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SECOND INTERIM ACTIVITY REPORT
For period March 2005 to February 2006

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A PROGRESS BY WORKPROGRAMME ITEM

1. Provision of essential epidemiologic information on congenital anomalies in Europe

1.1 Coverage of the European Population

<table>
<thead>
<tr>
<th>Country</th>
<th>EUROCAT Registry</th>
<th>Annual Births per Registry (year 2003)</th>
<th>Annual Births per Country (year 2005)*</th>
<th>% Country Covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU Countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td>Styria</td>
<td>10,500</td>
<td>82,000</td>
<td>12.8</td>
</tr>
<tr>
<td>Belgium</td>
<td>Antwerp, Hainaut</td>
<td>18,100, 12,000</td>
<td>115,500</td>
<td>26.1</td>
</tr>
<tr>
<td>Cyprus</td>
<td></td>
<td>0</td>
<td>8,100**</td>
<td>0.0</td>
</tr>
<tr>
<td>Czech Rep</td>
<td></td>
<td>0</td>
<td>10,200</td>
<td>0.0</td>
</tr>
<tr>
<td>Denmark</td>
<td>Odense</td>
<td>5,300</td>
<td>64,800</td>
<td>8.1</td>
</tr>
<tr>
<td>Estonia</td>
<td></td>
<td>0</td>
<td>13,000</td>
<td>0.0</td>
</tr>
<tr>
<td>Finland</td>
<td>#</td>
<td>56,800</td>
<td>57,200</td>
<td>99.3</td>
</tr>
<tr>
<td>France</td>
<td>Auvergne, Paris, Central East, Strasbourg</td>
<td>13,400, 38,300, 91,000</td>
<td>789,100</td>
<td>19.8</td>
</tr>
<tr>
<td>Germany</td>
<td>Mainz, Saxony-Anhalt</td>
<td>3,200, 17,000</td>
<td>742,500</td>
<td>2.7</td>
</tr>
<tr>
<td>Greece</td>
<td></td>
<td>0</td>
<td>99,900</td>
<td>0.0</td>
</tr>
<tr>
<td>Hungary</td>
<td>#</td>
<td>113,800</td>
<td>90,900</td>
<td>100.0</td>
</tr>
<tr>
<td>Ireland</td>
<td>Cork &amp; Kerry, Dublin, Galway, SE Ireland</td>
<td>8,500, 23,400, 2,700</td>
<td>65,600</td>
<td>62.4</td>
</tr>
<tr>
<td>Italy</td>
<td>Campania, Emilia Romagna, North East, Sicily, Tuscany</td>
<td>59,900, 27,400, 60,200, 16,100, 27,700</td>
<td>528,300</td>
<td>36.2</td>
</tr>
<tr>
<td>Latvia</td>
<td></td>
<td>0</td>
<td>20,700</td>
<td>0.0</td>
</tr>
<tr>
<td>Lithuania</td>
<td></td>
<td>0</td>
<td>30,600</td>
<td>0.0</td>
</tr>
<tr>
<td>Luxembourg</td>
<td></td>
<td>0</td>
<td>6,000</td>
<td>0.0</td>
</tr>
<tr>
<td>Malta</td>
<td></td>
<td>3,900</td>
<td>4,000</td>
<td>100.0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>North</td>
<td>20,000</td>
<td>195,600</td>
<td>10.2</td>
</tr>
<tr>
<td>Region</td>
<td>Sub-region 1</td>
<td>Sub-region 2</td>
<td>Total 1</td>
<td>Total 2</td>
</tr>
<tr>
<td>------------</td>
<td>--------------</td>
<td>--------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>Poland</td>
<td>Wielkopolska</td>
<td>Rest of Poland</td>
<td>33,600</td>
<td>217,900</td>
</tr>
<tr>
<td>Portugal</td>
<td>South</td>
<td></td>
<td>18,100</td>
<td>116,600</td>
</tr>
<tr>
<td>Slovakia</td>
<td></td>
<td></td>
<td>54,000</td>
<td>0.0</td>
</tr>
<tr>
<td>Slovenia</td>
<td></td>
<td></td>
<td>18,000</td>
<td>0.0</td>
</tr>
<tr>
<td>Spain</td>
<td>Asturias</td>
<td></td>
<td>7,200</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Barcelona</td>
<td></td>
<td>14,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Basque Country</td>
<td></td>
<td>19,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Madrid (ECEMC)</td>
<td></td>
<td>103,100</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>144,000</td>
<td>0.0</td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td></td>
<td>99,500</td>
<td>99,000</td>
</tr>
<tr>
<td>UK</td>
<td>Glasgow</td>
<td></td>
<td>9,700</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Merseyside</td>
<td></td>
<td>25,400</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Northern Region</td>
<td></td>
<td>30,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>North Thames</td>
<td></td>
<td>48,500</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Oxford</td>
<td></td>
<td>6,700</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Trent</td>
<td></td>
<td>64,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Wales (CARIS)</td>
<td></td>
<td>31,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Wessex</td>
<td></td>
<td>26,300</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>242,500</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td></td>
<td>1,404,500</td>
<td>4,747,000</td>
</tr>
<tr>
<td>Non-EU</td>
<td></td>
<td></td>
<td>79,900</td>
<td>662,000</td>
</tr>
<tr>
<td>Countries</td>
<td></td>
<td></td>
<td>1,484,400</td>
<td>5,409,000</td>
</tr>
</tbody>
</table>

