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Review Article

Paper 6: EUROCAT Member Registries: Organization and Activities†

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BACKGROUND: EUROCAT is a network of population-based congenital anomaly registries providing standardized epidemiologic information on congenital anomalies in Europe. There are three types of EUROCAT membership: full, associate, or affiliate. Full member registries send individual records of all congenital anomalies covered by their region. Associate members transmit aggregate case counts for each EUROCAT anomaly subgroup by year and by type of birth. This article describes the organization and activities of each of the current 29 full member and 6 associate member registries of EUROCAT. **METHODS:** Each registry description provides information on the history and funding of the registry, population coverage including any changes in coverage over time, sources for ascertaining cases of congenital anomalies, and upper age limit for registering cases of congenital anomalies. It also details the legal requirements relating to termination of pregnancy for fetal anomalies, the definition of stillbirths and fetal deaths, and the prenatal screening policy within the registry. Information on availability of exposure information and denominators is provided. The registry description describes how each registry conforms to the laws and guidelines regarding ethics, consent, and confidentiality issues within their own jurisdiction. Finally, information on electronic and web-based data capture, recent registry activities, and publications relating to congenital anomalies, along with the contact details of the registry leader, are provided. **CONCLUSIONS:** The registry description gives a detailed account of the organizational and operational aspects of each registry and is an invaluable resource that aids interpretation and evaluation of registry prevalence data. *Birth Defects Research (Part A) 91:S51–S100, 2011.* © 2011 Wiley-Liss, Inc.

Key words: congenital anomaly registries; population-based; ascertainment; organization; Europe

AUSTRIA, STYRIA – FULL MEMBER

History and Funding

The registry was set up in 1986 after the Chernobyl disaster. It registers fetuses/babies with congenital anomalies born after January 1, 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 10,000 births annually. See Table 1 for coverage of European birth populations.

Sources of Ascertainment

Pediatric cardiology centers supply systematic case lists and diagnostic details to the registry.

There is one central cytogenetic laboratory in Styria that covers the whole population and provides a list of all abnormal prenatal and neonatal karyotypes annually. The registry has no direct electronic link to cytogenetics, but has close contact almost every day. So the local cytogenetic database can be used easily, although indirectly.

The registry operates as a research program with voluntary participation of hospitals. Information is gathered from 48 sources once per year. Sources consist of 11 obstetric departments, 2 pathology services, 2 child health services with specialized departments for diagnosis and treatment, and 1 cytogenetic laboratory. Forty-eight percent of cases are reported by more than one source. In the remaining 52% of cases, only one source provided data. Since 2002, most of the information is gathered electronically (see below). Fetuses/babies with anomalies are registered if diagnosed before birth, at birth, or during the first year of life.

Maximum Age at Diagnosis

Up to 1 year of age.

Terminations of Pregnancy for Fetal Anomaly

Terminations of pregnancy after prenatal diagnosis of congenital anomalies are registered. (Termination of pregnancy for socio-economic reasons is legal up to 12 weeks postconception. It requires special counseling.)

For terminations of pregnancy for fetal anomaly (TOPFA), there is no upper limit of gestational age by law, if serious psychological or health problems for the mother or the fetus were to be expected, and labor has not started. But if a non-lethal congenital anomaly is diagnosed late, most obstetricians in Austria would follow the maternal wish for TOPFA only up to the end of 23 weeks' gestation. Thereafter, pregnancies with severe anomalies, but with a viable fetus, may be terminated after fetal analgesia and feticide, if a commission agrees with the maternal wish to terminate. Non-viable forms of congenital anomalies may of course be terminated at any stage of gestation.

Prenatal Screening Policy

The official policy regarding prenatal diagnosis is pregnant women are offered three ultrasound scans (8–12, 18–22, and 30–34 weeks' gestation) according to a booklet called ''Mother-child Passport.'' More scans are done in most cases, like combined testing and late assessment of fetal growth and wellbeing.

Stillbirth and Early Fetal Deaths

Stillbirths with congenital anomalies are registered. Stillbirth definition by law is late fetal death from a crown foot length >= 35 cm and from January 1, 1995, a limit of >= 500 g.

There is no lower gestational age or weight limit for registration of congenital anomalies in early fetal deaths/spontaneous abortions. Autopsy rates in 1999 were as follows: stillbirths 63%, induced abortions 68%, early neonatal death (0–7 days) 70% (estimate), later deaths 1 week to 1 year 70% (estimate), and almost all deaths with congenital anomalies.

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 systematically collected. Maternal residency is recorded and can be used for evaluating the subregional pattern of birth defects.

Denominators and Controls Information

Information on all births is available from birth certificates, registered nationally by Statistics Austria.

Registry Description References

Haeusler MC, Berghold A, Schoell W, et al. 1992. The influence of the post-Chernobyl fallout on birth defects and abortion rates in Austria. Am J Obstet Gynecol 167(4 Pt 1):1025–1031.

Haeusler MC, Berghold A, Stoll C, et al. 2002. Prenatal ultrasonographic detection of gastrointestinal obstruction: results from 18 European congenital anomaly registries. Prenat Diagn 22:616–623.

Ethics and Consent

The registry did not require ethics committee approval to collect and store data, but this will be sought in the near future.

Parental consent is not asked for, and we do not need maternal informed consent. The reason is that data are kept confidentially on a university computer for scientific use only, and data are published or transferred to central EUROCAT registry in a nonpersonalized form.

Electronic and Web-based Data Capture

The Styrian Malformation Registry has access since 2002 to the Styrian open Medical Documentation and Communication System where an annual search for patients born within the index year with an International Classification of Diseases (ICD) 10-Q-code (i.e., congenital anomaly) is performed. The hospital chart for each person is then looked up in the Medical Documentation and Communication System for details. Pathology and genetics institutes use their own electronic documentation system which the registry uses indirectly by asking for an annual search for subjects with congenital anomalies.

Recent Registry Activities and Publications (2007–2010)

The registry leader is a member of the project management committee of EUROCAT.

He presented the registry on various scientific meetings:

Haeusler M. Praenatale Diagnostik im Spiegel des Steirischen Fehlbildungsregisters. 32. Ultraschall Dreilaendertreffen, Davos, 24–27 September 2008.

Haeusler M. European malformation registries. 8th World Congress in Fetal Medicine, Portoros, Slovenia. 27 June–2 July 2009.

Haeusler M. Prevention of NTDs by folic acid supplementation. 9th World Congress in Fetal Medicine, Rhodos. 20–24 June 2010.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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BELGIUM, ANTWERP – FULL MEMBER

History and Funding

The registry started with a pilot study on procedures for registration of congenital anomalies in 1989. In 1990, the registry formally started. Since 1997, the whole province of Antwerp has been covered. The registry was 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 since 1990.

Population Coverage

The registry covers about 20,000 births annually; these are all births in the province of Antwerp, about 18% of the births in Belgium. The registry is population-based which means that all mothers resident in the province of Antwerp at the time of birth of their babies are included.

Sources of Ascertainment

Reports are actively collected form maternity, pediatric, and neonatologic units by registry staff who visit each maternity, pediatric, and neonatal unit in the covered region. We work with 20 participating hospitals. Basic information on children born with congenital anomalies is gathered from these hospital departments. More detailed information on diagnosis and exposure during pregnancy is gathered from gynecologist and pediatricians' records. Information about the parents is obtained from general practitioners and social welfare nurses. Clinical geneti-

Table 1
Coverage of European Birth Populations by EUROCAT Full or Associate Member Registries (October 2010)

Country	EUROCAT registry	Year started EUROCAT data transmission	Annual births 2007, registry	Annual births 2007, country[1]	% Country covered*
EU					
EU (Present EU Member States)			1,347,841	5,249,863	25.7
EU-15 (EU Member Countries since before 2004)			839,283	3,325,950	25.2
EU-NMS (Countries acceded in 2004–2007)			508,558	1,923,913	25.2
Belgium	Antwerp	1990	19,874		
	Hainaut	1980	12,717		
	Total		32,591	120,664	27.0
Bulgaria				75,257	0.0
Czech Republic	Czech Republic[2,3]	2000	114,947	114,947	100.0
Denmark	Odense	1980	5,429	63,731	8.5
Germany	Mainz	1990	3,323		
	Saxony–Anhalt	1987	17,470		
	Total		20,793	683,214	3.0
Estonia				15,840	0.0
Ireland	Cork & Kerry	1996	9,953		
	Dublin	1980	26,370		
	South east	1997	7,468		
	Total		43,791	69,863	62.7
Greece				111,717	0.0
Spain	Barcelona	1992	14,862		
	Basque Country	1990	20,681		
	Spain hospital network[2]	1980	102,540		
	Total		138,083	489,221	28.2
France	Isle de la Reunion	2002	15,002		
	Paris	1981	26,339		
	Rhone–Alpes[2]	2006	57,744		
	Strasbourg	1982	21,962		
	Total		121,047	814,377	14.9
Italy	Emilia–Romagna	1981	40,662		
	Tuscany	1980	30,957		
	Total		71,619	561,747	12.7
Cyprus				8,488	0.0
Latvia				23,269	0.0
Lithuania				32,495	0.0
Luxembourg				5,429	0.0
Hungary				97,642	0.0
Malta	Malta[3]	1986	3,898	3,898	100.0
Netherlands	Northern	1981	17,678	181,574	9.7
Austria	Styria	1985	10,209	76,203	13.4
Poland	Wielkopolska	1999	38,302		
	Rest of Poland[2,3]	1999	351,411		
	Total		389,713	389,713	100.0
Portugal	South	1990	18,874	102,811	18.4
Romania				215,651	0.0
Slovenia				19,702	0.0
Slovakia				54,476	0.0
Finland	Finland[2]	1993	58,574	58,574	100.0
Sweden	Sweden[2,3]	2001	101,688	101,688	100.0
United Kingdom	Northern England	2000	33,054		
	Thames Valley	1991	29,716		
	E Mid & S York	1998	72,549		
	Wales	1998	34,585		
	Wessex	1994	29,003		
	Total		198,907	771,923	25.8
Non EU					
Candidate countries in EUROCAT					
Croatia	Zagreb	1983	7,351	41,748	17.6
EFTA countries in EUROCAT					
Norway	Norway	1980	58,046	58,046	100.0
Switzerland	Vaud	1989	7,620	74,337	10.3
Ukraine	Ukraine[4]	2005	29,253	472,657	6.2

[1]Source: crude birth rate (accessed June 29, 2010) http://epp.eurostat.ec.europa.eu/portal/page/portal/population/data/main_tables.
[2]Associate EUROCAT Registries (transmit aggregate data only).
[3]Source of annual births in country provided by registry rather than EUROSTAT.
[4]http://www.ukrstat.gov.ua/operativ/operativ2007/ds/pp/pp_e/pp1207_e.html (accessed June 29, 2010).
*Including the 6 EUROCAT Affiliate registries (French West Indies, Hungary, Campania, Sicily, Slovenia, and South West United Kingdom) coverage of the EU population increased from 25.7% to 30.5%.
EU, European Union; NMS, New Member States; EFTA, European Free Trade Association.

Table 2
Published Papers Resulting from EUROCAT Projects (May 2010)

Name of Project Study Carried Out and Analysed by EUROCAT with Resulting Publication No:	Antwerp	Asturias	Auvergne	Barcelona	Basque Country	Campania	Cork & Kerry	Dublin	E Mid & S Yorks	Emilia Romagna	Finland	Galway	Glasgow	Hainaut	Hungary	Ile de la Reunion	Mainz	Malta	North East Italy	North Netherlands	Northern England	NW Thames	Norway	Odense	Paris	Poland	Saxony Anhalt	Sicily	South East Ireland	South Portugal	Strasbourg	Styria	Thames Valley	Tuscany	Ukraine	Vaud	Wales	Wessex	Wielkopolska	Zagreb
2010																																								
Congenital Hydrocephalus: A Population Based Study on Prevalence and Outcome [2010a]																								X								X			X				X
Late Terminations of Pregnancy After Prenatal Diagnosis of Fetal Abnormality (TOPFA) in Europe [2010b]	X					X			X	X				X						X	X		X	X	X		X			X		X	X	X	X	X	X		
Prenatal Diagnosis and Outcome of Pregnancy of Specified Sex-Chromosome Abnormalities in Europe [2010c]	X			X	X				X	X				X							X			X	X	X	X			X	X	X	X	X		X	X	X		
Paternal Age Risk for Chromosomal Anomalies [2010d]	X	X	X	X	X	X				X			X	X			X	X	X	X				X	X		X	X			X			X		X	X		X	X
Intrauterine Exposure to Valproic Acid and Specific Malformations: A Case-Control Study [2010e]	X				X		X			X				X			X	X		X			X	X	X	X	X				X			X		X	X	X		X
2009																																								
Renal Malformations – Prevalence and Regional Differences in Europe [2009a]				X	X	X	X			X				X			X	X		X				X	X				X	X	X	X		X		X	X	X	X	X
Maternal Age-Specific Risks of Non-Chromosomal Anomalies, 1990-2004 [2009b]	X	X		X	X		X	X		X							X	X		X				X	X		X		X	X	X	X	X	X		X	X		X	X
2008																																								
Epidemiology of Rare Syndromes in Europe [2008a]	X	X	X	X	X	X	X	X	X	X			X	X			X	X	X	X	X	X		X	X	X	X	X		X	X	X	X	X		X	X	X	X	X
Infantile Pyloric Stenosis [2008b]	X												X					X		X				X								X				X				
Lamotrigine and Orofacial Clefts[2008c]	X				X		X			X				X			X	X		X			X	X	X	X	X				X			X		X	X		X	X
Prenatal Screening Policies in Europe [2008d]		X		X	X	X		X		X	X			X			X	X		X	X		X	X	X		X			X		X	X	X		X	X	X	X	X
2007																																								
Gastro-Intestinal Atresias: Gestational Age at Diagnosis Indicative of Early Birth Induction? [2007a]	X	X								X							X	X		X		X		X						X	X			X		X	X			X
Gastroschisis: Maternal Age Specific Trends in Prevalence [2007b]	X	X		X	X	X	X	X	X	X	X		X				X	X		X				X	X		X			X	X	X		X		X	X	X		X
Epidemiology of Multiple Malformations: Presence of Congenital Malformations in Relatives [2007c]		X		X	X	X		X		X		X	X	X			X	X	X	X		X		X	X		X			X	X	X		X		X				X
Does Prenatal Diagnosis Increase Survival for Liveborn Infants with Transposition of Great Arteries? [2007d]	X				X												X			X		X		X											X					
Fortification of Staple Foods with Folic Acid [2007e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X	X

Table 2
Published Papers Resulting from EUROCAT Projects (May 2010) (continued)

Publication no:	full publication reference
2010a	Garne E, Loane M, Addor M-C, et al. 2010. Congenital hydrocephalus – prevalence, prenatal diagnosis and outcome of pregnancy in four European regions. Eur J Paediatric Neurol 14:150–155.
2010b	Garne E, Khoshnood B, Loane M, et al. 2010. Termination of pregnancy for fetal anomaly after 23 weeks of gestation: a European register-based study. Br J Gynaecol 117:660–666.
2010c	Boyd P, Loane M, Garne E, et al. 2010. Sex chromosome trisomies in Europe: prevalence, prenatal detection and outcome of pregnancy. Eur J Human Genet online publication 25 August 2010; doi: 10.1038/ejhg.2010.148.
2010d	de Souza E, Morris JK, and a EUROCAT Working Group. Case-control analysis of paternal age and trisomic anomalies. Arch Dis Child, DOI: 10.1136/adc.2009.176438.
2010e	Jentink J, Loane M, Dolk H, et al. 2010. Valproic acid monotherapy in pregnancy and major congenital malformations. N Eng J Med 362:2185–2193.
2009a	Garne E, Loane M, Wellesley D, et al. 2009. Congenital hydronephrosis: prenatal diagnosis and epidemiology in Europe. J Pediatr Urol 5:47–52.
2009b	Loane M, Dolk H, Morris JK, et al. Maternal age-specific risk of non-chromosomal anomalies. Br J Gynaecol 116:1111–1119.
2008a	Barisic I, Tokic V, Loane M, et al. 2008. Descriptive epidemiology of Cornelia de Lange syndrome in Europe. Am J Med Genet A 146A:51–59.
2008b	Pedersen RN, Garne E, Loane M, et al. 2008. Infantile hypertrophic pyloric stenosis: a comparative study of incidence and other epidemiologic characteristics in seven European regions. J Matern Fetal Neonat Med 21:599–604.
2008c	Dolk H, Jentink J, Loane M, et al. 2008. Does lamotrigine use in pregnancy increase orofacial cleft risk relative to other malformations. Neurology 71:714–722.
2008d	Boyd PA, de Vigan C, Khsohnood B, et al. 2008. Survey of prenatal screening policies in Europe for structure malformations and chromosome anomalies, and their impact on detection and termination rates for neural tube defects and Down's syndrome. Br J Gynaecol 115:689–696.
2007a	Garne E, Loane M, Dolk H, et al. 2007. Gastrointestinal malformations: impact of prenatal diagnosis on gestational age at birth. Paediatric Perinatal Epidemiol 21:370–375.
2007b	Loane M, Dolk H, Bradbury D, et al. Increasing prevalence of gastroschisis in Europe 1980–2002: a phenomenon restricted to younger mothers? Paediatric Perinatal Epidemiol 21:363–369.
2007c	Calzolari E, Pierini A, Astolfi G, et al. 2007. Associated anomalies in multi-malformed infants with cleft lip and palate: an epidemiologic study of nearly 6 million births in 23 EUROCAT Registries. Am J Med Genet A 143:528–537.
2007d	Garne E, Loane M, Nelen V, et al. 2007. Survival and health in liveborn infants with transposition of great arteries – a population based study. Congenital Heart Dis 2:165–169.
2007e	Abramsky L, Dolk H, and a EUROCAT Folic Acid Working Group et al. 2007. Should Europe fortify a staple food with folic acid? Lancet 369:641–642.

TOPFA, termination of pregnancy for fetal anomaly.

cists, surgeons, pathologists, and the center for detection of metabolic diseases are also contacted for more information. Pediatric cardiology centers supply diagnostic information when requested by the registry for specific cases. Cytogenetic information is gathered on the cases suspected with a genetic anomaly.

All cases with a congenital anomaly diagnosed prenatally or in the first year of life are registered. Reporting by hospitals and health workers is voluntary.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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 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 and spontaneous abortions with a gestational age of less then 20 weeks are not registered.

Exposure Data Availability

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

Denominators and Controls Information

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

Ethics and Consent

The registry's procedure was presented to the Belgian privacy committee. In this procedure, it was agreed that the registry provides information to the parents on aims and methods of registration, data protection, and the right to opt-out. If the parents do not opt-out, the data are registered. The registry does not require ethics committee approval to operate. No additional ethics committee approval is required for studies that use nonidentifiable data.

Information on the registration of congenital anomalies is given to the parents by medically qualified staff treating the child and other health care professionals treating the child.

Electronic and Web-based Data Capture

Not available.

Recent Registry Activities and Publications (2007–2010)

Registratie van aangeboren afwijkingen, Rapport 1989 to 2008, 2010.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

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BELGIUM, HAINAUT–NAMUR – FULL MEMBER

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 (Charleroi [Gosselies], Belgium). As a part of the Institute of Pathology and Genetics of Charleroi, it is supported by an annual grant from the Institute of Research in Pathology and Genetics of Charleroi. Since 2001, it is also partly supported by the Ministry of Public Health of Wallonia (www.wallonie.be).

Population Coverage

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

Sources of Ascertainment

Prenatal and delivery units, and neonatal and pediatric departments were divided into 13 hospitals. All cytogenetic, genetic, and pathologic data, including the examination of aborted fetuses, are regionally concentrated in the Institute of Pathology and Genetics of Charleroi (Gosselies). Children with malformations are registered up to 1 year of age.

Maximum Age at Diagnosis

Prenatal diagnosis, first week of life with follow-up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

Voluntary termination of pregnancy is legal in Belgium up to 12 weeks of gestation. However, if a severe congenital anomaly is diagnosed later, there is no upper age limit for termination, but this happens under the strict surveillance of an ethical committee.

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: weight ≥500 g or ≥22 weeks. 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 to 1994 compared to 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 Center of Human Genetics. Recently, a collaboration with the Centre d'Epidemiologie Périnatale has been initiated.

Address for Further Information

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CROATIA, ZAGREB – FULL MEMBER

History and Funding

Registration for EUROCAT network started in the Children's University Hospital Zagreb in 1983, after the preliminary favorable results of the pilot project on congenital anomaly registration. Collection and transmission of data was on a voluntary basis until the year 2000. After 2000, congenital anomaly registration was funded within the scientific project dedicated to epidemiologic surveillance of congenital anomalies, supported by the Ministry of Science, Education, and Sports of the Republic of Croatia.

Population Coverage

The registry is population based (population-based I = all mothers resident in defined geographic area). The registry covers northwestern Croatia – two regions at the seaside (Pula and Rijeka), and two continental provinces (Varaždin and Koprivnica). Births take place in four regional hospitals with practically no homebirths (only by accident). Total number of monitored births per year in these regions is around 7500, approximately 17.14% of the total annual births in Croatia. In 2009, we have started a pilot project in two additional delivery units: Vinkovci and Split, with the prospect to extend registry coverage in next years for additional 13% of annual births.

Sources of Ascertainment

In four maternity units, Varaždin, Koprivnica, Rijeka, and Pula, neonatologists and gynecologists record cases with congenital anomalies among livebirths, stillbirths, and terminations of pregnancies. Birth and stillbirth certificates include notification of congenital anomalies and are used as additional sources of information as well as hospital discharge lists.

Part of the population (local registry Rijeka) is covered by the pediatric cardiology diagnostic center. Children born in this neonatal unit have the cardiac ultrasound newborn screening. The pediatric cardiology center does not supply case lists with details and diagnostic details to the registry. In other local registries, there are no pediatric cardiology centers, but children suspected of having cardiac defects are referred to a pediatric cardiologist for evaluation. Cardiac ultrasound and diagnosis are made by a pediatric cardiologist. Data about patients with congenital heart defects are then collected by neonatologists employed in neonatal units and referred to the registry.

The Zagreb registry, at present, does not have direct access to cytogenetic laboratories. In local registries, personnel get data from cytogenetic and molecular laboratories, and, in case of death, from postmortem examination.

Maximum Age at Diagnosis

Maximum age at diagnosis is up to 1 week.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is regulated by Croatian law in 1978 (NN/18/78). The upper limit for termination of pregnancy for serious fetal anomaly is 24 gestational weeks.

Stillbirth Definition and Early Fetal Deaths

Official stillbirth definition in Croatia is 22 completed gestational weeks/500 g weight. The registry collects data about stillbirths and fetal deaths/spontaneous abortions from 20 weeks. The local registries also record results of autopsy of all termination of pregnancies after prenatal diagnosis, stillbirths, and early neonatal deaths (0–7 days). Autopsy rates in these cases are generally high, around 90 to 100%.

