Eurocat

European Surveillance of Congenital Anomalies

Special Report:

Congenital Heart Defects in Europe 2000-2005

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SUMMARY STATISTICS

The total prevalence rate for non-chromosomal congenital heart disease (CHD) in Europe is 7 per 1,000 births.

The average rate of livebirths affected by CHD surviving the first week of life is 6.4 per 1,000 births. Differences between countries in perinatal mortality rates and termination of pregnancy rates associated with CHD have little impact on this rate. An estimated 6% of these babies die before the age of 1 year.

Ventricular Septal Defect (VSD) and Atrial Septal Defect (ASD) are the most frequent CHD subtypes, accounting (with Pulmonary Valve Stenosis - PVS) for approximately three-quarters of non-chromosomal CHD cases. The vast majority of these children are liveborn and survive the first week, with 7% requiring surgery. A reasonable prevalence estimate for VSD/ASD/PVS combined is 5 per 1,000 births surviving the first week of life.

The remaining quarter of CHD mainly include conditions with higher perinatal mortality, high surgery rates, and conditions for which termination of pregnancy is the outcome for a significant proportion in some countries. The rate of cases surviving the first week of life for these conditions is 1.3 per 1,000 births, of whom an estimated 80% require surgery and 7% are too severe for surgery.

The average combined CHD mortality rate (perinatal deaths + terminations of pregnancy) in Europe is currently 0.7 per 1,000 births. However, a few countries have rates 50% or more in excess of this.

The main health service needs to reduce CHD burden are primary prevention, successful early treatment (possibly involving also improved prenatal diagnosis), and ongoing care for affected children and adults.

EUROCAT is the European network of population-based registries for the epidemiologic surveillance of congenital anomalies. It started in 1979 and now surveys approximately 1.5 million births per year in Europe across 40 registries in 20 countries, nearly one third of the EU annual birth population. A standardised central database on approx 400,000 cases of congenital anomaly among livebirths, stillbirths and terminations of pregnancy for fetal anomaly is held at the EUROCAT Central Registry at University of Ulster (UK), updated every year.

The objectives of EUROCAT are:

- To provide essential epidemiologic information on congenital anomalies in Europe
- To facilitate the early warning of teratogenic exposures
- To evaluate the effectiveness of primary prevention
- To assess the impact of developments in prenatal screening
- To act as an information and resource centre regarding clusters, exposures or risk factors of concern
- To provide a ready collaborative network and infrastructure for research related to the causes and prevention of congenital anomalies and the treatment and care of affected children
- To act as a catalyst for the setting up of registries throughout Europe collecting comparable, standardised data

EUROCAT is a WHO Collaborating Centre for the Epidemiologic Surveillance of Congenital Anomalies.

EUROCAT is funded by the EU Public Health Programme.

Extensive information on EUROCAT can be found on its website www.eurocat.ulster.ac.uk. This includes prevalence tables for 95 subgroups of congenital anomaly by registry, year and pregnancy outcome

(http://www.eurocat.ulster.ac.uk/pubdata/tables.html), as well as a series of Special Reports and scientific journal publications.

Introduction

This report has been designed as a contribution to the "Global Burden of Disease, Injuries and Risk Factors" (GBDIRF) project 2007-2010, led by the WHO and Universities of Harvard, Washington, Johns Hopkins and Queensland. Five clusters are responsible for collecting data, one of these being the Child and Maternal cluster, with a Neonatal expert sub-group consisting of five expert working groups of which the Congenital and Genetic Expert Working Group is one. EUROCAT is represented on this working group. The GBDRIF project has selected three congenital anomaly subgroupings for inclusion: chromosomal anomalies, congenital heart disease, and neural tube defects. This EUROCAT Special Report focuses on congenital heart disease.

The burden of disease relating to congenital heart disease (CHD) relates to:

- the burden to the affected child and family, and later adult, in terms of associated morbidity and impairment, reduced participation and quality of life
- the burden to the affected child and family in terms of fetal and infant mortality, and childhood mortality
- the continuing burden to the affected adult in terms of reduced life expectancy and quality of life
- the burden to the health service in terms of treatment costs.

CHD constitutes the largest group of congenital anomalies, accounting for nearly one third of babies with major congenital anomalies diagnosed prenatally or in infancy in Europe. Great advances in treatment in recent decades in Europe have led to a decrease in infant mortality and an increase in children and adults with CHD. Environmental risk factors such as socio-economic status, maternal infections, drugs taken during pregnancy, nutritional factors and environmental pollution have been associated with CHD in epidemiological research, but no concerted primary prevention strategy has emerged, and the prevalence of CHD diagnosed prenatally and up to the first year of life has not declined. Instead, improving early diagnosis has led to an increase in reported prevalence

and small muscular defects with early spontaneous closure are being diagnosed neonatally.

CHD is a diverse group of conditions in terms of severity and associated morbidity and mortality. Furthermore, a proportion of cases are associated with chromosomal anomalies, and a proportion of cases have multiple malformations of different organ systems. While EUROCAT has information on associated congenital anomalies, it has no information on associated intellectual, sensory or motor impairments for which children with CHD are at higher risk. EUROCAT research in collaboration with SCPE (network of cerebral palsy registries in Europe) is for example documenting the higher risk of cerebral palsy suffered by children with CHD.