** Livebirths only
# Registries with 100% coverage. Differences in annual births due to different years covered

1.2 Implementation of EUROCAT Data Management Program (EDMP) software by registries for data entry/import, validation and annual transmission to Central Registry

The revised EUROCAT Data Management Program (EDMP – version 3) compatible with Guide 1.3 coding system was released July 2005. All full member registries successfully implemented the program for data transmission to Central Registry.
Further refinements have been made to the EDMP software to incorporate the new EUROCAT subgroups of congenital anomalies (agreed by the Coding and Classification Committee June 2005). Prevalence rates for the new non-chromosomal subgroups will be reported both including chromosomal anomalies and excluding chromosomal anomalies. EDMP Version 4 will be ready for release June 2006. The new version will allow users to extract data based on any Guide 1.3 variable, whereas previously registries were only allowed to extract data based on congenital anomaly subgroups. Registries will also be able to output a table of all complete/incomplete variables locally, which is important for improving data quality.

1.3 Uploading of updated data to website to provide prevalence rates of 90 congenital anomaly subgroups

Please see Appendix 2 for table showing uploaded prevalence rates for EUROCAT congenital anomaly subgroups. The website tables (http://www.eurocat.ulster.ac.uk/pubdata/tables.html) show the most recent upload of data (07 November 2005). The upload of the new congenital anomaly subgroups up to and including year 2004 is underway. The upload process has taken longer on this occasion, as data for all the new subgroups, including and excluding chromosomal anomalies must be confirmed by the local registries before it can be uploaded to the website. Prevalence rates for the new subgroups are backdated to the beginning of the registry, hence the registries must check that the data are correct back to 1980. The tables for checking data are available on the membership-only section of the website.

Year 2004 data is available for the following registries: Antwerp, Hainaut (Belgium); Paris, Central East France (France); Saxony-Anhalt (Germany); Dublin (Ireland); Emilia Romagna, Tuscany (Italy); Malta; N Netherlands; Wielkopolska, Poland (Poland); Basque Country, Madrid (Spain); Vaud (Switzerland); Northern Regions, NW Thames, Oxford, Trent, Wales and Wessex (UK). This data will be uploaded to the website following confirmation that the data is correct (June 2006).

Updates up to and including year 2003 data are available for the following registries: Antwerp, Hainaut (Belgium); Zagreb (Croatia); Odense (Denmark); Finland; Paris, Central East France (France); Mainz, Saxony-Anhalt (Germany); Hungary; Dublin (Ireland); Campania, Emilia Romagna, NE Italy, Tuscany (Italy); Malta; N Netherlands; Norway; Wielkopolska, Poland (Poland); S Portugal; Asturias, Barcelona, Basque Country, Madrid (Spain); Sweden; Vaud (Switzerland); Northern Regions, NW Thames, Oxford, Trent, Wales and Wessex (UK).

A draft report on the European prevalence of the rare genetic syndrome Cornelia de Lange was sent to all contributing registries in December 2005 for comments. The report is being revised accordingly.

Analysis of the epidemiology of the following syndromes is on-going: Achondroplasia, Thanatophoric dysplasia, campomelic dysplasia, Apert, Osteogenesis Imperfecta Type II and III.
1.4 Provision of data to other organizations

a) Request from the UK CEMACH (Confidential Enquiry into Maternal and Child Health) cohort study of congenital malformations in diabetic mothers for EUROCAT maternal age-stratified rates of major organ system congenital anomalies (Table 1).