Exposure Data Availability

Exposure information includes: data on parental occupation, maternal drug use, maternal smoking and alcohol abuse, and maternal diseases before and during pregnancy.

Data about techniques of prenatal screening (ultrasound, serum markers) and assisted reproduction methods are collected as well and are available for most of the recorded cases.

Denominators

Information on annual births and maternal age distribution is obtained from the population databases and statistical units of the local authorities.

Ethics and Consent

To collect and store data, the registry requires ethics committee approval from the Ethics Committee of the Children's University Hospital Zagreb and Ethics

Committee of Medical School University of Zagreb. Approval is renewed every 5 years.

National legislation will probably require informed consent to register a baby with a congenital anomaly in the near future. At present, the registry collects data as hospital statistics needed for public health planning; for this we do not need informed consent for each case.

There is a possibility of case identification at the local level to avoid duplicate registration, to allow updating of information or diagnosis, and to assist children and their families in the future. The Zagreb Registry sends anonymous computerized data with a local serial number for each case for the use in communication with the local registries to the Central Registry. Safety measures are established to prevent unauthorized use of the records.

Electronic and Web-based Data Capture

The Zagreb registry does not receive electronic data or perfom web-based data capture.

Recent Registry Activities and Publications (2007–2010)

The Zagreb registry is a part of the referral center of the Ministry of Health and Social Welfare for Surveillance of Congenital Anomalies in the Republic of Croatia, located at the Children's University Hospital Zagreb. Activities in our registry include:

- Epidemiologic surveillance of congenital anomalies in Croatia.
- Center of expertise for rare genetic disorders in children – diagnostics (including clinical evaluation, cytogenetic, and molecular testing), multidisciplinary care for children affected with genetic disorders, and genetic counseling of families at risk.
- Primary prevention of congenital anomalies (investigation of fetal alcohol syndrome and use of folic acid supplementation in Croatia).
- Research in the field of genetic disorders (international projects EUROCAT, EUROPLAN, Projects of the Croatian Ministry of Science Education and Sports: Research on the Genetic Basis of Diseases in Childhood – Epidemiologic and Genetic Basis of Birth Defects, Telomeres, and chromosomal aberrations in childhood developmental disorders, celiac disease in children, and prevention and pathogenesis of chromosome instability).
- Participation in graduate and postgraduate training in genetics at Zagreb University School of Medicine, Zagreb University School of Pharmacy and Biochemistry, and Zagreb University School of Education and Rehabilitation Sciences.
- Organization of continuous medical training in the field of genetics at the University of Zagreb School of Medicine.
- Organization of congresses and symposia (Balkan Meeting of Human Genetics, 2009; Genes and Autism, 2010).
- Development of information for patients, health professionals, and the general public on genetic disorders.
- Partnership and collaboration with patientś organizations (e.g., The Croatian Society of Patients with Rare Diseases, Prader Willi Association, Croatian Association for Osteogenesis Imperfecta, Croatian Epidermolysis Bullosa Association, etc).
- Development of the National Plan for Rare Diseases (registry leader is a president of the interdisciplinary Committee for the Development and Implementation of the National Plan for Rare Diseases in Croatia).

A list of registry publications is available at the website of Croatian scientific bibliography: http://bib.irb.hr/lista-radova?sif_proj=072-1083107-0365&period=2007&lang=EN.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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CZECH REPUBLIC – ASSOCIATE MEMBER

History and Funding

The unofficial registration of congenital anomalies started in 1961 but the official population-covering registration in former Czechoslovakia started in 1964. The registration itself is compulsory and financed by the Government (Ministry of Health). The registry joined EUROCAT in 2009.

Population Coverage

The registry is population-based. Currently the Czech Republic is consisting of 13 regions and the capital, Prague (with regional status). The regions can be further divided into 76 districts in total. The population of the Czech Republic is approximately 10,509,377 inhabitants (March 31, 2010). The annual number of livebirths has increased to the current annual 120,000 livebirths (119,570 livebirths in 2008).

Sources of Ascertainment

The registry has multiple sources. The cases of the congenital anomalies are reported via the official reporting form. The reporting form is filled in by the medical doctor who first diagnosed the anomaly – most of the reports come from delivery units, pediatric and neonatology departments, departments of medical genetics (including cytogenetic and molecular-genetic laboratories), departments of ultrasound diagnostics, and surgery departments (cardio surgery, plastic surgery). Pediatric cardiology centers supply systematic case lists and some diagnostic details to the registry. Cytogenetic laboratories provide reports on both prenatally and postnatally diagnosed cases of congenital anomalies. All diagnoses from the XVII chapter of the ICD-10 (group Q00-Q99) are reported. We do not receive the verbal description of the reported anomalies, nor do we receive the complete lists

of pathologic karyotypes from cytogenetic laboratories. The ICD-10 (sub)code is the key. The age limit for the registration is 15 years; the prenatally diagnosed cases, cases in stillbirths, and cases in spontaneous abortions weighing over 500 g are also reported.

The reporting forms are collected in the Institute of Health Information and Statistics of the Czech Republic (UZIS CR, http://www.uzis.cz/), where the data are cleaned and the central database is created. The National Registry of the Congenital Anomalies is the part of The National Health Information System of the Czech Republic administered by UZIS. The reporting of a congenital anomaly is compulsory and does not require an informed consent.

Termination of Pregnancy

Termination of pregnancy is legal in the Czech Republic. After the 12th week of gestation, the termination of pregnancy is limited to the genetic indications. After the 24th week of gestation, the pregnancy can be terminated only if the mother's life is at risk.

Stillbirth Definition and Early Fetal Deaths

Stillbirth definition: non-viable fetuses, >28 weeks and >1000 g of weight. Early fetal deaths/spontaneous abortions definition: fetuses showing no signs of life, <28 weeks and <1000 g of weight, or fetuses showing one or more signs of life but <500 g and not surviving 24 hours after birth.

Cases in stillbirths and some cases in spontaneous abortions weighing over 500 g are also reported.

Exposure Data Availability

Maternal and paternal age and occupation, drugs in pregnancy (coded with the ATC (Anatomical Therapeutic Chemical classification system)), gravidity, and parity order.

Denominators and Controls Information

The information on all newborns born in the Czech Republic is available in the Czech Statistical Institute (http://www.czso.cz/) and Institute of the Health Information and Statistics of the Czech Republic (UZIS). The following information is available: birth weight, birth length, maternal and paternal age, birth date, and birth place.

Registry Description References

Sipek A, Gregor V, Horácek J, Masátová D. 2003. [Routine monitoring of congenital defects in children in the Czech Republic. History and present status]. [Article in Czech] Ceska Gynekol 68:71–80.

Sípek A, Gregor V, Horácek J, et al. 2009. [History and present of registration of congenital anomalies in the Czech Republic]. [Article in Czech] Cas Lek Cesk 148:505–509.

Ethics and Consent

The registry does not require ethics committee approval to collect and store data. Ethics committee approval is only required for some projects that use identifiable registry data (more complex studies, where other data sources are used).

National legislation does not require informed consent to register a baby with a congenital anomaly. Data from the National Registry of Newborns and from the National Registry of Mothers are also used. These registries do not require informed consent for data collection. Data collection is compulsory according to the internal law of the Ministry of Health of the Czech Republic.

Electronic and Web-based Data Capture

The registration process is based on the paper forms and paper reports. The electronic/web-based data collecting system is in preparation.

Recent Registry Activities and Publications (2007–2010)

Calda P, Sípek A, Gregor V. 2010. Gradual implementation of first trimester screening in a population with a prior screening strategy: population based cohort study. Acta Obstet Gynecol Scand 89:1029–1033.

Gregor V, Sípek A, Calda P, et al. 2008. [Ultrasound prenatal diagnostics of birth defects in the Czech Republic in 1994-2007]. [Article in Czech] Ceska Gynekol 73:340–350.

Gregor V, Sípek A, Horácek J, et al. 2008. [The analysis of incidence of selected types of bird defects in the Czech Republic according to a multiplicity of pregnancy]. [Article in Czech] Ceska Gynekol 73:199–208.

Gregor V, Sípek A, Sípek A Jr, et al. 2009. [Prenatal diagnostics of chromosomal aberrations Czech Republic: 1994-2007]. [Article in Czech] Ceska Gynekol 74:44–54.

Sípek A, Gregor V, Horácek J. 2007. [Birth defects in the Czech Republic in the period 1994 - 2005–perinatology data]. [Article in Czech] Ceska Gynekol 72:103–109.

Sípek A, Gregor V, Horácek J, et al. 2009. [Birth defects incidence in children from single and twin pregnancies in the Czech Republic–current data]. [Article in Czech] Ceska Gynekol 74:369–382.

Sípek A, Gregor V, Sípek A Jr, et al. 2010. [Incidence of congenital heart defects in the Czech Republic–current data]. [Article in Czech] Ceska Gynekol 75:221–242.

Sípek A, Malis J, Stěrba J, et al. 2009. [Tumors in children with birth defects. Current data from the Czech Republic]. [Article in Czech] Ceska Gynekol 74:105–117.

Quarterly reports are published electronically and are available on the registry's website: http://www.vrozene-vady.cz/congenital-anomalies/index.php?co=reports.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

None yet.

Address for Further Information

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Jiri Horacek, E-mail: jiri.horacek@gennet.cz.

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Antonin Sipek Jr., E-mail: admin@vrozene-vady.cz.

DENMARK, ODENSE – FULL MEMBER

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.

Population Coverage

The registry covers the 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 5600. Births take place in three hospitals with homebirths <1% of all births.

Sources of Ascertainment

The registry is based on active case finding. Data sources for the registry include electronic discharge and outpatient diagnosis from obstetric and pediatric departments, obstetric and pediatric hospital records with data on surgeries, and examinations performed on the cases (x-ray, magnetic resonance scans, and echocardiography), birth notifications, death certificates, postmortem examinations, and data from the cytogenetic laboratory.

The registry receives an annual list of all abnormal karyotypes diagnosed prenatally.

The outpatient list of diagnosis from the pediatric department includes diagnosis from the pediatric cardiology center.

Maximum Age at Diagnosis

Up to 5 years for cases seen at a pediatric department.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal before 12 weeks gestation without special permission. After 12 weeks of gestation, termination of pregnancy may be performed after permission from a local committee. If a congenital anomaly is diagnosed, the upper gestational age for termination is usually before viability. If a lethal malformation is diagnosed after fetal viability, it may be possible to have permission to induce the birth. Terminations of pregnancy for fetal anomalies are registered in the EUROCAT registry.

Stillbirth Definition and Early Fetal Deaths

From the beginning of the registry, stillbirth definition was gestational age ≥28 weeks. From April 2004, the stillbirth definition was changed to gestational age ≥22 weeks. Stillbirths and fetal deaths/spontaneous abortions from 20 weeks are registered in the EUROCAT registry. The autopsy rate in stillbirths is around 70%.

Exposure Data Availability

Exposure information: maternal occupation, 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 (www.statistikbanken.dk).

Registry Description References

Garne E. 2004. Congenital heart defects – occurrence, surgery and prognosis in a Danish County. Scand Cardiovasc J 38:357–362.

Garne E. 2006. Atrial and ventricular septal defects - epidemiology and spontaneous closure. J Matern Fetal Neonatal Med 19:271–276.

Ethics and Consent

The registry does not require ethics committee approval to collect and store data. The registry needs official approval for the database www.datatilsynet.dk.

National legislation does not require informed consent to register a case with a congenital anomaly.

Address for Further Information

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FINLAND – ASSOCIATE MEMBER

History and Funding

The national Malformation Register was established in 1963 and regular monitoring started in 1977. In 1974, the registry became a full member of the International Clearinghouse of Birth Defects Surveillance and Research (ICBDSR), and in 1998, it became an associate member of EUROCAT. The registry system (data collection) has been changed three times, in 1985, in 1993 and in 2005. The activities of the registry are regulated by specific law and statute on national health care registers that hold personal data. It is run and financed by THL (the governmental National Institute 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 defined geographic area. All births in Finland are covered, representing approximately 60,000 births annually. Selective terminations of pregnancy and spontaneous abortions with malformations have 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 (confirmation of the cases). The Pediatric Cardiology Center operating all pediatric heart defects supplies systematic case data with diagnostic details to the registry. Case information is also received from the national Medical Birth Register, Abortion Register, Hospital Discharge Register, and the Cause-of-Death Register. The diagnoses of the malformation cases received from other sources are confirmed from the hospitals. Informa-

tion on malformations is principally collected up to 1 year of age, but later information is also included. Aggregated data is transmitted to ICBDSR and EUROCAT.

Maximum Age at Diagnosis

Up to 1 year of age for surveillance purposes, but later diagnoses are also registered.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal. Termination of pregnancy for fetal reasons (severe congenital anomaly, other birth defect, or disease) can only be granted by a special permission from the National Supervisory Authority for Welfare and Health (Valvira). At the gestational age from >20 + 0 up to ≤24 + 0 weeks, termination of pregnancy can only be granted by Valvira'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 (≥22 + 0) or 500 g of birth weight (≥500 g) 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

Before 1986, extensive exposure information was obtained from maternity health centers and by personal interview for selected malformations and their controls. From 1987 to 1992, only parental occupation was reported. Exposure information, like maternal occupation, medication, x-rays, and diseases, 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

Epidemiologic background data are available on all births in the Medical Birth Register and in the Statistics Finland.

Registry Description References

More information on the registry can be found in the THL website in English: http://www.thl.fi/statistics/congenitalmalformations.

Ethics and Consent

According to the Act on Nationwide Health Care Registers and the Person Data Act, no informed consent is needed for collection of identifiable case data into the national health care registers (these registers are specified by the law and statutes). Thus, no informed consent is required to register a baby with a congenital anomaly into the registry. It is not allowed for the registry to contact the registered persons or their families. Because of the legislation, ethics committee approval to collect and store data in the national health care registers is neither required. It is obligatory for the health care personnel to notify the malformed cases.

It is possible to use the case data in the national health care registers for scientific studies with specific permission from the register administrators (governmental authorities like THL). The data protection authority also gives a statement on each study. Studies using only register data from national registers +/- hospital registers do not require ethical approval, but while it is not obligatory, it usually is highly recommended. Encrypted unidentifiable data are always preferably given out by THL instead of identifiable case data.

Address for Further Information

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FRANCE, ILE DE LA REUNION – FULL MEMBER

History and Funding

The registry was established in 2001 and has contributed data to EUROCAT from 2002 onward. The registry was funded by a private organization – Conseil General du Department (Provincial Council) until 2005, and since 2006, by a public organization: Agence Régionale d'Hospitalization regional agency for hospital care, and is run under guidance from a steering committee. Its qualification was obtained from INSERM and French Institute of Disease Monitoring (INVS) since November 18, 2008, and the registry was held by INVS and INSERM since 2009. The main purposes of the registry are to produce prevalence statistics, audit prenatal screening, assess reported clusters of environmental exposures, and to detect new teratogenic exposures.

Population Coverage

The registry is population-based III which is all mothers delivering in Isle of Reunion excluding non-residents. The registry covers an average of 14,650 births per year.

Sources of Ascertainment

Reporting is voluntary. Notification of cases to the registry comes from hospitals and other private institutions. Ascertainment is assisted by active searching of patient notes by registry staff. Ascertainment of cases by hospital doctors is thought to be virtually 100%. Sources include maternity units, pediatric departments, prenatal screening, pathology laboratories, cytogenetic laboratories, medical genetics, pediatric surgery, and cardiology units. Cases are registered if diagnosed before birth, at birth, or during the first year of life. All malformed babies are followed up until 1 year of age, especially cases with cardiac and urinary malformations, but ascertainment of these cases may be incomplete if the malformation is not prenatally diagnosed or the case is not seen at a hospital.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy has been legal in Isle of Reunion since 1975 and recorded by the registry since 2002. There is no upper limit on gestation age at termination. Information on terminations is provided by official legal pluridisciplinary prenatal diagnosis centers. There is a national prenatal screening policy.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is: gestational age >20 weeks of pregnancy. Gestational age of 14 weeks is the lowest age to be included as a fetal death/spontaneous abortion in the register. Autopsies may be carried out on stillbirths, early fetal deaths, and termination of pregnancies.

Exposure Data Availability

Exposure data (occupation of mother, assisted conception, illness before and during pregnancy, and drug use throughout pregnancy) are routinely recorded to a good degree of completeness and accuracy.

Denominators and Controls Information

National birth statistics are obtained from INSEE, the National Institute of Statistics and Economic Studies. Denominators can be provided by both maternal age and monthly distribution. Information is not available on controls.

Ethics and Consent

We propose a consent to parents before registration, with a respect of anonymous case, and without ethic approval. Informed consent is asked.

Electronic and Web-based Data Capture

Electronic and web-based data capture is not available for the registry.

Recent Registry Activities and Publications (2007–2010)

Bourdial H, Jamal-Bey K, Randrianaivo H, et al. Congenital cardiac malformations in Reunion Island from 2002 to 2007.

Letter N°30 of 20 November 2009 co-edited by ORS (Observatoire Régional de la Santé) and association ''Naitre Aujourd'hui'': indicators of trisomy 21 in Reunion Island during the period of 2003 to 2006. (National journey of the trisomy 21 of 22nd November 2009).

Letter N°2 of 11 February 2010 co-edited by ORS (Observatoire Régional de la Santé) and association ''Naitre Aujourd'hui'': indicators of congenital cardiopathy in Reunion Island (Journey of 14 February 2010 for sensibilisation to congénital cardiopathy).

Report on the register of congenital malformations of Reunion Island during the period 2002 to 2007. Co-editied by the Association ''Naître Aujourd'hui'' and the ORS.

Dietary request on the consommation of folates by women in age to procreation in Reunion Island for tube neural defects.

December 2008 saw the first meeting of the five French registries of congénital malformations. The program included presentations by J. L. Alessandri on Foetopathy with valproate, and Congenital diaphragmatic hernia and associated malformations by H. Randrianaivo on Foetopathy with Cytotec and by L. Lagarde and J. Baron on Trisomy 21 in Reunion Island.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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FRANCE, PARIS – FULL MEMBER

History and Funding

The registry was created in 1981 and it has 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 recognized by the French National Committee of Registries, and regularly renewed, most recently in 2008 for 4 years (2009–2012). The activities of the registry are partially supported by an annual grant from INSERM and Institut de la Veille Sanitaire (Institute for Health Surveillance).

Population Coverage

Until 2000, the registry population included all women residing in greater Paris (Paris and its surrounding suburbs) who delivered a baby in Paris maternity units (38,000 annual births). Beginning in 2001, the Paris population data for EUROCAT included only women residing in Paris and delivering in a Parisian maternity unit. The estimation of the coverage of the registry is around 95%.

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, the maximum age at diagnosis. Birth certificates include notification of congenital anomalies and are used as a source of notification. The registry systematically (at least once a year) consults the three main cytogenetic laboratories in Parisian hospitals.

By far, most cases of major congenital heart defects (CHDs) are diagnosed by specialized pediatric cardiology departments in our population or by prenatal ultrasound and/or autopsy reports for pregnancy terminations and fetal deaths. In addition, pediatric cardiology centers supply diagnostic confirmation when requested by the registry for specific cases.

Maximum Age at Diagnosis

Up to 1 week of age (or later if discharged from a maternity ward at a later date).

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal and there is no upper gestational age limit for termination after diagnosis of congenital anomaly. All terminations of pregnancy regardless of the gestational age at termination are registered.

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.

Exposure Data Availability

Information on maternal drug use, maternal and paternal diseases and occupations, and 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).

Registry Description References

Detailed description of the registry may be found in the following publications:

De Vigan C, Khoshnood B, Cadio E, et al. Le Registre des malformations de Paris : un outil pour la surveillance des malformations et l'évaluation de leur prise en charge. BEH Juillet 2008. (http://www.invs.sante.fr/beh/2008/28_29/index.htm).

De Vigan C, Khoshnood B, Lhomme A, et al. 2005. [Prevalence and prenatal diagnosis of congenital malformations in the Parisian population: twenty years of surveillance by the Paris Registry of congenital malformations.] J Gynecol Obstet Biol Reprod (Paris) 34(1 Pt 1):8–16.

Khoshnood B, Lelong N, Vodovar V, et al. Surveillance épidémiologique et diagnostic prénatal des malformations: Evolution sur vingt-sept ans (1981–2007), Registre des malformations congénitales de Paris, Juillet 2010 (http://www.u953.idf.inserm.fr/page.asp?page=4247).

Ethics and Consent

The registry requires ethics committee approval from the French National Committee of Freedom and Informatics (CNIL) to collect and store data. Review of procedures regarding confidentiality of data of the Paris Registry is overseen by both the French National Committee of Registries and the French National Committee of Informatics and Freedom.

The registry is allowed to register cases without explicit written consent of parents. Information letters are sent to chief of services for them to post in waiting rooms, patient rooms, or other areas of the maternity ward to inform parents that anonymous data are recorded for cases of congenital anomalies.

Electronic and Web-based Data Capture

None at this time.

Recent Registry Activities and Publications (2007–2010)

Our previous studies included population-based evaluations of prenatal diagnosis and pregnancy terminations for Down syndrome (Khoshnood et al., 2008; BJOG, 2004, Am J Public Health, 2004, Am J Public Health, 2006). In particular, we examined socioeconomic differences in the prenatal diagnosis and livebirth prevalence of Down syndrome. We also studied trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with CHDs (Khoshnood et al., 2008; Pediatrics, 2005).

Our main focus of research activities in the coming years will be on CHDs and particularly analysis of a cohort study of outcomes for children with CHD (the EPICARD study). We are also looking at the prevalence, prenatal diagnosis, and pregnancy terminations for CHD in both our registry data and in EPICARD. Another project is focused on studying the risks associated with assisted reproductive technologies; two ongoing studies are related to CHD and neural tube defects. We will also pursue our studies of the modalities of prenatal testing for Down syndrome and for CHD, in particular population-based evaluations of the performance of various prenatal tests/strategies of testing, in our population.

Registry Publications (2007–2010)

Bloch J, Cans C, deVigan C, et al. 2008. [Feasibility of the foetal alcool syndrome surveillance]. [Article in French] Arch Pediatr 15:507–509.

del Carmen Saucedo M, DeVigan C, Vodovar V, et al. 2009. Measurement of nuchal translucency and the prenatal diagnosis of Down syndrome. Obstet Gynecol 114:829–838.

de Vigan C, Khoshnood B, Cadio E, et al. 2008. [Prenatal diagnosis and prevalence of Down syndrome in the Parisian population, 2001-2005]. [Article in French] Gynecol Obstet Fertil 36:146–150.

Khoshnood B, De Vigan C, Blondel B, et al. 2008. Long-term trends for socio-economic differences in prenatal diagnosis of Down syndrome: diffusion of services or persistence of disparities? BJOG 115:1087–1095.

