced abortion is illegal, if residents sought abortion outside the country after prenatal diagnosis of malformation. Figures kept by the Office of Population Censuses and Surveys of England and Wales show that the number of Irish residents coming to England for induced abortion for fetal malformation is negligible (Botting B, personal communication) which suggests that this source of bias is not a major factor to consider. In two registries (Hainaut and Strasbourg) a good approximation to the results of a population based system is achieved by covering all maternity units in a sufficiently large geographical area. In Paris, births in all hospitals within the city boundary are covered by the registration system whether residence is in the city or in the outskirts since there is considerable migration across the city boundary in both directions. The possibility for some selection bias therefore exists, although comparisons of prevalence rates of anencephaly and spina bifida between inner and outer Paris residents do not suggest that this occurs to an important degree. Nevertheless, some caution should be used in the interpretation of Paris results.

A further difference between registries may lie in the degree of completeness of ascertainment of early fetal deaths of 20 to 27 weeks gestation. This cannot be directly assessed except in Marseille where thorough case-finding is assured due to a centralised necropsy service with coverage of all fetal deaths from 20 weeks gestation. However it can be estimated from a study of spontaneous abortions by Creasy and Alberman,[17] before the widespread utilization of prenatal diagnosis, that approximately 6% of fetuses affected by neural tube defects alive at 20 weeks are born before 28 weeks. This suggests that the effect of underascertainment of early fetal deaths on prevalence rates will be quite small. Conversely, since most induced abortions are relatively late, the increasing proportion of induced abortions is unlikely to lead to an artificial increase in total prevalence of any great magnitude.

High case ascertainment should have been achieved in most centres since neural tube defects are well defined and readily diagnosable conditions, and the centres are of relatively small size and use multiple sources of information. It is highly improbable that differences in case ascertainment, either between registries or within registries over time, could invalidate any of the major conclusions from this study.

The British Isles, as represented by six EUROCAT registries, continued in the period 1980–1986 as a high prevalence area for neural tube defects with rates two to three times higher than those in eight areas of continental Europe.

Clearly a considerable fall in neural tube defect prevalence in the British Isles, independent of the introduction of prenatal diagnosis, has occurred since the rates of 50 to 90 per 10 000 reported in the early to mid-1960s.[2–5 18–20] Regional comparison within the British Isles since the 1960s indicates that the Republic of Ireland and Northern Ireland are consistently higher prevalence areas, with medium prevalence in south Glamorgan, Glasgow, and Liverpool, although it is difficult to assess the role of differential ascertainment rates in apparent differences between published studies.[2–6 18–23] Reports from Liverpool and Glasgow show their prevalence figures to be quite similar up to the mid-1970s, and suggest that Glasgow may have emerged only recently as an area of high prevalence relative to other areas.[4 6 20] Little information exists specifically for Galway, but an Ireland wide study in 1961–62 and comparison of other Irish studies[19–23] for the years 1958–60 indicates that Galway has been a lower prevalence area than Dublin.

Relatively little published information is available for the last 30 years in the countries of continental Europe where EUROCAT registries now exist. A declining rate of anencephaly from 15 per 10 000 in the 1950s has been reported in the Netherlands.[7] In France, however, the anencephaly rate was reported to be only 5·4 per 10 000 in 1945–55.[24] In other European countries changes in prevalence have been observed, for example a reported increase in neural tube defects in Berlin to 50 per 10 000 during the immediate postwar period 1945–49,[9] a decline in spina bifida prevalence in Sweden from 11 per 10 000 in 1947 to 4 per 10 000 in 1970,[8] and a decline in total neural tube defect prevalence in Hungary from 28 per 10 000 in 1963–67 to 17 per 10 000 in the late 1970s.[10]

A continuation of the fall in neural tube defect prevalence in the British Isles into the mid 1980s could be shown among the six EUROCAT regions only in Dublin and Northern Ireland, where total prevalence had fallen to approximately 25 per 10 000 by 1985–86. A fluctuating or changing rate seemed to be characteristic of all the centres of the British Isles, however, in contrast to the stable situation in the rest of Europe. Of particular interest is the upturn in total prevalence in Glasgow in 1985–86. These results tend not to give much encouragement to any speculation that prevalence rates in the British Isles may be falling to the levels of the rest of Europe, and emphasise the need for the continuation of the search for aetiological differences between the two areas.

