This document contains the registry descriptions for 21 EUROmediCAT registries: Antwerp (BE), Basque Country (ES), Cork & Kerry (IE), Emilia Romagna (IT), Isle de la Reunion (FR), Mainz (DE), Malta (MT), Northern Netherlands (NL), Norway (NO), Odense (DK), Paris (FR), Poland (PL), Saxony Anhalt (DE), SE Ireland (IE), Tuscany (IT), Ukraine (UA), Valencia Region (ES), Vaud (CH), Wales (UK), Wielkopolska (PL), and Zagreb (HR).

Each description is comprised of the EUROCAT registry description as of December 2014 with extra EUROmediCAT medication exposure information added March 2016.

For updated EUROCAT registry descriptions please see the EUROCAT website:

http://www.eurocat-network.eu/aboutus/memberregistries

Prevalence rates for selected congenital anomalies in European countries can be accessed at the following link:

http://www.eurocat-network.eu/AccessPrevalenceData/PrevalenceTables
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Belgium, Antwerp

History and Funding
The registry started with a pilot study on procedures for registration of congenital anomalies in 1989. In 1990 the registry formally started. Since 1997, the whole province of Antwerp has been covered. The registry is developed in collaboration with the Provincial Government and the University of Antwerp. The programme is funded by the Provincial Government of Antwerp. The Registry has been a member of EUROCAT since 1990.

Population Coverage
The registry covers about 20,000 births annually, these are all births in the province of Antwerp, about 16% of the births in Belgium. The registry is population-based which means that all mothers resident in the province of Antwerp at the time of birth of their baby are included.

Sources of Ascertainment
Reports are actively collected from maternity, pediatric and neonatologic units by registry staff who visit each maternity, pediatric- and neonatal unit in the covered region. We work with 20 participating hospitals. Basic information on children born with congenital anomalies is gathered from these hospital departments. More detailed information on diagnosis and exposure during pregnancy is gathered from gynecologist and pediatricians’ records. Information about the parents is obtained from general practitioners and social welfare nurses. Clinical geneticists, surgeons, pathologists and the centre for detection of metabolic diseases are also contacted for more information. Paediatric cardiology centers supply diagnostic information when requested by the registry for specific cases. Cytogenetic information is gathered on the cases suspected with a genetic anomaly. All cases with a congenital anomaly diagnosed prenatally or in the first year of life are registered. Reporting by hospitals and health workers is voluntary.

Maximum Age at Diagnosis
Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy is registered. Termination of pregnancy is legal under 13 weeks. If congenital anomaly is diagnosed, the upper gestational age for termination is 23 to 24 weeks.

Stillbirth and Early Fetal Deaths
The stillbirth definition for denominators is: a baby which is not viable with a gestational age of >180 days. Stillbirths are registered. Early fetal deaths and spontaneous abortions with a gestational age of less than 20 weeks are not registered.

Exposure Data Availability
Exposure information includes: maternal drug use, maternal smoking and alcohol abuse, maternal and paternal diseases and family history, parental occupation.
Denominators and Controls Information
Background data on births are retrieved from the population databases of the local authorities and from the study center for perinatal epidemiology in the Flanders region. Controls are not included in the registry, but data can be ascertained for specific studies.

Ethics & Consent
The registries’ procedure was presented to the Belgian privacy committee. In this procedure that was agreed the registry provides information to the parents on aims and methods of registration, data protection and the right to opt out. If the parents don’t opt out the data are registered. The registry does not require ethics committee approval in order to operate. No additional ethics committee approval is required for studies that use non-identifiable data.

Information on the registration of CA is given to the parents by medically qualified staff treating the child and other HCPs treating the child.

Address for further Information
Dr Vera Nelen, Princiaal Instituut voor Hygiene, Kronenburgstraat 45, 2000 Antwerpen, Belgium
Tel: +32 3 2591270
Fax: +32 3 2591201
Email: vera.nelen@provincieantwerpen.be

Profile of Medication Exposure
- Reporting of CA cases is voluntary. For the period 1997-2013, 2.5% of all births resulted in a CA.
- Medication exposures are recorded for CA cases from 1997.
- Medication exposure prevalence for CA cases is low, ranging from 37 per 1,000 CA cases in 2009 to 101 per 1,000 CA cases in 2012 (see Figure 1).
- Data sources include obstetric/midwife records, medical geneticist records and paediatrician records. Detailed information on exposure during pregnancy is gathered from gynaecologists’ and paediatricians’ records. Information about the parents is obtained from general practitioners and social welfare nurses.
- Antwerp is unable to differentiate the proportion of LB, FD or TOPFA covered by their data sources.
- From 2010, Antwerp has access to electronic database records in certain hospitals. This explains the increase in medication exposure prevalence i.e. prevalence of medication exposure in 2012 surpassed the previous high rate in 1997 (see Figure 1).
- Antwerp has no explanation for the decrease in prevalence of congenital anomaly cases with drug exposure between 2002 and 2009 (see Figure 1)
- Most frequent drugs recorded in Antwerp are shown in Figure 2. The top 3 medications recorded are thyroid therapy, sex hormones and antibacterials for systemic use.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Antwerp, 1997-2013 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC Drug Group out of All CA Cases, Antwerp, 1997-2013*

*Only includes medications with prevalence >1 per 1,000 CA
**Croatia, Zagreb**

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

**Population Coverage**
The registry is population based (Population – based I = All mothers resident in defined geographic area). The registry covers North-western Croatia – two regions at the seaside (Pula, Rijeka) and two continental provinces (Varaždin, Koprivnica). Births take place in four regional hospitals with practically no homebirths (only by accident). In 2009 we have included in our registry a delivery unit Vinkovci, covering additional 1284 births. Total number of monitored births Croatia in 2009 was 9181, reaching the population coverage of 20.8% births.