Verret C, Jutand MA, De Vigan C, et al. 2008. Reproductuve health and pregnancy outcomes among French gulf war veterans. BMC Public Health 8:141.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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FRANCE, RHONE–ALPS – ASSOCIATE MEMBER

History and Funding

The Central East Registry began in 1973 within the Rhone–Alps area – the Auvergne region was added in 1983, the Jura area in 1985, the Cote d'Or & Nievre in 1989, and Saone-et-Loire in 1990. The registry joined EUROCAT as an associate member in 1999, and sent data backdated to 1980. 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 Central East France Registry is maintained and common results are to be published. At the start of 2007, the registry was renamed REMERA and limited to Rhone–Alpes region. Since January 2007, the financial support is provided only by public funds: by the Rhone–Alpes Region authority, the INVS, the French Health Products Safety Agency (AFSSAPS), the National Institute of Health and Medical Research (INSERM), and the Conseil Général of Isère.

Population Coverage

The registry is population-based II where all mothers delivering within a 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 area are included as well. The registry covers the Rhone–Alps region, with approximately 57,500 births annually which represents about 7% of all births in France. The geographic region changed over time as follows: Rhone–Alps was included from 1976 onward, Auvergne from 1983 to 1999, Jura from 1985 onward, Cote d'Or and Nievre from 1989 onward, and Saone-et-Loire from 1990 onward. From 2007, the registry is limited to a part of Rhone–Alpes region: Rhône, Loire, Isère, Savoie.

Sources of Ascertainment

Notification to the registry is voluntary. Reports are collected from multiple sources: maternity unit records, pediatric records, cytogenetic laboratory, pathology laboratory, child health services, specialized departments for medical genetics, pediatric surgeons, and birth notifications. We have difficulties accessing the pediatric cardiology department of one hospital in our region. Consequently, there will be some cases that are not reported. Active registration is performed by four data collectors assigned specifically to about 35 sources each. Confirmatory sources: every year a list of abnormal karyotypes is sent by cytogenetic laboratories, and copies of pathology reports are systematically sent to the registry if malformations are present. At least more than 145 sources collaborate with the registry. Infants up to the age of 1 year old are registered, as well as fetuses delivered after medical abortion. A cutoff 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 when noticed by the persons in charge of data collection in hospitals. 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, and inguinal and umbilical hernias). Aggregated data is transmitted to EUROCAT.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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 and early fetal death/spontaneous abortions are registered from 20 weeks' gestation onward. Before 1997, stillbirths were registered at 28 weeks or more after the last menstrual period. Stillbirth and infant death certificates are not routinely available as a source. 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, and diseases 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.

Registry Description References

See the description in the following link: http://www.invs.sante.fr/beh/2008/28_29/beh_28_29_2008.pdf.

Ethics and Consent

The registry does require ethics committee approval to collect and store data and this approval comes from the Commission Nationale Informatique et Liberte (CNIL) + Comite Consultatif du Traitement de l'Information Recherche en Sante. Approval has to be checked or renewed when there is a change in the database.

National legislation requires informed consent to register a baby with a congenital anomaly. Parents have to ask for removal of the child from the register (opt-out).

Electronic and Web-based Data Capture

The registry does not receive any electronic downloads. Nurses or midwives gather data on a daily or weekly basis in public and private hospital units using a laptop computer. To address the problem of security and management of the database, the registry decided to delegate the installation, configuration, hosting, maintenance, and monitoring of the server to the company Altitude Telecom, which provides a dedicated high security server REMERA. An integrated REMERA ''all web'' system has been developed internally to better meet the requirements of the profession, the aim being to have a unique up-to-date register reference available at all times to authorized persons. This highly secure intranet consists of management applications and query options to the database of registry tables and references (medical and geographical).

Like any web solution, it is based on a client/server system. The server is a DELL 1950 1U Linux housed in a clean room on a site with secure access, with proactive supervision, a 99.9% availability rate, 4H guaranteed recovery time, and with progressive and corrective maintenance. A production environment and an environment of pre-production exist and separate daily backups are performed.

Exchanges between client and server takes place through a virtual private network that guarantees the sealing of data traffic flow. We also use the web applications in secure mode, which requires a certificate of authenticity of the client and encryption. In addition, all personal information is encrypted in the database.

Recent Registry Activities and Publications (2007–2010)

Cordier S, Lehébel A, Amar E, et al. 2010. Maternal residence near municipal waste incinerators and the risk of urinary tract birth defects. Occup Environ Med 67:493–499.

Garne E, Dolk H, Krägeloh–Mann I, et al. 2008.Cerebral palsy and congenital malformations. Eur J Paediatr Neurol 12:82–88.

Tomson T, Battino D, French J, et al. 2007. Antiepileptic drug exposure and major congenital malformations: the role of pregnancy registries. Epilepsy Behav 11:277–282.

Perthus I, Amar E, De Vigan C, et al. 2008. État des lieux des registres de malformations congénitales en France en 2008. BEH 28–29:246–248.

Amar E. 2008. Création d'un registre: exemple du Registre des malformations en Rhône-Alpes (Remera). BEH 28–29:249.

Perthus I, de Brosses L, Amar E, Francannet C. 2008. La vérification du caryotype fetal est-elle justifiée devant la découverte anténatale de pieds varus équins isolés? BEH 28–29:258–260.

Leoncini E, Baranello G, Orioli IM, et al. 2008. Frequency of holoprosencephaly in the International Clearinghouse Birth Defects Surveillance Systems: searching for population variations. Birth Defects Res A Clin Mol Teratol 82:585–591.

Weber–Schoendorfer C, Hannemann D, Meister R, et al. 2008. The safety of calcium channel blockers during pregnancy: a prospective, multicenter, observational study. Reprod Toxicol 26:24–30.

Chevrier C, Bahuau M, Perret C, et al. 2008. Genetic susceptibilities in the association between maternal exposure to tobacco smoke and the risk of nonsyndromic oral cleft. Am J Med Genet A 146A:2396–2406.

Cordier S, Lehébel A, Amar E, et al. 2008. Maternal residence near municipal waste incinerators and risk of urinary tract birth defects. Epidemiology 19:S234.

Cordier S, Léhebel A, Amar E, et al. 2010. Maternal residence near municipal waste incinerators and risk of urinary tract birth defects. Occup Environ Med 67:493–499.

Rankin J, Cans C, Garne E, et al. 2010. Congenital anomalies in children with cerebral palsy: a population-based record linkage study. Dev Med Child Neurol 52:345–351.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Emmanuelle Amar (leader of REMERA registry from 2007), Registre des Malformations en Rhône Alpes, Faculté de médecine Laennec, 7-9 rue Guillaume Paradin, 69372 Lyon, France. E-mail: emmanuelle.amar@remera.fr.

FRANCE, STRASBOURG – FULL MEMBER

History and Funding

The registry was started in 1979 and became a member of EUROCAT in 1982. The registry has been officially recognized by the French National Committee of Registries in 2007 for the next 3 years (2008–2010). It is partially supported by an annual grant from INSERM and Institut National de Veille Sanitaire (Institute for Health Surveillance).

Population Coverage

The registry is population-based III and includes all mothers delivering in the covering area, excluding non-residents. A total of 3.5% of non-residents give birth in the covered hospitals and 2% of the residents deliver outside the area. Up until 2004, the geographic area covered by the registry was the ''Department of Bas-Rhin'', Northeastern France, including Strasbourg, and covered about 13,500 births. Since 2005, the geographic area concerns the two departments of Alsace, ''Bas-Rhin'' and ''Haut-Rhin'', including urban and rural areas. The registry covers about 23,000 births which represents approximately 3% of all births in France.

Sources of Ascertainment

Registration is active. Sources of information are multiple including reports obtained from pediatricians, hospital discharge records, maternity records, fetal ultrasound screening, laboratory records (cytogenetic, molecular, and pathology), and specialized departments. Birth certificates include notification of congenital anomaly and are also used as a source of notification. The registry has direct access to cytogenetics laboratories; the laboratories do not

send data, but all prenatal and postnatal karyotypes are actively verified. Concerning heart malformations, there are two pediatric cardiology departments. The lists of all consultations including date and place of birth and parental address, age at the time of consultation, and diagnosis are easily available and compared to other pediatric or surgical reports.

Maximum Age at Diagnosis

Up to 2 years of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal and there is no upper gestational age limit set for either social terminations or terminations as a result of a 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 amenorrhea (20 weeks of gestation) gestation. There is no limit with regard to either gestational age or weight that impedes notification of a fetal death/spontaneous abortion to the registry. Stillbirths and fetal death/spontaneous abortions are registered. All autopsies are carried out by fetopathologists.

Exposure Data Availability

Information on maternal drug use, maternal and paternal diseases and occupations, and outcome of previous pregnancies is available for the malformed cases. The children are followed to the age of 2 years old.

Denominators and Controls Information

Background data on births are available from the National Institute of Statistics (INSEE).

Ethics and Consent

The registry does not require ethics committee approval to function but has approval of both Comite Consultatif du Traitement de l'Information Recherche en Sante and CNIL.

Individual parental consent is not systematically asked for but a parental information form is available in all care units.

Electronic and Web-based Data Capture

Our electronic database corresponds to the EUROCAT Data Management Program (EDMP) with some minor local modifications. Moreover, we collect data from several electronic sources of information:

- Electronic database from gynecologists named DIAMM (Dossier Informatisé Adaptatif Monde Médical).
- Local website from Strasbourg Hospital.

Recent Registry Activities and Publications (2007–2010)

Osteosclerotic bone dysplasia in siblings with a Fam20C mutation.

Fradin M, Stoetzel C, Muller J, et al. 2010. Osteosclerotic bone dysplasia in siblings with a Fam20C mutation. Clin Genet [Epub ahead of print].

Cocchi G, Gualdi S, Bower C, et al. 2010. International trends of Down syndrome 1993–2004: births in relation to maternal age and terminations of pregnancies. Birth Defects Res A Clin Mol Teratol 88:474–479.

Sananes N, Guigue V, Vayssiere C, et al. 2010. Contribution of 3D ultrasound and fetal face studies to the prenatal diagnosis of Pallister-Killian syndrome. J Matern Fetal Neonatal Med 23:558–562.

Bloch J, Cans C, de Vigan C, et al. 2008. [Feasibility of the fetal alcool syndrome surveillance]. [Article in French] Arch Pediatr 15:507–509. French.

Leoncini E, Baranello G, Orioli IM, et al. 2008. Frequency of holoprosencephaly in the International Clearinghouse Birth Defects Surveillance Systems: searching for population variations. Birth Defects Res A Clin Mol Teratol 82:585–591.

Doray B, Dott B, Cordier C, Dollfus H. 2008. Epidémiologie, génétique et diagnostic prénatal des malformations diaphragmatiques en Alsace, France. BEH 28–29:254–258.

International Meetings

Doray B. 2009. Fetal alcohol syndrome. Knowledge, training and experience of pediatricians, gynecologists and midwives in the care of fetal alcohol syndrome. EUROCAT Registry Leader Meeting. Bilbao.

Doray B. 2008. Fetal alcohol syndrome. Knowledge, training and experience of pediatricians and gynecologists in the care of fetal alcohol syndrome. Communication orale: 35th Annual Meeting of the International Clearinghouse for Birth Defects Surveillance and Research Padoue 13–17 September 2008.

Doray B, Dott B, Cordier C, et al. Ten years of congenital eye malformations in Alsace, north-eastern France (1995–2004). Epidemiologic and genetic study of 140 cases and evaluation of prenatal diagnosis. ISGEDR Strasbourg, 28–30 August 2008.

Doray B. 2008. Fetal alcohol syndrome. Animation d'un workshop sur le syndrome d'alcoolisation fetale à l'occasion du EUROCAT Registry Leaders' Meeting, Helsinki, June 2008.

Doray B, Dott B, Rinkenbach R, Dollfus H. 2007. Epidemiologic and genetic study and evaluation of prenatal diagnosis of oral clefts in Alsace, north-eastern France (1995-2004): analysis of 266 cases.

EUROCAT Registry Leaders' Meeting, Naples, 7–9 May 2007.

Doray B. Registry of Congenital Malformations of Alsace, France. EUROCAT Registry Leaders' Meeting, Graz, 9–10 June 2006.

National Meetings

Doray B. Microcéphalies syndromiques et métaboliques. XIIèmes Journées de la SOFFOET Strasbourg October 2008.

Doray B. Registre de Malformations et Dépistage. Communication orale dans le cadre du Séminaire Pierre Royer, Paris, 13–14 March 2008.

Doray B. Embryologie, Epidémiologie et Génétique des Malformations Oesophagiennes. Communication orale dans le cadre de la Société Française de Chirurgie Pédiatrique Mont Saint-Odile, 4–5 December 2006.

Local and Regional Seminars

Doray B. Trisomie 21. Epidémiologie, génétique, clinique et prise en charge. Communication dans le cadre d'un colloque sur les nouvelles procédures nationales de dépistage. CMCO, Schiltigheim. 16 October 2009.

Doray B. Syndrome d'Alcoolisation fetale. Réseau Maternité et Addictions. Journées de formation Erstein, 24 October 2008.

Doray B. Syndrome d'Alcoolisation Fetale. Communication orale dans le cadre d'une FMC Médecins Généralistes, Strasbourg, 24 January 2008.

Doray B. Syndrome d'Alcoolisation Fetale. Communication orale dans le cadre d'une FMC Médecins Pédiatres. Molsheim, 25 January 2007.

Doray B. Cardiologie et Génétique. Communication orale dans le cadre d'une FMC Médecins Cardiologues. Schiltigheim, December 2006.

Doray B. Génétique et Médecine Fetale. La quête de l'Enfant parfait? Communication orale dans le cadre des séminaires de réflexion éthique, Rosheim, May 2006.

Posters

Doray B, Badila–Timbolschi D, Cordier C, et al. Twelve years of esophageal malformations in Alsace (France): epidemiologic, genetic and clinical study and evaluation of prenatal diagnosis. First International Workshop about esophageageal atresia. Lille 27–28 May 2010.

Doray B, Badila–Timbolschi D, Dott B, et al. Etude épidémiologique et génétique et évaluation du diagnostic prénatal de la Trisomie 21 en Alsace: Analyze de 274 cas entre 1995 et 2004. Assises de Génétique Humaine et Médicale. Strasbourg, January 2010.

Doray B, Badila–Timbolschi D, Dott B, et al. Etude épidémiologique et évaluation du diagnostic prénatal des dysgonosomies en Alsace entre 1995 et 2004. Assises de Génétique Humaine et Médicale. Strasbourg, January 2010.

Doray B, Cordier C, Dott B, et al. Etude épidémiologique et génétique des malformations oculaires: analyze de 140 cas entre 1995 et 2004 à partir du Registre de Malformations Congénitales d'Alsace. Assises de Génétique Humaine et Médicale. Strasbourg, January 2010.

Doray B, Dott B, Cordier C, et al. Etude épidémiologique et génétique et évaluation du diagnostic prénatal de la trisomie 21 en Alsace: analyze de 279 cas entre 1995 et 2004. Communication affichée aux Journées de Médecine Fetale. Morzine, March 2009.

Doray B, Dott B, Cordier C, et al. Syndrome d'alcoolisation fetale : Connaissances et pratiques des pédiatres, gynécologues et sages-femmes d'Alsace. Communication affichée aux Journées de Médecine Fetale. Morzine, March 2009.

Doray B, Dott B, Cordier C, et al. Ten years of diaphragmatic malformations in Alsace, North-Eastern France: epidemiologic and clinical study and evaluation of prenatal diagnosis. Clearing House (ICDBMS) meeting, Padova, September 2008.

Doray B, Dott B, Favre R, et al. Etude épidémiologique et génétique et évaluation du diagnostic prénatal des malformations diaphragmatiques en Alsace: analyze de 65 cas entre 1995 et 2004. Communication affichée aux Journées de Médecine Fetale Morzine, April 2008.

Doray B, Dott B, Favre R, et al. Etude épidémiologique et génétique et évaluation du diagnostic prénatal des malformations diaphragmatiques en Alsace: analyze de 65 cas entre 1995 et 2004. Communication affichée aux deuxièmes Assises de Génétique Humaine et Médicale. Lille, January 2008.

Doray B, Dott B, Rinkenbach R, et al. Etude épidémiologique et génétique et évaluation du diagnostic prénatal des fentes oro-faciales en Alsace: analyze de 266 dossiers entre 1995 et 2004. Communication affichée aux deuxièmes Assises de Génétique Humaine et Médicale. Lille, January 2008.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Berenice Doray, Service de Genetique Medicale, Hopital de Hautepierre, Avenue Moliere, F-67098 Strasbourg Cedex, France. E-mail: Berenice.Doray@chru-strasbourg.fr; berenice.doray@neuf.fr.

GERMANY, MAINZ – FULL MEMBER

History and Funding

The Mainz Model was launched in 1990. The aim of this screening project was to determine prevalence and etiologic causes of birth defects. The registry and its associated research are funded by the Ministry of Health of the Federal Republic of Germany from 1990 to 1995 and by the Ministry of Labor, 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 and area of Rheinhesse (370,000 inhabitants; population coverage 94.7% in 2008 according to federal statistics office) of Rhineland–Palatinate in southwest Germany with approximately 3300 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, neonatology, 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 the heart, the 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 and terminations of pregnancy (voluntary) are also obtained from pathology reports. Information concerning terminations of pregnancy is obtained from pathology reports and from the one center in the district doing the final prenatal diagnosis. Cases of microcephaly are not transmitted to the EUROCAT Central Registry. Cases of hydronephrosis are available in more detailed diagnoses. Karyotyping in all suspicious and prenatally diagnosed cases in the monitored area is initiated by the registry. All cytogenic laboratory results are available for all relevant cases. All cases with prenatally detected signs or relevant medical history, as well as all suspicious children (clinics, persisting cardiac murmur for more than 3 days), are referred to the cardiology department for diagnosis. Pediatric cardiology centers supply diagnosis when requested by the registry.

Maximum Age at Diagnosis

Up to 1 week of age.

Termination of Pregnancy for Fetal Anomaly

Terminations of pregnancy after prenatal diagnosis are registered. Terminations of pregnancy for fetal malformation are performed in one of the hospitals and included in the data. It is relatively common for prenatal diagnosis of congenital anomalies not to result in a decision to terminate the pregnancy. Sixty percent of terminations have an autopsy examination as this is on a voluntary basis and these are not legally registered.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition in Germany is a baby born with no signs of life weighing >= 500 g. 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. Sources: the pregnancy pass filled out throughout pregnancy by the obstetrician and his staff and data collected by midwives 6 to 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.

Registry Description Reference

Queisser–Luft A, Stolz G, Wiesel A, et al. 2002. Malformations in newborn: results based on 30,940 infants and fetuses from the Mainz congenital birth defect monitoring system (1990–1998). Arch Gynecol Obstet 266:163–167.

Ethics and Consent

Informed consent to use all routinely acquired data for scientific research is part of the admission contract between the patient and the hospital and thus given (opt-in).

The registry requires approval from the ethics committee of Rhineland Palatinate since its beginning. The approval does not have to be checked or renewed periodically. The registry includes only pseudonymous data. An approval of the data protection committee is necessary ever since.

Electronic and Web-based Data Capture

Electronic data capture has been designed, planned implementation is scheduled in 2011.

Recent Registry Activities and Publications (2007–2010)

- Birth defects in the vicinity of nuclear power plants (2006–2009, under review 2010).
- Occupational maternal exposure to ionizing radiation in health care and birth defects in their offspring (under review 2010).
- Artificial reproductive techniques and birth defects (continuous).
- Feasibility on recruiting pregnant women in the second trimester (2008, for publication 2010).
- Gestational diabetes over time (2010, for publication 2011).
- Follow-up of a birth cohort (started January 2010).
- Developing a survey system to avoid familial/social child health dangers as soon as possible (started November 2010).

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Annette Queisser–Wahrendorf, and Awi Wiesel, Birth Registry Mainz Model, Children's Hospital, University Medical Center of the Johannes Gutenberg University Mainz, Langenbeckstr. 1, 55131 Mainz, Germany. E-mail: queisser@kinder.klinik.uni-mainz.de.

GERMANY, SAXONY–ANHALT – FULL MEMBER

History, Funding, and Legal Legitimacy

The registry joined EUROCAT in 1992. The registry started in 1980. The years 1980 to 1989 were funded by the Ministry of Health of former German Democratic

Republic. The years 1990 to 1992 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 Health and Social Affairs State of Saxony Anhalt, Germany. On December 11, 2009, a new law by the parliament of Saxony–Anhalt was unanimously adopted. In § 7 states: ''The Federal state of Saxony–Anhalt promotes the widespread detection of birth defects in babies under a permanent observation. The task of this observation was to identify data on the prevalence of congenital malformations and watch over a defined period of time, to analyze the scientific data, and to evaluate the effectiveness of measures for primary and secondary prevention.''

Population Coverage

The registry started in 1980 in the city of Magdeburg with about 4000 annual births. After that, there was a successive enlargement of the registry from 1981 to 1986. In 1981, we expanded to include some rural districts around the city of Magdeburg and this process continued until 1987 when we registered the whole area of the former ''District of Magdeburg'' (about 17,000 births per year). Then we had a stable system from 1987 to 1989, and then 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 of Germany. After the reunification, a similar process of territorial enlargement took place. In the year 2000, registration expanded to the entire Federal State of Saxony–Anhalt (21 districts and 3 major cities). In the year 2007, a reform reduced the 21 districts to 11 districts.

Saxony–Anhalt has 2.375 million inhabitants (March 31, 2009) and annual births at a rate of about 17,200 children (2009).

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

Sources of Ascertainment

Multiple sources, such as delivery units (January 1, 2010: 27 clinics), pediatric departments, laboratories, prenatal diagnostic centers, departments of pathology, and other specialities report children/fetuses with malformations and healthy children as a control group.

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 during pregnancy, including periconceptional folic acid intake) and the father is documented on a standardized documentation sheet. From 1987 onward, cases are registered if diagnosed with a congenital anomaly up to 1 year of age. The registry receives some results from cytogenetic laboratories but not through direct access or via electronic transfer. Some are received indirectly via gynecology or pediatric notes.

We get notification from the pediatric cardiology department and a regional cardiology outpatient clinic via our standardized form twice a year.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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 January 4, 1994, and >= 1000 g before 1994.

Exposure Data Availability

Maternal and paternal occupation, drugs in pregnancy (ATC coded), alcohol, nicotine, and 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 standardized documentation sheet is used.

Additional Services

Since January 8, 2006, the Malformation Monitoring Center is collecting and tracking the results of the newborn hearing screening in Saxony–Anhalt. This test is made regular in the delivery units.

We closely collaborate with the newborn screening center Saxony–Anhalt which is located at the Medical Faculty of Otto-von-Guericke University Magdeburg.

An annual report is available with results of malformation interpretation, newborn hearing screening, and newborn metabolic screening (in German). The report can be downloaded from our website.

