Congenital Anomalies as Preventable Rare Diseases

*International Conferences for Rare Diseases and Orphan Drugs*

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on behalf of the EUROCAT Network and the EUROPLAN Project

*The authors declare no conflict of interest*

Visit [www.eurocat-network.eu](http://www.eurocat-network.eu)
European Surveillance of Congenital Anomalies

WHO Collaborating Centre for the Epidemiological Surveillance of Congenital Anomalies
Supported by the EU-Commission Public Health Directorate
Programme of Community Action on Rare Diseases
What is EUROCAT?

- European network of population-based registries for the epidemiologic surveillance of congenital anomalies.

- Started in 1979

- More than 1.7 million births surveyed per year in Europe, around 31% of the EU birth population

- 48 registries in 21 countries of Europe

- Standardised central database on cases of congenital anomaly among livebirths, stillbirths and terminations of pregnancy for fetal anomaly

  www.eurocat.ulster.ac.uk
EUROCAT: Mission

• to support primary prevention of congenital anomalies (CA) and provision of appropriate services to pregnant women, affected children and their families by the collection, analysis, interpretation and dissemination of population-based epidemiologic data. Epidemiological surveillance should inform policies and interventions to reduce the size of, and inequalities in, the public health burden of CA.

• Through the network of high quality multiple source population-based CA registries ascertaining live births, still births/fetal deaths, and terminations of pregnancy following prenatal diagnosis of CA, EUROCAT enables the provision and dissemination of accessible and updated epidemiological information, including prevalence, prenatal diagnosis and perinatal mortality data, and the pooling of population-based data on monogenic syndromes and rare chromosomal abnormalities.
What epidemiological information can be found on the EUROCAT website?


- The prevalence of selected Monogenic Syndromes in Europe


- EUROCAT Statistical Monitoring for both trends and clusters in time in order to detect signals of new or increasing teratogenic exposures which may require public health action.

  Prevalence data by individual anomaly (eg. Spina bifida) or subgroup (eg. Neural tube defects)
EUROCAT contribution to RD prevalence

- EUROCAT prevalence of CA is the proportion of births affected by a CA:

  - EUROCAT **Live birth prevalence** = (No. Cases (LB)/No. Births (LB)) x 10,000

- The “actual” current EU population prevalence depends on past LB prevalence and past survival to adulthood and is therefore unknown.

- EUROCAT LB prevalence provides the future maximum EU population prevalence - survival to adulthood of babies with CA is lower than in the general population.

- EUROCAT registers cases of CA diagnosed prenatally or in infancy with some conditions added later.
EUROCAT contribution to RD prevalence

- Congenital anomalies occur in around 2% of births in Europe: (173.08 per 10,000 live births in 2012)
- 70 of 89 EUROCAT subgroups were rare (< 5 per 10,000)
- For the rare subgroups LB prevalence is 96 per 10,000 births
- Estimate 4.8M affected persons in Europe
- > 50,000 affected babies per year

16% of rare disease patients in Europe have a rare congenital anomaly

Sources:
EUROCAT Website Database: http://www.eurocat-network.eu/ACCESSPREVALENCEDATA/PrevalenceTables (data uploaded 24/03/2014)
EUROCAT data sharing