The prevalence patterns of anencephaly and spina bifida were similar, both in terms of geographic differences and secular change. The one exception was the increase of anencephaly in Florence, in the absence of any increase in the spina bifida rate. The geographical pattern of encephalocele however differed, with a much lower increase in risk in the British Isles than for other neural tube defects. A further analysis of the data in some EUROCAT centres will be looking more specifically at the question of aetiological and phenotypic heterogeneity of neural tube defects.

It is notable that the ratio of livebirths to stillbirths is very variable in the spina bifida case series reported by the various registries. This does not seem to be correlated with the total prevalence. There may be a number of reasons for this, relating to medical practice, to the social, religious, or welfare implications of livebirth compared to stillbirth, to variation in severity of the condition, and to selection of cases where early prenatal diagnosis had not been made. It is clear that a "livebirth prevalence rate" has little real meaning. To evaluate fully the impact of prenatal diagnosis on the prevalence of spina bifida related handicaps in surviving children, figures concerning survivors beyond the neonatal period are needed.

In 11 centres the impact of prenatal screening on prevalence at birth could be evaluated. Maternal serum α fetoprotein screening programmes exist in Glasgow, Liverpool, and south Glamorgan, although in south Glamorgan the test is available for only two thirds of the population of pregnant women (depending on the antenatal clinic attended). The proportion of pregnant women tested was estimated at 75% in Glasgow in 1985 and 47% in south Glamorgan in 1984. Maternal serum α fetoprotein tests are recommended between 16 and 18 weeks gestation. None of the continental European centres nor Northern Ireland have population based maternal serum α fetoprotein screening programmes, but tests may be offered by individual clinicians or clinics.

Obstetric ultrasound is available in all centres but screening policy and practice regarding gestational age at scanning varies. In some centres ultrasound is limited to women with certain indications (Odense) or attending certain types of antenatal care (Groningen), and routinely performed obstetric ultrasound, while it may detect anencephaly, needs to be supplemented by diagnostic fetal ultrasound to achieve a high detection rate of all neural tube defects. Even where a serum α fetoprotein screening programme is in place, ultrasound screening may provide the first indication of an anomaly.[25] In Glasgow and south Glamorgan, for example, it is known that in the latter half of the study period the majority of cases of anencephaly were first detected by ultrasound (Laurence KM, personal communication, and[26]).

In all centres, anencephaly was more frequently diagnosed prenatally and aborted than spina bifida, and prenatal diagnosis of anencephaly was made earlier during pregnancy. This is to be expected from the greater sensitivity of screening and diagnostic methods for anencephaly. An increase over time in the proportion of cases prenatally diagnosed and terminated was seen for both anencephaly and spina bifida. This could be due to an improvement in screening and diagnostic methods or the skill of operators, or to a changing organisation and uptake of services.

The British centres with a serum α fetoprotein screening programme achieved a greater proportion of early prenatal diagnoses than centres lacking such a programme. A number of factors affect the time of detection of an anomaly, including time of presentation for antenatal care, recommended gestational age at screening, and

the time dependent sensitivity of the screening method used. A combination of these factors may have explained the small difference between British and other centres in time of detection of anencephaly. For spina bifida, the presence of a serum α fetoprotein screening programme was linked to a much greater shift towards earlier diagnosis, indicating that in current routine practice conditions, the population sensitivity at earlier gestational ages of serum α fetoprotein screening for spina bifida is greater than that of ultrasound screening. Other studies have also shown a rather late mean age at detection of spina bifida with ultrasound screening.[27 28]

Given the disparity between the results of ultrasound and α fetoprotein screening for spina bifida, it should not be assumed that with the increasing sophistication of ultrasound the need for serum α fetoprotein screening has disappeared. Serum α fetoprotein screening at 16–18 weeks may serve an important role as an early indicator of high risk cases for diagnostic investigation. It is important that any evaluation of the cost-effectiveness of different screening methods should take into account the benefits of early diagnosis as well as the fact that the sensitivity of population screening is commonly below the potential indicated by single centre studies. Until primary prevention of neural tube defects becomes a reality, the potential for a further diminution in the public health impact of neural tube defects lies in increasing the rate of prenatal detection and in achieving earlier prenatal diagnosis.

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