Table 1: EUROCAT Prevalence rates per 10,000 births, 2002 (May 2005)

<table>
<thead>
<tr>
<th>Major system groups</th>
<th>&lt;20</th>
<th>20-24</th>
<th>25-29</th>
<th>34</th>
<th>35+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Nervous system,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Neural Tube Defects</td>
<td>31.53</td>
<td>22.77</td>
<td>22.31</td>
<td>22.62</td>
<td>24.19</td>
<td></td>
</tr>
<tr>
<td>1.2 Eye</td>
<td>4.06</td>
<td>3.89</td>
<td>3.89</td>
<td>4.79</td>
<td>4.13</td>
<td></td>
</tr>
<tr>
<td>1.3 Ear</td>
<td>4.38</td>
<td>4.13</td>
<td>4.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 Congenital heart disease</td>
<td>35.93</td>
<td>35.93</td>
<td>35.93</td>
<td>35.93</td>
<td>35.93</td>
<td></td>
</tr>
<tr>
<td>1.5 Cleft lip with or without palate</td>
<td>8.41</td>
<td>8.41</td>
<td>8.41</td>
<td>8.41</td>
<td>8.41</td>
<td></td>
</tr>
<tr>
<td>1.6 Cleft palate</td>
<td>5.29</td>
<td>5.29</td>
<td>5.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.7 Digestive system</td>
<td>15.04</td>
<td>15.04</td>
<td>15.04</td>
<td>15.04</td>
<td>15.04</td>
<td></td>
</tr>
<tr>
<td>1.8 Internal urogenital system</td>
<td>36.7</td>
<td>36.7</td>
<td>36.7</td>
<td>36.7</td>
<td>36.7</td>
<td></td>
</tr>
<tr>
<td>1.9 Limb</td>
<td>14.48</td>
<td>14.48</td>
<td>14.48</td>
<td>14.48</td>
<td>14.48</td>
<td></td>
</tr>
<tr>
<td>1.10 Musculoskeletal and Connective tissue</td>
<td>40.90</td>
<td>40.90</td>
<td>40.90</td>
<td>40.90</td>
<td>40.90</td>
<td></td>
</tr>
</tbody>
</table>

Notes: Groups 1-12 exclude chromosomal cases

b) Updated data on oro-facial clefts (2001-2003) was forwarded to ICBDMS in December 2005.

c) A number of individuals requested data on EUROCAT prevalence rates for various congenital anomalies. When appropriate, these individuals were directed to the EUROCAT website tables (http://www.eurocat.ulster.ac.uk/pubdata/tables.html) with instructions on how to access the prevalence information. Requests included:

I. UK General Practice Research Database (GPRD). Comparison of GPRD prevalence of all heart defects, ventricular septal defects, coarctation of aorta and tetralogy of fallot with EUROCAT prevalence rates.

II. UK Evidence Base Medicine Journal. Request for prevalence of chromosomal anomalies

III. International PPB Registry, Minnesota, USA. Request for prevalence of lung malformations.

IV. Spina Bifida and Hydrocephalus Association of Quebec, Canada. Request for prevalence of Hydrocephalus and Spina Bifida in France.
1.5 **Revision of common dataset for births from 2005**: revised coding of drugs, prenatal screening/diagnosis, assisted conception, survival, new coding of folic acid supplementation, civil registration status, social class, migrant status. Consultation with EU Health Monitoring indicator development for compatibility

EUROCAT Guide 1.3 incorporating these revisions has been published (see Appendix 10)

1.6 **Expansion of range of indicators of data quality and harmonization**, including registry descriptions, data manual and validations of prevalence data

The set of 30 Data Quality Indicators have been revised (see Appendix 11). EUROCAT Guide 6 on the Coding of Syndromes has been published (see Appendix 6). A questionnaire relating to Genetic Services was sent to all Registries and results will be presented to Registry Leaders in June 2006. A new List of Minor Anomalies for Exclusion has been incorporated in EUROCAT Guide 1.3

2. **To co-ordinate the establishment of new registries throughout Europe collecting comparable, standardised data**

2.1 **Assistance to and exchange with new/applicant members**

A number of interested Registries from Central and Eastern Europe attended the Registry Leaders Meeting in Poznan in June 2005 (See Appendix 4) – they include two teams from the Ukraine as well as Latvia, Moscow and Belarus.

Applications for membership were received from South East Ireland, Ukraine and Ile de la Reunion. Guadeloup has made contact with a view to future membership. Slovenia is also working towards membership.

2.2 **Organisation of one day induction workshop for new/applicant members**

Coding workshops were organized for all EUROCAT members in Dublin (26 April 2005, 13 participants), London (12 April 2005, 23 participants) Rome (6-7 October 2005, 50 participants). In addition, “EDMP clinics” were held at the Registry Leaders Meeting in Poznan to teach new and old registries how to use the EDMP software.