Developments in prenatal screening and diagnosis by ultrasound have led to an increasing proportion of cases being prenatally diagnosed. Screening practice and resulting detection rates vary by country. For very severe CHD, prenatal diagnosis is in some countries followed by termination of pregnancy. For most CHD, prenatal diagnosis prompts further diagnostic investigation, gives the family and health professionals early warning, and may increase the chances of treatment success.

This report will present a brief overview of the epidemiology of CHD in Europe, in terms of the prevalence of livebirths with CHD, proportion undergoing surgery, fetal and perinatal mortality, and frequency of different types of CHD.

The figures presented here are for the period 2000-2005. Prevalence data from 1980 to 2007 can be found on the EUROCAT website at http://www.eurocat.ulster.ac.uk/pubdata/tables.html.

Methods

Data were extracted from the EUROCAT database, fully described in EUROCAT Guide 1.3 Instructions for the Registration and Surveillance of Congenital Anomalies (http://www.eurocat.ulster.ac.uk/pdf/EUROCAT-Guide-1.3.pdf). A description of all EUROCAT member registries contributing data to this Report can be found at http://www.eurocat.ulster.ac.uk/memberreg/memberreg.html.

Twenty-nine population-based registries contributed data included in this Report, as shown in Table 1. The total population coverage for 2000-2005 was 3.3 million births. Only full member registries contributing individual anonymised case data to the central database were included. Registries were excluded which had not updated their data since before 2004 (birth year) or which according to their data quality indicators (www.eurocat.ulster.ac.uk/memberreg/DQI.html) had less than 75% of EUROCAT average major malformation prevalence and less than half the EUROCAT average prevalence of selected severe CHD indicating recent problems with CHD case ascertainment.

Cases of CHD include livebirths, late fetal deaths/stillbirths from 20 weeks gestational age, and terminations of pregnancy following prenatal diagnosis of fetal anomaly of any gestational age.

Cases can have up to nine syndrome or malformation codes. The following International Classification of Disease codes are used to define cases of congenital heart disease:

Anomaly	Description Of Anomaly	ICD9	ICD10	Comments
Congenital heart disease		745, 746, 7470-7474	Q20-Q26	exclude PDA in preterm babies (<37 weeks) - ICD9: 7470; ICD10: Q250
Common arterial truncus	Presence of a large single arterial vessel at the base of the heart (from which the aortic arch, pulmonary and coronary arteries originate), always accompanied by a large subvulvar septal defect.	74500	Q200	
Transposition of great vessels	Total separation of circulation with the aorta arising from the right ventricle and the pulmonary artery from the left ventricle	74510	Q203	
Single ventricle	Only one complete ventricle with an inlet valve and an outlet portion even though the outlet valve is atretic	7453	Q204	
Ventricular septal defect	Defect in the ventricular septum	7454	Q210	
Atrial septal defect	Defect in the atrial septum	7455	Q211	ICD9: 74550 ICD10: Q2111
Atrioventricular septal defect	Central defect of the cardiac septa and a common atrioventricular valve, incl primum ASD defects	7456	Q212	
Tetralogy of Fallot	VSD close to the aortic valves, infundibular and pulmonary valve stenosis and over-riding aorta across the VSD	7452	Q213	
Tricuspid atresia and stenosis	Obstruction of the tricuspid valve and hypoplasia of the right ventricle	7461	Q224	
Ebstein's anomaly	Tricuspid valve displaced with large right atrium and small right ventricle	7462	Q225	
Pulmonary valve stenosis	Obstruction or narrowing of the pulmonary valves which may impair blood flow through the valves	74601	Q221	
Pulmonary valve atresia	Lack of patency or failure of formation altogether of the pulmonary valve, resulting in obstruction of the blood flow from the right ventricle to the pulmonary artery	74600	Q220	
Aortic valve atresia/stenosis	Occlusion of aortic valve or stenosis of varying degree, often associated with bicuspid valves	7463 (no code for atresia)	Q230	
Hypoplastic left heart	Hypoplasia of the left ventricle, outflow tract and ascending aorta resulting from an obstructive lesion of the left side of the heart	7467	Q234	
Hypoplastic right heart	Hypoplasia of the right ventricle, always associated with other cardiac malformations	no code	Q226	
Coarctation of aorta	Constriction in the region of aorta where the ductus joins aorta	7471	Q251	
Total anomalous pulmonary venous return	All four pulmonary veins drain to right atrium or one of the venous tributaries	74742	Q262	

Cases with only patent ductus arteriosus associated with preterm birth are excluded.

Prevalence rates are calculated as follows for this report:

Livebirth prevalence rate: (no. liveborn cases)/(total births live and still)
Fetal death prevalence rate: (no. fetal deaths)/(total births live and still)
Termination of pregnancy (TOPFA) rate: (no. TOPFA)/(total births live and still).

Total prevalence rate = livebirth prevalence rate + fetal death prevalence rate + TOPFA prevalence rate.