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

Part of population (local registry Rijeka) is covered by paediatric cardiology center diagnostic. Children born in this neonatal unit have the cardiac ultrasound newborn screening. Paediatric cardiology center doesn’t supply case list with details and diagnostic details to the registry. In other local registries there is no paediatric cardiology centers but children suspected of having cardiac defect are referred to paediatric cardiologist for estimation. Cardiac ultrasound and diagnosis are made by paediatric cardiologist. Data about patients with congenital heart defects are then collected by neonatologist employed in neonatal units and referred to the registry. Zagreb registry at present does not have direct access to cytogenetic labs from local registries. In local registries personnel gets data from cytogenetic and molecular laboratories and in case of death from post-mortem examination.

**Maximum Age at Diagnosis**
Maximum age at diagnosis is up to one week.

**Termination of Pregnancy for Fetal Anomaly**
Termination of pregnancy is regulated by Croatian law in 1978 (NN/18/78). Upper limit for termination of pregnancy for serious foetal anomaly is 24 gestational weeks.

**Stillbirth Definition and Early Fetal Deaths**
Official stillbirth definition in Croatia is 22 completed gestational weeks/500g weight. Registry collects data about stillbirths, and foetal deaths/ spontaneous abortions from 20 weeks. The local registries also record results of autopsy of all termination of pregnancies following prenatal
diagnosis, stillbirths and early neonatal deaths (0-7 days). Autopsy rates in these cases are generally high, around 90-100%.

**Exposure Data Availability**
Exposure information includes: data on parental occupation, maternal drug use, maternal smoking and alcohol abuse, maternal diseases before and during pregnancy. Data about techniques of prenatal screening (ultrasound, serum markers) and assisted reproduction methods are collected as well and are available for most of the recorded cases.

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

**Ethics & Consent**
In order to collect and store data the registry requires ethics committee approval from Ethics Committee of the Children's University Hospital Zagreb and Ethics Committee of Medical School University of Zagreb. Approval is renewed every 5 years.

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

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

**Address for Further Information**
Prof Ingeborg Barisic, Registry Leader and Medical Geneticist,
Children's University Hospital Zagreb,
Department of Pediatrics, Klaiceva 16,
10-000 Zagreb, Croatia
Tel: +385 1 4600107
Fax: +385 1 4600160
Email: ingeborg.barisic@kdb.hr

**Profile of Medication Exposure**
- Reporting of CA cases in Zagreb was voluntary until year 2000. For the period 1995-2013, 1.8% of all births resulted in a CA.
- The registry recorded information on medication exposures in pregnancy from 1995.
- Medication exposure prevalence ranged from 0 per 1,000 CA cases in 1998 to 234 per 1,000 in 2013 (see Figure 1). Prevalence fluctuates a lot. Zagreb is a small registry which may explain the fluctuation.
- Data sources include obstetric/midwife medical records and paediatric medical records.
- Medication data are available for LB, FD and TOPFA.
- Medications are recorded for the whole of the pregnancy and not just the first trimester.
The most frequent drugs recorded in Zagreb are shown in Figure 2. The top 3 medications recorded are antibacterials for systemic use, sex hormones and thyroid therapy.

Figure 1: Prevalence of medication exposure* per 1,000 CA cases, Zagreb, 1995-2013 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent drug exposure by ATC Drug Group out of All CA Cases, Zagreb, 1995-2013*

*Only includes medications with prevalence >1 per 1,000 CA
Denmark, Odense

History and Funding
The registry started in 1979 and joined the EUROCAT network from the beginning of EUROCAT. The registry has been approved by the "Data Tilsynet" as a private registry for the purpose of research. There is no specific funding.

Population Coverage
The registry covers the island of Funen with surrounding small islands, situated in the middle of Denmark (Population-based I = All mothers resident in defined geographic area). The total number of births per year in Funen County is around 5,600. Births take place in 3 hospitals with homebirths less than 1% of all births.

Sources of Ascertainment
The registry is based on active case finding. Data sources for the registry include electronic discharge and out-patient diagnosis from obstetric and pediatric departments, obstetric and pediatric hospital records with data on surgeries and examinations performed on the cases (x-ray, MR scans, echocardiography), birth notifications (up to 1999), death certificates (up to 1999), post-mortem examinations and data from the cytogenetic laboratory. The registry receives an annual list of all abnormal karyotypes diagnosed prenatally and postnatally in the registry area. The out-patient list of diagnosis from the pediatric department includes diagnosis from the pediatric cardiology center.

Maximum Age at Diagnosis
Up to 5 years for children seen at a pediatric department.

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

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

Exposure Data Availability
Exposure information: medication during first trimester of pregnancy, maternal illness before and during first trimester of pregnancy.
Denominators and Controls Information
Data on births per year and maternal age distribution covering Funen County is available from National Danish Statistics (www.statistikbanken.dk).