2.3 **Survey of confidentiality and consent issues in EUROCAT registries**


Registries collecting personal medical data must, under EC Directive 95/46/EC, obtain consent for the processing of such data, unless national law or a national supervisory body
allows for an exemption. Member states have not always taken advantage of the ability to exempt health care or disease registries. There has been much debate about the consequent effect on epidemiologic research and surveillance. We conducted a survey of congenital anomaly registries with regard to the requirement for informed consent and its implementation. A questionnaire designed by the EUROCAT Committee on Ethics and Confidentiality was sent to 37 EUROCAT registries in February 2003. 29 registries from a total of 15 EU countries (and 2 registries from 2 non-EU countries subsequently excluded from further analysis) replied. Information was updated in June 2004.

Nine countries have enacted legislation or created a supervisory body which allows registries to operate without informed consent. In three of these, registries effectively operate opt-out consent (every effort is made to ensure families are aware of the registry’s activities; parents must explicitly ask for their children to be removed).

Eight registries (from 6 countries) report experience of informed consent. Of five registries relying on clinician notification or access to medical records, four report marked reduction in case reporting after introducing consent and considerable difficulty maintaining high ascertainment levels, largely due to logistic difficulty associated with tracing parents. Less than 1% of parents refuse consent or opt-out of participation.

EUROCAT experience indicates that opt-in consent poses a serious threat to the operation of congenital anomaly registries. The debate about informed consent has eclipsed more relevant consideration of procedures to maintain confidentiality of data or ensure the ethical operation of registries.

3. **To co-ordinate the detection of and response to clusters and early warning of teratogenic exposures**

3.1 **Testing, training and implementation of new statistical surveillance software (compatible with EDMP) for rapid monitoring in member registries**

Registries received further training in use of the software at the EDMP clinics in Poznan. Work continued on resolving some methodological issues resulting in a new version of the Statistical Software. Major improvements have been estimating date of conception in cluster detection and the facility to analyse non-chromosomal anomalies separately. These improvements will be implemented in annual monitoring in April 2006.

3.2 **Annual Central Registry monitoring of validated data to detect trends and clusters**

Statistical Monitoring results were communicated to all Registries in April 2005 and Registries presented the results on preliminary cluster investigations at the Registry Leaders Meeting in Poznan (see Appendix 4)
3.3 Response to clusters or public health concerns through analysis of central database, co-ordination of extra data collection

Gastroschisis is a rare abdominal wall anomaly which has been increasing in prevalence in Europe and worldwide. It is well established that young maternal age is a strong risk factor for this anomaly. Smoking, recreational drug use and some therapeutic drugs are also risk factors. A paper investigating trends in prevalence by maternal age has been submitted for publication. The following is the abstract:


Summary

Gastroschisis is an abdominal wall defect more prevalent in offspring of young mothers. It is known to be increasing in prevalence despite the general decrease in the proportion of births to young European women. We investigated whether the increase in prevalence was restricted to the high risk younger mothers. We analysed 936 cases of gastroschisis from 25 population-based registries in 15 European countries, 1980-2002. Bayesian analogue of ridge regression allowed us to estimate trend, to estimate which registries were significantly different from the common distribution, and to adjust simultaneously for maternal age, time (in grouped years) and registry. The maternal age standardised prevalence (standardised to the year 2000 European maternal age structure) rose almost fourfold from 0.54 [95% Credible Interval 0.37, 0.75] per 10,000 births in 1980-84 to 2.12 [95% Credible Interval 1.85, 2.40] per 10,000 births in 2000-2002. The relative risk of gastroschisis for mothers <20 years of age 1995-2002 was 7.0 [95% Credible Interval 5.6, 8.7]. There were geographical differences within Europe, with higher rates of gastroschisis in the United Kingdom, and lower rates in Italy after adjusting for maternal age. After standardising for regional variation, our results showed that the increase in risk over time was the same for mothers of all ages – the increase for mothers <20 years was 3.96-fold compared to an increase of 3.95-fold for mothers in the other age groups. These findings indicate that the phenomenon of increasing gastroschisis prevalence is not restricted to younger mothers only.

A more general analysis of the link between congenital anomaly risk and maternal age is on-going.