Note that these rates are slightly unconventional e.g. the livebirth prevalence rates includes all births rather than just livebirths in the denominator, and the TOPFA prevalence rate does not include TOPFA in the denominator. This is to facilitate use of a standard denominator, and means that the three rates add up exactly to the total rate. Since stillbirths and TOPFA each account for less than 1% of total births, the difference with rates using "correct" denominators is minimal.

Each case is counted once only in any given prevalence rate. A case with more than one type of cardiac defect would be counted within the prevalence rate for each type.

Cases were further classified as follows:

- Non-chromosomal: Cases without a chromosomal syndrome (ICD10 codes Q90-93, 96-99 excl Q936).
- Isolated cardiac: Non-chromosomal cases without an additional major non-cardiac anomaly coded to a non-cardiac EUROCAT subgroup (as defined in Guide 1.3).
- Single isolated cardiac: Non-chromosomal cases without an additional major non-cardiac anomaly and with only one of the cardiac subgroups coded. This group was defined to facilitate estimating surgery and mortality rates associated with a particular CHD type that were not affected by its association with other cardiac

anomalies. This was considered sufficient for the purposes of this report which aims to estimate burden of disease in general terms, rather than describing detailed clinical outcomes for which a more clinically oriented classification would be needed. 72% of isolated CHD cases were coded to one CHD subgroup only, and thus considered "single" isolated CHD.

"Severity" of CHD subtype was classified according to the combined perinatal mortality and TOPFA rate as follows:

- Very Severe: single ventricle, hypoplastic left heart, hypoplastic right heart, Ebstein's anomaly, tricuspid atresia
- Severe: Pulmonary valve atresia, common arterial truncus, atrioventricular septal defects (AVSD), aortic valve atresia/stenosis, transposition of great vessels, tetralogy of fallot, total anomalous pulmonary venous return, coarctation of aorta; without additional CHD anomalies classified as very severe.
- VSD/ASD/PVS: Ventricular septal defect, atrial septal defect, pulmonary valve stenosis without additional CHD anomalies classified as very severe or severe. VSD only: VSD without other cardiac or non-cardiac anomalies.

Note that there are a few subtypes of CHD which are not included in any of the above severity categories, as they are not standard EUROCAT subgroups (5% of all CHD cases).

There are other schemes for the classification of congenital heart disease needing expert review of cases and consideration of specific combinations of CHD codes. Our classification schemes shown above are pragmatic, using information as coded by registries without further review.

Results and Commentary

The average reported total prevalence of CHD in Europe is 8.0 per 1,000 births, including livebirths, stillbirths and TOPFA (Table 1).

Twelve percent of these are associated with chromosomal anomalies, 7% Down Syndrome, 1% Trisomy 13 and 2% Trisomy 18. Chromosomal anomalies are particularly common among atrioventricular septal defects (57% chromosomal). The prevalence of CHD associated with chromosomal anomalies (Table 2) depends on the maternal age profile in the country (since chromosomal anomalies are much more frequent among older mothers), the proportion of chromosomal cases diagnosed prenatally followed by termination of pregnancy without there being an ultrasound examination of the heart or fetal pathology, and the proportion of chromosomal fetal deaths where a full autopsy is performed. In terms of calculating the burden of disease, it is best therefore to group chromosomal CHD with chromosomal conditions (in particular they are an important part of the burden of disease associated with Down Syndrome), rather than with CHD, and henceforth we exclude them from this analysis.

Excluding cases associated with chromosomal anomalies, the average total prevalence of CHD is 7.0 per 1,000 (Table 2), the vast majority of which are livebirths (6.6 per 1,000). The prevalence of very severe cases was 0.5 per 1,000, severe cases 1.3 per 1,000 and VSD/ASD/PVS 4.3 per 1,000 (including VSD only at 2.2. per 1,000) (Table 3). Eighteen percent of CHD cases were associated with other major non-cardiac anomalies, a similar proportion (16-21%) regardless of severity category.

Five EUROCAT countries report a CHD livebirth prevalence of above 10 per 1,000 births (Table 2): Austria (13.7), Germany (10.2), Malta (13.3), Poland (10.2) and Switzerland (11.6). Higher prevalence may be associated with a true higher risk of CHD. It may also however be associated with earlier diagnosis, more extensive prenatal ultrasound or neonatal screening, with better ascertainment by the registries of later postneonatally diagnosed cases or with more registration of the least severe cases.

- Overall 15% of liveborn cases were reported as diagnosed (ie. first suspicion of malformation) after one month of age, but this proportion was one quarter or more in Austria, Denmark, Malta, Netherlands, Switzerland and UK (Table 2) suggesting better ascertainment of postneonatally diagnosed cases by these registries and/or later age at diagnosis. VSD/ASD/PVS and aortic valve atresia/stenosis are the most likely CHD types to be diagnosed after the first month of life (Annex 1).
- Austria has a higher than average prevalence across all categories of severity (Table 3), but a low prevalence of VSD only, suggesting that a true higher prevalence of CHD needs to be further investigated. Switzerland and Malta both have a high prevalence of VSD/ASD/PVS (including VSD only), suggesting more registration of the least severe cases that close spontaneously. Croatia has a lower prevalence across all categories (Table 3), possibly associated with general underascertainment. The Netherlands has a low prevalence of milder CHD cases due to underascertainment of cases that may not require hospitalisation, and ascertainment has improved recently. Further investigation is needed to distinguish differences in true prevalence from diagnostic and reporting differences.