Registry Description References

Ethics & Consent
The registry does not require ethics committee approval in order to collect and store data. The registry needs official approval for the database http://www.datatilsynet.dk/
National legislation does not require informed consent in order to register a case with a congenital anomaly.

Address for Further Information
Dr Ester Garne,
Paediatric Department
Hospital Lillebaelt, Kolding
Skovvangen 2-6
DK -6000 Kolding
Denmark
Tel: +45 7636 2219
Fax: +45 7636 3474
Email: mailto:ester.garne@rsyd.dk

Profile of Medication Exposure
• In Odense, for the period 1995-2012, 2.8% of all births were born with a CA.
• Medication exposure data is available from 1995.
• Medication exposure prevalence ranges from 48 per 1,000 CA cases in 1999 to 256 per 1,000 CA cases in 2007 (see Figure 1). Medication prevalence was at its lowest in the early years.
• Easier access to data sources explains (most of) the improvement in the prevalence of medication exposure. Some of the increase in prevalence is a true increase in maternal medication use for chronic diseases
• Data sources include obstetric/midwife medical records and paediatric medical records.
• Medication data are available for LB, FD and TOPFA.
• The most frequent first trimester drugs recorded in Odense are shown in Figure 2. The top 3 medications recorded are drugs for obstructive airway disease, psychoanaleptics and analgesics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Odense, 1995-2012 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Odense, 1995-2012

*Only includes medications with prevalence >1 per 1,000 CA*
France, Ile de la Reunion

History and Funding
The Registry was established in 2001 and has contributed data to EUROCAT from 2002 onwards. The Registry was funded by a private organisation – Conseil General du Department (Provincial Council) until 2005 and since 2006 by a public organisation : Agence Régionale d'Hospitalisation (ARH) regional agency for hospital care, and is run under guidance from a steering committee. Its qualification was obtained from INSERM and INVS since November 18th 2008 (requalified until 2020) and the registry was supported by InVS, INSERM and ARS since 2009. The main aims of the Registry are to produce prevalence statistics, audit prenatal screening, assess reported clusters of environmental exposures and to detect new teratogenic exposures.

Population Coverage
The Registry is population-based III which is all mothers delivering in Isle of Reunion excluding non-residents. The Registry covers an average of 14,650 births per year. In our island, there is a high prevalence of obesity, diabetes and high blood pressure.

Sources of Ascertainment
The registry is based on a voluntary hospital participation. Notification of cases to the registry comes from hospitals and other private institutions. Reports are received from multiple sources: paediatric records, cytogenetics laboratories, pathology laboratory, child health services, midwives, birth notifications, maternity unit records, specialised departments for medical genetics, orthopaedics, cardiology, paediatric surgery, paediatric radiology, and department of prenatal diagnosis. Active registration is performed by a data collector. The register has so directly access to the computing files of the patients of the university hospital (mother or infants with birth defect). Cases are registered if diagnosed before birth by prenatal screening, at birth or during the first year of life. All malformed babies are followed up until 1 year of age, in order to have the survival, an eventual evolution of the diagnosis and the procedure of surgery.

Maximum Age at Diagnosis
Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy has been legal in Isle of Reunion since 1975 and recorded by the Registry since 2002. There is no upper limit on gestation age at termination. Information on terminations are provided by official legal pluridisciplinary prenatal diagnosis centres. There is a national prenatal screening policy. Exhaustivity for TOPFAs is estimated close to 100%, as all TOPFAs must be authorized by CPDP.

Stillbirth Definition and Early Fetal Deaths
The official stillbirth definition is: gestational age >20 weeks of pregnancy. Early fetal deaths/spontaneous abortions are included 22 weeks after the last menstrual period. All terminations of pregnancy for fetal malformation are included at any gestational age. Autopsies maybe carried out on stillbirths, early fetal deaths and termination of pregnancies.

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

Denominators and Controls Information
National birth statistics are obtained from INSEE. Denominators can be provided both by maternal age and monthly distribution. Information is not available on controls.

Ethics & Consent
The registry requires ethics committee approval from the French National Committee of Freedom and Informatics (CNIL) in order to collect and store data. Review of procedures regarding confidentiality of data of the Paris Registry is overseen by both the French National Committee of Registries and the French National Committee of Informatics and Freedom. The registry is allowed to register cases without explicit written consent of parents. Information letters are sent to chief of services for them to post in waiting rooms, patient rooms or other areas of the maternity in order to inform parents that anonymous data are recorded for cases of congenital anomalies.