A project funded by the Department of Health, London on congenital anomaly risk in Britain in relation to air pollution is on-going.
3.4 Drug surveillance through analysis of drug-malformation associations and collaboration with International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) ICBDMS Madre project

Members of the Drug Committee are: Lolkje de Jong van den Berg (Chair), Hermien de Walle, Lorentz Irgens, Marian Bakker, Jan Mejnartowicz, Amanda Neville, Annette Queisser-Luft, Elisabeth Robert and Margery Morgan (since September 2005).

Summary of the activities of the Drug Committee of the past three years:

a) We investigated the potential of the EUROCAT collaboration for pharmacoepidemiology and drug safety surveillance through exploring the drug information in the individual EUROAT registries. From this investigation we concluded that practices vary widely between registries regarding how to record drug exposure information. EUROCAT has the potential to be an effective collaborative framework to contribute to postmarketing drug surveillance in relation to teratogenic effects, but work is needed to implement ATC drug coding more widely, and to diversify the sources of information used to determine drug exposure in each registry. The results will be published in the Journal of Pharmacoepidemiology and Drug Safety.

b) A case-control study was carried out to investigate the relation of Loratadine and hypospadias. We used data from the central database from 1991 to 2000. The summarized table (all years, all registries) is given below:

<table>
<thead>
<tr>
<th>Births in database</th>
<th>81603</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosomal+monogenic</td>
<td>12239</td>
</tr>
<tr>
<td>Exposed to antihistaminic</td>
<td>34</td>
</tr>
<tr>
<td>Exposed to loratadine</td>
<td>5</td>
</tr>
<tr>
<td>Non-chromosomal</td>
<td>69364</td>
</tr>
<tr>
<td>Exposed to antihistaminic</td>
<td>226</td>
</tr>
<tr>
<td>Exposed to loratidine</td>
<td>8</td>
</tr>
<tr>
<td>Hypospadias</td>
<td>4623</td>
</tr>
<tr>
<td>Exposed to antihistaminic</td>
<td>12</td>
</tr>
<tr>
<td>Exposed to loratidine</td>
<td>1</td>
</tr>
</tbody>
</table>

Thus in total we have 1 exposed case with hypospadias. When we calculated an odds ratio (OR) with this number, using all non-hypospadias as controls (13 exposed controls), we found an OR of 1.36 with very wide confidence intervals. The numbers were too small to proceed with this study. In addition we did sub-analyses with selected registries: those who use ATC-coding and registries who interviewed women after birth. The conclusion of these sub-analyses will be worked out in a short report or letter for publication in a journal.

c) Since January 2005 EUROCAT Central Registry introduced the international ATC coding system. In Autumn 2005 we sent a short questionnaire to the registry Leaders to evaluate the implementation of the ATC-coding system. Results will be presented at the Registry Leaders Meeting in Graz, Austria.
d) Plans for the coming years

Our general goal for the near future is to come to a birth defect case-control surveillance monitoring system of EUROCAT Registries. This will include:

- More detailed explanation of the sources of information for first trimester drug exposure
- Which registries can presently, or in the future, include information about controls? Are there other ways to get information regarding specific drug exposure in the general pregnant population?
- At the moment the Dutch group is initiating a study with data from the Central Registry looking at 3 types of drug use for chronic diseases (diabetes, asthma and epilepsy) based on the "old" EUROCAT” drug code. The first phase is to assess data quality.
- To prepare a combined meeting with a group of pharmaco-epidemiologists about reproductive toxicity and the ways to detect this in humans. We have to discuss this with the next President of ISPE, Allen Mitchell. April 2007.
- The possibility of setting up a 1 or 2-day course for ATC coding is being considered. This could be in co-operation with the WHO working group. This group is teaching these courses every year.

3.5 Collaboration with ICBDSR for multiple malformation monitoring

Due to methodological differences between ICBDSR and EUROCAT it was decided at a meeting in Poznan to delay collaboration in routine monitoring and re-draw a protocol for collaboration. Meanwhile, EUROCAT has implemented a computer algorithm for identifying potentially multiply-malformed cases and meetings of a sub-committee of the Coding and Classification Committee were held to agree on classification of resulting case lists. Large differences in the prevalence of multiply-malformed children were found to exist between Registries and results will be presented to Registry Leaders in June 2006.

3.6 EUROCAT network communications as a rapid reaction and response facility

19 EUROCAT network communications were sent out. These related to all aspects of management of the project but there were no external cluster or exposure concerns during this period.

3.7 Maintenance and updating of EUROCAT Cluster Advisory Service on the web and translation of key parts into five languages

Translation will be made in the next phase of this project.
4. To evaluate the effectiveness of primary prevention

4.1 Annual production and website dissemination of commented yearly updated prevalence rates of neural tube defects (births and terminations)

Data up to 2004 were transmitted to Central Registry in February 2006 but there was a delay in making them available on the website due to the implementation of the new EUROCAT subgroups. Data will be on the website in June 2006.