Fetal deaths from 20 weeks gestation with CHD were reported for 0.09 per 1,000 births (Table 2), ranging from 0 per 1,000 (Malta) to 0.19 per 1,000 (Ukraine). The rate of first week deaths with CHD is 0.17 per 1,000 births, or 2.7% of all livebirths with CHD. Perinatal deaths including fetal deaths and first week deaths accounted for 0.26 per 1,000 births, ranging from 0.07 (Italy) to 0.93 (Ukraine) per 1,000. The high perinatal mortality rate with CHD in the Ukraine stands out against all other countries Since the total prevalence of CHD is not higher in Ukraine than elsewhere, the high perinatal mortality rate may be mainly associated with low treatment success. The next highest rates are 0.37-38 per 1,000 in Ireland, Malta and Netherlands, where there are no or very few terminations of pregnancy for fetal anomaly. Very low perinatal mortality rates, such as in Italy, may be associated with low autopsy rates or poor cause of death recording.

A separate analysis was made for deaths in the first year of life but after the first week for 2005-6. This information was known for all CHD cases by five registries (Odense, Dublin, SE Ireland, N Netherlands, N England). The data suggest that approximately 6% of babies surviving the first week with CHD died within the first year, an average prevalence of such deaths of 0.4 per 1,000 births, greater than the prevalence of first week deaths.

TOPFA associated with non-chromosomal CHD were more frequent than perinatal mortality, at 0.39 per 1,000, but this also varied more strongly between countries (Table 2). The TOPFA rate was 0 in Ireland, Malta, and Poland; varying up to 0.4 to 0.5 per 1,000 in Germany, Switzerland, Spain and UK; with a maximum of 1.06 per 1000 in France (Table 2). CHD cases which have other major non-cardiac anomalies accounted for nearly half of TOPFA cases. To some extent, this variation will reflect differences in prenatal screening and diagnosis between countries. It also reflects the frequency with which prenatal diagnosis results in termination of pregnancy, and there are also be some differences in definition and practice regarding the distinction between a late fetal death and a termination of pregnancy.

The high perinatal mortality and TOPFA rates are found among the rare CHD types. Two types of CHD result in a fetal death rate over 10% when present as single isolated anomalies: single ventricle, and Ebstein's anomaly (Table 4). Single ventricle and hypoplastic left heart are associated with particularly high first week deaths rates (15% each). Overall, perinatal mortality is high for single ventricle (26.7%), Ebstein's anomaly (19.8%), and Hypoplastic Left Heart (17.2%). Hypoplastic left heart contributed one quarter of all cardiac perinatal deaths. Termination of pregnancy (TOPFA) rates by single isolated subtype were generally very low except for single ventricle (40%), Tricuspid atresia and stenosis (22.8%), Ebstein's anomaly (18.8%), hypoplastic left heart (38.8%) and hypoplastic right heart (31.3%). Thus TOPFA is mainly performed for CHD with high risk of perinatal mortality. Whereas countries differed in their overall TOPFA rates, they generally performed TOPFA for the same range of CHD subtypes, with the exception of France which additionally had a TOPFA rate of 32-33% for pulmonary

valve atresia and aortic valve atresia/stenosis when present as single isolated cardiac anomalies (data not shown).

Two registries, Vaud (Switzerland) and Odense (Denmark) could provide data on surgery for liveborn cases for the years 2005-6, as this variable was only introduced in EUROCAT in 2005. One percent of CHD cases were judged too severe for surgery. Overall, 17% of cases of isolated CHD who survived the first week of life had surgery* (a prevalence of isolated CHD requiring surgery of 1.4 per 1,000 births), but this varied enormously by type, with many of the less frequent types usually resulting in surgery, whereas the surgery rate for isolated VSD/ASD/PVS was only 7% (higher in PVS than VSD and ASD). The surgery rate in isolated CHD cases other than isolated VSD/ASD/PVS was 82%, and 7% were too severe for surgery. These data on surgery are probably fairly representative of the European situation, whereby surgery is not normally conducted on less severe isolated CHD anomalies.

* This proportion was the same for all livebirths and not just those that survived the first week of life

Recommendations Regarding European Burden of Disease Estimates for GBDIRF Project.

The livebirth prevalence rate for non-chromosomal CHD in Europe is 6.6 per 1,000 births. It is possible that some areas experience up to twice this rate, but geographic differences in reported livebirth prevalence may be mainly diagnostic and reporting differences. There is some evidence in the literature of socioeconomic differences in CHD prevalence; while it is possible these may translate into differences between countries, such differences cannot be seen within Europe against the "noise" of variation in diagnostic and reporting factors.