Address for Further Information
Dr Hanitra RANDRIANAIVO
Scientific director of the registry
Centre Hospitalier Universitaire Sud Réunion
ILE DE LA REUNION
Tel: 33 260 35 92 56 /33 260 35 97 71
Fax: 33 260 35 92 48
Email: hanitra.randrianaivo@chu-reunion.fr

Profile of Medication Exposure

- For the period 2005-2014, 2.9% of all births were born with a CA.
- Medication exposure data is available from 2005. ATC codes are not yet recorded for 2005, but the drug names are available.
- Based on ATC codes, medication exposure prevalence ranges from 65 per 1,000 CA cases in year 2014, to 140 per 1,000 CA cases in 2011(see Figure 1).
- Prevalence of medication exposure in 2005 is based on drug name only (115 per 1,000 CA cases)
- Data sources are mainly patient hospital records.
- The most frequent drugs recorded in Isle de la Reunion are shown in Figure 2. The top 3 medications recorded are drugs for diabetes, antihypertensives and antiepileptics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Isle de la Reunion, 2005-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC Drug Group out of All CA Cases, Isle de la Reunion, 2005-2014*

*Only includes medications with prevalence >1 per 1,000 CA
France, Paris

History and Funding
The registry was created in 1981 and it has been a member of EUROCAT since 1982, and a member of EUROMEDICAT since the beginning. The registry is part of a research unit of INSERM (French National Institute of Health and Medical Research). The registry has been officially recognised by the French National Committee of Registries, and regularly renewed, most recently in 2012 for the period 2013-2016. The Registry is supported in part an annual grant from the INSERM and the Institut de la Veille Sanitaire (French National Institute for Health Surveillance).

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

Sources of Ascertainment
Notification to the registry is voluntary. Reports are actively collected from delivery units, paediatric departments, cytogenetic laboratories, and pathology departments. Terminations of pregnancy are included. Case information is also received from the information in health certificates for the first week of life. Birth certificates also include notification of congenital anomalies and are used as a source of case registration. The registry systematically (at least once a year) consults the three main cytogenetic laboratories for the Parisian hospitals.

By far, most cases of major CHD are diagnosed by specialized paediatric cardiology departments in our population or by prenatal ultrasound and/or autopsy reports for pregnancy terminations and foetal deaths. In addition, by request, paediatric cardiology centres supply diagnostic confirmation for specific cases.

Maximum Age at Diagnosis
Up to 1 week of age (or later if discharged from maternity at a later date)

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

Stillbirth Definition and Early Fetal Deaths
Stillbirths of 22 weeks after the last menstrual period or more are registered. Early foetal deaths/spontaneous abortions are registered and included when the gestational age is 16 weeks.

Exposure Data Availability
Information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies, is available for the malformed cases.
Denominators and Controls Information
Background data on births are available from the National Institute of Statistics (INSEE).

Registry Description References
Detailed description of the Registry may be found in the following publication:


Ethics & Consent
The registry requires ethics committee approval from the French National Committee of Freedom and Informatics (CNIL) in order to collect, store and analyse data. Review of procedures regarding confidentiality of data is overseen by both the French National Committee of Registries and the French National Committee of Informatics and Freedom.

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

Address for Further Information
Babak Khoshnood, MD, PhD and Nathalie Lelong, MS
Paris Registry of Congenital Malformations
INSERM U1153 – Equipe EPOPé
Maternité Port-Royal
53 avenue de l’Observatoire
75014 PARIS

Tel : +33 1 42 34 55 87
Email: babak.khoshnood@inserm.fr
Email: nathalie.lelong@inserm.fr

Profile of Medication Exposure
- Paris conducts active case ascertainment using multiple sources of information. For the period 2001-2014, 3.2% of all births were born with a CA. CA cases are only ascertained up to 1 week of age.
- Medication exposure data is available from 2001 for Paris.
- Medication exposure prevalence in Paris ranges from 70 per 1,000 CA cases in 2007 to 129 per 1,000 CA cases in 2013 (see Figure 1).
- Medical files from maternities are used for ascertainment of drug exposure. Data sources include obstetric/midwife medical records.
- Medication data are available for LB, FD and TOPFA.
The most frequent first trimester drugs recorded in Paris are shown in Figure 2. The top 3 medications recorded are drugs for thyroid therapy, analgesics, and drugs used in diabetes.

Figure 1: Prevalence of medication exposure* in the first trimester per 1,000 CA cases, Paris, 2001-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Paris, 2001-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Germany, Mainz

History and Funding
The Mainz Model was launched in 1990. The aim of this screening project was to determine prevalence and etiological causes of birth defects. The registry and its associated research are funded by the Ministry of Health of the Federal Republic of Germany from 1990-1995 and by the Ministry of Labor, Social Affairs and Health of Rhineland-Palatine from 1990 until now. The Registry joined EUROCAT in 1992.

Population Coverage
The registry covers births in three maternity hospitals which serve the Mainz district and area of Rheinhesse (370,000 inhabitants; population coverage 94.7% in 2008 according to federal statistics office) of Rhineland-Palatinate in SW Germany with approximately 3,300 births per year. Births to non-residents of the area are excluded (population-based III).

Sources of Ascertainment
The registry employs three pediatricians specially trained in clinical genetics, neonatalology and pediatric ultrasonography who examine each baby born in the participating hospitals within the first week of life. Routine sonography of kidneys is performed. For particular indications (e.g. microcephaly or heart murmur, history of hip dysplasia) further ultrasound examinations and other examinations are made. Both major and minor anomalies are recorded according to a standard examination protocol, but only major anomalies are transmitted to the EUROCAT Central Registry, according to its guidelines. In addition information on stillbirths, spontaneous abortions and TOPFA are obtained from pathology reports. Information on TOPFA is also obtained from the center checking the final prenatal diagnosis. Cases of Microcephaly are not transmitted to EUROCAT Central Registry. Cases of Hydronephrosis are available in more detailed diagnosis. Karyotyping in all suspicious and prenatally diagnosed cases in the monitored area is initiated by the registry. All lab results are available. All cases with prenatally detected signs or relevant medical history, as well as all suspicious children (clinics, persisting cardiac murmur > three days), are referred to the cardiologic department and provide diagnosis on request.