4.2 Annual survey in member countries of policy changes regarding periconceptional folic acid supplementation, health education initiatives undertaken, available data on folic acid uptake and analysis of available data on protective effect for other congenital anomalies

In 2005 we completed the update of the earlier NTD and folic acid report. The Update includes one more country (Sweden) and two more recent years’ NTD prevalence data (births from 2001 and 2002). It documents policy changes in a few countries, especially Italy, and the extremely slow progress with regard to fortification of food with folic acid. Although fortification has been advised in a few countries, it has not yet been implemented. This updated report is now on the EUROCAT website. EUROCAT continues to advocate the recommendations from the earlier report. Country representatives have agreed to supply information about policy and practice changes in their country periodically so that the report can be updated

EUROCAT findings have been and will continue to be widely reported in journals and conferences including (but not limited to):


Abramsky L, Busby A, Dolk, H, Promotion of periconceptional folic acid has had limited success: Journal of the Royal Society for the Promotion of Health, September 2005; 125 (5) (special issue on health promotion during pregnancy).

A field about whether and when folic acid supplementation was taken periconceptionally has been added to the EUROCAT database, and member registers are being encouraged to collect this information.

In January 2006, we sent a questionnaire to NTD patient support groups in 25 Europe countries asking about their position regarding mandatory fortification of flour with folic acid. A reminder was sent to non-responders in March. To date, representatives from 12 countries have replied. The results of this questionnaire will be made available through a journal publication.

Maria Loane, presentation to food Standards Agency Belfast, 22 February 2006.

5. To assess the impact of developments in prenatal screening

5.1. Annual updating of website regarding the frequency of terminations of pregnancy following prenatal diagnosis

Information on the number of terminations of pregnancy following prenatal diagnosis per type of anomaly, registry and year was updated at the website with 2003 data from 33 registries after the second deadline in October 2005 and has been available at the EUROCAT website since November 2005. As the 2004 data has to be uploaded to the website using the new EUROCAT subgroups, the 2004 data on terminations of pregnancy has been delayed until June 2006. In autumn 2005 it was decided to give website data on the proportion of cases diagnosed prenatally for selected subgroups of congenital anomalies: anencephalus, spina bifida, transposition of great arteries, hypoplastic left heart, bilateral renal agenesis and Down syndrome for the most recent 5 years. The data is now ready to be approved by the local registries and then uploaded to the website.

5.2. Analyses of Central Database regarding impact of prenatal screening and maternal age changes on geographic inequalities in livebirth prevalence and perinatal mortality

At the meeting in the Prenatal Diagnosis Working Group in Bergen in June 2004 it was decided to write a EUROCAT Special Report on prenatal screening and diagnosis policies, including policies regarding termination of pregnancy, in the European countries. A chapter on their national policies was written by a representative from 11 countries and the final report was available at the website in July 2005. This report is important in informing interpretation of EUROCAT data from different countries. Further a scientific paper for publication on the European policies on prenatal diagnosis is under preparation by Tricia Boyd, Catherine de Vigan and Ester Garne. The paper will compare the policies with the prenatal detection rates on Down syndrome and NTD in the European countries.

In order to keep up with the progress in the field of prenatal diagnosis the variables have been changed in EUROCAT Guide 1.3 from birth year 2005. From 2005 it will be reported for each case which prenatal diagnostic test was the first positive test and thereby led to the diagnosis of the congenital anomaly. In future, this information should be available routinely on the EUROCAT website.
A study has been carried out on gestational age at live-birth for infants with gastrointestinal malformations. Gestational age at birth seems to be significantly lower for infants with a prenatal diagnosis of a gastro-intestinal malformation compared to infants with a postnatal diagnosis, potentially adding to the risk of mortality and morbidity. The paper has been submitted to “Paediatric and Perinatal Epidemiology” for publication: Garne E, Loane M, Dolk H and a EUROCAT Working Group: Prenatal diagnosis of congenital malformations – Are we inducing birth too early?

A study on the impact of prenatal diagnosis of Transposition of Great Arteries (TGA) on postnatal outcome has being carried out in 7 EUROCAT registries. A total of 97 liveborn infants with TGA are included. The first draft of the paper has been written (Ester Garne).

A preliminary analysis of perinatal mortality data was made and presented to the Registry Leaders Meeting in Poznan (see Appendix 4). Publication has been delayed due to staff departure.


