Eurocat

European Surveillance of Congenital Anomalies

WHO COLLABORATING CENTRE FOR THE EPIDEMIOLOGIC SURVEILLANCE OF CONGENITAL ANOMALIES

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Terms of reference:

1. To provide essential epidemiologic information on congenital anomalies in Europe
2. To facilitate the early warning of teratogenic exposures and act as an information and resource centre regarding clusters or exposures or risk factors of concern
3. To evaluate the effectiveness of primary prevention and assess the impact of developments in prenatal screening
4. To promote the exchange of experience on population-based registration methods, classification and coding of congenital anomalies, and surveillance methods.

Terms of reference 1: To provide essential epidemiologic information on congenital anomalies in Europe

EUROCAT now has 41 members in 20 countries (see Table 1), new members including Poland, Hungary, Sweden and 4 UK regions. Of these, 36 are full members transmitting individual level data on congenital anomalies and 5 are associate members transmitting only yearly aggregate numbers. In total, more than one million births per year are surveyed, one quarter of the births in EU member states and more than half of births in seven non-EU countries. The central database holds a total of more than 250,000 cases of congenital anomaly since 1980 including livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis. Average total prevalence rates for 85 congenital anomaly subgroups 1996-2001 are given in Table 2.

The EUROCAT Website, under Publications and Data, gives open access to prevalence data on 85 subgroups of congenital anomalies, with user choice regarding congenital anomaly(s) of interest, years of interest, and registries or countries of interest in order to produce a range of table formats that can be readily printed. Prevalence rates are given as livebirth prevalence rates, birth prevalence rates, and total prevalence rates (the latter including also terminations of pregnancy following prenatal diagnosis). Prevalence data were updated to the birth year 2001. A modification was also made to the website to allow the user to select "basic tables" with default selections for their congenital anomaly of choice, which would also enable ready linkage with other websites giving information on diagnosis and treatment (e.g. Orphanet). The website has now replaced printed data reports as it is considered the most efficient and accessible method of dissemination of information.

In 2003, EUROCAT began to provide the WHO Craniofacial Anomalies database with data from European countries. A data extract concerning cases of cleft palate, cleft lip, and cleft lip and palate, was provided to the International Centre for Birth Defects in Rome (Prof Pierpaolo Mastrioacovo and Dr Elisabeth Robert), and the results will appear on the WHO Genomic Resource Centre website http://www.who.int/genomics/anomalies/idcfa/en/. A study of EUROCAT data on cleft palate led by Prof Elisa Calzolari is available on the EUROCAT website:

> *EUROCAT Special Report. 2003. The epidemiology of orofacial clefts in 30 European Regions. www.eurocat.ulster.ac.uk/pubdata/*
>
> *Calzolari E, Bianchi F, Rubini M, Ritvanen A, Neville A and a EUROCAT Working Group. Epidemiology of Cleft Palate in Europe: Implications for Genetic Research. The Cleft Palate-Craniofacial Journal (in press).*

In 2004, work will proceed to produce prevalence data on a list of approximately 20 rare congenital syndromes which have not previously been extracted from the EUROCAT database.

Table 1. Coverage of the European Population by EUROCAT Registries

Country	Registry	Annual Births per Registry	Annual Births per Country	% Country Covered
EU Countries				
Austria	Styria	10,800	75,800	14.2
Belgium	Antwerp	17,700		
	Hainaut	12,800		
	Total	30,500	116,900	26.1
Denmark	Odense	5,700	65,300	8.7
Finland		56,100	56,100	100.0
France	Auvergne	13,000		
	Paris	38,500		
	Central East	93,700		
	Strasbourg	13,800		
	Total	159,000	772,500	20.6
Germany	Mainz	3,300		
	Saxony-Anhalt	18,100		
	Total	21,400	743,500	2.9
Greece		0	107,000	0.00
Ireland	Cork & Kerry	7,700		
	Dublin	22,000		
	Galway	2,700		
	Total	32,400	56,100	57.8
Italy	Campania	47,400		
	Emilia Romagna	24,800		
	North East	54,400		
	Sicily	17,000		
	Tuscany	26,600		
	Total	170,200	545,000	31.2
Luxembourg		0	5,500	0.0
Netherlands	North	20,500	200,200	10.2
Portugal	South	18,200	114,800	15.9
Spain	Asturias	6,700		
	Barcelona	12,300		
	Basque Country	17,400		
	Madrid (ECEMC)	103,400		
	Total	139,800	407,400	34.3
Sweden		91,800	91,800	100.0
UK	Glasgow	9,700		
	Merseyside	26,600		
	Northern Region	29,100		
	North Thames	45,700		
	Oxford	5,300		
	Trent	62,000		
	Wales (CARIS)	31,400		
	Wessex	26,000		
	Total	235,800	669,000	35.2
	Total	**992,200**	**4,026,900**	**24.6**
Non-EU Countries				
Bulgaria	Sofia	10,200	68,200	15.0
Croatia	Zagreb	5,700	47,500	12.0
Hungary		98,100	98,100	100.0
Malta		3,900	3,900	100.0
Norway		57,000	57,000	100.0
Poland		197,200	363,200	54.3
Switzerland	Vaud	7,300	73,600	9.9
	Total	**379,400**	**711,500**	**53.3**
	GRAND TOTAL	**1,371,600**	**4,738,400**	**28.9**