The average rate of livebirths surviving the first week of life is 6.4 per 1,000 births. Differences between countries in perinatal mortality rates and termination of pregnancy rates associated with CHD have very little impact on this rate. An estimated 6% of these babies die before the age of 1 year.

VSD and ASD are the most frequent CHD subtypes, accounting (with PVS) for approximately three-quarter of CHD cases. The vast majority of these children are liveborn and survive the first week, and less than 10% require surgery. A reasonable prevalence estimate for VSD/ASD/PVS combined is 5 per 1,000 births surviving the first week.

The remaining quarter of CHD mainly include conditions with higher perinatal mortality, high surgery rates, and conditions for which termination of pregnancy is the outcome for a significant proportion in some countries. The rate of cases surviving the first week of life is 1.3 per 1,000, of whom an estimated 80% require surgery and 7% are too severe for surgery. We recommend that an average weighting for impact on quality of life for surviving cases be derived for this group and for VSD/ASD/PVS separately.

The average combined CHD mortality rate (perinatal + TOPFA) in Europe is currently 0.7 per 1,000 births. However, Ukraine has a higher rate of 1.0 per 1,000 due to a high

perinatal mortality rate, which may be more representative of other non-EUROCAT countries with similar health services to Ukraine. France also has a higher mortality rate of 1.3 per 1,000 due to a high termination of pregnancy rate, associated also with more terminations being performed for cases who would otherwise have survived the first week of life.

Terminations of pregnancy are mainly performed for CHD with high perinatal mortality. We recommend that in terms of burden of disease, the GBDIRF project should treat fetal deaths, first week deaths and terminations of pregnancy with CHD very similarly. If a perinatal death is given a greater impact weighting than a surviving severe CHD case, then this will result in a country with more terminations have a greater estimated burden of disease associated with CHD than a country with less terminations. In order to reflect societal choices in terms of quality of life of the child and family, it may be best to cap the impact of a TOPFA on burden of disease at that of a surviving case of severe CHD.

The main health service needs in relation to CHD are primary prevention, successful early treatment, and ongoing care for affected children and adults. Termination of pregnancy is not currently, and is unlikely to become, a major health service impact on CHD burden. Improved prenatal diagnosis may have the potential to improve early treatment success further in Europe.

Conclusion

Congenital heart disease is the most frequent group of major congenital anomalies, with a total prevalence of 7.0 per 1,000 births. The majority survive the first week of life, of whom an estimated one in six require surgery. Although perinatal deaths and terminations of pregnancy for fetal anomaly are infrequent in relation to livebirths with CHD, they are a major cause of fetal and perinatal mortality, with a combined mortality of 0.7 per 1,000 births, varying between countries.

Further Relevant Information

The EPICARD study (Epidemiological cohort study of the outcomes for infants with congenital heart diseases) in Paris is currently following up children with Congenital Heart Disease. Principal Investigators: F. Goffinet, C De Vigan, B Khoshnood, Paris Registry of Congenital Malformations, Inserm (National Institute of Health and Medical Research) U953, Paris, France

EPICARD study

Background: Despite continuing medical progress, considerable mortality, morbidity and adverse neuro-developmental outcomes still affect many children with congenital heart disease (CHD). By far most of the currently available data on outcomes for children with CHD are from hospital-based studies in specialized centers. Population-based studies are rare, though they have important strengths, particularly since they are not affected by selection bias related to selective referrals to specialized centers and are more generalizable.

Objectives: Use population-based data from a large cohort of patients with CHD to: i) estimate the prevalence, pre- and postnatal diagnosis of congenital heart diseases; ii) assess the medical and surgical management of children with CHD, iii) evaluate neonatal mortality and morbidity and neuro-developmental outcomes of children with CHD; and iv) identify the factors associated with prognosis, especially the role of events during the neonatal period and of the initial medical and surgical management of children

Methods: The EPICARD study is a prospective cohort study of all children with a congenital heart disease born in the Greater Paris area (Paris and its surrounding suburbs) between 2005 and 2008 (base of 300 000 births), including a total number of approximately 2900 cases of CHD diagnosed in the prenatal period or up to one year of age. Once the diagnosis has been confirmed in a specialized pediatric cardiology department, the children are seen routinely by a pediatrician at one year of age for a general and cardiac work-up. At the age of 3 years, an extensive evaluation is done, which includes detailed assessment of cardiac and neuro-

developmental outcomes and the standardized cognitive and developmental test Kauffman Assessment Battery for Children (K-ABC).

Progress Report: The recruitment phase of the study has ended (birth cohorts of May 2005-April 2008) except for some of the cases diagnosed after the sixth month of age for the birth cohort of 2008. We have included more than 2800 cases, including about 2250 newborns (~80%), 500 pregnancy terminations (~18%) and 50 fetal deaths (~2%). The database of the study is in construction and we have begun preliminary analyses of data at inclusion. So far, more than 80% of infants eligible have completed the first-year examination and very few parents have refused the follow-up (< 5%). The three-year follow up examinations, including the K-ABC tests administered by trained psychologists, began in October 2008 and are in progress.