6. To provide an information and resource centre and ready collaborative research network to address the causes and prevention of congenital anomalies and the treatment, care and outcome of affected children

6.1 Organisation of European Workshop on methodological approaches to the assessment of the impact of environmental pollution on the risk of congenital anomalies

Not yet held.

6.2 Organisation of 8th European Symposium on the Prevention of Congenital Anomalies (for objectives 3,4, 5 and 6)

Held in Poznan, Poland, Friday 10 June 2005 (see Appendix 4)

6.3 Collaboration with International Centre for Birth Defects (ICBD) on WHO World Craniofacial Anomalies Registry and world study of risk factors for gastroschisis

EUROCAT has continued to update its data which are available on the WHO Genomic Research Center Website (http://www.who.int/genomics/anomalies/idcfa/en)
6.4 Central Registry administrative and database support for research, and provision of anonymised data extracts on request

A collaborative project was undertaken with SCPE (Surveillance of Cerebral palsy in Europe) on the association between cerebral palsy and congenital anomalies. The proportion of cerebral palsy cases with cerebral and non-cerebral anomalies in the SCPE database was compared to EUROCAT prevalence figures. Recommendations were made for improving cerebral palsy registry data with regard to congenital anomalies. This analysis will be submitted for publication.

A paper on the Epidemiology of Cleft Lip in Europe was published "Epidemiology of Cleft Palate in Europe: Implications for Genetic Research Strategy", The Cleft Palate-Craniofacial Journal, Vol 41, No 3, pp 244-249. A draft paper was prepared “Associated Anomalies in Multi-Malformed Infants with Cleft Lip and Palate: An Epidemiological Study Based on 6 million Births in 23 Registries” by the Emilia Romagna, Italy partner using the EUROCAT database.

A new study Arthrogryposis Multiplex Congenita (AMC) has been initiated by the Norwegian partner using the EUROCAT database.

A new study on paternal age related risk of Down Syndrome has been initiated in England using the EUROCAT database.

7. Organisation of Annual Registry Leaders’ Meeting (to support all above tasks)

This was held in Poznan, Poland, June 2005 (see Appendix 4).

8. Rare Diseases Task Force and Other DG Sanco Related Activities

EUROCAT participated in the RDTF (as Deputy Leader). EUROCAT was a partner in organizing the European Rare Diseases Conference in Luxembourg in June 2005 and a presentation was given entitled “Strategies for Prevention”. The issue of the need to improve prevention of neural tube defects by raising periconceptional folate status was also highlighted.
B. ORGANISATION OF EUROCAT: PARTNER ROLES

1. Central Registry

Carried out co-ordination functions and analyses of the central database.

Administratively based at University of Ulster, but scientific and medical expertise also provided by other Institutions. Most staff are part-time (see Budget for number of hours spent on EUROCAT).

Prof Helen Dolk:
EUROCAT Project Leader, University of Ulster (sabbatical from September 2005 to March 2006)

Dr Carol Curran:
Head of School, University of Ulster

Maria Loane:
Database Manager & Research Officer, University of Ulster

Elaine Hand:
Statistician, University of Ulster (left in July 2005)

Ian Bradbury:
Statistician, University of Ulster

Barbara Norton:
Administrator, University of Ulster

Suzhuang Hong:
PhD Student, University of Ulster

Dr Araceli Busby:
Epidemiologist, London School of Hygiene & Tropical Medicine (left in August 2005)

Lisa Grisolia:
Administrator, London School of Hygiene & Tropical Medicine

Dr Ester Garne:
Pediatric Epidemiologist, University of Southern Denmark and Chair of Prenatal Diagnosis Working Group and on Classification and Coding Committee

Dr Lolke de Jong v d Berg
Pharmaco Epidemiologist, University of Groningen and Chair of Drug Exposure During Pregnancy Working Group

Marlies Guerts
Pharmaco Epidemiologist, University of Groningen

Dr Alan Kelly
Statistician, Trinity College Dublin

Conor Teljeur:
Statistician, Trinity College Dublin

Lenore Abramsky:
Chair of NTD and Folic Acid Working Group, Northwick Park Hospital
2. **Project Management Committee**

The Project Management Committee consists of the Project Leader, elected Registry Leaders and Working Group Chairs:

Lenore Abramsky (UK)  
Ingeborg Barisic (Croatia)  
Fabrizio Bianchi (Italy)  
Elisa Calzolari (Italy)  
Catherine de Vigan (France)  
Hermien de Walle (The Netherlands)  
Helen Dolk (Project Leader)  
Ester Garne (Denmark)  
Anna Latos-Bielenska (Poland)  
David Lillis (Ireland: President of EUROCAT Association)  
Annette Queisser-Luft (Germany)