Table 2. Number of cases among livebirths, stillbirths and terminations of pregnancy following prenatal diagnosis, and prevalence per 10,000 births, of 85 congenital anomaly subgroups in 34 EUROCAT full member registries, 1996-2001.

Birth year(s) = 1996, 1997, 1998, 1999, 2000, 2001

Total births: 3883879

Centre(s) = Hainaut (B), Odense (DK), Paris (F), Tuscany (I), Dublin (IRL), Galway (IRL), N Netherlands (NL), Glasgow (UK), Emilia Romagna (I), Straszburg (F), Switzerland (CH), Zagreb (YU), Malta (M), North East Italy (I), S Portugal (P), Antwerpen (B), Basque Country (E), Asturias (SP), Saxony Anhalt (D), Mainz (D), Barcelona (SP), El Valles (SP), Styria (AU), Sofia (BG), North Thames (UK), Cork and Kerry (IRL), ISMAC (I), Campania (I), Merseyside & Cheshire (UK), CARIS (UK), Poland (PL), Oxford (UK), Wessex (UK), Trent (UK)

Anomaly	LB (n)	FD (n)	IA (n)	LB+FD+IA (n)	LB+FD+IA (rate)
Nervous system	4014	460	3972	8446	21.75
Neural Tube Defects	1290	258	2347	3895	10.03
Anencephalus and similar	191	152	1081	1424	3.67
Encephalocele	181	26	281	488	1.26
Spina Bifida	918	80	985	1983	5.11
Hydrocephaly	1011	106	894	2011	5.18
Microcephaly	618	25	82	725	1.87
Arhinencephaly/holoprosencephaly	146	30	306	482	1.24
Eye	1537	42	144	1723	4.44
Anophthalmos/microthalmos	348	17	68	433	1.11
Anophthalmos	65	10	23	98	0.25
Microthalmos	283	7	45	335	0.86
Cataract	307	1	12	320	0.82
Ear	1254	81	176	1511	3.89
Anotia/microtia	266	7	28	301	0.77
Anotia	84	2	10	96	0.25
Microtia	182	5	18	205	0.53
Congenital heart disease	20912	455	2250	23617	60.81
Anomalies of cardiac chambers and connections	1844	62	337	2243	5.78
Common arterial truncus	228	13	57	298	0.77
Transposition of great vessels (complete)	977	12	77	1066	2.74
Single ventrical	204	15	73	292	0.75
Malformations of cardiac septa	14832	265	1264	16361	42.13
Ventricular septal defect	9031	138	699	9868	25.41
Atrial septal defect	5685	85	201	5971	15.37
Atrioventricular septal defect	1056	39	354	1449	3.73
Tetralogy of Fallot	989	23	105	1117	2.88
Malformations of valves	3255	83	610	3948	10.17
Tricuspid atresia and stenosis	308	5	73	386	0.99
Ebstein's anomaly	107	6	13	126	0.32
Aortic valve atresia/stenosis	403	10	38	451	1.16
Hypoplastic left heart	561	29	352	942	2.43
Malformations of the great arteries and veins	3990	75	353	4418	11.38
Coarctation of aorta	1119	17	70	1206	3.11
Cleft lip with or without palate	3086	84	368	3538	9.11
Cleft palate	2045	53	170	2268	5.84