Registry Description References

Krause H, Pötzsch S, Haβ HJ, et al. 2009. Ventrale Bauchwanddefekte – Darstellung der Entwicklung in Prävalenz und operativem Vorgehen anhand von Gastroschisis und Omphalozele. Zentralblatt für Chirurgie 6:524–531.

Pötzsch S, Hoyer–Schuschke J. 2009. Angeborene Fehlbildungen – Hintergrundwissen für die Beratung der Eltern. Die Hebamme 2:88–94.

Bade A, Rohden L von, Hoyer–Schuschke J, Pötzsch S. 2008. Ultraschallscreening des Schädels bei Neugeborenen – Pro und Kontra. Päd Praktische Pädiatrie 3:178–188.

Ethics and Consent

The registry has the ethics committee approval from the Medical Faculty, Otto-von-Guericke University, Magdeburg.

Because of the data protection law in Germany, since 1992, national legislation requires informed consent to register a baby with a congenital anomaly. Parents have to agree to the inclusion of the child on the Register (opt-in).

Electronic and Web-based Data Capture

The registry does not receive web-based data because of the data protection law.

Recent Registry Activities and Publications (2007–2010)

Lindinger A, Schwedler G, Hense HW, for the participants of the PAN study. 2010. Prevalence of congenital heart defects in newborns in Germany: results of the first registration year of the PAN study (July 2006 to June 2007). Klinische Pädiatrie 5:321–326.

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Pötzsch S, Bretschneider D, Hoyer–Schuschke J, et al. 2010. Neugeborenes mit frontonasaler Schwellung. Monatsschrift Kinderheilkunde 5:427–429.

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Hoyer–Schuschke J, Pötzsch S, Böttger R, et al. 2008. Kongenitale alveolar-kapilläre Dysplasie. Seltene Ursache der persistierenden pulmonalen Hypertension beim Neugeborenen. Monatsschrift Kinderheilkunde 1:57–62.

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Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Anke Rissmann, Malformation Monitoring Centre Saxony–Anhalt, Medical Faculty, Otto-von-Guericke University, Leipziger Strasse, Haus 39, D-39120 Magdeburg, Germany. E-mail: monz@med.ovgu.de. Website: http://www.angeborene-fehlbildungen.com.

IRELAND, CORK, AND KERRY – FULL MEMBER

History and Funding

The registry started in 1996 and was granted approved membership of EUROCAT in 1998. The Clinical Research Ethics Committee of the Cork Teaching Hospitals approved the registry for research. Staffing includes a part-time nurse/researcher plus a part-time specialist in public health medicine and surveillance scientist support. The Department of Health and Children through the Health Services Executive provides funding for the registry.

Population and Coverage

The registry covers the counties of Cork and Kerry in the southwest of Ireland (population-based, all mothers resident in a geographic area). In 2002, <1% of resident mothers gave birth outside the registry area. The total number of births each year is around 9950.

Sources of Ascertainment

The registry is based on active case finding. Data for the registry includes hospital records from obstetric and neonatal departments, antenatal and orthopedics outpatient letters, pediatric cardiology center (local outreach clinic), supplies systematic case lists, and diagnostic details to the registry, Hospital In-patient Enquiry Data (HIPE), birth notifications, stillbirth certificates, CSO data on deaths in children up to the age of 2 years and postmortem examinations. There is no direct access to a cytogenetics laboratory.

Maximum Age at Diagnosis

Seven years of age (this is under review at present).

Termination of Pregnancy for Fetal Anomaly

Abortion is illegal in Ireland. However, women in Ireland have the option to travel outside of Ireland for termination of pregnancy after prenatal diagnosis. Where information is available to the registry about these cases, they are included.

Stillbirth Definition and Early Fetal Deaths

Babies born without signs of life with a gestational age of >= 24 weeks or a weight of >= 500 g are registered. Early fetal deaths/spontaneous abortions are not registered. National autopsy rates for stillbirths and early neonatal death (0–7 days) have decreased due to controversy arising from the issue of consent.

Exposure Data Availability

Information on parental occupation, maternal drug use, smoking and alcohol use, illness during pregnancy, and outcome of previous pregnancies is gathered.

Denominators and Controls Information

Denominator data is available from the national CSO. The CSO now publishes national perinatal statistics in respect of all births annually and provides rates for the Republic of Ireland and is broken down by county.

Registry Description Reference

http://www.lenus.ie/hse/bitstream/10147/68034/1/Congenital%20Anomalies%20Newsletter%20%28final%29.pdf.

Ethics and Consent

Approval is required from an ethics committee representing medical, paramedical, legal, lay, and academic interests and is reviewed as indicated. Additional approval would be required for any studies that require identifiable patient data or the merging of data sources. To date, no such studies have been done.

National legislation does not require informed consent to register a baby with a congenital anomaly. No plans to introduce a requirement for informed consent – in accordance with long established practice for longitudinal population-based registers. Balance is in favor of public interests as minimal individual risk.

Electronic and Web-based Data Capture

Electronic download from:

1. HIPE once a year with 2 year delay.
2. CSO – Stillbirth certificates once a year with a 3 year delay and vital statistics data once a year with a 1 year delay.

Recent Registry Activities and Publications (2007–2010)

No journal articles, book chapters, or books. A local newsletter is published.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Mary O'Mahony, Specialist in Public Health Medicine, Department of Public Health, Health Service Executive – South, Sarsfield House, Sarsfield Road, Wilton, Cork, Ireland. E-mail: maryt.omahony@hse.ie.

IRELAND, DUBLIN – FULL MEMBER

History and Funding

The registry was established in 1979 and joined EUROCAT in 1980. The registry is located within the Quality and Clinical Care Directorate (Health Intelligence) of the Health Service Executive. Staffing includes a full-time pediatric nurse/researcher and a specialist in public health medicine who works part-time with the registry. In addition, there is limited secretarial support. Funding is provided by the Department of Health through the Health Service Executive.

Population Coverage

The registry is population-based I, which includes all mothers resident in the Health Service Executive area covering the counties of Dublin, Wicklow, and Kildare in the east of Ireland. A little more than one-third (25,000 births) of all births in Ireland occur in the area of coverage.

Sources of Ascertainment

There is surveillance of all livebirths and stillbirths. Children with a congenital anomaly are included in the registry when diagnosed up to the age of 5 years. Multiple sources of ascertainment are used, including information from maternity and pediatric hospitals, governmental vital statistics, medical genetics services, and hospital discharge information. As a consequence of data protection restrictions, most of the data used by the registry in the ascertainment of cases is anonymized. This is more a passive process than the active approach formerly used by the registry. As such, the use of multiple sources of ascertainment is, therefore, essential in the verification and validation of cases, but is more time consuming and has led to a time-delay in the ascertainment of many categories of anomaly. There is no electronic data access or transfer by the registry from data sources, nor web transfer process. The registry receives an anonymized case list with diagnoses from the local pediatric cardiology center; the center would include virtually all cases resident in the registry catchment area. The cytogenetic center within the region supplies an annual anonymized list to the registry of samples tested, with karyotyping and diagnostic details. The center includes the majority of samples tested within the registry population, although not all.

Maximum Age at Diagnosis

Up to the age of 5 years.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy for congenital anomaly is not legal 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 >= 500 g are registered. Early fetal deaths/spontaneous abortions are not registered. National autopsy rates only were available for 1999 for the following: stillbirths 50 to 60% and early neonatal death (0–7 days) 50 to 60%. There has been a decrease in the proportions having an autopsy in the registry catchment area to approximately 50% due to controversy arising from the issue of consent.

Exposure Data Availability

For each malformed infant reported, very limited or no information is given on certain exposures.

Denominators and Controls Information

Denominator data are supplied by the government body – the CSO. No information is available on controls.

Ethics and Consent

The registry operates according to Data Protection Legislation in Ireland/European Union. As the data on the vast majority of cases held by the registry are received on an anonymized basis, no consent is currently sought or required. No data are provided to third parties and any reports or papers using registry data are on an aggregate basis.

New national legislation on information governance in relation to all health data (including that obtained and held, and analyzed by registries) will be published by the Irish Government in late 2010. The legislation will provide the basis for the obtaining and use of all aspects of data/information, including ethical and confidentiality considerations. The precise contents of the Bill in relation to congenital anomaly registries were unknown by mid-2010, although submissions were made by the registry during the prior consultation period.

Electronic and Web-based Data Capture

The registry does not have access to electronic data held by other organizations. Likewise, there is no electronic data transfer, nor web transfer process, to the registry from its data sources.

Recent Registry Activities and Publications (2007–2010)

The main activity of the registry is to monitor trends and clusters on an ongoing basis in its catchment area. The registry has also been involved for many years in a number of collaborative research projects with EUROCAT and the International Clearinghouse for Birth Defects and Research, and has co-authored a number of research articles.

At a local level, the registry has carried out surveys on the use of folic acid by women in the periconceptional period, consequent to a high birth prevalence of neural tube defects historically in Ireland. The findings are documented in a number of journal publications in past years.

The registry has also examined the epidemiology of a number of other congenital anomalies over the past that have shown changes in trend or have been of special significance in an Irish context, including Down syndrome, gastroschisis, and neural tube defects.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

The registry collaborates on a regular and ongoing basis with EUROCAT in research projects on congenital anomalies and related issues. Recent collaborative published articles resulting from such research are shown in Table 2.

Address for Further Information

Bob McDonnell/Virginia Delany, Health Service Executive (HSE) Registry of Congenital Anomalies – East, Quality and Clinical Care Directorate, Room G29, Health Service Executive, Dr. Steeven's Hospital, Dublin 8, Ireland. E-mail: bob.mcdonnell@hse.ie/virginia.delaney@hse.ie.

IRELAND, SOUTH EAST – FULL MEMBER

History and Funding

The Southeast Ireland Congenital Anomaly Register was established in the year 2000 and data was retrospectively collected from 1997 onward. The Department of Health and Children funds the registry through the HSE.

Population Coverage

The registry is population-based and includes babies born to all mothers resident in the southeast. The registry covers approximately 6500 births per year, which represents 11% of all births in the Republic of Ireland.

Sources of Ascertainment

The registry is based on active case findings. A child with a malformation, born after January 1, 1997, can be registered at any age. There is no upper age limit imposed for registration of a case.

Multiple sources of data are used in ascertainment and verification of cases. They include:

- Child Health Information System.
- Death and Still Birth Certificates.
- Postmortem Examinations.
- Disability Care Allowance systems.
- Hospital Inpatient Enquiry System (HIPE).
- Cytogenetic Laboratories – no direct access, information received on an annual basis.
- Information from maternity and pediatric hospitals.

Pediatric cardiology centers do not supply information to the registry, but other sources of information cover pediatric cardiac surgery (i.e., copies of letters from pediatric cardiology centers in respect of each case are always available in medical notes at hospital level).

Medical notes are reviewed in each instance to assist in the confirmation of the diagnosis.

Registration covers babies born with prenatally diagnosed anomalies, affected fetuses spontaneously lost from 24 weeks gestation, or with a birth weight >500 g.

EUROCAT guidelines are adhered to in respect of inclusions and exclusions.

There has been a decrease in the proportions of stillbirths and early neonatal death (0-7 days) having an autopsy, due to controversy arising from the issue of consent.

Maximum Age at Diagnosis

There is no upper age limit.

Terminations of Pregnancy for Fetal Anomaly

Induced abortions are illegal in Ireland. We do not currently obtain information about terminations of pregnancy for fetal anomaly carried out under other jurisdictions.

Stillbirth Definition and Early Fetal Deaths

Registration covers affected fetuses spontaneously lost from 24 weeks' gestation or with a birth weight >500 g.

Exposure Data Availability

Maternal health, drug, and lifestyle exposure data is collected primarily from pediatric medical records.

Denominators and Controls Information

Denominator data is available from the national CSO.

Ethics and Consent

The registry requires ethics committee approval to collect and store data. This approval was sought at the time of setting up the registry and there has been no requirement for renewal of the approval.

Currently, consent is not obtained for inclusion of cases on the register. Women are given information antenatally, telling them about the register. New legislation (The Health Information Bill) due to be published in autumn 2010 will place new requirements on registers in the areas of data protection and consent.

Electronic and Web-based Data Capture

We currently have three electronic downloads of notifications:

1. HIPE (Hospital inpatient enquiry) system. We receive HIPE downloads on cases of congenital anomalies as soon as the data has been collected and quality audited at hospital level. This is conducted in a timely manner, for example, 2008 year's data will be available to us within the first 6 months of 2009. Any cases that do not have a confirmed diagnosis at that stage will be followed up by registry staff at a later date.
2. Cytogenetic laboratory electronic reports. We receive electronic reports on neonates, infants, and older children from the cytogenetic laboratories on an annual basis via another registry.
3. Oral clefts. We receive electronic reports on neonates and infants on an annual basis from a tertiary referral hospital that specializes in these cases.

Recent Registry Activities and Publications (2007–2010)

In addition to data collection and transmission to EUROCAT Central Registry, and contribution to studies via EUROCAT Central Registry, the Southeast Ireland registry is involved in educational activities, is linked in with EUROPLAN activities in Ireland, and is part of a national group with the other Irish EUROCAT registries under the auspices of the HSE National Directorate for Quality and Clinical Care.

'Congenital Anomalies in the East of Ireland 1997–2001'. Published by Eastern Regional Health Authority 2004; Authors Eastern Regional Health Authority, North Eastern Health Board, South Eastern Health Board.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Carmel Mullaney/Johanna Costigan, Department of Public Health, Health Service Executive – South, Lacken, Kilkenny, Ireland. E-mail: carmel.mullaney@hse.ie/johanna.costigan@hse.ie.

ITALY, EMILIA–ROMAGNA – FULL MEMBER

History and Funding

The registry started its activities in 1978 with the participation of a few collaborating centers rising to cover all delivery units in the region.

Since 1980, the registry is recognized and supported by the Emilia–Romagna region with the following objectives:

- To produce prevalence data on congenital malformations.
- To provide temporal and spatial surveillance and management for alarms.
- To conduct studies to evaluate health interventions (pre-natal and neonatal screening).
- To provide a reference center, both clinical and epidemiologic, for congenital malformations.

The registry joined EUROCAT in 1980 and in 1981 transmitted the first birth year of data to EUROCAT. The registry joined the International Clearinghouse for Birth Defects in 1995. The Emilia–Romagna Registry also participates in the coordination of the Italian Congenital Malformation Registries set up by The Italian National Institute for Health (l'Istituto Superiore di Sanità) with the aim of sharing the experiences of the various registries, create common lines of research, and produce epidemiologic data on congenital malformations at a national level (http://www.iss.it).

Since 2003, the registry has been in collaboration with the health information systems service and social policy body of the Emilia–Romagna region formally involved in the Scientific Steering Committee.

In 2004, a link with the Regional Medical Genetics Service network was formed (www.geneter.it) with the aim of providing genetic counseling and evaluating genetic conditions diagnosed within the network.

Population Coverage

The Emilia–Romagna region covers an area of 22,123 square killometers with a population of around 4 million people. The total number of births in the Emilia–Romagna region is growing with 42,397 births in 2008. The registry includes in its coverage the Republic of San Marino with 349 births in 2008.

The program is population-based II (includes all mothers delivering within the region of Emilia–Romagna, irrespective of place of residence). In 2008, 92.3% of births were to resident mothers. Since 2006, the registry, in collaboration with the Regional births database (CeDAP) has reached a population coverage ~100% involving all 34 delivery units in the region. In recent years, immigration has created an important demographic change with an increase in births. The births to non-Italian citizens represented 26.1% of the total births in the region in 2008.

Sources of Ascertainment

The Emilia–Romagna Registry has multiple sources of ascertainment:

1. Voluntary hospital participation. Reporting is carried out using the Emilia–Romagna Registry form by neonatologists, pediatricians, and obstetricians during the first week of the infant's life. We do not have specific notification from pediatric cardiology units. Pediatric cardiology centers supply diagnostic confirmation when requested by the registry for specific cases. Notification of a congenital anomaly is recorded up to 1 week. Selected malformations are followed up (e.g., Down syndrome, cardiovascular defects, and clefts). The clinical activities and genetic counseling conducted by medical geneticists who form part of the registry staff provides an opportunity to stimulate colleagues to notify cases.
2. The Regional Births database (CeDAP) also provides the registry with a source of denominator and control data.
3. The hospital discharge database Scheda di Dimissione Ospedaliera (SDO) provides further sources of ascertainment. This source can be used to investigate pediatric surgery cases for specific studies.

Birth certificates do not notify congenital anomalies. Death certificates do not allow for the notification of a congenital anomaly as a cause of death. We do not currently have direct access to cytogenetic laboratory results across the region but we are working toward this objective with the Regional Health Authority.

Maximum Age at Diagnosis

Up to 1 week of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy became legal in Italy in 1978. Termination is legal when there is no possibility of autonomous life for the fetus. The Italian law (L.N. 194/78) states that termination is allowed in the case of diagnosis of serious fetal pathology which may detrimentally affect the woman's physical or psychological health. The upper gestational age limit for terminations is 23 weeks. Induced abortions after prenatal diagnosis of birth defects are systematically included. Data for induced abortions first became available in 1982.

A ministerial decree (decreto 10.09.1998 GU no. 245 del 20.10.98) details a protocol covering laboratory and diagnostic tests for pregnant women (ultrasound, amniocentesis, chorionic villus sampling, and AFP/triple test). Three ultrasound examinations at 10, 20, and 30 weeks gestation are foreseen in the protocol. Cytogenetic testing is provided routinely for women over 35 years of age. After genetic counseling, cytogenetic and genetic testing are offered independent of age; these services are free of charge.

Stillbirth Definition and Early Fetal Deaths

The official definition of stillbirth in this registry is now 180 gestational days in line with the Regional Births database (CeDAP). Fetal deaths of 20 weeks or more gestation are systematically included (with no lower weight limit exclusion criteria). The autopsy rates in 2008 were: ~50% in stillbirths, ~60% 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 anomalies. A regional project on perinatal deaths is ongoing.

Exposure Data Availability

Exposure information is obtained by interviews of the mothers of malformed infants. From 2003, data regarding maternal drugs in the first trimester is recorded as ATC codes and jobs are recorded using the International Standard Classification of Occupations (ISCO) work codes. Previously, these data were recorded using internal codes.

Denominators and Controls Information

Birth statistics are provided by the Regional births database (CeDAP) recorded by maternal age group and birth month. This source also provides information for control cases. General demographic information is available for all births in the area (e.g., mean maternal and paternal ages, percentage of mothers 35 years or older). In recent years, immigration has created an important demographic change with an increase in births. As births to non-Italian citizens represented 26.3% of the total births in the region in 2006, the nationality of the mother is now coded for all births.

Further information regarding the reference population can be gained from the Emilia–Romagna region websitehttp://www.regione.emilia-romagna.it/index.htm.

Ethics and Consent

The registry is recognized as part of the health system information flow and regulated by regional laws. The

parents have to agree to the inclusion of the child on the register (opt-in).

Electronic and Web-based Data Capture

The registry website allows the participating centers to download a pdf of the case notification form but does not allow electronic data transmission. The majority of cases (75%) are still received from neonatologists, pediatricians, and obstetricians using the paper form. The Regional Births database (CeDAP) provides the registry with a source of denominator and control data and we receive an annual download of malformed cases. In November, we receive the file of the previous year so it has an 11-month delay. We also receive an electronic download annually for terminations during the second trimester. The delay for receiving data is around 9 months from year-end. The centers are then alerted to integrate the cases with further details from this summary data. Around 20% of cases are provided by this source. We do not receive regular downloads of data from the hospital discharge database (Scheda di Dimissione Ospedaliera) but we can request data for specific studies.

Recent Registry Activities and Publications (2007–2010)

II° IMER course: ''Aggiornamento sulla epidemiologia e percorsi diagnostico-assistenziali congenite'' Ferrara. 14 April 2007.

XXI IMER Congress ''30 anni di indagine sulle malformazioni congenite in Emilia Romagna'' Bologna. 11 April 2008.

XXII IMER Congress ''Le problematiche assistenziali del concepito con anomalie congenite multiple'' Bologna. 27 March 2009.

Neville A, Calzolari E. 2007.Womens knowledge of and uptake of folic acid for the prevention of neural tube defects. Workshop Network Italiano Promozione Acido Folico Prevenzione primaria di Difetti Congeniti. Istituto Superiore di Sanità Roma ISTISAN Congressi. Abstracts.

Astolfi G, Calzolari E, Cocchi G, et al. 2009. Rapporto annuale sulle malformazioni congenite – 2006. IMER Number 19.

Astolfi G, Calzolari E, Cocchi G, et al. 2008. Rapporto annuale sulle malformazioni congenite – 2005. IMER Number 18.

Astolfi G, Calzolari E, Cocchi G, et al. 2007. Rapporto annuale sulle malformazioni congenite – 2004. IMER Number 17.

Lisi A, Botto LD, Robert–Gnansia E, et al. 2010. Surveillance of adverse fetal effects of medications (SAFE-Med): findings from the international Clearinghouse of birth defects surveillance and research. Reprod Toxicol 29:433–442.

Ghirri P, Scaramuzzo RT, Bertelloni S, et al. 2009. Prevalence of hypospadias in Italy according to severity, gestational age and birthweight: an epidemiologic study. Ital J Pediatr 35:18.

Rittler M, López–Camelo JS, Castilla EE, et al. 2008. Preferential associations between oral clefts and other major congenital anomalies. Cleft Palate Craniofac J 45:525–532.

Leoncini E, Baranello G, Orioli IM, et al. 2008. Frequency of holoprosencephaly in the International Clearinghouse Birth Defects Surveillance Systems: searching for population variations. Birth Defects Res A Clin Mol Teratol 82:585–591.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Registry Staff and Computing

Professor Elisa Calzolari – Registry Leader (part time).
Dr. Gianni Astolfi – Database management (full time).
Dr. Amanda J Neville – EUROCAT coordinator (part time).

Address for Further Information

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ITALY, TUSCANY – FULL MEMBER

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 program included in the Regional Statistics System; it is formally recognized and supported by the Tuscany Region Health Authority. The registry joined EUROCAT in 1979.

Population Coverage

The program 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 29,000 births per year). Exchanges between regional informative systems indicate that 3.3% of resident mothers gave birth in a hospital outside Tuscany in 2007.

Sources and Ascertainment

Multiple sources are used to ascertain malformed infants; records are obtained from all obstetrical and maternity units, pediatric departments, pediatric cardiology departments, pediatric cardiac surgery units, prenatal diagnostic centers, medical genetics units, and pathology services. Pediatric cardiology centers covering part of the registry population supply systematic case lists and diagnostic details to the registry. Cytogenetic laboratories only confirm karyotype for cases already known. Mothers are interviewed by using a standardized questionnaire. Malformed babies diagnosed within the first year of life are also registered.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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 women'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.

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, with no lower weight limit exclusion criteria.