- Many genetic syndromes are amongst the “rarest” of the CA

- When CA are so rare EUROCAT pools data across registries to show prevalence

- EUROCAT can provide total prevalence (LB, FD, and TOPFA) of selected Monogenic Syndromes in Europe with ICD10-BPA codes
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>ICD10-BPA</th>
<th>Number of cases</th>
<th>Prevalence per 10,000 births</th>
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</thead>
<tbody>
<tr>
<td>Aarskog syndrome</td>
<td>Q8710</td>
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<td>0.03</td>
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<tr>
<td>Acrocephalopolysyndactyly (all types)</td>
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<td>Alagille syndrome</td>
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<td>Angelman syndrome</td>
<td>Q8785</td>
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<td>Apert's syndrome (acrocephalosyndactyly type I and II)</td>
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<td>Bardet-Biedl syndrome</td>
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<td>Beckwith-Wiedemann syndrome (EMG syndrome)</td>
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<td>Cleidocranial dysplasia</td>
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<td>Cockayne's syndrome</td>
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<td>Crouzon's disease (craniofacial dysostosis type I)</td>
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<td>Di George syndrome</td>
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<td>Dubowitz syndrome</td>
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<td>Ehlers-Danlos syndrome</td>
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<td>Frontonasal dysplasia</td>
<td>Q7581</td>
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<tr>
<td>Holt-Oram syndrome (heart-hand syndrome)</td>
<td>Q8720</td>
<td>11</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Continued........
Special Report: Congenital Anomalies are a Major Group of Mainly Rare Diseases

(December 2012)

Why did EUROCAT create this report?

• To address issues including: Are all CA rare, or just some?

• To highlight that EUROCAT registries differ from RD as they are population based ie. register all cases in a defined geographical area, and are aimed at surveillance underpinning primary prevention

• To address confusion regarding prevalence: population vs at birth

• The highlight the contribution of EUROCAT to European Action on RD

• To emphasise the importance of:
  – pooling data
  – being population based
  – primary prevention of CA
Many CA are Potentially Preventable

EUROCAT data:
- 1.9% of CA are monogenic syndromes,
- 13% chromosomal anomalies
- 0.65% teratogenic syndromes - maternal infections, drugs or alcohol.

- The precise cause of most congenital anomalies is not known
- Most CA are probably caused by an interaction of environmental and genetic factors.
- Genetic factors play an important role but by changing exposures we can prevent CA.
- Environmental – used in the broadest sense as non-genetic (although interacting with genetic factors), encompassing physical, chemical, biological and social factors, concentrating on factors that are modifiable.
- Examples: Spina bifida, Fetal Alcohol spectrum disorder
EUROCAT Surveillance: Underpinning Prevention

• Provision of essential epidemiological information on CA in Europe
• Detection, investigation, reporting of clusters/trends in CA
  – Facilitation of early warning of new/changing teratogenic exposures
  – Improved capacity for rapid response
• Establishment of a strategy to include primary prevention of CA in national plans for RD
• Evaluation of the effectiveness of primary prevention at population level
• Contribution to the development and implementation of a European postmarketing pharmacovigilance system (EUROmediCAT www.euromedicat.eu)
  – Evaluation and provision of early warning of teratogenic risk of CA related to medication use in early pregnancy
  – Focus on medication for chronic diseases: new antiepileptics, insulin analogues, anti-asthmatics, antidepressants
• Provision of a ready collaborative network and infrastructure for research related to the causes and prevention of CA
PRIMARY PREVENTION OF CONGENITAL ANOMALIES

EUROCAT (European Surveillance of Congenital Anomalies) and EUROPLAN (European Project for Rare Diseases National Plans Development)

Recommendations on policies to be considered for the primary prevention of congenital anomalies in National Plans and Strategies on Rare Diseases

Endorsed by

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EUROPLAN
European Project for Rare Diseases National Plans Development
Co-ordinated by the Italian National Centre for Rare Diseases
Italian National Institute of Health
2012-2015

Grant N.: 2010 22 04
www.eurocat-network.eu

Grant N.: 2011 22 01
www.europlanproject.eu
The Scope of Policy Actions Needed for Primary Prevention of CA

- In the field of medicinal drugs
- In the field of food/nutrition and lifestyle
- In the field of health services
- In the field of environmental pollution including the workplace
EUROCAT

- Collects epidemiological data
- Looks for causes
- Looks for how causes can be prevented
- Provides scientific data for policy makers, health professionals, patients and the public
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"We thank the many people throughout Europe involved in providing and processing information, including affected families, clinicians, health professionals, medical record clerks, and registry staff"