Maximum Age at Diagnosis
First week of life.

Termination of Pregnancy for Fetal Anomaly (TOPFA)
TOPFA are registered as they are performed in one of the hospitals and thus included in the data. It is relatively common for prenatal diagnosis of congenital anomalies not to result in a decision to terminate the pregnancy. In 60% of terminations an voluntary, not legally registered, autopsy examination follows, but the numbers decrease rapidly.

Stillbirth Definition and Early Fetal Deaths
The official stillbirth definition in Germany is a baby born with no signs of life weighing >=500g. The registry records information on all fetal deaths (including both stillbirths and spontaneous abortions) from 16 weeks gestation. Autopsy rates were as follows in 1995: in stillbirths 70%, in induced abortions 70%, in early neonatal deaths (0-7 days) 55%, in later deaths 1 week to 1 year - not applicable and in deaths with congenital anomaly – not known.
Exposure Data Availability
Exposure information on the EUROCAT form is obtained for both malformed and non-malformed babies (all population based birth). Sources: the pregnancy pass filled out throughout pregnancy by the obstetrician and his staff and data collected by midwives 6-8 weeks before birth. Additional exposure data is held which is not transmitted to EUROCAT. Drugs are ATC coded.

Denominators and Controls Information
As Mainz maintains a birth register rather than a CA register, there is comparable information on all non-malformed babies in the population from the same process of pediatric examination and information gathering. Pathology reports are included as well as the prenatal centres for ultrasound and invasive diagnostics for all children. The number of births is taken from this database. Information on the total number of fetal deaths from 16 weeks is available and included in “stillbirth” statistics.

Registry Description References

Ethics & Consent
Informed consent to use all routinely acquired data for scientific research is part of the admission contract between the patient and the hospital and thus given (opt in). The registry holds an approval from the ethics committee and the data security office of Rhineland Palatinate since its beginning. The approval does not have to be checked or renewed periodically. The registry includes only pseudonymous data.

Address for Further Information
PD Dr Annette Queisser-Wahrendorf, Dr Awi Wiesel, MSc
Birth Registry Mainz Model, Children’s Hospital
University Medical Center of the Johannes Gutenberg University Mainz, Germany
Langenbeckstr.1, 55131 Mainz
Tel and Fax ++49 6131 172773
Annette.queisser@unimedizin-mainz.de,
Awi.wiesel@unimedizin-mainz.de

Profile of Medication Exposure
- The Mainz registry employs 3 specialist trained paediatricians who examine each baby once in the first week of life, including an ultrasound scan of the kidneys.
- Active ascertainment (examination) and coding by the same person.
- For the period 1996-2014, 4.7% of all births were born with a CA.
- Although medication exposures have been recorded since the registry began in 1990, ATC codes are only available from 1996.
Medication exposure prevalence ranged from 37 per 1,000 CA cases in 1997 to 394 per 1,000 CA cases in 2014 (see Figure 1). Prevalence is lower prior to 2005, as generally only the 4 drug groups for chronic conditions (antidepressants, antiasthmatics, antiepileptics and insulin analogues) were coded using ATC codes. Post 2005, the medication exposure prevalence is generally higher in Mainz compared to the other EUROmediCAT registries combined.

Data sources include obstetric/midwife records, paediatric records and maternal medical records not related to the pregnancy such as child health records held by, for example, paediatrician, geneticist, neonatologist, paediatric cardiologist /neurologist/ surgeon. A maternity “pass” is filled out throughout the pregnancy by the obstetrician and staff for all pregnant women in Germany. Data is also collected by midwives 6-8 weeks before birth.

Medication data are available for LB, for FD and TOPFA the data has different sources. There are some differences in coding of medication exposure for TOPFAs due to the availability of post mortem information.

The most frequent first trimester drugs recorded in Mainz are shown in Figure 2. The top 3 medications recorded are thyroid therapy, antibacterials for systemic use and drugs used in diabetes.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Mainz, 1996-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Mainz 1996-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Germany, Saxony-Anhalt

History, funding and legal legitimacy

The registry joined EUROCAT in 1992. The registry started in 1980. The years 1980-89 were funded by Ministry of Health of former German Democratic Republic. The years 1990-92 were funded by the Academy of Medicine, Magdeburg whereas the period between 1993 and 1995 was sponsored by the Ministry of Health, Federal Republic of Germany. Since 1995, the registry has been funded by the Ministry of Labour and Social Affairs of the Federal State of Saxony-Anhalt. On 12.11.2009, a new law under the federal by the parliament of Saxony-Anhalt was unanimously adopted. In § 7 Child protection Act Saxony-Anhalt states: "The Federal state of Saxony-Anhalt promotes the widespread detection of birth defects in babies under a permanent observation. The task of this observation is to identify data on the prevalence of congenital malformations and watch over a defined period of time, to analyze the scientific data and to evaluate the effectiveness of measures for primary and secondary prevention".