Exposure Data Availability

Maternal and paternal occupation, life-style and socio-economic characteristics are obtained by interviews of mothers of malformed infants.

Denominators and Controls Information

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

Ethics and Consent

The registry does not require ethics committee approval to collect and store data.

At the moment informed consent is not required by national legislation, but the registry asks for oral authorization from the mother, the parents have to agree to the inclusion of the child on the register (opt-in).

Electronic and Web-based Data Capture

Until 2009, personal and diagnosis information were transmitted separately by hard copy; from 2010, appointed gynecologists, neonatologists, and/or pediatricians of the maternity units and the centers of Pediatrics, Medical Genetics, Pediatric Cardiology, and Pediatric Cardiosurgery have a personal account and send data via web. Sensitive data are kept separate from medical information. For security, data are encrypted and transmitted across the internet network using the secure http protocol HTTPS, instead of the standard HTTP.

Recent Registry Activities and Publications (2007–2010)

Cocchi G, Gualdi S, Bower C, et al. 2010. International trends of Down syndrome 1993–2004: births in relation to maternal age and terminations of pregnancies. Birth Defects Res A Clin Mol Teratol 88:474–479.

Leoncini E, Botto LD, Cocchi G, et al. 2010. How valid are the rates of Down syndrome internationally? Findings from the International Clearinghouse for Birth Defects Surveillance and Research. Am J Med Genet A 152A: 1670–1680.

Mastroiacovo P, Working Group IP. 2010. Prevalence at birth of cleft lip with or without cleft palate. Data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). Cleft Palate Craniofac J [Epub ahead of print].

Lisi A, Botto LD, Robert–Gnansia E, et al. 2010. Surveillance of adverse fetal effects of medications (SAFE-Med): findings from the International Clearinghouse of birth defects surveillance and research. Reprod Toxicol 29:433–442.

EUROCAT. 2010. Special report: prenatal screening policies in Europe 2010. EUROCAT Central Registry, University of Ulster. http://www.eurocat-network.eu/content/Special-Report-Prenatal-Screening-Policies.pdf.

Salerno P, Bianchi F, Pierini A, et al. 2008. [Folic acid and congenital malformation: scientific evidence and public health strategies]. [Article in Italian] Ann Ig 20:519–530.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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MALTA – FULL MEMBER

History and Funding

The registry 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 January 1997, the Department of Health Information resumed the functions of the registry increasing coverage to all hospitals on the islands making it a national population-based register. The registry is now run and funded by the Government Department of Health Information and Research. The aim of the registry is to provide accurate epidemiologic information regarding the occurrence of congenital anomalies in Malta and Gozo.

Population Coverage

The registry is population-based 1: covering all resident mothers in Malta, Gozo, and Comino, and presently covers about 4000 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 considered 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

backdated 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 uses active data collection from multiple sources including delivery, obstetric, and pediatric wards, pediatric echo cardiology records, genetic clinics records, National Mortality Register, National Obstetric System database, Hospital Activity Analysis database, National Cancer Register, and the hypothyroid screening program. Voluntary reporting by doctors is also available. These sources cover the whole population of the Maltese Islands. Registry staff regularly visits the pediatric echo cardiology department to go through their records and identify cases. Consultant geneticists send the registry a list of positive genetic results on an annual basis.

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 in combination with other major defects. There is no legal requirement for notification of congenital anomalies without parental consent.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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, or a birth weight equal to or >500 g. 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 2009 were 57% for stillbirths and 32% for infant deaths.

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

Epidemiology background data on all births are available from the National Obstetric Information Systems database and the National Statistics Office.

Registry Description Reference

https://ehealth.gov.mt/HealthPortal/strategy_policy/healthinfor_research/registries/birth_defects.aspx.

Ethics and Consent

The Superintendant of Public Health, within his legal responsibility, requires that a Malta Congenital Anomalies Register be kept in the interest of public health (DH circular 36/09). Ethics committee approval is needed before data is released for individual studies, projects, or theses.

Malta became a member of the European Union in 2004 and complies with directive EC95/46. There is no national legislation requiring informed consent to register a baby with a congenital anomaly.

Electronic and Web-based Data Capture

Not yet available.

Recent Registry Activities and Publications (2007–2010)

Recent registry activities and publications for the Malta Registry can be found at: https://ehealth.gov.mt/HealthPortal/strategy_policy/healthinfor_research/registries/birth_defects.aspx.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Miriam Gatt, Malta Congenital Anomalies Registry, Department of Health Information and Research, 95 Guardamangia Hill, Guardamangia PTA 1313, Malta. E-mail: miriam.gatt@gov.mt.

NETHERLANDS, NORTH – FULL MEMBER

History and Funding

EUROCAT Northern Netherlands started in 1981, and was a member of the EUROCAT network since that year. The registry is funded by the Dutch Ministry of Health, Welfare, and Sports and is associated with the Department of Genetics of the University Medical Centre of Groningen (UMCG).

Population Coverage

The registry is population-based, including all mothers resident in the registration area. In the beginning, the program covered 7500 births annually in the province of Groningen and the northern part of the province of Drenthe. From 1989 onward, coverage was gradually increased to 20,000 births annually in the provinces of Groningen, Friesland, and Drenthe. In recent years, the number of births in the region decreased to 18,500, approximately 10% of all births in The Netherlands. Home deliveries (35% 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

Children and fetuses with congenital anomalies diagnosed before or after birth are eligible for registration at the EUROCAT Northern Netherlands registry, if the mother lived in the region at the time of birth and the child has not reached the age of 16 at notification. There is no lower limit for gestational age, spontaneous and induced abortions are included. Notification of children and fetuses with congenital anomalies is voluntary. Registry personnel are actively involved in case ascertainment, using multiple sources such as obstetric records,

hospital administration data, and pathology records. Cytogenetic laboratory results are electronically downloaded from the genetics department and include all abnormal karyotype reports, both from prenatal and postnatal samples. For cases reported to the registry, it is verified whether any genetic tests were performed and test results are registered in the database. The only pediatric cardiology center in the registration area, also part of the UMCG, supplies systematic case lists and diagnostic details to the registry. A number of frequently occurring mild anomalies is not registered unless they occur in combination with other serious congenital anomalies. If new information becomes available for registered children before 16 years of age, the files are updated.

Maximum Age at Diagnosis

Up to 16 years of age.

Termination of Pregnancy for Fetal Anomaly

TOPFA is legal. The upper age limit for termination of pregnancy (for social reasons and for fetal anomaly) is 24 weeks, based on the viability criteria. Termination of pregnancy after 24 weeks is allowed when the fetus is affected with a congenital anomaly that is considered lethal.

Stillbirth Definition and Early Fetal Deaths

A stillbirth is defined as a fetus of at least 24 weeks' gestation that died in the uterus or during birth. There are no age or weight limits for inclusion of early fetal deaths/spontaneous abortions. Autopsy rates per year are not available.

Exposure Data Availability

Since 1997, parents have been asked to fill out a questionnaire including questions on occupational activities, smoking habits, alcohol consumption, recreational drug use, and socioeconomic status. In addition, data from community pharmacies are used to collect data on medication dispensed in the period from 3 months before and during pregnancy. After the information of the pharmacy is received, a telephone interview with the mother is done to verify whether she has actually taken the medication dispensed from the pharmacy and if she has taken any over-the-counter medication. The response rate to the questionnaire is 80%.

Denominators and Controls Information

General statistics are available from the Central Bureau of Statistics. No information on non-malformed infants is collected.

Ethics and Consent

The registry does not require ethics committee approval to collect and store data. The registry operates within the scope of the Dutch data protection act (Wbp) and the Code of Good Conduct, set up by the Dutch Federation of Biomedical Scientific Societies. National legislation requires informed consent to register a baby with a congenital anomaly. Parents have to agree to the inclusion of the child on the register (opt-in). The positive response rate is 80%.

Electronic and Web-based Data Capture

Although the ascertainment of cases uses electronically derived lists of children with certain clinical diagnoses or cytogenetic laboratory results, no automatically electronic or web-based data capture has been implemented so far.

Recent Registry Activities and Publications (2007–2010)

The research activities are focused in particular on knowledge and use of folic acid and its protective effect on congenital malformations and on medication use in pregnancy. Selected local publications in international journals include:

Bakker MK, de Walle HE, Dequito A, et al. 2007. Selection of controls in case-control studies on maternal medication use and risk of birth defects. Birth Defects Res A Clin Mol Teratol 79:652–656.

de Walle HE, de Jong-van den Berg LT. 2007. Growing gap in folic acid intake with respect to level of education in the Netherlands. Community Genet 10:93–96.

Felix JF, Steegers–Theunissen RP, de Walle HE, et al. 2007. Esophageal atresia and tracheoesophageal fistula in children of women exposed to diethylstilbestrol in utero. Am J Obstet Gynecol 197:38.e1–38.e5.

Bakker MK, Kölling P, van den Berg PB, et al. 2008. Increase in use of selective serotonin reuptake inhibitors in pregnancy during the last decade, a population-based cohort study from the Netherlands. Br J Clin Pharmacol 65:600–606.

De Walle HE, de Jong–van den Berg LT. 2008. Ten years after the Dutch public health campaign on folic acid: the continuing challenge. Eur J Clin Pharmacol 64:539–543.

Bakker MK, De Walle HE, Wilffert B, de Jong–van den Berg LT. 2010. Fluoxetine and infantile hypertrophic pylorus stenosis: a signal from a birth defects-drug exposure surveillance study. Pharmacoepidemiol Drug Saf 19:808–813.

Bakker MK, Kerstjens–Frederikse WS, Buys CH, et al. 2010. First-trimester use of paroxetine and congenital heart defects: a population-based case-control study. Birth Defects Res A Clin Mol Teratol 88:94–100.

Jentink J, Bakker MK, Nijenhuis CM, et al. 2010. Does folic acid use decrease the risk for spina bifida after in utero exposure to valproic acid? Pharmacoepidemiol Drug Saf 19:803–807.

van Beynum IM, Kapusta L, Bakker MK, et al. 2010. Protective effect of periconceptional folic acid supplements on the risk of congenital heart defects: a registry-based case-control study in the northern Netherlands. Eur Heart J 31:464–471.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Marian Bakker, EUROCAT Northern Netherlands, Department of Genetics, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands. E-mail: eurocat@medgen.umcg.nl. Website: www.eurocatnederland.nl or www.geneticsgroningen.nl.

NORWAY – FULL MEMBER

History and Funding

The program ie, the Medical Birth Registry of Norway was started in 1967. The program is run and funded by the governmental National Institute of Public Health. The registry joined EUROCAT in 1998.

Population Coverage

The program is population-based and covers all mothers delivering within Norway, irrespective of place of residence, with approximately 58,000 annual births. Nonresident mothers delivering with the registry area account for approximately 0.2% of all births.

Sources of Ascertainment

Reporting to the registry is compulsory. The registry is based on the notification of births from the delivery units and, since 1999, also from the neonatal units for infants transferred to such units after birth. Congenital anomalies are registered up to 1 year of age and there is no maximum age for registration of mortality. Autopsy reports are collected for stillbirths with birth weight >500 g, and for TOPFAs where autopsy has been done.

The Medical Birth Registry of Norway (MBRN) does not currently receive direct notification from cytogenetic laboratories or specific notification from pediatric cardiology departments.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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 onward. If a congenital anomaly is diagnosed, the upper gestational age limit is 18 weeks (with exemptions). Since December 1, 1998, all TOPFAs are registered in the MBRN database. Autopsy reports are collected.

Stillbirth Definition and Early Fetal Deaths

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 onward. Official birth rates are published for births ≥22 weeks (or 425 g). 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 (with consent) is collected on all infants, malformed or not.

Denominator and Controls Information

All information available for the reported malformed infants is also available for the total population of births.

Registry Description Reference

Irgens LM. 2000. The Medical Birth Registry of Norway. Epidemiologic research and surveillance throughout 30 years. Acta Obstet Gynecol Scand 79:435–439.

Ethics and Consent

Research using anonymized data from the Medical Birth Registry are exempt from institutional review board approval in Norway. All studies must be approved by the Publication board at the Medical Birth Registry.

Electronic and Web-based Data Capture

Electronic notification to the registry was made compulsory from 2006, and by June 2010 was adopted for 82% of births. Notifications are transmitted as encrypted XML messages using the ''National Health Net'' for transportation, and with unique, specific certificates for all delivery units, neonatal intensive care units (NICUs), and the Medical Birth Registry. Notifications should be sent from delivery units to the Birth Registry within the first month after birth, and is usually sent daily, depending on the size of the delivery unit. Notifications from NICUs should be sent within 1 month after discharge. Reminders of missing notifications (based on records in the Central Population Registry, to which the MBRN is routinely linked) are sent to the delivery units each month.

In September 2010, there were three different software packages in use at the delivery units providing medical birth notifications, while all NICUs providing neonatal notifications used the same software.

Recent Registry Activities and Publications (2007–2010)

The main registry activities, outside research work, have been to establish electronic notification of births from all delivery units in the country, and to rebuild the registry's local database. Electronic notification is a prerequisite for another major goal at present: to publish updated institution-specific statistics, which may be used for quality work at the institutions. Some validation studies have been done, in addition to research activities in several fields, both within obstetrics and neonatology, birth defects, genetic epidemiology, and within the field of ''fetal origin of adult diseases''.

Eskedal LT, Hagemo PS, Eskild A, et al. 2007. A population-based study relevant to seasonal variations in causes of death in children undergoing surgery for congenital cardiac malformations. Cardiol Young 17:423–431.

Harville EW, Wilcox AJ, Lie RT, et al. 2007. Epidemiology of cleft palate alone and cleft palate with accompanying defects. Eur J Epidemiol 22:389–395.

Nguyen RH, Wilcox AJ, Moen BE, et al. 2007. Parent's occupation and isolated orofacial clefts in Norway: a population-based case-control study. Ann Epidemiol 17:763–771.

Sivertsen A, Lie RT, Wilcox AJ, et al. 2007. Prevalence of duplications and deletions of the 22q11 DiGeorge syndrome region in a population-based sample of infants with cleft palate. Am J Med Genet A 143:129–134.

Wilcox AJ, Lie RT, Solvoll K, et al. 2007. Folic acid supplements and risk of facial clefts: national population based case-control study. BMJ 334:464.

DeRoo LA, Wilcox AJ, Drevon CA, Lie RT. 2008. First-trimester maternal alcohol consumption and the risk of infant oral clefts in Norway: a population-based case-control study. Am J Epidemiol 168:638–646.

Engesaeter IØ, Lie SA, Lehmann TG, et al. 2008. Neonatal hip instability and risk of total hip replacement in young adulthood: follow-up of 2,218,596 newborns from the Medical Birth Registry of Norway in the Norwegian Arthroplasty Register. Acta Orthop 79:321–326.

Gjessing HK, Lie RT. 2008. Biometrical modelling in genetics: are complex traits too complex? Stat Methods Med Res 17:75–96.

Shi M, Mostowska A, Jugessur A, et al. 2009. Identification of microdeletions in candidate genes for cleft lip and/or palate. Birth Defects Res A Clin Mol Teratol 85:42–51.

Beaty TH, Murray JC, Marazita ML, et al. 2010. A genome-wide association study of cleft lip with and without cleft palate identifies risk variants near MAFB and ABCA4. Nat Genet 42:525–529.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Stein Emil Vollset, Medical Birth Registry of Norway, Kalfarveien 31, N-5018 Bergen, Norway. E-mail: stvo@fhi.no.

Kari Klungsøyear, E-mail: kmel@fhi.no.

POLAND – ASSOCIATE MEMBER

History and Funding

The Polish Registry of Congenital Malformations (PRCM) 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, financed by the Polish Ministry of Health. As part of this program, the registry provides the Polish Ministry of Health with important information needed in health care management. In 2003, it was decided that data for the Wielkopolska region, which is part of the territory covered by the PRCM, would be transferred to EUROCAT separately and treated as full member registry data.

Population Coverage

The PRCM is a population-based registry of type I (all mothers resident in defined geographic area). For the years 1998 to 2000, data for Poland (Associate registry) comes from nine provinces of Poland: Pomorskie, Zachodniopomorskie, Arminsko–Mazurskie, Kujawsko–Pomorskie, Wielkopolskie, Lubuskie, Lodzkie, Dolnoslaskie, and Opolskie. In 2001, the Slaskie Province (Silesia) was added, in 2002, the Lubelskie and Podkarpackie regions joined the registry, and in 2004 – Mazowieckie. In 2006, the next two provinces joined the PRCM – Swietokrzyskie and Podlaskie. In 2007, Malopolskie Province joined the PRCM. Since 2007, all of Poland has been covered by the registry. Since the year 2007, the whole of Poland has been covered by the Polish Registry, and in 2010, data for 15 provinces has been transferred to the EUROCAT (the data for the 16th province – Wielkopolska – is sent separately). In 2008, in these 15 provinces, 375,304 livebirths and stillbirths occurred which corresponds to 90.12% of all births in Poland.

Sources of Ascertainment

Notification is recommended by the Ministry of Health (as an official government program, however, notification is not obligatory) and consists of multi-source reporting. The sources include: delivery unit staff, ultrasound staff, postnatal ward staff, pediatric intensive care unit staff, fetal medicine unit staff, pediatricians, postmortem reports, regional genetic and cytogenetic services (direct access to cytogenetic laboratories and genetic clinic), and pediatric cardiology referral centers. The main source of information is a double-sided notifications form filled out by a physician responsible for diagnosing the malformations. The notification forms are sent immediately to the PRCM Central Working Group. Additionally, all birth records in Wielkopolska are reviewed and abstracted by trained staff with the aim of ascertainment of cases. Birth certificates do not record congenital anomalies. Death certificates allow for notification of congenital anomaly as a cause of death and, therefore, they are used as a source. Electronic and web-based data capture has been implemented (about 15% of all notifications). Well visited website www.rejestrwad.pl.

Maximum Age at Diagnosis

Up to 2 years of age.

Termination of Pregnancy for Fetal Anomaly

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 women; (2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease; and (3) there is a plausible suspicion the pregnancy has arisen from a prohibited act. The upper gestational age limit for termination of a severe congenital anomaly-affected pregnancy is 24 weeks. Although the termination of pregnancy is legal, in Poland there is public pressure not to perform such a procedure and that is why the data on pregnancy terminations might be underestimated. Hence, the registry currently does not register terminations of pregnancy after prenatal diagnosis.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is as follows: fetal death (stillbirth) is a death before 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 g at the moment of birth, having reached the 22nd week of gestational age, if the weight is unknown, or reaching 25 cm of the body length (crown-heel). We do not include early fetal deaths or spontaneous abortions. Autopsy rates vary between regions or even between health care units, the ranges for performance are as follows: stillbirths 10 to 30%, early neonatal deaths 20 to 30%, later deaths 1 week to 1 year 10 to 20%, and deaths with congenital anomaly 30 to 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, the country of residence, family history of congenital malformations, and genetic conditions in family members, father's and mother's occupational and environmental hazards, and the father's and mother's education.

Denominators and Controls Information

Information on all births (live and stillbirths) is available from birth certificates gathered by the Central Statistical Office for Poland. Since 2005, information on controls has been gathered by the registry.

Registry Description Reference

Latos–Bieleńska A, Materna–Kiryluk A, PRCM Working Group. 2005. Polish Registry of Congenital Malformations – aims and organization of the registry monitoring 300,000 births a year. J Appl Genet 46:341–348.

Ethics and Consent

The registry does not require ethics committee approval for all studies based on the registry data solely, but requires an approval for other projects (using registry data but focusing on genetic or clinical studies).

Electronic and Web-based Data Capture

Electronic and web-based data capture has been implemented (about 15% of all notifications).

Recent Registry Activities and Publications (2007–2010)

''Genetic studies on congenital urinary system malformations'' collaborative project with Division of Nephrology, Columbia University. PRCM main investigator – Dr. A. Materna–Kiryluk.

''Identification of novel genes for limb malformations'' collaborative project with Development & Disease Working Group, Max Planck Institute for Molecular Genetics in Berlin. PRCM main investigator: Dr. A. Jamsheer.

Publications (2007–2010)

Materna–Kiryluk A. 2010. Genetyczne aspekty najczęstszych wrodzonych wad rozwojowych układu moczowego u dzieci (Genetic aspects of common malformations of the kidney and urinary tract in children). Standardy Medyczne (in press).

Wiśniewska K, Wysocki J. 2010. [Primary prevention of neural tube defects by means folic acid supplementation – a summary of current recommendations in some European countries]. Standardy Medyczne (in press).

Jezela–Stanek A, Ciara E, Małunowicz E, et al. 2010. The Smith-Lemli-Opitz syndrome (SLOS) Collaborative Group. Differences between predicted and established diagnoses of Smith-Lemli-Opitz syndrome in the Polish population: underdiagnosis or loss of affected fetuses? J Inherit Metab Dis (Epub ahead of print).

Latos-Bieleńska A, Materna-Kiryluk A. 2010. [Congenital malformations in Poland in 2003–2004. Data from the Polish Registry of Congenital Malformations]. II ed. (Ed. A. Latos-Bieleńska, A. Materna-Kiryluk), Ośrodek Wydawnictw Naukowych PAN, Poznań.

Materna–Kiryluk A, Wiśniewska K, Badura–Stronka M, et al. 2009. Parental age as a risk factor for isolated congenital malformations in a Polish population. Paediatr Perinat Epidemiol 23:29–40.

Jamsheer A, Materna–Kiryluk A, Badura–Stronka M, et al. 2009. Comparative study of clinical characteristics of amniotic rupture sequence with and without body wall defect: further evidence for separation. Birth Defects Res A Clin Mol Teratol 85:211–215.

Engels H, Eggermann T, Caliebe A, et al. 2008. Genetic counseling in Robertsonian translocations der13,14: frequencies of reproductive outcomes and infertility in 101 pedigrees. Am J Med Genet A 146A:2611–2616.

Jamsheer A, Materna–Kiryluk A, Latos–Bieleńska A. 2008. Valproic acid and pregnancy: clinical presentation of 3 cases with valproate embryopathy. Archives of Perinatal Medicine 14:57–60.

Mazurczak T, Latos–Bieleńska A. 2007. Wady wrodzone. (Congenital Malformations) ,,Raport: Zdrowie Kobiet w wieku prokreacyjnym 15-49 lat. Polska 2006.'' (Report: Women's reproductive health in Poland 2006) Program Narodów Zjednoczonych ds. Rozwoju. Warszawa 93–98:148–151.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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Genetics, ul. Grunwaldzka 55 paw. 15, 60-352 Poznan, Poland. E-mail: alatos@ump.edu.pl.

POLAND, WIELKOPOLSKA – FULL MEMBER

History and Funding

The PRCM 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 Program of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland, financed by the Polish Ministry of Health. As part of this Program, the registry provides the Polish Ministry of Health with important information needed in health care management. In 2003, it was decided that data for the Wielkopolska Region, which is part of the territory covered by the PRCM, would be transferred to EUROCAT separately and treated as full member registry data.