Digestive system	5326	202	708	6236	16.06
Tracheo-oesophagal fistula-Oesophageal atresia and stenosis	946	22	84	1052	2.71
Congenital absence, atresia and/or stenosis of the small intestine	762	27	62	851	2.19
Congenital absence, atresia and/or stenosis of the duodenal	381	20	41	442	1.14
Congenital absence, atresia and/or stenosis of other specified parts of small intestine	252	5	15	272	0.7
Ano-rectal atresia and stenosis	900	38	188	1126	2.9
Internal urogenital system-ovaries uterus and renal system	8808	302	1711	10821	27.86
Bilateral renal agenesis	221	73	345	639	1.65
Cystic kidney disease	1413	46	475	1934	4.98
Congenital hydronephrosis	3149	35	234	3418	8.8
Bladder extrophy	86	4	34	124	0.32
External genital system	4825	75	190	5090	13.11
Hypospadias	3634	14	29	3677	9.47
Indeterminate sex	215	20	38	273	0.7
Limb	12422	335	1464	14221	36.62
Limb reduction	1634	91	467	2192	5.64
Upper limb reduction	1153	66	311	1530	3.94
Complete absence of upper limb	18	6	16	40	0.1
Absence of upper arm and forearm with hand present	21	1	9	31	0.08
Absence of both forearm and hand	115	3	28	146	0.38
Absence of hand and fingers	447	29	94	570	1.47
Longitudinal reduction defect/shortening of arm	397	32	152	581	1.5
Lower limb reduction	517	35	198	750	1.93
Complete absence of lower limb	16	0	16	32	0.08
Absence of thigh and lower leg with foot present	8	2	11	21	0.05
Absence of both lower leg and foot	16	3	5	24	0.06
Absence of foot and toe	177	10	41	228	0.59
Longitudinal reduction defect/shortening of leg	203	18	103	324	0.83
Polydactyly	2837	55	288	3180	8.19
Syndactyly	1900	54	164	2118	5.45
Musculoskeletal and connective tissue	6180	385	2047	8612	22.17
Choanal atresia	244	2	12	258	0.66
Craniosynostosis	437	9	28	474	1.22
Pierre Robin Syndrome	279	2	6	287	0.74
Mandibulofacial dystosis (Treacher-Collins and Franceschetti)	28	0	3	31	0.08
Goldenhar's Syndrome	88	1	4	93	0.24
Chondodystrophies and osteodystrophies	430	31	353	814	2.1
Diaphraghmatic hernia	720	39	203	962	2.48
Omphalocele	499	80	467	1046	2.69
Gastroschisis	637	33	115	785	2.02
Prune Belly Syndrome	38	6	53	97	0.25
Chromosomal	5829	433	6219	12481	32.14
Down Syndrome	3857	139	3324	7320	18.85
Patau syndrome (trisomy 13)	169	33	394	596	1.53
Edward syndrome (trisomy 18)	334	110	958	1402	3.61
Other trisomies and partial trisomies of autosomes	281	57	479	817	2.1
Monosomies and deletions from the autosomes	444	12	143	599	1.54
Turner's syndrome	228	56	525	809	2.08
Klinefelters syndrome	156	5	169	330	0.85

Anomalies outside normal range *	2701	163	448	3312	8.53
All Cases**	68357	1954	13374	83685	215.47

LB - Live Births

FD - Fetal deaths / Still Births from 20 weeks gestation

IA - Induced Abortions following prenatal diagnosis

* Any case coded outside the range 740 to 759 of ICD 9 (International Classification of Disease, 9th edition, WHO Geneva 1977) or the Q chapter of ICD 10 (10th edition, WHO Geneva 1992)
** excluding minor anomalies according to the specifications in EUROCAT Guide 1.2.

Terms of reference 2: To facilitate the early warning of teratogenic exposures and act as an information and resource centre regarding clusters or exposures or risk factors of concern

Development of the Cluster Advisory Service

In February 2003, a meeting was held of the EUROCAT Working Group on the Management of Clusters and Environmental Exposure Incidents to discuss the development of a web-based cluster advisory service. In preparation for this meeting, the literature regarding clusters of congenital anomalies and cluster investigation protocols was reviewed, and a questionnaire about local practice was sent to EUROCAT members. Work has also proceeded on a EUROCAT Special Report: A Review of Environmental Causes of Congenital Anomalies, to be one of the elements of the CAS. The CAS area of the website will become active in 2004.
The Cluster Working Group meanwhile responded to a number of requests for advice about clusters from EUROCAT members and non-members.

