Un système à l'échelle Européenne:
EUROCAT
EUROPEAN SURVEILLANCE OF CONGENITAL ANOMALIES

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EUROCAT Overview

- **EUROCAT**: European Surveillance of Congenital Anomalies (CA)

- Network of the population-based registries of CA in Europe, since 1979

- Currently surveys more than 1.7M births per year in Europe (31% of birth population in the EU) via 38 registries in 21 countries

- Registries ascertain cases of all major structural and chromosomal anomalies among livebirths (LB), still births/late fetal deaths, and terminations of pregnancy for fetal anomaly (TOPFA), using multiple sources of information

- Using common software, each member registry transmits either anonymised individual case data (full members) or summary data (associate members) to a central database at EUROCAT Central Registry at University of Ulster, now >320,000 cases in database (full members)

- Funded by DGSanco Public Health Programme as a Rare Diseases Action
- WHO Collaborating Centre for the Surveillance of Congenital Anomalies
## Percentage of births in population covered by EUROCAT registries

*(should it be 100%? – quality vs quantity)*

<table>
<thead>
<tr>
<th>Country (no. registries)</th>
<th>% Country Covered</th>
<th>Country</th>
<th>% Country Covered</th>
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<tr>
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<td>30</td>
<td>NON EU</td>
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<tr>
<td>Belgium (2)</td>
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<td>Candidate countries in EUROCAT</td>
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<tr>
<td>Czech Republic (1)</td>
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<td>Denmark (1)</td>
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<td>EFTA countries in EUROCAT</td>
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<tr>
<td>Germany (2)</td>
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<td>UK (6)</td>
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The Objectives of EUROCAT:
Prevalence, Prevention, Prenatal Diagnosis

• To provide essential epidemiologic information on congenital anomalies in Europe

• To facilitate the early warning of new teratogenic exposures [cf thalidomide]

• To evaluate the effectiveness of primary prevention

• To assess the impact of developments in prenatal screening

• To act as an information and resource centre for the population and health professionals regarding clusters or exposures 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
Why European Collaboration?

- Pooling of data
- Comparison of data
- Sharing of expertise
- Joint approach to European public health questions
- Sharing of resources (e.g. website, software)
Types of surveillance based on CA registries

- **Statistical Monitoring (without prior hypothesis)**
  - Recent Clusters in time, clusters in space
  - Trends in time, geographical differences
- **Response to exposure incidents/health threats/disasters**
  - Chernobyl
  - Swine Flu/H1NI
- **Surveillance oriented to identifying environmental causes (with different levels of hypothesis)**
  - Pharmacovigilance
  - Envirovigilance
- **Surveillance oriented to evaluating primary prevention**
  - NTD prevalence and prevention by periconceptional folic acid
- **Surveillance oriented to health service needs and evaluation**
  - Prenatal screening and diagnosis, TOPFA, mortality rates
  - Children needing services
Some Figures for the EU

- 2.3% of babies in EU registered with major CA, including livebirths (LB), Stillbirths (SB/FD), Terminations of Pregnancy following prenatal diagnosis (TOPFA)
  - more than 115,000 babies affected by major congenital anomalies in the EU each year
  - Congenital heart disease the largest group: 40,000/year

- 1.8% of babies are livebirths with major CA
  - more than 1% of liveborn babies have surgery for a congenital anomaly
  - Most of these children need specialist services during childhood and adulthood

- 0.9% of babies in the EU have a major congenital anomaly prenatally diagnosed, of which 0.4% result in termination of pregnancy

- Perinatal mortality with CA: 1.0 per 1,000 births (0.1%)
  - Half stillbirths and late fetal deaths from 20 weeks gestation
  - Half first week deaths
  - Important cause of perinatal mortality

Perinatal Mortality and Termination of Pregnancy due to congenital anomaly, per 1,000 births, 2004, by country
Lack of Success of Primary Prevention: Need for Renewed Policy Efforts
implement what we know, research what we do not know

Prevalence per 10,000 births of All Anomalies, for All Full Member Registries, from 1991 - 2010

*Still births and Fetal Deaths from 20 weeks gestation
Primary Prevention of Congenital Anomalies