Population Coverage

The PRCM is a population-based registry of type I (all mothers resident in defined geographic area). In the year 2009, Wielkopolska Region had a population of 34,083 people (8.93% of Poland) spread over an area of 29,827 square kilometers (9.54% of the Poland territory) with 41,043 births per year (livebirths and stillbirths), corresponding to 9.79% of total births in Poland.

Sources of Ascertainment

Notification is recommended by the Ministry of Health as an official government program; however, notification is not obligatory and consists of multi-source reporting. The sources include: delivery unit staff, ultrasound staff, postnatal ward staff, pediatric intensive care unit staff, fetal medicine unit staff, pediatricians, postmortem reports, regional genetic and cytogenetic services (direct access to cytogenetic laboratories and genetic clinics), and pediatric cardiology referral centers. The main source of information is a double-sided notifications form filled out by a physician responsible for diagnosing the malformations. The notification forms are sent immediately to the PRCM Central Working Group. Additionally, all birth records in Wielkopolska are reviewed and abstracted by trained staff with the aim of ascertainment of cases. Birth certificates do not record congenital anomalies. Death certificates allow for notification of congenital anomaly as a cause of death and, therefore, they are used as a source. Electronic and web-based data capture has been implemented (about 15% of all notifications). Well visited website www.rejestrwad.pl.

Maximum Age at Diagnosis

Up to 2 years of age.

Termination of Pregnancy for Fetal Anomaly

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 women; (2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease; and (3) there is a plausible suspicion the pregnancy has arisen from a prohibited act. The upper gestational age limit for termination of a severe congenital anomaly-affected pregnancy is 24 weeks. Although the termination of pregnancy is legal in Poland, there is public pressure not to perform such a procedure and that is why the data on pregnancy terminations might be underestimated. Hence, the registry currently does not register terminations of pregnancy after prenatal diagnosis.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is as follows: fetal death (stillbirth) is a death before 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 g at the moment of birth, having reached the 22nd week of gestational age, if the weight is unknown, or reaching 25 cm of the body length (crown-heel). We do not include early fetal deaths or spontaneous abortions. Autopsy rates vary between regions or even between health care units, the ranges for performance are as follows: stillbirths 10 to 30%, early neonatal deaths 20 to 30%, later deaths 1 week to 1 year 10 to 20%, and deaths with congenital anomaly 30 to 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, the country of residence, family history of congenital malformations, genetic conditions in family members, father's and mother's occupational and environmental hazards, and the father's and mother's education.

Denominators and Controls Information

Information on all births (live and stillbirths) is available from birth certificates, gathered by the CSO for Poland. Since 2005, information on controls has been gathered by the registry.

Registry Description Reference

Latos–Bieleńska A, Materna–Kiryluk A, PRCM Working Group. 2005. Polish Registry of Congenital Malformations – aims and organization of the registry monitoring 300,000 births a year. J Appl Genet 46:341–348.

Ethics and Consent

The registry does not require ethics committee approval for all studies based on the registry data solely, but requires an approval for other projects (using registry data but focusing on genetic or clinical studies).

Electronic and Web-based Data Capture

Since July 2005, electronic reporting of malformations has been made possible on the PRCM website (www.rejestrwad.pl).

Currently, at least 15% of all notifications are electronic.

Recent Registry Activities and Publications (2007–2010)

Genetic studies on congenital urinary system malformations. Collaborative project with Division of Nephrology, Columbia University. PRCM main investigator – Dr. A. Materna–Kiryluk.

Identification of novel genes for limb malformations. Collaborative project with Development & Disease Working Group, Max Planck Institute for Molecular Genetics in Berlin. PRCM main investigator: Dr. A. Jamsheer.

Registry Publications (2007–2010)

Materna–Kiryluk A. 2010. [Genetic aspects of common malformations of the kidney and urinary tract in children]. Standardy Medyczne (in press).

Wiśniewska K, Wysocki J. 2010. [Primary prevention of neural tube defects by means folic acid supplementation – a summary of current recommendations in some European countries]. Standardy Medyczne (in press).

Jezela–Stanek A, Ciara E, Małunowicz E, et al. 2010. ,,The Smith-Lemli-Opitz syndrome (SLOS) Collaborative Group. Differences between predicted and established diagnoses of Smith-Lemli-Opitz syndrome in the Polish population: underdiagnosis or loss of affected fetuses?'' J Inherit Metab Dis (Epub ahead of print).

Latos–Bieleńska A, Materna–Kiryluk A. 2010. [Congenital malformations in Poland in 2003–2004. Data from the Polish Registry of Congenital Malformations]. II ed. In: Latos–Bieleńska A, Materna–Kiryluk A, editors. Ośrodek Wydawnictw Naukowych PAN.

Materna–Kiryluk A, Wiśniewska K, Badura–Stronka M, et al. 2009. Parental age as a risk factor for isolated congenital malformations in a Polish population. Paediatr Perinat Epidemiol 23:29–40.

Jamsheer A, Materna–Kiryluk A, Badura–Stronka M, Latos–Bieleńska A. 2009. ,,Comparative study of clinical characteristics of amniotic rupture sequence with and without body wall defect: further evidence for separation.'' Birth Defects Res A Clin Mol Teratol 85:211–215.

Engels H, Eggermann T, Caliebe A, et al. 2008. ''Genetic counseling in Robertsonian translocations der13,14: frequencies of reproductive outcomes and infertility in 101 pedigrees.'' Am J Med Genet A 146A:2611–2616.

Jamsheer A, Materna–Kiryluk A, Latos–Bieleńska A. 2008. Valproic acid and pregnancy: clinical presentation of 3 cases with valproate embryopathy. Archives of Perinatal Medicine 14:57–60.

Mazurczak T, Latos–Bieleńska A. 2007. [Congenital Malformations. Report: Women's reproductive health in Poland 2006]. Program Narodów Zjednoczonych ds. Rozwoju 93–98:148–151.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Anna Latos–Bielenska, Registry Director; Anna Materna–Kiryluk, Organizing Coordinator, Polish Registry of Congenital Malformations, Department of Medical Genetics, ul. Grunwaldzka 55 paw. 15, 60-352 Poznan, Poland. E-mail: alatos@ump.edu.pl.

PORTUGAL, SOUTH – FULL MEMBER

History and Funding

The registry started in 1988 and it became a member of EUROCAT in 1989. The registry is funded by the National Institute of Health, a body within the Ministry of Health.

Population Coverage

The registry is population-based which includes all mothers resident in the regions of Algarve, Alentejo, and part of the Lisboa e Vale do Tejo Region (Setubal and part of Santarem Districts). It covers approximately 18,000 births annually representing 14% of the total number of births in Portugal.

Sources of Ascertainment

Pediatricians, obstetricians, and clinical geneticists are responsible for case notification in each region, up to the end of the neonatal period. Other sources of ascertainment are fetal pathology hospital departments. At this moment, only two pediatric cardiology departments participate in the registry, but no cytogenetic laboratory. Data are validated and coded at the central level in Lisbon.

Maximum Age at Diagnosis

Up to 1 month of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal up to 24 weeks' gestation and requires the permission of a technical committee. Non-viable anomalies have no upper limit. Terminations as results of diagnosis of a congenital anomaly are included in the registry.

Stillbirth Definition and Early Fetal Deaths

The definition is 22 weeks of gestation of 500 g. Most stillborn fetuses in the covered area have an autopsy performed. Stillbirths with congenital anomalies are included in the registry. Fetal deaths of earlier gestation or lower weight are not included.

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.

Registry Description Reference

The operation of the registry is described in the website of the National Institute of Health.

Ethics and Consent

Data on cases is transmitted by attending doctors at hospital departments to the Central Registry and registered centrally without personal information. A specific numeric code permits linking registry data with clinical data at local levels by the attending medical doctor.

Electronic and Web-based Data Capture

Approximately 30% of all EUROCAT registries from the South Portugal region come through an electronic web-based system. Data is input at local levels by participating physicians into the central database template. This has the same variables than the paper-based questionnaire. Each participating center can use and download only data from that center. The web-based tool has data input, data analysis, and data transfer capabilities. Data from the remaining centers is received in paper and centrally input into the informatics database.

Recent Registry Activities and Publications (2007–2010)

Portugal, Registo Nacional de Anomalias Congénitas. Relatório 2000–2001. Lisboa, Instituto Nacional de Saúde, 2008.

Portugal, Registo Nacional de Anomalias Congénitas. Nota Informativa 1. Lisboa, Instituto Nacional de Saúde, 2009.

Portugal, Registo Nacional de Anomalias Congénitas. Nota Informativa 2. Lisboa, Instituto Nacional de Saúde, 2009.

Portugal, Registo Nacional de Anomalias Congénitas. Relatório 2002–2007. Lisboa, Instituto Nacional de Saúde, 2010.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Carlos Matias Dias, Departamento de Epidemiologia, Registo Nacional de Anomalias Congénitas, Av Padre Cruz, 1649-016, Lisbon, Portugal. E-mail: carlos.dias@insa.min-saude.pt.

SPAIN, BARCELONA – FULL MEMBER

History and Funding

The Barcelona Birth Defects Registry (Registre de Defectes Congènits de Barcelona –REDCB) was initiated in 1990 and reached a population-based status by 1992, when it became a member of the EUROCAT. The REDCB is part of the Service of Health Information Systems (Servei de Sistemes d'Informació Sanitaria) in the Public Health Agency of Barcelona (Agència de Salut Pública de Barcelona). It is funded by Regional (Generalitat de Catalunya) and Local (Ajuntament de Barcelona) Administrations.

Population Coverage

The REDCB is population-based and covers pregnancies of women resident in Barcelona City ending in live or stillborn babies of 22+ weeks of gestation or in induced abortions (IAs) due to prenatal detection of birth defects (i.e., the registry does not include birth defects in spontaneous abortions –<22 weeks of gestation, or IAs not due to prenatal detection of birth defects).

Some 3% of residents' newborns occur at maternity units of the city limits. The REDCB controls 50% of these newborns (1.5%), delivering in a hospital near the city. Since Barcelona City is a pole of attraction for at risk pregnancies, the remaining 1.5% of newborns not controlled by the registry probably provides <1% of cases.

Currently, (2008) the REDCB covers about 14,500 births annually. In the last 5 years, the number of births has increased from about 12,500, mainly due to a higher fertility rate among immigrant women of developing countries coming to the city.

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 with the mother is the main source of general information. Delivery units, pediatric departments, cytogenetic laboratories, pathology departments, prenatal diagnosis units, and pediatric cardiology services are the main sources of clinical information. The registry has direct access to some cytogenetic laboratories, but not to all. Some of the collaborating laboratories send their data by e-mail, but for most of them, registry staff personally go to collect the case information.

Direct Access to Cytogenetic Laboratories Covers only Part of our Population

Pediatric cardiology centers covering part of the registry population supply systematic case lists and diagnostic details to the registry.

Maximum Age at Diagnosis

Up to 3 days of age. When a suspicion of birth defect exists, follow-up is made until a diagnosis or normality is stated. This affects mainly birth defects as CHD.

Termination of Pregnancy for Fetal Anomaly

IA after prenatal detection of a birth defect is legal in Spain until 22 weeks of gestation. A probable future modification in the Spanish IA law will affect birth defects: some fetuses with major birth defects detected in the third trimester of pregnancy (i.e., after 22 weeks) could be induced for abortion.

Case Definition

Cases are defined as fetuses or newborns with at least 1 major or 2+ minor anatomic birth defects or with unbalanced chromosomal anomalies. The follow-up period is 2 to 3 days after delivery. Due in part to this short follow-up period, poor ascertainment exists for birth defects as mild hypospadias, some cardiovascular defects, and other anomalies of internal organs not detected using prenatal ultrasounds. The ascertainment of unbalanced chromosomal anomalies without neonatal anatomic defects (as some sexual chromosome anomalies like XXX, XXY, XYY) is never complete and depends on the rate of karyotyped pregnancies.

Controls Selection

A random sample (not case-matched) of about 2% of the newborns expected in each maternity unit is selected as controls.

Data Availability and Information Sending to EUROCAT

Information on maternal drug use, maternal and paternal diseases, and occupations is available for cases and controls, but it is not sending to the EUROCAT Central Registry. The REDCB systematically sends data to the EUROCAT Central Registry on all ''core'' variables but two (civil registration status and McKusick code), and on a ''non-core'' variable (karyotype).

Denominators Information

Background data on births are available from birth certificates and the Barcelona Perinatal Mortality Registry.

Ethics and Consent

The registry is located in a health authority setting (Barcelona Public Health Agency).

Parental consent is asked for during interview with the mothers of cases and controls.

Address for Further Information

Joaquín Salvador, Servei de Sistemes d'Informació Sanitària (SESIS), Agencia de Salut Pública de Barcelona (ASPB), Avda. Princep d'Astúries, 63, 2°, 08012 Barcelona, Spain. E-mail: jsalvado@aspb.cat.

SPAIN, BASQUE COUNTRY – FULL MEMBER

History and Funding

Registration of congenital anomalies in the Basque Country started on January 1, 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 2,162,944 inhabitants. It is a population-based registry that, therefore, includes all mothers delivering in the Basque Country excluding any non-residents. The average number of annual births 2003 to 2008 is 20,174. It is estimated that 1 to 2% of outside resident mothers deliver in the covered hospitals.

Sources of Ascertainment

Reporting is voluntary, although the capture of data is now systematic for 80% of cases using the automated hospital database. There is an active search for cases (livebirths, stillbirths, and induced abortions), through multiple sources of information: hospital discharge records, hospital automated data, neonatal units, specialist pediatric department, cytogenetics and pathology laboratories, and private maternity hospitals.

Pediatric cardiology centers supply diagnostic confirmation when requested by the registry for specific cases.

We do not have direct access to cytogenetic laboratories. We ask for the results personally from the geneticists at each of the hospitals involved in the registry. Usually laboratories supply the list of prenatal and infant abnormal karyotypes when requested.

Maximum Age at Diagnosis

Routinely reported to the registry up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

Since March 2010, ''sexual and reproductive health and abortion'' in Spain is governed by a new law. Termination of pregnancy is now legal for certain indications, including prenatal diagnosis of severe anomaly, at any time during pregnancy. 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 and Spain is a gestational age of 22 weeks or a birth weight of 500 g. 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). The autopsy rate after termination of pregnancy is high (70%), but the quality varies, depending on hospitals.

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).

Ethics and Consent

No ethics committee approval is required to operate the registry. No approval is needed for studies that require identifiable patient data. The hospitals have an ethics committee if further ethical recommendations are considered necessary.

Legislation complies with the EC95/46 directive with respect to disease registers and surveillance since 1999.

There is no national legislation requiring informed consent to register a baby with a congenital anomaly.

Electronic and Web-based Data Capture

Information about all newborns in the Basque Country is automatically collected and stored in an oracle application server. This application is the property of the Health Department of the Basque Government from which the registry can complete information for newborns with any congenital anomaly. We have unrestricted access to the application. The application follows high levels of security specified in the Official Disposition of June 17, 2005.

Recent Registry Activities and Publications (2007–2010)

The 10th European Symposium on Prevention of Congenital Anomalies was held in Bilbao (Basque Country) on June 10, 2009. We have a new registry leader since April 2010.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Larraitz Arriola, Registro Anomalías Congénitas CAV, Subdirección de Salud Pública, Av. Navarra 4, 20013 San Sebastian, Spain. E-mail: l-arriola@ej-gv.es.

SPAIN, SPAIN HOSPITAL NETWORK – ASSOCIATE MEMBER

ECEMC–Spanish Collaborative Study of Congenital Malformations

History and Funding

This is a research program created in 1976 by Professor Dr. María Luisa Martínez–Frías, as a hospital-based case-control study and surveillance system, with voluntary participation of hospitals but mandatory subjugation to the operating rules for those participating. It contributes to EUROCAT with data since 1980, and is also a member of the ICBDSR. In January 2002, the ECEMC Program became integrated into CIAC (Research Center on Congenital Anomalies), of the Instituto de Salud Carlos III (ISCIII), from the Ministerio de Ciencia e Innovación. It is also directed by Professor Martínez–Frías. In 2006, the ECEMC was recognized as an excellent research program to be integrated into Centre for Biomedical Research on Rare Diseases. ECEMC has two teratogen information services since 1991, one for the general population and another one for physicians. The program is financed mainly by the Spanish Administration and, partially, by non-governmental organizations.

Population Coverage

Data are obtained from about 70 hospitals distributed all over Spain. The annual number of births is about 100,000, representing more than 21% of all Spanish births. Stillbirths of at least 24 weeks or 500 g have been included since 1980. Data on terminations of pregnancy due to the presence of congenital anomalies, which can be legally performed within the first 22 weeks of gestation, can only be gathered in some participating hospitals.

Sources of Ascertainment

The detection period is the first 3 days of life, including major and/or minor/mild defects. The information comes from delivery units and pediatric departments of the participating hospitals. The pediatric/neonatology units ask for specialized cardiologic evaluation of patients in whom cardiac anomalies were prenatally or neonatally suspected, and those with other congenital defects. Mothers are interviewed directly by the participating physicians during those first 3 days after the infant's delivery to fill in the ECEMC standard protocols, which include more than 310 data for each child, whether case or control. The information for each case and its control is gathered by the same physician. Controls are defined as the next non-malformed infant born at the same hospital than the case with the same sex of the malformed infant. In many instances, photographs, imaging studies, high-resolution bands karyotype, and molecular analyses when needed (which are performed at the central group of the ECEMC), and other complementary studies, are available. ECEMC's laboratory, to which the program has direct access, provides karyotype and molecular analyses for cases the program already knows about, and some registered cases are studied in external laboratories. Biologic samples are stored in the ECEMC registry for those cases for which the collaborating physicians send them, with the informed consent of the parents, for diagnosis as well as for further research.

Maximum Age at Diagnosis

Up to 3 days of age. A longer follow-up is achieved in selected cases.

Termination of Pregnancy for Fetal Anomaly

Up to 1985, termination of pregnancy was illegal in Spain. From 1985 onward, induced abortions have been legal but they are registered by the ECEMC only for some hospitals that can report them. The upper gestational age limit for termination is 22 weeks in cases of congenital anomaly.

Stillbirth Definition and Early Fetal Deaths

The official definition of stillbirth in the Spain Hospital Network is 24 weeks or later or weighing at least 500 g. Stillbirths have been included since 1980. Autopsy rates in the period from 2007 to 2009 were 58.18% for stillbirths and 22.22% for deaths with a congenital anomaly.

Exposure Data Availability

The mother of each reported infant (case or control) is interviewed within the first 3 days after delivery to obtain data on several exposures (parental occupation, maternal acute or chronic diseases, drug usage, illicit drugs, alcohol and tobacco maternal consumption, exposure to other chemical or physical factors), apart from the other data gathered (family history, obstetrical and de-

mographic data, among others). It is important to note that when the pediatricians detect the cases and select the control children, they are blinded to the different maternal and family data that they are going to collect.

Denominators and Controls Information

Total number of births by sex and number of twin pairs in each participating hospital are gathered. Other background information is obtained from the control material. The information for controls is obtained with the same methodology that is used for cases (interview to the mother) and, as for cases, data on more than 300 variables are gathered.

Registry Description Reference

Martínez–Frías ML. 2007. Postmarketing analysis of medicines: methodology and value of the Spanish case-control study and surveillance system in preventing birth defects. Drug Safety 30:307–316.

Ethics and Consent

The registry obtained approval to function from the Ethics Committee of the Instituto de Salud Carlos III, Ministry of Science and Innovation. National legislation requires informed consent to register a baby with a congenital anomaly. Parental consent is always asked for and parents have to agree to the inclusion of the child on the register (opt-in).

Electronic and Web-based Data Capture

Neither electronic nor web-based data capture is used in this program. All the notifications are received in paper forms from the neonatal or delivery units of the participating hospitals.

Recent Registry Activities and Publications (2007–2010)

ECEMC, which is organized in three sections (epidemiology, genetics, and clinical teratology), maintains its international participation in EUROCAT, ICBDSR, and ENTIS (European Network of Teratology Information Services). It participates in the activities and several research projects of Centre for Biomedical Research on Rare Diseases, as one of its 61 integrating Spanish research groups. Annually, ECEMC organizes a scientific meeting with the attendance of outstanding researchers, together with representatives from the 70 collaborating hospitals in the program. During that meeting, the most burning methodological issues of the program are also discussed. Every year, ECEMC publishes a report (ECEMCs Annual Bulletin), in which some results of its activity are shown. Such bulletin (http://www.ciberer.es/documentos/ECEMC_2009_AF.PDF) is distributed among 7000 physicians (pediatricians and obstetricians) from all over Spain.

These are some selected publications of the group for the period 2007 to 2010 (the complete list can be accessed through the above detailed link to the ECEMC's Annual Bulletin):

Chabchoub E, Rodríguez L, Galán E, et al. 2007. Molecular characterisation of a mosaicism with a complex chromosome rearrangement: evidence for coincident chromosome healing by telomere capture and neo-telomere formation. J Med Genet 44:250–256.

de Frutos CA, Vega S, Manzanares M, et al. 2007. Snail1 is a transcriptional effector of FGFR3 signaling during chondrogenesis and achondroplasias. Dev Cell 13:872–883.

Galán–Gómez E, Sánchez EB, Arias-Castro S, Cardesa-García JJ. 2007. Intrauterine growth retardation, duodenal and extrahepatic biliary atresia, hypoplastic pancreas and other intestinal anomalies: further evidence of the Martínez–Frías syndrome. Eur J Med Genet 50:144–148.

Martínez–Frías ML. 2007. Postmarketing analysis of medicines: methodology and value of the Spanish case-control study and surveillance system in preventing birth defects. Drug Saf 30:307–316.

Martínez–Frías ML. 2008. The biochemical structure and function of methylenetetrahydrofolate reductase provide the rationale to interpret the epidemiologic results on the risk for infants with Down syndrome. Am J Med Genet A 146A:1477–1482.

Martínez–Frías ML, Grupo de trabajo del ECEMC. 2008. Epidemiologic association between isolated skin marks in newborn infants and single umbilical artery (SUA). Does it have biological plausibility? Am J Med Genet A 146A:26–34.

Martínez–Frías ML, Bermejo E, Rodríguez–Pinilla E, et al. 2008. Does single umbilical artery (SUA) predict any type of congenital defect? Clinical-epidemiologic analysis of a large consecutive series of malformed infants. Am J Med Genet A 146A:15–25.

Martínez–Frías ML; ECEMC Working Group. 2009. Epidemiology of acephalus/acardius monozygotic twins: new insights into an epigenetic causal hypothesis. Am J Med Genet A 149A:640–649.

Martínez–Frías ML, Bermejo E, Mendioroz J, et al. 2009. Epidemiologic and clinical analysis of a consecutive series of conjoined twins in Spain. J Pediatr Surg 44:811–820.