Population Coverage

The registry started in 1980 in the city of Magdeburg with about 4,000 annual births. After it there was a successive enlargement of the registry from 1981 to 1986. In 1981 we expanded to include some rural districts around the city of Magdeburg and this process continued until 1987 when we registered the whole area of the former “district Magdeburg” (about 17,000 births per year). Then we had a stable system from 1987 to 1989 and in 1990 there was a dramatic political change. Since the reunification there has been a two-third decrease in the number of births in the so-called ‘new’ Federal states of Germany. After the reunification, a similar process of territorial enlargement took place. In year 2000, registration expanded to the entire Federal State of Saxony-Anhalt (21 districts and 3 major cities). In the year 2007 a reform reduced the 21 districts to 11 districts.

Saxony-Anhalt has 2.237 million inhabitants (30.06.2014) and annual births at a rate of about 16 797 children (2013).

By comparison to 1987, we currently survey a much larger area in our registry with approximately twice as many inhabitants but the births rate is the same as the 1980s.

Registration concerns deliveries within surveyed region excluding non-residents (Population-based III).

Sources of Ascertainment

Multiple sources, such as delivery units (01.01.2014: 25 maternity hospital), paediatric departments, laboratories, prenatal diagnostic centres, departments of pathology and other specialities (pediatric surgery, orthopedics) report children/foetuses with malformations and healthy children as a control group.

The registration of a child requires the informed consent of the parents. The registration sheet does not include much personal identifiable data, thus making follow-up investigations almost impossible. Exposure information of the mother (including drug intake before and in pregnancy, including periconceptional folic acid intake) and the father is documented on a standardized documentation sheet. From 1987 onwards, cases are registered if diagnosed with a congenital
anomaly up to 1 year of age. The registry receives some results from cytogenetic labs but not through direct access or via electronic transfer. Some are received indirectly via gynaecology or paediatric notes.
Second source is the notification in form of a basis dataset (month of birth, malformation, age of mother) not acquiring parents consent.
We get notification from the paediatric cardiology department and a regional cardiology outpatient clinic via our standardized form twice a year.

**Maximum Age at Diagnosis**
Up to 1 year of age

**Termination of Pregnancy for Fetal Anomaly**
Terminations of pregnancy (“medical indication”) have no time limitation by law in Germany. We have had complete information about terminations of pregnancy after prenatal diagnosis of foetal malformations since 1987.

**Stillbirth Definition and Early Foetal Deaths**
Stillbirths and spontaneous abortions with malformations from 16 weeks gestation are registered. The stillbirth definition has been >=500 g from 1.4.94 and >= 1000g before 1994.

**Exposure Data Availability**
Maternal and paternal occupation, drugs in pregnancy (ATC coded), alcohol, nicotine, drug abuse.

**Denominators and Controls Information**
Statistics on the total number of births comes from Statistical Office Saxony-Anhalt. There is the opportunity to exclude non-resident mothers with assistance of the postal code. A woman who gives birth outside Saxony-Anhalt, but is a result here is included in the statistics. The denominators include only live births and stillbirths. Information about maternal age for all births is available at the level of the entire state of Saxony-Anhalt and also the single counties.
Information is also reported about two control infants per malformed child. The two control infants, theoretically, are those born directly before and directly after the malformed child. The information about the control children is the same as malformed because a standardized documentation sheet is used.

**Additional services**
Since 01.08.2006 the Malformation monitoring centre is collecting and tracking the results of the newborn hearing screening in Saxony Anhalt. The hearing screening is made regular in all delivery units in Germany.
We closely collaborate with the newborn screening centre Saxony-Anhalt which is located at the Medical Faculty of Otto-von-Guericke University Magdeburg.
Annual report is available with results of malformation interpretation, newborn hearing screening and newborn metabolic screening (in German and English). The report can be downloaded from our website.

**Registry Description References**


**Ethics & Consent**
The registry has the ethics committee approval from the Medical Faculty, Otto-von-Guericke University, Magdeburg. Because of the data protection law in Germany, since 1992 national legislation requires informed consent in order to register a baby with a congenital anomaly. Parents have to agree to the inclusion of the child on the Register (opt-in) with a standardized full description dataset.

**Address for Further Information**
Dr Anke Rißmann MD
Malformation Monitoring Centre Saxony-Anhalt
Medical Faculty, Otto-von-Guericke University
Leipziger Strasse, Haus 39
D-39120 Magdeburg, Germany
Tel: +49 391 67 14174
Fax: +49 391 67 14176
Email: monz@med.ovgu.de
www.angeborene-fehlbildungen.com

**Profile of Medication Exposure**
- For the period 2000-2014, 3.2% of all births were born with a CA.
- Medication exposure data is available in the EUROmediCAT central database from 2000 for Saxony Anhalt.
- Medication exposure prevalence ranged from 122 per 1,000 CA cases in 2002 to 213 per 1,000 CA cases in 2011 (see Figure 1)
- Sources of medication exposures include prospectively recorded maternity records and maternal interview after birth
- The most frequent first trimester drugs recorded in Saxony Anhalt are shown in Figure 2. The top 3 medications recorded are drugs for thyroid therapy, antibacterials and drugs for diabetes
Figure 1: Prevalence of medication exposure* in the first trimester per 1,000 CA cases, Saxony-Anhalt, 2000-2014 compared to all other EUROmediCAT registries combined.