A general presentation of the epidemiology of congenital anomalies in Europe, including the place of congenital heart disease, based on EUROCAT data, can be found in two recent reports:

EURO-PERISTAT Project, in collaboration with SCPE, EUROCAT, EURONEOSTAT **(2008)**, "European Perinatal Health Report: Better Statistics for Better Health for Pregnant Women and Their Babies", EURO-PERISTAT. [www.eurocat.ulster.ac.uk/pdf/EUROPERISTAT-Report.pdf]

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Syndrome", *BJOG*, Vol 115, pp 689-696. [www.blackwell-synergy.com/doi/full/10.1111/j.1471-0528.2008.01700.x?prevSearch=allfield%3A%28Survey+of+Prenatal+Screening+Policies%29].

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Knoshnood B, De Vigan C et al **(2005)** "Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983-2000: a population-based evaluation." *Pediatrics*, Vol 115, No 1, pp 95-101.

General information on EUROCAT activities can be found in:

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Table 1 Population Coverage by EUROCAT Registry 2000-2005

Countries	Annual birth population 2005	% annual births covered in country 2005	Total births covered in report 2000-2005
Austria			
Styria	10473	13	62667
Belgium		27	
Antwerp	19176	16	108365
Hainaut	12517	11	74102
Croatia			
Zagreb	5935	14	33933
Denmark			
Odense	5258	8	32003
France		7	
Ile de la Reunion	14779	2	58528
Paris	26715	3	220911
Strasbourg*	12569	2	64276
Germany		3	
Mainz	3146	0.5	18695
Saxony-Anhalt	17232	2.5	106257
Ireland		62	
Cork & Kerry**	8425	14	32617
Dublin	22627	38	135635
SE Ireland	6580	11	38151
Italy	29411	16	
Emilia Romagna	37605	7	178331
Sicily*	19880	4	87756
Tuscany	29411	5	165640
Malta	3865	100	23668
Netherlands			
Northern Netherlands	18552	10	119104
Norway	57667	100	346838
Poland			
Wielkopolska	35445	10	206170
Spain		7	
Barcelona	14711	3	82079
Basque Country	19792	4	112155
Switzerland			
Vaud	7222	10	42874
UK		26	
E Midlands & S Yorkshire	67318	9	362415
Northern England	31611	4	181377
Thames Valley	27298	4	60119
Wales	32768	5	189191
Wessex	26963	4	157899
Ukraine	25835	6	25835
Total	621375	12	3327591

Footnote
* Strasbourg, Sicily: Period covered 2000-2004; 2004 birth population used as annual birth estimate for 2005.
** Cork & Kerry: Period covered 2000-2003; 2003 birth population used as annual birth estimate for 2005.
All annual births calculated using EUROSTAT figures, except for Ukraine, which was based on WHO

Table 2 Prevalence of CHD and Non-Chromosomal CHD per 1,000 Births, by Outcome of Pregnancy

Country	Total* prev CHD per 1,000 births	Total* prev chromosomal CHD per 1,000 births	Total* prev non-chromosomal CHD per 1,000 births	Birth prev (LB+FD) non-chromosomal CHD per 1,000 births	Prev non-chromosomal CHD LB per 1,000 births	% non-chromosomal LB diagnosed after 1 month	Prev non-chromosomal CHD FD per 1,000 births	Prev non-chromosomal CHD perinatal deaths per 1,000 births	Prev non-chromosomal CHD TOPFA per 1,000 births
Austria	15.34	1.42	13.91	13.79	13.69	24	0.10	0.34	0.13
Belgium	6.66	0.84	5.82	5.56	5.51	6	0.04	0.27	0.26
Croatia	5.39	0.62	4.77	4.77	4.69	8	0.09	0.21	0.00
Denmark	8.91	0.81	8.09	7.84	7.75	35	0.09	0.31	0.25
France	8.38	1.18	7.19	6.13	6.04	7	0.09	0.28	1.06
Germany	11.90	1.14	10.76	10.26	10.14	4	0.12	0.27	0.50
Ireland	6.60	1.60	5.00	5.00	4.88	13	0.12	0.38	0.00
Italy	6.86	0.47	6.40	6.05	6.02	2	0.02	0.07	0.35
Malta	15.25	1.99	13.27	13.27	13.27	34	0.00	0.38	0.00
Netherlands	6.08	0.77	5.31	5.23	5.12	46	0.11	0.37	0.08
Norway	10.27	0.90	9.37	9.08	9.01	-	0.07	-	0.29
Poland	11.18	0.92	10.26	10.26	10.19	4	0.08	0.33	0.00
Spain	5.58	0.91	4.67	4.23	4.18	8	0.06	0.22	0.44
Switzerland	13.62	1.47	12.15	11.64	11.59	33	0.05	0.23	0.51
Ukraine	7.78	0.81	6.97	6.89	6.70	11	0.19	0.93	0.08
UK	6.88	1.03	5.86	5.39	5.25	28	0.14	0.26	0.47
Total	8.03	0.98	7.05	6.66	6.57	15	0.09	0.26	0.39

* Total includes LB (livebirth), FD (Fetal death), and TOPFA (termination of pregnancy for fetal anomaly)
- means data not available