Martínez–Frías ML. 2010. Can our understanding of epigenetics assist with primary prevention of congenital defects? J Med Genet 47:73–80.

Martínez–Frías ML, de Frutos CA, Bermejo E, et al. 2010. Review of the recently defined molecular mechanisms underlying thanatophoric dysplasia and their potential therapeutic implications for Achondroplasia. Am J Med Genet Part A 152A:245–255.

Mastroiacovo P, Lisi A, Castilla EE, et al. 2007. Gastroschisis and associated defects: an international study. Am J Med Genet A 143:660–671.

Rittler M, López–Camelo JS, Castilla EE, et al. 2008. Preferential associations between oral clefts and other major congenital anomalies. Cleft Palate Craniofac J 45:525–532.

Rodríguez L, Martínez–Fernández ML, Mansilla E, et al. 2008. Screening for subtelomeric chromosome alteration in a consecutive series of newborns with congenital defects. Clin Dysmorphol 17:5–12.

Rodríguez–Pinilla E, Mejías C, Prieto–Merino D, et al. 2008. Risk of hypospadias in newborn infants exposed to valproic acid during the first trimester of pregnancy: a case-control study in Spain. Drug Saf 31:537–543.

Address for further information

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SWEDEN – ASSOCIATE MEMBER

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) 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 Center 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 fetuses with malformations are included since 1999.

Sources of Ascertainment

Since 1999, the register does not receive notifications from pediatric cardiology centers. However, information from detailed cardiovascular examinations could be attached to the reports sent by the reporting unit (pediatric or obstetric department).

Notification to the registry is compulsory. Reports are obtained from departments of pediatrics, obstetrics, clinical genetics, and cytogenetic laboratories. The diagnoses of the malformed cases are often received from more than one source. Pediatric cardiology centers do not supply information to the registry, but other sources of information cover pediatric cardiac surgery. The cytogenetic information is obtained through annual reports from all cytogenetic laboratories in the country, and contains information on all prenatal and infant abnormal karyotypes.

Aggregated data are transmitted to EUROCAT.

Maximum Age at Diagnosis

Information on malformations is principally reported before 1 month of age except for congenital heart malformations, which are reported up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal. Termination of pregnancy for fetal 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 22 weeks of gestation. Since 1999, all fetal deaths with congenital malformations >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

Epidemiologic background data are available on all births in the Medical Birth Register and in the Statistics of Sweden.

Ethics and Consent

The registry does not require ethics committee approval to collect and store data. The register is ruled under a special law for the registers of health care run by the Swedish National Board of Health and Welfare. For investigations run by other groups of researchers than those working within the Swedish National Board of Health and Welfare, approval from ethics committee is compulsory.

National legislation does not require informed consent to register a baby with a congenital anomaly.

Electronic and Web-based Data Capture

All reports to the Swedish Register of Birth Defects are sent by paper forms (September, 2010).

Recent Registry Activities and Publications (2007–2010)

Information from the register has been used in several publications, but this is not centrally recorded, and no publication list is available.

Annual reports have been published by the Swedish National Board of Health and Welfare in 2007, 2008, and 2009 (covering data on births/terminations in 2006, 2007, and 2008, respectively). The 2010 annual report is in preparation covering data from 2009.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Karin Källén, The Swedish National Board of Health and Welfare and Department of Reproduction Epidemiology Institution of Clinical Sciences, University of Lund, Sweden. E-mail: karin.kallen@med.lu.se.

SWITZERLAND, VAUD – FULL MEMBER

History and Funding

The Registry of Switzerland was originally established in collaboration with 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 to 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 program: Zurich, Fribourg, Argovie, Tes-

sin, Vaud, Valais, Neuchatel, and Jura. The registry is located in the Division of Medical Genetics in the University Hospital of 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 was 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 to 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 7500 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 units. Data about different methods of prenatal diagnosis are collected (ultrasound, serum markers, cytogenetic, and molecular).

Pediatric cardiology centers supply systematic case lists and diagnostic details to the registry.

The registry is situated in the Department of Medical Genetics and we thus have direct access to the cytogenetic and DNA laboratories; they systematically supply the registry with abnormal karyotypes and molecular studies prenatally and postnatally diagnosed.

Twice a year we contact the other laboratories covering the residual population of the canton to check for anomalies.

There is no upper age limit for registration of a child with a malformation.

Maximum Age at Diagnosis

There is no upper age limit.

Termination of Pregnancy for Fetal Anomaly

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 after prenatal diagnosis are included in the register.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is a gestation age of >= 27 weeks or length >= 30 cm, which 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, and outcome of previous pregnancies is available for the malformed infants.

Denominators and Controls Information

Background data on births are available from the Service Cantonal de Recherche et d'Information Statistique.

Ethics and Consent

The registry does not require ethics committee approval to collect and store data.

National legislation does not require informed consent to register a baby with a congenital anomaly. However, since 2007, according to a national law about genetic analysis, the parents have to sign informed consent for these analyses.

Electronic and Web-based Data Capture

We receive some data mainly from pediatricians only on a paper-based system.

We have no website notification system.

Recent Registry Activities and Publications (2007–2010)

Beretta L, Hauschild M, Jeannet PY, et al. 2007. Atypical presentation of Prader–Willi syndrome with cerebral venous thrombosis: association or fortuity? Neuropediatrics 38:204–206.

Magyar I, Colman D, Arnold E, et al. 2009. Quantitative sequence analysis of FBN1 premature termination codons provides evidence for incomplete NMD in leukocytes. Hum Mutat 30:1355–1364.

Martinet D, Filges I, Besuchet Schmutz N, et al. 2008. Subtelomeric 6p deletion: clinical and array-CGH (comparative genomic hybridization) characterization in two patients. Am J Med Genet A 146A:2094–2102.

Narumi Y, Aoki Y, Niihori T, et al. 2008. Clinical manifestations in patients with SOS1 mutations range from Noonan syndrome to CFC syndrome. J Hum Genet 53:834–841.

Rieubland C, de Viragh PA, Addor MC. 2007. Uncombable hair syndrome: a clinical report. Eur J Med Genet 50:309–314.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Marie–Claude Addor, Registre Vaudois des Anomalies Congenitales and Swiss Registry for EUROCAT, Division of Medical Genetics, Maternite, CH-1011 CHUV-Lausanne, Switzerland. E-mail: marie-claude.addor@chuv.ch. monique.devolz@chuv.ch. Website: www.hospvd.ch/public/

chuv/genmol/eurocat/euro-home.htm (username: eurocat, password: tropic).

UKRAINE – FULL MEMBER

History and Funding

Population-based birth defects surveillance began in 2000 in the framework of the Ukrainian–American Birth Defects Program funded by the United States Agency for International Development. The program became an associate member of ICBDSR in 2001. In 2005, the United States Agency for International Development component was completed and the program was assumed by OMNI-Net, a not-for-profit international organization incorporated in Ukraine, and is continued as OMNI-Net Ukraine Birth Defects Program. OMNI-Net represents five resource OMNI-centers all of which provide care for children with birth defects, promote prevention programs, participate in parental organizations, and engage in collaborative programs with national and international partners.

Program objectives include universal folic acid flour fortification, methods to reduce alcohol impact on child development in collaboration with partners, and promoting international partnerships.

OMNI-Net personnel are financed from regional budgets. The legislation and rules by the Ministry of Health mandates the reporting of birth defects. Birth defect data is reported by Oblast Vital Statistics Centrum who aggregates, formats, and forwards the data to the Ministry of Health.

Population Coverage

Birth defect surveillance annually covers about 28,000 births in two oblasts (provinces) of Western Ukraine – Rivne and Khmelnytsky, representing approximately 6% of births in Ukraine. The population is relatively homogeneous and stable (data is pooled from these two oblasts). The registry is of type III (all mothers delivering in the defined geographic area excluding non-residents of that area).

Sources of Ascertainment

Relevant hospital admission/discharge summaries are systematically reviewed. Qualified registry specialists also routinely review all medical records of regional pediatric cardiology centers and obtain ascertainment of diagnostic details. Data from specialty clinics, laboratories (including cytogenetic one), and other services are explored. Our cytogenetic laboratories are the only ones in the region and they provide us with study reports. Pregnancy, obstetrics, delivery, neonatal, and pediatrics records are reviewed. The information is substantial regarding service providers located in regional centers, but limited regarding service providers in rural environments.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

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

Up until December 31, 2005, the upper gestational age limit for termination of pregnancy in Ukraine was 28 weeks and/or 1000 g.

From January 1, 2006, Ukraine redefined the definition and the current upper gestational age limit for termination of pregnancy is 22 weeks and/or 500 g.

Stillbirth Definition and Early Fetal Deaths

The stillbirth definition is as follows: fetal death (stillbirth) is a death before the complete expulsion or extraction of a product of conception. Until January 1, 2006, for statistical purposes, we include all fetuses weighing 1000 g or more at the moment of birth or/and gestational age above 28 weeks; spontaneous abortions include fetuses weighing $<$1000 g and gestational age $<$28 weeks.

From January 1, 2006, Ukraine redefined stillbirth definition as all fetuses weighing 500 g or more at the moment of birth and/or gestational age above 22 weeks.

In Ukraine, Certificates of Neonatal Death are NOT medical documents, they are issued by civil authorities.

Exposure Data Availability

Routine information collection is limited except when ad hoc circumstances are noted. An expansion of exposure data collection is in progress.

Denominators and Controls Information

Information on all births (live and stillbirths) is available from birth certificates gathered by the Regional Vital Statistics. There are 2 control cases for each birth defect case.

Background Information

The northern counties (rayons) of one of the two oblasts are contaminated from the Chernobyl disaster. Data regarding ionizing radiation pollution in contaminated rayons is available by special agreements. Data from a population-based neonatal registry is also available by special agreements.

Ethics and Consent

Registration of birth defects and follow-up is an integral part of health care protocols.

The registry does not require ethics committee approval to collect and store data.

National legislation does not require informed consent to register a baby with a congenital anomaly.

Electronic and Web-based Data Capture

Maternity departments transfer data on all newborns, including newborns with birth defects, to a Central Regional Newborn Registry Database every month. Web-based data capture is not used.

Recent Registry Activities and Publications (2007–2010)

Bohatyrchuk–Kryvko S, Novak V, Shumlyanski I, et al. 2008. Linking birth defects surveillance with early intervention services-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 127.

Dancause KN, Yevtushok L, Lapchenko S, et al. 2010. Chronic radiation exposure in the Rivne–Polissia region of Ukraine: implications for birth defects. Am J Hum Biol 22:667–674.

Leoncini E, Botto LD, Cocchi G, et al. 2010. How valid are the rates of Down syndrome internationally? Findings from the International Clearinghouse for Birth Defects Surveillance and Research. Am J Med Genet A 152A:1670–1680.

Kfir M, Yevtushok L, Onishchenko S, et al. 2009. Can prenatal ultrasound detect the effects of in utero alcohol exposure? A pilot study. Ultrasound Obstet Gynecol 33:683–689.

Kfir M, Hull A, Yevtushok L, et al. 2007. Evaluation of early markers of prenatal alcohol exposure. Abstract of the platform presentation at the American Institute of Ultrasound in Medicine Annual Convention (March 15–18, 2007, New York, NY).

Wertelecki W, Yevtushok L, Zymak–Zakutnya N, et al. 2007. Elevated rates of NTD and conjoined twins in Polissya, a region impacted by Chernobyl. Abstract submitted to the 48th European Society of Pediatric Research Conference.

Wertelecki W, Afanasyeva N, Baryliak I, et al. 2008. OMNI-Net BD Ukrainian Consortium: impact and lessons learned from ''de-centralized'' strategies-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 95.

Wertelecki W, Yevtushok L. 2008. Elevated neural tube defects (NTD) rates in Ukraine – highest in Polissia-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 67.

Wertelecki W. 2010. Malformations in a Chernobyl-impacted region. Pediatrics 125:836–843.

Yevtushok L, Zymak–Zakutnya N, Polishchuk S, et al. 2007. Elevated prevalence of NTD and conjoined twins in a Chernobyl impacted region of Ukraine. Abstract submitted to the European Teratology Society.

Yevtushok L, Onishchenko S, Wertelecki W, et al. 2008. Predictors of binge drinking during pregnancy among women in Ukraine-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 163.

Yevtushok L, Needham K, Lapchenko S, et al. 2008. Dietary and activity patterns and implications on birth defects in the Chernobyl impacted Rivne–Polissia Region in Ukraine-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 16.

Zymak–Zakutnya N, Ropotan A, Shumlyanski I, et al. 2008. Reduction of infant morbidity and mortality – Gastroschisis as one Index-1-st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects. August 27–30, 2008. Budapest, Hungary. Program & Abstract Book. p 165.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Addresses for Further Information

Wertelecki W, ''OMNI-Net for Children'', 36, 16 Lypnya st., r. 709, Rivne, Ukraine, 33028. Email: omninetukr@gmail.com

UNITED KINGDOM, EAST MIDLANDS, AND SOUTH YORKSHIRE – FULL MEMBER

History and Funding

Data collection began on January 1, 1997, and included any baby delivered on or after the date diagnosed or suspected of having a congenital anomaly. There is no exclusion list. EMSYCAR was originally known as Trent Congenital Anomaly Register (CAR) and funded by the former Trent National Health Service (NHS) Executive Regional Research & Development Department. In April 2003, it expanded to include Northamptonshire and funding transferred to the NHS Primary Care Trusts within the former region. Since January 1999, the register has been responsible for contributing data for the region directly to the National Congenital Anomaly System (NCAS) organized by the Office for National Statistics.

Population Coverage

All mothers normally resident within South Yorkshire and the counties of Derbyshire, Nottinghamshire, Lincolnshire, Leicestershire, Rutland, and Northamptonshire, irrespective of the actual place of delivery. The annual number of births for the registry is approximately 74,000.

Sources of Ascertainment

Reporting is voluntary from multiple sources in all the hospitals across the region, including antenatal clinics, delivery suites, neonatal screening, neonatal and special care baby units, cytogenetics laboratories, clinical genetics, pathology, pediatric surgery, and departments of child health. Registration includes pre-natally diagnosed fetuses, with no lower age limit, thus including early terminations and fetal losses.

There are three cytogenetic laboratories in the region, each with a different method of communication with the registry. One laboratory provides a monthly electronic list of all abnormal prenatal and infant karyotyptes. One laboratory provides this on paper notification forms, while the third confirms karyotypes for cases already notified to the register. An annual data validation exercise is undertaken with this laboratory to identify missing cases.

The central pediatric cardiology center situated within the region provides systematic case lists and diagnostic details for all surgical and non-surgical cases to the registry on request (usually made annually). Two other cen-

ters outside the registry area, covering parts of the western and southern population, supply diagnostic information for cases already known to the registry, or neighboring registers, upon request. A fourth center, also outside the region but covering part of its northern population, currently does not supply data, but is expected to routinely exchange data with EMSYCAR once the new Yorkshire CAR becomes fully operational in 2011.

There is no time limit for registration or for updating diagnostic details.

Maximum Age at Diagnosis

There is, at present, no upper age limit.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal up to 24 weeks' gestation. There is no upper gestational age limit for termination if a major anomaly is diagnosed. Terminations for anomaly reasons and anomalies found at postmortem after social terminations are included in the register.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is fetal death after 24 completed weeks. There is no lower gestational age or weight limit for anomalies identified in early fetal deaths.

Exposure Data Availability

Not specifically requested but recorded if relevant information is provided by the notifier.

Denominators and Controls Information

The denominator data for births in the region is provided by the Office for National Statistics on an annual basis.

Ethics and Consent

All United Kingdom registries require ethics committee approval to collect and store data. This is obtained centrally from Trent Multicentre Research Ethics Committee (NHS) and requires renewal every 5 years.

National legislation also requires informed consent, but United Kingdom registries are exempted from this by National Information Governance Board (formerly Patient Information Advisory Board, PIAG) approval. This allows the Secretary of State for Health to permit a specified dataset to be collected without individual consent. This approval requires annual renewal. All parents have to be made aware that they can request the removal of personal identifiers from their local register should they wish.

Electronic and Web-based Data Capture

Electronic downloads are received from one of three cytogenetic laboratories (monthly), and the main pediatric cardiac center (annually). All abnormal scan reports from the second largest delivery suite are received electronically, with plans for the largest unit to adopt this method during late 2010. All other notifications are paper based. EMSYCAR does not use web-based data capture.

Recent Registry Activities and Publications (2007–2010)

Budd J. 2007. ''Regional Congenital Registers in the UK'', Obstetrics, Gynaecology and Reproductive Medicine 17:333–334.

Congenital Anomalies in Births 2004–2008. 2010. http://www2.le.ac.uk/departments/health-sciences/research/ships/timms/documents/congenital-anomalies-in-births-2004-2008.pdf.

Draper ES, Rankin J, Tonks AM, et al. 2007. Recreational drug use: a major risk factor for gastroschisis? Am J Epidemiol 167:485–491.

Wright J, Budd J, Field D, Draper E. 2010. Epidemiology of diaphragmatic hernia: a nine year experience. Perinatal and Pediatric Epidemiology (in press).

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Elizabeth Draper, Director EMSYCAR, Department of Health Sciences, University of Leicester, 22-28 Princess Road West, Leicester, United Kingdom, LE1 6TP. E-mail: msn@leicester.ac.uk.

Judith Budd, CAR Coordinator, Department of Health Sciences, University of Leicester, 22-28 Princess Road West, Leicester, United Kingdom, LE1 6TP. E-mail: jlsb1@leicester.ac.uk.

UNITED KINGDOM, NORTHERN ENGLAND – FULL MEMBER

History and Funding

The Northern Congenital Abnormality Survey (United Kingdom, Northern England) was established in 1985 after a 1-year pilot study. The Northern England register is funded by the Healthcare Quality Improvement Partnership until April 2011. The registry is one of four databases linked through the mother's details, held at the Regional Maternity Survey Office in Newcastle – the others being perinatal and infant deaths, diabetic pregnancy, and multiple births. The Northern England register has been the source of congenital anomaly data for our reporting area for United Kingdom National Statistics from January 2003 to December 2009.

Population Coverage

The Northern England register records all congenital anomalies that occur in pregnancies of mothers' resident in North East England and North Cumbria (population-based). This area extends from North Cumbria to the Tees area up to the Scottish border and includes North Cumbria, Northumberland, Newcastle upon Tyne, North Tyneside, Gateshead, South Tyneside, County Durham, Darlington, and Tees. Until 1994, South Cumbria was included in the reporting area. The population of the current area is approximately 3 million. The annual number of births for the registry area is currently approximately 32,000, which represents about 5% of the total births in England. Minor anomalies are not reported. The EUROCAT list of exclusions is used.

Sources of Ascertainment

Reporting is voluntary from multiple sources. The Northern England register has a strong relationship with clinicians and non-medical staff in all the hospitals in the region. Sources of reporting include ultrasonographers, geneticists, midwives, radiographers, obstetricians, pediatricians from a wide range of specialties, pathologists, cardiologists, fetal medicine specialists, and surgeons. Cross validations with other regional databases occur regularly, including the Northern Genetics Service (cytogenetics service), the Fetal Medicine Unit at the Royal Victoria Infirmary (regional tertiary center), and the Pediatric Cardiology database at Freeman Hospital which supplies case lists and diagnostic details to the register. The registry receives quarterly downloads of all prenatal and infant abnormal karyotypes for the population of the region from the Northern Genetics Service.

Registration includes all anomalies discovered in fetuses, including early pregnancy losses and terminations after prenatal diagnosis, and babies and children up to the age of 12. The registry has extremely good ascertainment of late fetal deaths and stillbirths affected by congenital anomalies as it is run in parallel with the Northern Perinatal Mortality Survey, which was established in 1981. All registered deaths are cross-validated with U.K. National Statistics annually.

There is no time limit for updating diagnostic detail. Ascertainment of anomalies diagnosed after the neonatal period is less complete than those usually diagnosed in the neonatal period, although there is good ascertainment of all chromosomal and cardiac anomalies, whenever diagnosed. Ascertainment of ophthalmological anomalies is low. Karyotype details of cases with abnormal karyotypes are now being recorded. These are available for cases from 2004.

Maximum Age at Diagnosis

Up to 12 years of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is potentially legal, subject to proper process, for fetuses without identified anomalies up to 24 weeks' gestation. There is no upper gestational age limit for termination if a major anomaly is diagnosed that is considered to be life threatening for the newborn baby.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is fetal death after 24 completed weeks. There is no lower gestational age or weight limit for anomalies identified in early fetal deaths. Miscarriages under 20 weeks' gestation that have abnormal karyotypes which have not been detected antenatally and are not accompanied by structural anomalies are not included in the database.

Exposure Data Availability

We have good data on exposure to diabetes in pregnancy, due to a linked database (Northern Diabetes in Pregnancy Survey) that has run since 1995. Maternal drug exposure, whether or not they smoke, and major medical problems are recorded when available. In mid-2004, maternal weight and height data were added to the reporting form.

Denominator Information

At present, denominator data is provided by the U.K. National Statistics. There is work at the national level to provide information on gestation for all registered births, which is currently lacking.

Registry Description Reference

Richmond S, Atkins J. 2005. A population-based study of prenatal diagnosis of congenital malformation over 16 years. BJOG 112:1349–1357.

Ethics and Consent

The registry requires ethics committee approval to collect and store data and this is granted by the Trent Multi-center Research Ethics Committee. Approval is renewed annually.

National legislation requires informed consent to register a baby with a congenital anomaly. However, through its membership of the British Isles Network of Congenital Anomaly Registers (BINOCARs), the registry collects non-consented data under Section 251 of the NHS Act 2006 (originally enacted under Section 60 of the Health and Social Care Act 2001), which allows the common law duty of confidentiality to be set aside in specific circumstances where anonymous information is not sufficient and where patient consent is not practicable.

Electronic and Web-based Data Capture

The Northern England register does not have web-based data capture facilities at present. While cases are reported electronically, there is no system for uploading this information directly to the database. Therefore, information received electronically is added to the database manually. Electronic downloads of cases are received via internal secure email from the regional cleft lip and palate team (monthly) and the cytogenetic laboratory (quarterly). The cases included in these lists are the most recent available. Cases for cross validation are received from the Hospital Episode Statistics on an ad hoc basis. These are hand delivered or sent by courier on an encrypted disk or memory stick.

Recent Registry Activities and Publications (2007–2010)

Armstrong BG, Dolk H, Pattenden S, et al. 2007. Geographic variation and localised clustering of congenital anomalies in Great Britain. Emerg Themes Epidemiol 4:14.

Bythell M, Bell R, Taylor R, et al. 2008. The contribution of late termination of pregnancy to stillbirth rates in Northern England, 1994–2005. BJOG 115:664–666.

Dadvand P, Rankin J, Rushton S, Pless–Mulloli T. 2010. Association between maternal exposure to ambient air pollution and congenital heart disease: a register-based, spatiotemporal analysis. Am J Epidemiol 2011;173:171–82.