As an example of response to environmental exposure incidents, a preliminary analysis of congenital anomalies data from Belgium in relation to the 1999 dioxin contamination incident has been performed. Results will be reported in 2004.

A study has been conducted in five British regions 1991-99 of Geographical Variation in the prevalence of congenital anomalies, and sociodemographic risk factors, funded by the Department of Health (UK), led by Dolk and Armstrong (UK). Geographical variation and clustering was looked for at the level of region, hospital catchment area, census ward (10,000 households) and enumeration district (1,000 households). Generalised geographical variation was found at the level of region and hospital catchment area, but not below this. The prevalence of non-chromosomal congenital anomalies was positively associated with deprivation of the area of residence, and the prevalence of chromosomal anomalies was negatively associated with deprivation because of the higher average maternal age in more affluent areas. Raised risks persisted near the hazardous waste landfill sites previously included in the EUROHAZCON study. A full report will be published in 2004. The same dataset is now being used to look at risks associated with air pollution and drinking water contamination.

Surveillance of Hypospadias in relation to Exposure to Endocrine Disrupting Chemicals

Concern about apparent increases in the prevalence of hypospadias, a congenital male reproductive tract abnormality, in the 1960s to 1980s and the possible connection to increasing exposures to endocrine disrupting chemicals, have underlined the importance of effective surveillance of hypospadias prevalence in the population. We analysed the prevalence of hypospadias from 1980 to 1999 in 20 regions of Europe with EUROCAT population-based congenital anomaly registers, thirteen of which implemented a guideline to exclude glanular hypospadias. Our results do not

suggest a continuation of rising trends of hypospadias prevalence in Europe. However, a survey of the registers and a special validation study conducted for the years 1994-96 in nine EUROCAT registers identified a clear need for a change in the guidelines for registration of hypospadias. We recommend that all hypospadias should be included in surveillance, but that information from surgeons must be obtained to verify location of the meatus, and whether surgery was performed, in order to interpret trends. Investing resources in repeated special surveys may be more cost-effective than continuous population surveillance. We conclude that it is doubtful whether we have had the systems in place worldwide for the effective surveillance of hypospadias in relation to exposure to potential endocrine disrupting chemicals. Work in 2004 will proceed to put a more effective prospective surveillance system in place in Europe.

Two publications in 2003 relate to this study:

> *EUROCAT Special Report 2003. An assessment and analysis of surveillance data on hypospadias in Europe.* www.eurocat.ulster.ac.uk/pdf/hypospadias.pdf
>
> *Dolk H, Vrijheid M, Scott JES, Addor M-C, Botting B, de Vigan C, de Walle H, Garne E, Loane M, Pierini A, Garcia-Minaur S, Physick N, Tenconi R, Wiesel A, Calzolari E, Stone D. 2003. Towards the Effective Surveillance of Hypospadias. Environ Health Perspect: doi:10.1289/ehp.6398. [Online 18 November 2003]* http://ehpnet1.niehs.nih.gov/docs/2003/6398/abstract.html

Surveillance of maternal drug exposures.

A Working Group on Drug Surveillance chaired by Prof Martina Cornel (Netherlands) and then by Prof Lolkje van den Berg (Netherlands) and co-chaired by Dr Elisabeth Robert (France) and Dr Maurizio Clementi (Italy, President of ENTIS) have advised on the introduction of international ATC coding for drug exposures which will be implemented from 2005. A summary of information in the EUROCAT database relating to drug exposures has also been made, including methods of data collection and numbers of cases by drug category, which will be published in 2004. Twenty registries collect data on drug exposure in the first trimester of pregnancy, with the main source of information being obstetric records. For the 5 years from 1996-2000, nearly two thousand cases were recorded in the EUROCAT database of at least one drug exposure by 14 registries using the 18-category EUROCAT drug code, 12% of all cases in these registers. Despite the difficulties of collecting complete information on drugs, the database represents a considerable resource for further investigations. A pilot project examining evidence for an association between hypospadias and loratidine exposure is underway. After the introduction of ATC coding, EUROCAT will also contribute data to the ICBDMS Madre project, which looks for associations between specific drugs and specific malformations in registry data.