Table 3 Prevalence of Non-Chromosomal CHD per 1,000 Births, by Severity, Country, Birth Outcome, 2000-2005

Countries	Prev non-chromosomal CHD per 1,000 births	Prev of selected very severe CHD	Prev of severe CHD	Prev VSD/ ASD/ PVS	Prev VSD only
Total	7.05	0.47	1.34	4.30	2.20
Austria	13.91	0.70	1.76	10.47	1.04
Belgium	5.82	0.41	1.32	3.22	1.61
Croatia	4.77	0.27	0.83	3.18	0.68
Denmark	8.09	0.50	1.31	5.75	4.44
France	7.19	0.71	1.62	3.99	2.89
Germany	10.76	0.54	1.34	7.59	3.01
Ireland	5.00	0.47	1.51	2.33	1.17
Italy	6.40	0.37	1.24	3.98	2.59
Malta	13.27	0.51	1.52	10.48	3.84
Netherlands	5.31	0.45	1.60	2.78	1.58
Norway	9.37	0.46	1.09	5.81	3.51
Poland	10.26	0.36	0.93	8.27	2.25
Spain	4.67	0.49	1.40	2.31	1.14
Switzerland	12.15	0.47	1.75	8.58	4.57
Ukraine	6.97	0.31	1.24	4.80	3.44
UK	5.86	0.46	1.37	3.19	1.69
Total LB	6.57	0.30	1.22	4.22	2.15
Total FD	0.09	0.02	0.02	0.02	0.01
Total Perinatal deaths	0.26	0.08	0.07	0.05	0.03
Total TOPFA	0.39	0.16	0.10	0.06	0.04
Total isolated	5.76	0.39	1.14	4.00	1.95
Total isolated LB	5.51	0.25	1.07	3.95	1.94
Total isolated FD	0.05	0.01	0.01	0.02	0.01
Total isolated Perinatal deaths	0.14	0.06	0.05	0.03	0.01
Total isolated TOPFA	0.20	0.12	0.06	0.04	0.01

Very severe CHD = Single ventricle, Hypoplastic left heart, Hypoplastic right heart, Ebstein's anomaly, Tricuspid atresia

Severe CHD = Pulmonary valve atresia, Common arterial truncus, Atrioventricular septal defect, Aortic valve atresia/stenosis, Transposition of great vessels, Tetralogy of Fallot, Total anomalous pulmonary venous, Coarctation of aorta

VSD/ ASD/ PVS = Ventricular septal defect, atrial septal defect, pulmonary valve stenosis

Prevalence of VSD only (i.e. no other cardiac or non-CHD anomaly)

Table 4 **CHD Subtype: Total Prevalence per 1,000 Births, Isolated CHD Prevalence, Single Isolated* CHD Prevalence, % LB Single Isolated Cases, % FD Single Isolated Cases, % Single Isolated First Week Deaths, % Single Isolated Perinatal Death, % Single Isolated TOPFA**

	Total** non-chromosomal CHD prev per 1,000 births	Total isolated CHD prev per 1,000 births	Single isolated CHD prev per 1,000 births	Single isolated CHD LB %	Single isolated CHD FD %	Single isolated CHD 1st week deaths %	Single isolated CHD perinatal deaths %	Single isolated CHD TOPFA %
All CHD	7.05	5.76	4.12	96.1	0.8	1.5	2.3	3.1
Common arterial truncus	0.09	0.07	0.04	92.4	0.8	5.9	6.8	6.8
Transposition of great vessels	0.35	0.31	0.17	97.5	0.9	5.7	6.5	1.6
Single ventricle	0.07	0.05	0.02	48.3	11.7	15.0	26.7	40.0
Ventricular septal defect	3.06	2.65	1.95	99.2	0.3	0.2	0.5	0.5
Atrial septal defect	2.05	1.60	0.98	99.3	0.5	0.3	0.9	0.2
Atrioventricular septal defect	0.19	0.13	0.07	90.2	2.4	2.4	4.9	7.3
Tetralogy of Fallot	0.28	0.20	0.17	93.9	1.7	0.3	2.1	4.4
Tricuspid atresia and stenosis	0.08	0.07	0.02	75.9	1.3	6.3	7.6	22.8
Ebstein's anomaly	0.05	0.04	0.03	69.8	11.5	8.3	19.8	18.8
Pulmonary valve stenosis	0.40	0.34	0.20	99.5	0.2	0.5	0.6	0.3
Pulmonary valve atresia	0.09	0.07	0.03	86.0	2.3	3.5	5.8	11.6
Aortic valve atresia/stenosis	0.14	0.12	0.08	92.7	1.9	1.5	3.5	5.4
Hypoplastic left heart	0.26	0.22	0.18	58.5	2.7	14.5	17.2	38.8
Hypoplastic right heart	0.04	0.03	0.01	65.6	3.1	6.3	9.4	31.3
Coarctation of aorta	0.34	0.28	0.15	98.2	0.6	3.0	3.7	1.2
Tot anom pulmonary venous return	0.05	0.04	0.03	100.0	0.0	5.7	5.7	0.0