- EUROCAT in collaboration with EUROPLAN have developed recommendations on policies to be considered for the primary prevention of congenital anomalies in National Plans (and Strategies) on Rare Diseases
  - Awaiting EUCERD approval

- In the field of:
  - Medicinal drugs
  - Food/nutrition and lifestyle (e.g. folic acid, obesity)
  - Health Services (e.g. vaccination, women with chronic diseases, genetic counselling)
  - Environmental pollution incl. the workplace

- Mechanisms:
  - Preconceptional care (one to one) – high vs low risk parents
  - Health promotion to future parents and awareness raising: major health determinants + pregnancy specific issues
  - Public health approaches: vaccination, food fortification
  - Regulatory policies (pharmaceutical, food, environmental, tobacco, alcohol)
  - Research and surveillance (CA and exposure), and expert review
Has periconceptional folic acid supplementation in Europe prevented neural tube defects?

1991: MRC RCT results

Prevalence per 10,000 births of Neural Tube Defects, for All Full Member Registries, from 1991 – 2010
*Still births and Fetal Deaths from 20 weeks gestation

Neural Tube Defects

Prevalence (per 10,000 births)

YEAR

1991
1993
1995
1997
1999
2001
2003
2005
2007
2009

Legend:
- Total Prevalence
- Live Births
- Fetal Deaths *
- TOPFA
Proportion of all births to mothers 35 years and older, 1990-99, 2000-09.

Countries are ordered by % mothers 35+ years in 2000-2009
Total and livebirth prevalence of trisomy 21 (Down Syndrome) in Europe v Paris-Strasbourg.
EUROCAT Annual Statistical Monitoring

- With common software, registries format and validate data to standard guidelines
- February data transmission to Central Registry
  - February Year X+2 e.g. Feb 2012 for 2010 births
  - Website tables produced, confirmed by registries
- March Central Registry statistical monitoring
  - Clusters: Scan “moving window” technique (by est DOC)
  - Ten year trends
- April: EUROCAT Steering Committee prioritises trends and clusters needing investigation
- Member registries conduct preliminary investigation of any identified clusters and trends according to standard protocol
  - presented at June Registry Leaders Meeting
  - Registries communicate results regionally/nationally for RESPONSE
  - Publication of Annual Statistical Monitoring Report in December

- **Neural Tube Defects**
  - Anencephalus and similar
  - Encephalocele
  - Spina Bifida
  - Hydrocephaly
  - Microcephaly
  - Arhinencephaly/holoprosencephaly
  - Eye
  - Anophthalmos/microphthalmos
  - Anophthalmos
  - Congenital cataract
  - Congenital glaucoma

- **Ear, face and neck**
  - Anotia

- **Congenital heart disease**
  - Severe CHD
  - Common arterial truncus
  - Transposition of great vessels
  - Single ventricle
  - Ventricular septal defect
  - Atrial septal defect
  - Atrioventricular septal defect
  - Tetralogy of Fallot
  - Tricuspid atresia and stenosis
  - Ebstein's anomaly
  - Pulmonary valve stenosis
  - Pulmonary valve atresia
  - Aortic valve atresia/stenosis
  - Hypoplastic left heart
  - Hypoplastic right heart
  - Coarctation of aorta
  - Total anomalous pulm venous return

Average annual change in prevalence:
- 20% dec
- 10% dec
- No change
- 10% inc
- 20% inc
Cluster output: Scan method

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Lambda: 2324.46
No cases: 6
Expected: 0.9
Start case: 7
Start date: 14/08/2006
End date: 07/12/2006
p value: 0.021
cluster group: 1
Type: Cluster

Distribution of cases
* = cases with gestation entered, ? = cases with estimated gestation
Tick marks for the 1st of each month.
Solid line represents span of most significant cluster, dotted lines indicate span of cases in clusters of the same group.
50 years after Thalidomide: early detection of teratogenic medications

- Lack of premarketing involvement of pregnant women in clinical trials means that safety information lacking
  - Postmarketing surveillance and research essential
  - Large population sizes crucial, especially for rare exposures/rare CA

- EUROCAT two-pronged pharmacovigilance:
  - Routine monitoring for recent time clusters
    - Annual Statistical Monitoring
    - could we detect “another thalidomide”?
      - Depends on strength of teratogenic effect, % population exposed
  - Targeted investigation of specific medications
    - Case-malformed control studies
    - Signal testing and signal generation

- EUROMediCAT: daughter of EUROCAT
  - Systematic specific CA-medication association detection
  - Improving exposure data by electronic prescription data linkage
  - Medication for chronic diseases
Welcome to the EUROMedICAT website. On this website you will find information on the EUROMedICAT project: what we aim to do, who are involved, the contents of the work packages, information on meetings and publications related to the project. As the project develops, the website will be regularly updated with new information.
September 2011.