Statistical monitoring over time

The aim of general statistical monitoring over time is to identify increases or clusters that may be due to changing exposure to teratogens in the environment. In practice, statistical monitoring also operates as a data quality monitoring system.

Statistical monitoring based on the Scan method has been developed for use by Central Registry and local registries by Dr Alan Kelly (Ireland). The software has been integrated into the EUROCAT Data Management Programme by Biomedical Computing Ltd and a workshop was held on the new software at the Registry Leaders Meeting in Heidelberg June 2003. Results of cluster investigations will be discussed at the Registry Leaders Meeting in 2004. At present, statistical monitoring is applied to the standard EUROCAT congenital anomaly subgroups. Work has been underway also to routinely

identify multiply malformed cases in the EUROCAT database for additional monitoring. This will be done in collaboration with the International Clearinghouse for Birth Defects Monitoring Systems, who have developed a methodology for multiple malformation monitoring.

Other risk factors

The risks of congenital anomaly related to assisted conception and to the rise in multiple births related to assisted conception is of high interest at present. A session of the European Symposium on Prevention of Congenital Anomalies in Heidelberg June 2003 was devoted to this issue, followed by a meeting during the Registry Leaders Meeting to plan the analysis of available EUROCAT data. Following a presentation to the Symposium by Prof Peter Pharoah, on the evidence that the risk of congenital anomalies and cerebral palsy is increased by in utero death of a co-twin, it has been agreed to provide EUROCAT data to investigate this hypothesis further.

Observations worldwide of a rise in the prevalence of gastroschisis, a high relative risk among young mothers, and an association with socioeconomic deprivation, have also led to increased research activity into this anomaly. EUROCAT data have been provided for a case-control study of gastroschisis using available registry data concerning risk factors (Prof Pierpaolo Mastrioacovo and Dr Fabrizio Bianchi, Italy) and further analysis of trends in prevalence in EUROCAT data is being undertaken.

Terms of reference 3: To evaluate the effectiveness of primary prevention and assess the impact of developments in prenatal screening

Prevention of neural tube defects by folic acid supplementation

Approximately 4000 pregnancies every year in Europe result in a livebirth, stillbirth or termination of pregnancy of a baby/fetus affected by Neural Tube Defects (NTD), mainly anencephaly and spina bifida. Periconceptional folic acid supplementation has been shown over a decade ago to be an effective method of preventing potentially two thirds of cases. A study was conducted by the EUROCAT Working Group on NTD and Folic Acid, led by Lenore Abramsky (UK), to review progress in the last decade in European countries in terms of developing and implementing public health policies to raise periconceptional folate status, and analyse 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 have been prevented up to the year 2000. Representatives from seventeen countries participating in EUROCAT provided information about policy, health education campaigns and surveys of folic acid supplement uptake in their country. At the beginning of 2002, an official governmental recommendation that women planning a pregnancy should take 0.4 mg of folic acid supplementation daily was in operation in nine of the seventeen countries. The earliest countries to introduce an official supplementation policy were the UK, Ireland and Netherlands in 1992-3 and the latest were Spain and France in 2000-2001. In the remaining eight participating countries, no official government recommendation about supplementation was in place, however, professional bodies within a subset had in fact recommended supplementation, and two countries had an official policy of encouraging women to increase their dietary intake of folate periconceptionally. Only seven countries had official health education initiatives: UK, Ireland, France, 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 periconceptionally. 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 the 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, predating folic acid advice.

We conclude that 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 staple foods is likely to avoid widening socio-economic inequalities in NTD prevalence and result in large scale prevention of NTDs.

In view of the findings that there has been a lack of substantial decline in neural tube defect prevalence in Europe in the last decade and even countries which have pursued supplementation policies relatively actively have found a limited preventive impact, EUROCAT has issued the following recommendations:

1) Countries should review their policies regarding folic acid fortification and supplementation, taking account of WHO Europe recommendations.

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 malformations.

A full report of this work is available on the EUROCAT website:

> *EUROCAT Working Group. EUROCAT Special Report: Prevention of Neural Tube Defects by Periconceptional Folic Acid Supplementation in Europe. May 2003.*
> *http://www.eurocat.ulster.ac.uk/pubdata/folic%20acid.html*

A session of the European Symposium on Prevention of Congenital Anomalies in Heidelberg June 2003 was devoted to presentations by EUROCAT registries of studies on periconceptional folic acid supplement uptake in their areas.