*Excludes Vitamins, minerals and folic acid.
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Saxony Anhalt, 2000-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Ireland, Cork & Kerry

History and Funding
The registry started in 1996 and was granted approved membership of EUROCAT in 1998. The Clinical Research Ethics Committee of the Cork Teaching Hospitals approves the Registry for research. Staffing includes a nurse (0.48 WTE) and specialist in public health medicine (0.1 WTE) with support sessions by surveillance scientist, IT, technical and administrative staff. The Department of Health through the Health Services Executive provides funding for the register.

Population and Coverage
The Registry covers the counties of Cork and Kerry in the SW of Ireland (population-based, all mothers resident in a geographic area). Between 2007 and 2013, 1% of resident mothers gave birth outside the registry area. Since 1996, the total number of births each year has varied between 8 and 10 thousand births. The average number of births per year over the most recent ten years (2004-2013) is 9777 births per annum.

Sources of Ascertainment
The registry is based on active case finding. Data for the registry includes hospital records from obstetric and neonatal departments, paediatric cardiology and orthopaedics outpatient letters, Hospital In-patient Enquiry Data (HIPE), birth notifications, stillbirth certificates, Central Statistics Office (CSO) data on deaths in children up to the age of 2 years, post mortem examinations, and social allowance records. The national cytogenetic laboratory and the national centre for paediatric cardiology and cardiac surgery database are additional sources of confirmatory data.

Maximum Age at Diagnosis
Most cases are identified before the first birthday. The registry seeks HIPE data up to age 7 years. Some rare disease cases e.g. Marfan Syndrome or Ehlers-Danlos Syndrome are diagnosed later than this and come to the registry in routine data sources e.g. paediatric cardiology or orthopaedic outpatient letters and are registered.

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

Stillbirth Definition and Early Fetal Deaths
Babies born without signs of life with a gestational age of >= 24 weeks or a weight of >= 500g are registered in national statistics. Early fetal deaths / spontaneous abortions following prenatal diagnosis of congenital anomaly are also entered on the registry and reported to EUROCAT (those <20 weeks gestation are not included in prevalence data). National autopsy rates for stillbirths and early neonatal death (0-7 days) have decreased due to controversy arising from the issue of consent.

Exposure Data Availability
Information on parental occupation, maternal drug use, smoking and alcohol use, illness during pregnancy and outcome of previous pregnancies is gathered.
Denominators and Controls Information
Denominator data is available from the national Central Statistics Office (CSO). The CSO publishes national statistics in respect of all births annually and provides rates for the Rep. of Ireland and broken down by county.

Registry Description References

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

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

Address for Further Information
Dr. Mary O'Mahony, Specialist in Public Health Medicine, Department of Public Health, HSE South (Cork & Kerry), Floor 2, Block 8, St. Finbarrs Hospital, Douglas Road, Cork, Ireland.
Tel: +353 21 4927601-4
Fax: +353 21 4923257
E-mail: maryt.omahony@hse.ie
In Cork & Kerry, for the period 1996-2012, 2.6% of all births resulted in a CA. The registry recorded information on medication exposures in pregnancy from 1996. Ascertainment of medication exposures is currently on-going for the years 2007, 2010 and 2011. Excluding these 3 years, medication exposure prevalence ranged from 99 per 1,000 CA cases in 2004 to 211 per 1,000 CA cases in 2009 (see Figure 1).

Only medical files from maternal healthcare providers in relation to pregnancy are used. Data sources include obstetric/ midwife/ gynaecologist records i.e. information on medication is extracted directly from the mother’s medical chart. However, some medications such as anti-asthmatics are regarded as innocuous and not routinely noted on the maternal record even when taken throughout pregnancy.

The midwife administers a standard questionnaire to the pregnant woman. This is supplemented by information from the GP referral letter, hence the maternal medical file / record depends on information supplied directly by the pregnant woman/ GP letter.

A section of the maternal chart includes a text box for recording medication used in the first trimester – all pregnancy medication tends to be entered into this section.

The maternal chart also includes a separate question on over the counter (OTC) medication so it would usually be noted if used.

A paper copy of the maternity record, stored in the registry, is used for confirming medication exposures for CA cases. The primary information source is not reviewed.

Records are available for 96% of LB and 99% of FD recorded in the registry. Maternal medication is recorded at the first (booking) and subsequent antenatal visits during the pregnancy. As a result the same information is available on maternal medication use during pregnancy irrespective of pregnancy outcome whether LB, or FD.

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

The most frequent first trimester drugs recorded in Cork & Kerry are shown in Figure 2. The top 3 medications recorded are drugs for obstructive airway diseases, sex hormones and analgesics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Cork and Kerry, 1996-2012 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Cork and Kerry, 1996-2012*

*Only includes medications with prevalence >1 per 1,000 CA
Ireland, South East

History and Funding
The South East Ireland Congenital Anomaly Register was established in the year 2000 and data was retrospectively collected from 1997 onwards. The Department of Health funds the registry through the Health Service Executive (HSE).

Population Coverage
The registry is population based and includes babies born to all mothers resident in the South East. The registry covers approximately 7500 births per year, which represents 10% of all births in the Republic of Ireland.

Sources of Ascertainment
The registry is based on active case finding. A child with a malformation, born after 01/01/1997, can be registered at any age. There is no upper age limit imposed for registration of a case.