EUROMedICAT is a research project, conducted within the European Union’s 7th Framework Programme. Its aim is to build a European system for the evaluation of safety of medication use in pregnancy in relation to the risk of congenital anomalies.

EUROMedICAT is a project funded under the European Union’s 7th Framework Programme

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All studies use a case-malformed control design, 3.9 million births, 19 registries

- LTG: Response to OC signal from North American AED cohort. LTG monotherapy vs no AED OR 0.67 (95% CI 0.10–2.34) for OC relative to other malformations.
- CBZ: Only spina bifida confirmed OR 2.6 (95% CI 1.2 to 5.3) among 5 signals tested.
- VPA: 6/14 signals confirmed: spina bifida, 12.7 (95% CI 7.7 to 20.7); atrial septal defect, OR 2.5; cleft palate OR 5.2; hypospadias, 4.8; polydactyly, 2.2; and craniosynostosis, 6.8.
Envirovigilance using biomarkers of exposure to pollutants, and other exposure assessment approaches ("exposome"):

- Endocrine disrupting chemicals-hypospadias
- Pesticides
- Solvents
- Air pollutants
- Drinking water disinfection byproducts

Rare chromosome abnormalities, prevalence and prenatal diagnosis rates from population-based congenital anomaly registers in Europe

Diana Wellesley, Helen Dolk, Patricia A Boyd, Ruth Greenlees, Martin Haeusler, Vera Nelen, Ester Garne, Babak Khoshnood, Berenice Doray, Anke Rissmann, Carmel Mullaney, Elisa Calzolari, Marian Bakker, Joaquin Salvador, Marie-Claude Addor, Elizabeth Draper, Judith Rankin and David Tucker

Epidemiology of small intestinal atresia in Europe: a register-based study

Kate E Best, Peter W G Tennant, Marie-Claude Addor, et al.

Sex chromosome trisomies in Europe: prevalence, prenatal detection and outcome of pregnancy

Patricia Anne Boyd1, Maria Loane2, Ester Garne3, Babak Khoshnood4,5 and Helen Dolk6, a EUROCAT working group6

Spectrum of Congenital Anomalies in Pregnancies with Pregestational Diabetes

Ester Garne,7 Maria Loane,2 Helen Dolk,2 Ingeborg Barisic,1 Marie-Claude Addor,1 Larraitz Arriola,3 Marian Bakker,1 Elisa Calzolari,2 Carlos Malias Dias,3 Berenice Doray,2 Miriam Gatt,10 Kari Klyungsoy Melve,1 Vera Nelen,12 Mary O'Mahony,12 Ania Pierini,14 Hanitra Randrianarivo-Ranjitorena,12 Judith Rankin,9 Anke Rissmann,7 David Tucker,10 Christine Verellum-Dumsoulin,12 and AwI Wiesel12

For more information, visit http://www.eurocat-network.eu/aboutus/publications/publications
Key messages

• Major congenital anomalies affect more than 115,000 babies in the EU each year

• Fifty years after Thalidomide, we need to raise our expectations, implement known preventive measures effectively and invest in basic, epidemiologic and public health research and surveillance

• Surveillance at a European level adds value to regional and national systems
  – National response to surveillance

• Surveillance shows disappointing progress in preventing NTD by folic acid supplementation

• Postmarketing surveillance of medications (pharmacovigilance) in relation to use in pregnancy should give risk information for women/clinicians to weigh against benefits

• Envirovigilance - to develop
You can make selections on which registries, anomalies, years to include.
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Dr. Ieve Grinfelde and Dr. Ieve Cirule (Latvia)
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Dr. Martine Vrijheid (CREAL, Spain)
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