EUROCAT participated at the WHO Euro meeting “Folic Acid: from Research to Public Health Practice” Rome, Italy 2 November 2002 and is contributing to the Report of that meeting due to be published in 2004.

Work in 2004 will proceed to update the analysis of trends in Neural Tube Defect Prevalence, to update the information on current policy regarding folic acid supplementation and its implementation in European Countries, and to promote the recording of information in maternity units about folic acid supplementation for all cases of congenital anomaly as well as for unaffected pregnancies.

Prenatal diagnosis of congenital anomalies

Prenatal diagnosis of congenital anomaly may lead to preparation for the birth of an affected child by the family and health services, or in severe cases to termination of the pregnancy. Information on the number of terminations of pregnancy following prenatal diagnosis is available on the EUROCAT website, and can also be seen in Table 2.

Two studies were conducted in 2003 using the EUROCAT database with respect to prenatal diagnosis, led by Dr Ester Garne (Denmark), with papers now submitted for publication. The first of these analysed data from 17 registries 1995-99, to establish the frequency at a population level of prenatal diagnosis of severe congenital malformations that can be detected by ultrasound investigation. The analysis concerned all livebirths, fetal deaths and terminations of pregnancy diagnosed with one or more of the following malformations: anencephalus, encephalocele, spina bifida, hydrocephalus, transposition of great arteries, hypoplastic left heart, limb reduction defect, bilateral renal agenesis, diaphragmatic hernia, omphalocele and gastroschisis. The 17 registries reported 4366 cases diagnosed with the 11 severe malformations and of these 2300 were livebirths (53%) and 1863 terminations of pregnancy (43%). Overall prenatal detection rate was 64% (range 25-88% between regions). The proportion of terminations of pregnancy varied from 15%-59% of all cases. Gestational age at discovery for prenatally diagnosed cases was less than 24 weeks for 68 % (range 36-88%). There was a significant relation between high prenatal detection rate and early diagnosis. For the individual malformations prenatal detection rate was highest for anencephalus (94%) and lowest for transposition of great arteries (27%). Termination of pregnancy was performed in more than half of the prenatal diagnosed cases except for transposition of great arteries, diaphragmatic hernia and gastroschisis where 30-40% of the pregnancies with a prenatal diagnosis were terminated. We concluded that European countries currently vary widely in the provision and uptake of prenatal screening and its quality, as well as the "culture" in terms of decision to carry on the pregnancy. This inevitably contributes to variation between countries in perinatal and infant mortality, in childhood prevalence and in cost to health services of congenital anomalies.

The second study analysed data from fourteen registries 1995-99 to investigate outcomes of ultrasound investigations (US) and invasive diagnostic procedures in cases of congenital malformations (CM), and to compare the use of invasive prenatal test techniques (amniocentesis (AC) versus chorionic villus sampling (CVS)) among European populations. 25,400 cases of CM recorded by 14 EUROCAT registries covering a total population of 1,013,352 births 1995-99. US were performed in 91% of cases, and positively detected CM in 35% of cases. AC was performed in 24% of the cases and CVS procedures in 3% of cases. Thirty-eight percent of invasive tests performed gave positive results. Fifty-two percent of cases with maternal age ≥ 35 years had an invasive test performed compared to 20% of cases with younger mothers. Considerable variation was found between registries in the uptake rate of invasive tests in cases with older maternal age and on the use of invasive tests, with only four regions employing CVS techniques in at least a third of cases with invasive tests performed. For chromosomal anomalies US gave positive results in 46% of cases with maternal age <35 years with US performed and in 36% of cases with maternal age ≥35 years with US performed. The study highlighted the counselling implications of the large number of children being born with congenital anomalies after negative prenatal investigations, the large regional variation in the uptake and type of invasive tests performed, the relatively infrequent use of CVS compared to amniocentesis, and the now extremely important role of ultrasound in diagnosing both chromosomal and non-chromosomal anomalies.

A presentation of these and other data on prenatal diagnosis was made to the EURORDIS conference in Paris, October 2003, by Prof Martina Cornel (Netherlands).