* single isolated cases refers to cases with a single CHD only and no other malformations

** Total includes LB (livebirth), FD (Fetal death), and TOPFA (termination of pregnancy for fetal anomaly)

Table 5 Number and Proportion of Isolated Livebirth (LB) CHD Cases by Type with Information on Surgery in Odense (Denmark) and Vaud (Switzerland), 2005-2006

	Prev per 1,000 births of single isolated cardiac	LB surviving > 1 week (n)	Surgery performed (%)	No surgery required (%)	Too severe for surgery (%)	Not Known (%)
All isolated CHD	8.33	208	17	81	1	1
VSD/ASD/PVS (isolated)	6.66	168	7	93	0	1
Very severe and severe CHD (isolated)	1.19	28	82	7	7	4

LB= livebirth
VSD/ ASD/ PVS = Ventricular septal defect, atrial septal defect, pulmonary valve stenosis
Very severe CHD = Single ventricle, Hypoplastic left heart, Hypoplastic right heart, Ebstein's anomaly, Tricuspid atresia
Severe CHD = Pulmonary valve atresia, Common arterial truncus, Atrioventricular septal defect, Aortic valve atresia/stenosis, Transposition of great vessels, Tetralogy of Fallot, Total anomalous pulmonary venous, Coarctation of aorta

Annex 1a Time of Diagnosis of All Non-Chromosomal CHD Cases

Countries	CHD (n)	Prenatal (%)	At birth (%)	<1 week (%)	1-4 weeks (%)	1-12 months (%)	After 1 year (%)	Not known (%)
Austria	872	14.0	9.4	35.9	14.9	19.6	3.2	3.0
Belgium	1062	17.9	20.6	39.5	5.2	4.9	0.0	11.9
Croatia	162	2.5	34.0	38.3	17.3	7.4	0.6	0.0
Denmark	259	6.9	8.1	42.9	8.9	25.9	7.3	0.0
France	2473	42.5	33.0	13.9	3.4	5.0	0.9	1.3
Germany	1344	8.0	23.1	14.1	1.0	1.3	0.3	52.2
Ireland	1032	6.8	22.4	19.4	4.4	7.2	0.6	39.3
Italy	2761	16.0	33.7	35.1	4.0	1.5	0.5	9.2
Malta	314	1.0	15.6	36.6	12.4	34.1	0.0	0.3
Netherlands	632	9.5	15.2	18.4	11.6	32.9	10.3	2.2
Norway	3250	-	-	-	-	-	-	-
Poland	2116	3.6	25.4	37.3	7.9	2.9	0.1	22.7
Spain	907	25.8	50.1	7.4	7.5	6.6	0.7	2.0
Switzerland	521	10.9	8.3	30.9	18.6	29.4	1.9	0.0
Ukraine	180	5.0	46.1	26.1	11.1	10.6	0.0	1.1
UK	5570	18.4	13.6	5.5	4.4	12.1	1.7	44.4
Total	23455	14.8	20.0	17.9	5.1	7.8	1.1	33.2

At birth includes cases diagnosed at abortion and cases diagnosed at postmortem

- time of diagnosis not specified in EUROCAT Central Registry database

Annex 1b Time of Diagnosis of All Non-Chromosomal CHD Cases by Type of Isolated CHD

	CHD (n)	Prenatal (%)	At birth (%)	<1 week (%)	1-4 weeks (%)	1-12 months (%)	After 1 year (%)	Not known (%)
Common arterial truncus	222	19	36	9	1	2	2	32
Transposition of great vessels	1048	22	33	12	3	1	0	28
Single ventricle	161	50	14	11	3	2	0	19
VSD	8834	6	19	27	6	7	1	33
ASD	5324	4	17	23	8	10	1	36
AVSD	417	35	13	13	4	7	1	25
Tetralogy of Fallot	663	20	22	17	3	5	0	32
Tricuspid atresia and stenosis	232	42	24	7	3	3	0	22
Ebstein's anomaly	139	45	17	7	3	3	1	24
Pulmonary valve stenosis	1128	7	18	17	7	19	2	25
Pulmonary valve atresia	227	35	18	13	3	2	0	27
Aortic valve atresia/stenosis	390	13	18	17	3	13	2	31
Hypoplastic left heart	721	52	11	10	1	0	0	26
Hypoplastic right heart	101	44	21	3	2	0	0	31
Coarctation of aorta	934	17	20	17	8	6	2	29
Tot anom pulmonary venous return	126	11	18	15	8	6	0	40
Very severe CHD (isolated)	1573	51	14	8	2	1	0	24
Severe CHD (isolated)	4472	24	24	13	4	5	1	29
VSD/ASD/PVS (isolated)	14322	7	20	23	6	10	1	34
Very severe CHD (isolated)*	586	53	11	8	2	2	0	23
Severe CHD (isolated) *	1758	20	19	12	5	9	2	34
VSD/ASD/PVS (isolated)*	4816	8	10	17	9	21	3	31

* Based on data from Austria, Denmark, Malta, Netherlands, Switzerland, UK