3. **Participating Registries**

In EU Countries (See Appendix 1 for addresses)

Ms Lenore Abramsky (UK)  
Dr Sebastiano Bianca (Italy)  
Dr Fabrizio Binachi (Italy)  
Dr Patricia Boyd (UK)  
Prof Elisa Calzolari (Italy)  
Dr Catherine de Vigan (France)  
Dr Hermien de Walle (The Netherlands)  
Dr Elizabeth Draper (UK)  
Dr Maria Feijoo (Portugal)  
Dr Christine Francannet (France)  
Dr Ester Garne (Denmark)  
Dr Miriam Gatt (Malta)  
Dr Yves Gillerot (Belgium)  
Dr Martin Haeusler (Austria)  
Prof Anna Latos-Bielenska (Poland)  
Dr David Lillis (Ireland)  
Prof Maria-Luisa Martinez-Frias (Spain)  
Dr Bob McDonnell (Ireland)  
Dr Carmen Mosquera-Teneiro (Spain)  
Dr Vera Nelen (Belgium)  
Dr Birgitta Ollars (Sweden)  
Dr Mary O’Mahony (Ireland)  
Dr Isabel Portillo (Spain)  
Dr Simone Poetzsch (Germany)  
Dr Annette Queisser-Luft (Germany)  
Dr Annukka Ritvanen (Finland)  
Dr Elisabeth Robert (France)  
Dr Joaquin Salvador (Spain)  
Dr Janos Sandor (Hungary)
Dr Gioacchino Scarano (Italy)
Prof Claude Stoll (France)
Dr David Stone (UK)
Prof Romano Tenconi (Italy)
Mr David Tucker (UK)
Dr Martin Ward Platt (UK)
Dr Diana Wellesley (UK)

In Non-EU Countries (see Appendix 1 for addresses)

Dr Marie-Claude Addor
Dr Ingeborg Barisic
Prof Lorentz Irgens
C. MEETINGS, WORKSHOPS, TRAVEL AND INFORMATION REQUESTS

1. Project Committee Meetings

The EUROCAT Project Management Committee met on 11 April 2005 and 29 November 2005.

2. 20th Registry Leaders’ Meeting and 8th European Symposium on the Prevention of Congenital Anomalies

The EUROCAT Registry Leaders’ Meeting was held in Poznan, Poland, 11 June 2005. A total of 55 people attended this meeting and can be broken down as follows:

- 28 Registry Leaders or their Representatives
- 7 Central Registry staff
- 6 New Applicant Registry Leaders and their staff
- 11 Local registry staff
- 3 other guests

The attendance list can be found in Appendix 3 and the Minutes (including Programme) can be found in Appendix 4.

Poznan, Poland was also the venue for the 8th European Symposium on the Prevention of Congenital Anomalies. This meeting took place on 10 June 2005. The programme and abstracts (which were published in the Archives of Perinatal Medicine, September 2005, ISSN 1505-0580) can be found in Appendix 5. These events were hosted by the EUROCAT Registry of Poland.

3. Workshops

The following workshops and committee meetings were held and minutes of these and the Registry Leaders’ Meeting can be found in the Minutes of the 20th Registry Leaders’ Meeting (see Appendix 4) – Coding and Classification, NTD and Folic Acid, Prenatal Diagnosis, Drugs, Genetics Services, Hospital Activity Data, and Monitoring of Multiple Malformations.

Three Coding Workshops were held on 12 April 2005 in London, UK, 26 April 2005 in Dublin, Ireland and 6-7 October 2005 in Rome, Italy.
4. Travel and Presentations


5. Central Registry Co-ordination Travel

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<tr>
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<tr>
<td>Ian Bradbury</td>
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<td>Araceli Busby</td>
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<td>James Densem</td>
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<td>Helen Dolk</td>
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<td>Maria Loane</td>
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<td>Ian Bradbury</td>
<td>Coleraine - Belfast</td>
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<td>Helen Dolk</td>
<td>Belfast - Luxembourg</td>
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<td>Helen Dolk</td>
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<td>Babak Khoshnood</td>
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D. PUBLICATIONS (*copies attached in Appendix 12)

2006 and In Press


2005


*EUROCAT (2005), "EUROCAT Guide 6: Definition and Coding of Syndromes", *EUROCAT Central Registry*, University of Ulster.


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