Dr Ester Garne (Denmark) is leading a study in a small number of EUROCAT registries of the impact of prenatal diagnosis of Transposition of Great Arteries on postnatal outcome. Data collection is nearly finished for this study.

A presentation of EUROCAT data on the combined impact of maternal age and prenatal diagnosis and termination of pregnancy on the livebirth prevalence of Down Syndrome was made by Prof Helen Dolk to the INSEE/INSERM/EAPS meeting on Health Implications of Late Parenthood in Paris, May 2003. EUROCAT data show how the steep rise in maternal age across Europe since 1980 (the proportion of mothers of over 35 years of age more than doubling in some regions) has led to an increasing proportion of pregnancies affected by Down Syndrome. Livebirth prevalence varies between regions and countries depending on the maternal age structure of the population and the extent to which prenatal diagnosis and termination of pregnancy has counteracted the increase in numbers due to maternal age.

Following a presentation by Dr Joan Morris (UK) to the European Symposium on Prevention of Congenital Anomalies in Heidelberg June 2003, EUROCAT has supplied data with which to independently confirm the findings of the England and Wales Down Syndrome register that the maternal age specific rates of Down Syndrome for women of 44 years and over level off, rather than continuing to increase exponentially as previously assumed. This has implications for prenatal screening and counselling among these mothers. The results will be available in 2004.

Terms of reference 4: To promote the exchange of experience on population-based registration methods, classification and coding of congenital anomalies, and surveillance methods.

The 18th annual Registry Leaders Meeting was held in Heidelberg in June 2003, together with the 7th European Symposium on the Prevention of Congenital Anomalies. These events were hosted by the EUROCAT Registries of Mainz and Saxony. Some additional exchanges were also held e.g. Dr Fabrizio Bianchi (Italy) visited the registries of Barcelona and Lisbon and Maria Loane (UK) visited the registries of Auvergne and Barcelona. News about EUROCAT was mailed to all contacts in Eastern Europe, and we are seeking funds to support travel exchanges with Eastern European partners.

In order to facilitate data transmission to the Central Registry, the EUROCAT Data Management Programme ("EDMP") has been developed in Microsoft Access. This interfaces with the EUROCAT Central Database. New versions are downloadable from the membership area of the EUROCAT website, and a copy is provided to all new members. The EDMP allows a choice between data entry or data import, and runs a standard validation programme on data which is expanded over time to ensure progress toward higher quality data and greater data standardisation. Data can be exported in standard format for transmission to EUROCAT Central Registry. Additional developments during 2003 include the binary (present or absent) coding of 85 EUROCAT congenital anomaly subgroups based on a range of ICD9-BPA and ICD10-BPA codes, a facility to produce standard Excel Tables identical to the tables on the website for these subgroups, and the statistical monitoring facility discussed above. In 2004, work will proceed to finalise revisions to EUROCAT Guide 1.2: Instructions for the Registration of Congenital Anomalies and the EDMP with the addition of new variables to the EUROCAT common dataset.

The Coding and Classification Committee have been working on developing guides to the coding of limb defects and syndromes, which will be ready in 2004.

The development of Data Quality Indicators is an important part of EUROCAT activity. Development to date includes: standardized Registry Descriptions, validation checks in the EDMP (above), missing data summaries, analysis of the ratio of anencephaly to spina bifida to identify underascertainment of

pregnancy terminations (included in the EUROCAT report on NTD and folic acid, see above) and capture-recapture analysis:

> *EUROCAT Special Report 2003. Using capture-recapture methods to ascertain the completeness of a register: case study and methodological considerations. www.eurocat.ulster.ac.uk/pubdata.*

In recent years, the issue of parent consent for registration of affected individuals has been raised in a number of European countries. A survey was carried out in 2003 of current practice. Ten registries are consent-based or about to become so. However, registries note that the requirement for consent (unless operated on an opt-out basis) is a grave logistic difficulty, with considerable resource implications, and a considerable actual or potential impact on case ascertainment. Experience is that while parents rarely refuse permission, underascertainment comes about through clinicians not asking consent or not completing the paperwork of notification. Since high ascertainment is dependent on multiple sources of notification, systems must be put in place to avoid asking parents repeatedly for their consent. In some countries, there are legal provisions for registration without consent, and the emphasis is instead on strict data protection.

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