Dadvand P, Rankin J, Shirley MD, et al. 2008. Descriptive epidemiology of congenital heart diseases in Northern England. Paediatr Perinat Epidemiol 23:58–65.

Dolk H, Armstrong B, Lachowycz K, et al. 2010. Ambient air pollution and risk of congenital anomalies in England, 1991–1999. Occup Environ Med 67:223–227.

Draper ES, Rankin J, Tonks A, et al. 2009. Congenital abnormalities: data needed to establish causes. BMJ 339:b3428.

Draper ES, Rankin J, Tonks AM, et al. 2008. Recreational drug use: a major risk factor for gastroschisis? Am J Epidemiol 167:485–491.

Fillingham A, Rankin J. 2008. Prevalence, prenatal diagnosis and survival of gastroschisis. Prenat Diagn 28:1232–1237.

Glinianaia SV, Rankin J, Wright C. 2008. Congenital anomalies in twins: a register-based study. Hum Reprod 23:1306–1311.

Hemming V, Rankin J. 2007. Small intestinal atresia in a defined population: occurrence, prenatal diagnosis and survival. Prenat Diagn 27:1205–1211.

Irving C, Richmond S, Wren C, et al. 2010. Changes in fetal prevalence and outcome for trisomies 13 and 18: a population-based study over 23 years. J Mat-Fet Neonat Med 2011;24:137–141.

Irving C, Basu A, Richmond S, et al. 2008. Twenty-year trends in prevalence and survival of Down syndrome. Eur J Hum Genet 16:1336–1340.

McNally RJ, Rankin J, Shirley MD, et al. 2008. Space-time clustering of Down syndrome: results consistent with transient pre-disposing contagious agent. Int J Epidemiol 37:1169–1179.

Pharoah PO, Glinianaia SV, Rankin J. 2009. Congenital anomalies in multiple births after early loss of a conceptus. Hum Reprod 24:726–731.

Rankin J, Tennant P, Stothard K, et al. 2010. Maternal obesity and congenital anomaly risk: a cohort study. Int J Obes 34:1371–1380.

Rankin J, Cans C, Garne E, et al. 2010. Congenital anomalies in children with cerebral palsy: a population-based record linkage study. Dev Med Child Neurol 52:345–351.

Rankin J, Chadwick T, Natarajan M, et al. 2009. Maternal exposure to ambient air pollution and risk of congenital anomalies. Environ Res 109:181–187.

Rankin J, Silf KA, Pearce MS, et al. 2008. Congenital anomaly and childhood cancer: a population-based, record linkage study. Pediatr Blood Cancer 51:608–612.

Rankin J. 2007. Congenital anomalies in the British Isles. Congenital diseases and the environment. In: Nicolopoulou–Stamati P, Hens L, Howard C, editors. New York: Springer. pp 359–377.

Swamy R, Embleton N, Hale J. 2008. Sacrococcygeal teratoma over two decades: birth prevalence, prenatal diagnosis and clinical outcomes. Prenat Diagn 28:1048–1051.

Tennant PW, Pearce MS, Bythell M, Rankin J. 2010. 20-year survival of children born with congenital anomalies: a population-based study. Lancet 375:649–656.

Wren C, Reinhardt Z, Khawaja K. 2008. Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. Arch Dis Child Fetal Neonatal Ed 93:F33–35.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contributions to EUROCAT studies.

Contacts for Further Information

Judith Rankin, Register Lead, Regional Maternity Survey Office, 1-2 Claremont Terrace, Newcastle upon Tyne, NE2 4AE, United Kingdom. E-mail: j.m.rankin@ncl.ac.uk. Web address: www.rmso.org.uk.

Judith Rankin, Institute of Health & Society, Baddiley-Clarke Building, Newcastle Univeristy, Richardson Road, Newcastle upon Tyne, NE4 2AX.

Mary Bythell, Regional Maternity Survey Office Coordinator, Regional Maternity Survey Office, 1-2 Claremont Terrace, Newcastle upon Tyne, NE2 4AE, United Kingdom. E-mail: mary.bythell@ncl.ac.uk. Web address: www.rmso.org.uk.

Martin Ward Platt, Regional Maternity Survey Office Clinical Director, 1-2 Claremont Terrace, Newcastle upon Tyne, NE2 4AE, United Kingdom. E-mail: m.p.ward-platt@ncl.ac.uk. Web address: www.rmso.org.uk.

UNITED KINGDOM, THAMES VALLEY – FULL MEMBER

History and Funding

The Congenital Anomaly Register of Oxfordshire, Berkshire, and Buckinghamshire (CAROBB) was awarded funding by the Department of Health in 2003 to maintain and expand the previously established Oxford Congenital Anomaly Register to include Berkshire and Buckinghamshire. Oxford Congenital Anomaly Register was established in 1991. It started to contribute Oxfordshire data to EUROCAT in 2002 and has now expanded to include cases for the three counties. CAROBB is an active member of BINOCAR.

Population Coverage

- For births 1991 to 2004 – Information is collected on all malformations suspected prenatally and/or confirmed in fetuses/babies booked for delivery at the two maternity hospitals in Oxfordshire or in the community. Cases submitted to EUROCAT must have an Oxfordshire postcode – this gives the best approximation available to the unselected local Oxfordshire population (7000 births).
- For births from 2005 onward – The register uses the same malformation inclusion criteria to cover the whole of Oxfordshire, Berkshire, and Buckinghamshire. This region is defined by the Local Authority boundaries that make up the three counties. The population coverage is approximately 30,000 births per annum.
- For 2005 births – ascertainment in Berkshire and Buckinghamshire is likely to be lower than would be expected because systems for registration were still being established. Therefore, prevalence rates will be misleading for this year.

Sources of Ascertainment

Data are obtained voluntarily from multiple sources across the region, such as antenatal clinics, obstetric ultrasound, delivery suites, special care baby units, cytogenetic laboratory, pediatric pathology, and the Down

syndrome service. Information is collected on all fetuses identified antenatally with a suspected congenital anomaly or ultrasound soft marker and on all babies born with a congenital anomaly. The aim is to collect data concerning all infants aged up to age 1 year, but in practice, this is not achieved. There is under ascertainment of cardiac, orthopedic, and renal defects diagnosed after the mother has left the maternity unit and methods to improve ascertainment are being explored.

Maximum Age at Diagnosis

Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal up to 24 weeks of gestation with no gestation limit for serious congenital defects. Cases are ascertained via the prenatal diagnosis unit and from postmortem reports.

Stillbirth Definition and Early Fetal Deaths

The definition of still birth is ''a child born with no signs of life after complete expulsion from the mother after the 24th week of pregnancy''. All stillbirths with a congenital anomaly are registered. Early fetal deaths/spontaneous abortions are included with no lower gestational age limit.

Exposure Data Availability

Information is collected where it is available (not on every case) on chronic illness in the mother, details of assisted conception, invasive tests in pregnancy, and alcohol abuse.

Denominators and Controls Information

Oxford Maternity Data system provides denominator data for 1991 to 2004 births. The Office for National Statistics (ONS) provide denominators for births after 2005.

Registry Description Reference

www.npeu.ox.ac.uk/carobb/annualreport.

Ethics and Consent

The registry requires ethics committee approval to collect and store data and this comes from Trent, United Kingdom for all BINOCAR. Approval is renewed every 5 years.

National legislation requires informed consent but the registry is exempt. Patient Information Advisory Group (PIAG) approval given for all BINOCAR registries. Parents have to ask for the removal of the child from the register (opt-out).

Electronic and Web-based Data Capture

There is direct access to the cytogenetic laboratory covering the whole area, providing six-monthly electronic lists of all abnormal karyotypes for prenatal and postnatal diagnoses. Pediatric cardiology centers covering part of the registry population supply systematic electronic case lists to the registry on cases undergoing surgical procedures. Monthly electronic lists of relevant pediatric admissions (by ICD10 code) are received from the tertiary referral center.

Recent Registry Activities and Publications (2007–2010)

Thames Valley Register activities include regular feedback to staff in all contributing hospitals by presenting local data and encouraging use of the data for audit and research. Recent collaborations include one with experimental psychologists, clinical and cytogeneticists on a project concerning sex chromosome trisomes; BINOCAR collaborations (e.g., with the Fetal Anomaly Screening Program) to develop a means of monitoring the National Program and collaboration concerning the future of national surveillance in England and Wales.

Bishop DV, Barnicoat A, Boyd PA, et al. 2010. Autism spectrum disorders, language and communication in children with sex chromosome trisomies. Arch Dis Child doi:10.1136/adc.179747.

Dolk H, Armstrong B, Lachowycz K, et al. 2010. Ambient air pollution and risk of congenital anomalies in England, 1991-1999. Occup Environ Med 67: 223–227.

Choudhry MS, Rahman N, Boyd P, Lakhoo K. 2009. Duodenal atresia: associated anomalies, prenatal diagnosis and outcome. Pediatr Surg Int 25:727–730.

Sherwood W, Boyd P, Lakhoo K. 2008. Postnatal outcome of antenatally diagnosed intra-abdominal cysts. Pediatr Surg Int 24:763–765.

Nieuwenhuijsen MJ, Toledano MB, Bennett J, et al. 2008. Chlorination disinfection by-products and risk of congenital anomalies in England and Wales. Environ Health Perspect 116:216–222.

Zaki M, Boyd PA, Impey L, et al. 2007. Congenital myotonic dystrophy: prenatal ultrasound findings and pregnancy outcome. Ultrasound Obstet Gynecol 29:284–288.

Choudhry M, Boyd PA, Chamberlain PF, Lakhoo K. 2007. Prenatal diagnosis of tracheo-esophageal fistula and oesophageal atresia. Prenat Diagn 27:608–610.

Armstrong BG, Dolk H, Pattenden S, et al. 2007. Geographic variation and localised clustering of congenital anomalies in Great Britain. Emerg Themes Epidemiol 4:14.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

Patricia Boyd and Cath Rounding, National Perinatal Epidemiology Unit, University of Oxford, Old Road Campus, Headington, Oxford OX3 7LG. E-mail: carobb@npeu.ox.ac.uk. Website: www.npeu.ox.ac.uk/carobb.

UNITED KINGDOM, WALES – FULL MEMBER

History and Funding

The Congenital Anomaly Register and Information Service (CARIS) collect data on all cases of congenital anomaly born to mothers normally resident in Wales. Data collection commenced on January 1, 1998, and

includes any baby where pregnancy ended on or after this date. The Wales Register joined EUROCAT in 1998. The register is based at Singleton Hospital, Swansea and, since October 1, 2009, became part of Public Health Wales NHS trust. The register aims to collect data that 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 coordinate provision of health services for affected babies and children.
- Assess possible clusters of birth defects and their causes.

The register has a lead clinician, who is an obstetrician and a director of information, and who is a consultant in Public Health.

In 2005, an expert advisory group was set up to help set objectives for the register. The group consists of a fetal medicine consultant, an obstetrician, a pediatrician, a medical geneticist, a consultant radiologist, a lay representative, a consultant in public health, the director of Antenatal Screening Wales, and a senior medical officer from the Welsh Assembly Government. The group meets twice yearly.

Population Coverage

The registry is population-based and covers the entire country of Wales with an annual number of births of currently around 35,000.

Sources of Ascertainment

Reporting is voluntary. The register relies upon multisource reporting including antenatal clinics, delivery units, pediatric departments, ophthalmology, cytogenetics, pathology, orthopedics, and maxillofacial and regional centers of pediatric surgery. Each delivery unit has a nominated coordinator to help ensure good reporting. Register staff also visit units to help with data collection. Registration covers all fetuses with prenatally diagnosed anomalies. There is no lower age limit so fetal losses and early terminations with anomalies are registered. All live born babies with structural anomalies are registered if diagnosed before their first birthday, but all chromosomal anomalies and syndromes are registered, even if diagnosed later.

Babies in North Wales needing specialist services are referred to Liverpool and in South Wales, they travel to Bristol for cardiac surgery. Both pediatric cardiology centers in Cardiff and Liverpool supply systematic case lists and diagnostic details to the registry, including details of antenatally-detected cases. These lists cover the whole population requiring pediatric cardiology services and are provided annually.

The cytogenetic laboratory in Cardiff provides a download of data of all abnormal karyotypes on a quarterly basis. This includes details of demographic details, procedure, and reason for karyotying. Cases reported include antenatal and all children born since 1998. This covers most of the population. Some cases in North Wales are karyotyped in Liverpool, while a few cases in Mid Wales are referred via Shrewsbury to Birmingham. This means that the register cannot guarantee 100% coverage of the Welsh population; although many of these cases are known and reported back to the register.

Maximum Age at Diagnosis

Maximum age at diagnosis is set at 1 year of age. This is currently under review. Chromosomal anomalies and syndromes are an exception to this rule. In these cases, it is often found that a registration has already been made for other anomalies diagnosed within the first year.

Electronic reporting of inpatient data has presented a challenge, as it has highlighted unreported cases from years before. It is not always clear precisely when the diagnosis was originally made. These cases require follow-up to ensure that the diagnosis is correct as well as to verify the time of diagnosis. Regular data downloads should lessen this problem in the future and give better ascertainment.

Termination of Pregnancy for Fetal Anomaly

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

Stillbirth Definition and Early Fetal Deaths

Stillbirth definition is 24 weeks' gestation (late fetal death after 23 weeks + 6 days gestation). Stillbirths of 24 weeks or more are registered. Early fetal deaths/spontaneous abortions have no lower limit for inclusion on the register (earliest recorded is 8 weeks' gestation).

Exposure Data Availability

Exposure information on maternal drug use, smoking, alcohol, maternal and paternal diseases and occupations, outcomes of previous pregnancies, and assisted conception is available. Folic acid supplementation before and during pregnancy is also collected. Drugs are coded to the ATC classification. Since 2005, body mass index has also been added to the dataset.

Denominators and Controls Information

Denominator data is obtained from the Office for National Statistics. Where this is not timely or readily available, then data may be used from the National Community Child Health System.

Registry Description Reference

The registry's description and work was most recently described in our 10th annual report. This is available on: www.wales.nhs.uk/sites3/Documents/416/Caris%20Ann%20rep%20%28Eng%29%20final.pdf.

Ethics and Consent

The registry requires ethics committee approval to collect and store data and this comes from Leicester Regional Multicentre Research Ethics Committee, under

the auspices of the BINOCAR. Approval is renewed every 5 years, next due in 2014.

National legislation requires informed consent but the registry is exempt from this. The register has been granted exemption under section 251 of the Health Service Act 2006. Parents have to ask for the removal of the child from the register (opt-out).

Information Governance Standards, Policies and Protocols are Agreed and Set by a Committee within Public Health Wales

Electronic and Web-based Data Capture

Data are reported electronically to the register from cytogenetics, medical genetics, child health system, and inpatient data. Antenatal ultrasound reports are sent electronically from 10 delivery units. These are downloaded monthly. The remaining four units are expected to have the same system in place by the end of 2010. We will start work on developing a web-based reporting system for clinical staff in 2011.

Recent Registry Activities and Publications (2007–2010)

Oral presentation at the British International Congress of Obstetrics and Gynaecology. Congenital anomalies in clomiphene induced pregnancies: review from a congenital anomaly register (London – July 2007).

CARIS Annual report – Risk factors in pregnancy. Published November 2007.

www.wales.nhs.uk/sites3/Documents/416/Caris%20Ann%20rep%202006.pdf.

Oral presentation at EUROCAT Registers Leaders Meeting. Update on gastroschisis in Wales (Helsinki – June 2008).

Oral presentation – International Clearing House of Birth Defects Surveillance and Research annual conference. Evaluation of a congenital anomaly register (Padua – September 2008).

Poster presentation – International Clearing House of Birth Defects Surveillance and Research annual conference. Cystic fibrosis in Wales (1998–2007). (Padua – September 2008.)

CARIS Annual report – 10 years of reporting. Published November 2008.

www.wales.nhs.uk/sites3/Documents/416/Caris%20Ann%20rep%20%28Eng%29%20final.pdf.

Poster presentation at UKPA conference. Congenital Anomalies and Socioeconomic deprivation in Wales 1998 to 2007 (Brighton – April 2009).

Poster presentation at EUROCAT Registers Leaders meeting. Congenital anomalies, smoking and deprivation in Wales (Bilbao – June 2009).

Draper ES, Rankin J, Tonks A, et al. Congenital abnormalities: data needed to establish causes. BMJ 339:b3428.

Oral presentation – International Clearing House of Birth Defects Surveillance and Research annual conference. Outcome of antenatally suspected congenital cystic adenomatoid malformation of the lungs (CCAM) and sequestration of the lungs in Wales, United Kingdom: 7 years experience 2000 – 2006 (Salt Lake City – Sept 2009). Abstract to be published in Birth Defects Research A 2010.

Poster presentation – 9th World Congress of Perinatal Medicine. Outcome of antenatally suspected sequestration of lung (Berlin – October 2009).

CARIS Annual Report. Focus on skeletal anomalies. Published November 2009.

www.wales.nhs.uk/sites3/Documents/416/Caris%20Ann%20rep%20%28Eng%29%20%286%29.pdf.

Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

Address for Further Information

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UNITED KINGDOM, WESSEX – FULL MEMBER

History and Funding

The Wessex Antenatally Detected Anomalies Register (WANDA) was started in 1988 as a local database. In 1994, funding was obtained and the regional register established under the auspices of the Wessex Clinical Genetics Service. Funding is provided by each of the 10 districts covered through the genetics budget. The registry joined EUROCAT in 2002, and has sent backdated data from 1994. From 2001, data have been transmitted electronically to the ONS. WANDA is an active member of BINOCAR and the Follow-up of Congenital Anomalies Long-term study (FOCAL). Data collection is enhanced by regular specialized meetings in each district. Thus, the aims of WANDA are to improve communication between all clinicians involved in the care of pregnant women and their babies; to monitor clusters and provide relevant data to allow further investigation and research; to evaluate new and established prenatal screening tests; to monitor incidence and population trends of selected malformations; to provide data for research into the etiology and natural history of certain anomalies and for the investigation of potential teratogens; and to provide data for health care policies and planning.

Population Coverage

All women living within the old 'Wessex' region, Jersey and Guernsey, who deliver within the hospitals in the region are included (population-based III). Annual births are approximately 27,000 and the population is 2.8 million.

Sources of Ascertainment

Information is collected on all fetuses in which an anomaly, a suspected anomaly, or an ultrasound soft marker, has been detected antenatally. Data are also ascertained on all babies born with a congenital anomaly or a genetic condition. Anomalies are accepted at any age of detection, but in reality, reporting is unreliable if diagnosed outside the neonatal period. Exceptions are chromosome errors and surgical conditions for which the

register has full ascertainment at any age. All cardiac defects detected antenatally and those that require treatment or further investigation postnatally are included in the register, hence, small ventricular septal defects, mild pulmonary stenosis, and other conditions with minimal or no morbidity are not included. This information is available directly from the cardiology department.

Reporting of hypospadias is good from January 2001 but was poor until this date.

The cytogenetic laboratories provide data on all abnormal prenatal and infant karyotypes (and now array comparative genomic hybridization results) for the entire population covered by WANDA. Routine downloads are also sent on all cases every 6 months to ensure no case is missed.

Data are obtained voluntarily from multiple sources. Sources used include ultrasonographers, radiologists, obstetricians, fetal medicine, pediatricians, pediatric cardiologists, pediatric surgeons, pediatric neurologists, pediatric pathologists, plastic surgeons, orthopaedic nurse, CESDI (Confidential Enquiry into Stillbirths and Deaths in Infancy), central records for Primary Care Trusts for postnatal cases, cytogenetics, molecular genetics, clinical genetics, pathologists, and biochemistry. Ascertainment is excellent for anomalies detected antenatally but less complete for those diagnosed postnatally. Both active and passive ascertainment procedures are used. Data are good where there has been a postmortem examination, for all significant cardiac and chromosomal defects, and for all conditions requiring surgery such as abdominal wall defects or clefts. Ascertainment is incomplete for neurologic and orthopedic conditions, although serious efforts are underway to improve these. Cerebral palsy or isolated hearing or sight impairment are not included.

Maximum Age at Diagnosis

There is no upper age limit.

Termination of Pregnancy for Fetal Anomaly

Termination of pregnancy is legal up to 24 weeks of gestation with no gestation limit for very serious congenital anomalies. Cases are ascertained from the department of fetal medicine and from postmortem reports.

Stillbirth Definition and Early Fetal Deaths

The definition of stillbirth is ''a child born with no signs of life after complete expulsion from the mother after the 24th week of pregnancy.'' All stillbirths with a congenital anomaly are registered. Early fetal deaths/spontaneous abortions are included with no lower gestational age limit.

Exposures Data Availability

Information is collected where it is available (not on every case) on chronic illness in the mother, details of assisted conception, invasive tests in pregnancy, and alcohol abuse. In practice, this information is very underreported.

Denominators and Controls Information

Data on the number of births in each district are provided through the labor wards of each hospital (i.e., referring to the births in each hospital to residents of the region). Maternal age is supplied by ONS with at least a one year delay. No control information is collected.

Ethics and Consent

National legislation requires informed consent but the registry is exempt. National Information Governance Board approval (formerly PIAG) – Health & Social Care Act 2001 – allows for the Secretary of State for Health to permit certain data to be collected without consent. However, parents/patients can opt-out of registers.

Electronic and Web-based Data Capture

The register is able to access other data sources electronically for information but we do not receive regular case reports through this route.

Recent Registry Activities and Publications (2007–2010) Local Studies

Outcome of fetal 'absent stomach' or 'small stomach' found at routine ultrasound scan.

Prenatal detection rate of postnatally diagnosed esophageal atresia +/- tracheo-esophageal fistula.

Long-term outcome of duodenal atresia.

Prenatal detection of heart abnormalities in Wessex.

National Studies

With four other U.K. registers and the Small Areas Health Authority Unit at Imperial College, 'chlorination disinfection byproducts and risk of congenital anomalies in England and Wales' study. Complete and published.

The Follow-up of Congenital Anomalies Long-term study, under the umbrella of the National Perinatal Epidemiology Unit in Oxford, commenced in 2006 with funding from Newlife. 'Etiology of gastroschisis: a prospective case control study to investigate the effects of lifestyle, dietary, and environmental exposures.' Case collection is complete but the control data are still awaited.

In conjunction with the Department of Experimental Psychology in Oxford, Clinical Genetics and the local congenital anomaly registers in Southampton, Oxford, Bristol, Manchester, and London, and the parental support group Unique, children aged from 4 to 16 years who were diagnosed prenatally with a sex chromosome anomaly were followed up. The findings from this study have been published.

We thank the many people throughout Europe involved in providing and processing information, including affected families, clinicians, health professionals, medical records clerks, and registry staff.

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Registry Contribution to EUROCAT Collaborative Papers (2007–2010)

Table 2 shows the registry contribution to EUROCAT studies.

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