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

- Hospital Inpatient Enquiry System (HIPE)
- Child Health Information System
- Births Notification Form
- Labour ward and NICU registers
- Paediatric and Obstetric case records
- Post-mortem Examinations
- Cytogenetic Laboratories – no direct access, information received on an annual basis
- Information from maternity and paediatric hospitals
- Information from disability nursing service
- Prenatal screening records in some centres
- Maternity hospital clinical reports

Paediatric cardiology centres do not supply information to the registry, but other sources of information cover paediatric cardiac surgery, i.e. copies of letters from paediatric cardiology centres in respect of each case which are available in medical notes at local hospital level.

Medical notes are reviewed to assist in the confirmation of the diagnosis. EUROCAT guidelines are adhered to in respect of inclusions and exclusions.

Maximum Age at Diagnosis
There is no upper age limit

Terminations of Pregnancy for Fetal Anomaly
Abortion is illegal in Ireland. However, women in Ireland have the option to travel outside of Ireland for termination of pregnancy following prenatal diagnosis. Where information is available to the registry about these cases, they are included.
Stillbirth Definition and Early Fetal Deaths
Registration covers affected fetuses spontaneously lost from 24 weeks gestation or with a birth weight > 500g.

Exposure Data Availability
Maternal health, drug and lifestyle exposure data is collected primarily from paediatric and obstetric medical records.

Denominators and Controls Information
Denominator data is obtained from the national Central Statistics Office (CSO)

Ethics & Consent
The registry required ethics committee approval in order to collect and store data. This approval was sought at the time of setting up the registry and there has been no requirement for renewal of the approval. Currently consent is not obtained for inclusion of cases on the register. Information about the registry is available through the antenatal service and at www.hse.ie

Address for Further Information
Dr Catherine Lynch / Ms Johanna Costigan
Department of Public Health
Health Service Executive – South
Lacken, Kilkenny, Ireland
Eircode R95 P231
Tel: + 00 353 56 7784142
Email: catherine1.lynch@hse.ie / johanna.costigan@hse.ie

Profile of Medication Exposure
- For the period 2007-2014, 1.7% of all births were born with a CA.
- Medication exposure data is available from 2007.
- Medication exposure prevalence ranges from 29 per 1,000 CA cases in year 2012, to 220 per 1,000 CA cases in 2014 (see Figure 1).
- Data sources include clinical case records.
- In 2012, it was only possible to access approx. 55% of maternal charts which would be lower than normal and may have resulted in a decrease in drug data ascertainment.
- The most frequent first trimester drugs recorded in SE Ireland are shown in Figure 2. The top 3 medications recorded are sex hormones, thyroid therapy and antithrombotic drugs.
Figure 1: Prevalence of medication exposure* in the first trimester per 1,000 CA cases, SE Ireland, 2007-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA Cases, SE Ireland, 2007-2014*
**Italy, Emilia Romagna**

**History and Funding**
The Registry started its activities in 1978 with the participation of a few collaborating centres rising to cover all delivery units in the Region.

Since 1980 the Registry is recognised and supported by the Emilia Romagna Region with the following objectives:

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

The Registry joined EUROCAT in 1980 and in 1981 transmitted the first birth year of data to EUROCAT. The Registry joined the International Clearinghouse for Birth Defects in 1995. The Emilia Romagna Registry also participates in the co-ordination of the Italian Congenital Malformation Registries set up by The Italian National Institute for Health (I'Istituto Superiore di Sanità) with the aim of sharing the experiences of the various registries, create common lines of research and produce epidemiological data on congenital malformations at a national level (http://www.iss.it). The Registry created a website in 2000 which has since been expanded and developed. [www.registroimer.it](http://www.registroimer.it)

Since 2003 the Registry has been in collaboration with the Health Information systems service and Social policy body of the Emilia Romagna Region formally involved in the Scientific Steering Committee.

In 2004 a link with the Regional Medical Genetics Service network was formed (www.geneter.it) with the aim of providing genetic counselling and evaluating genetic conditions diagnosed within the network and in the same year with the Regional birth assistance database Cedap (Certificate of Assistance at delivery). From 2004 additional information on maternal medication is available from the Regional Prescription Database.

From 2005, the Registry has progressively moved away from paper data collection developing an integrated system of ascertainment based on linking regional healthcare databases and specific competence in database management. An algorithm has now been developed to integrate and validate cases.

From 2009 the IMER Registry ascertains cases for the 1st year of life.

The exchange of data between IMER and the registry of rare diseases allows better identification of recognized conditions in IMER. The collaboration that has been established has resulted, for example, in a contribution to the Annual Report on Rare Diseases from IMER and a
chapter on Rare Diseases in the IMER Annual Report so maximising dissemination and providing a unique source of information for decision making.

We are now launching an IMER FORUM in order to involve clinicians in the definition of difficult cases and to provide skill development in congenital anomalies.

Every year the Registry provides a scientific convention, course for reference centres, and an annual report.

Population Coverage
The Emilia–Romagna region covers an area of 22,123 sq.kms with a population of around 4.4 million people. The total number of births in Emilia Romagna, which has grown significantly in recent years has now plateaued at 39415 births in 2012. From 2011 the registry no longer includes in its coverage the republic of San Marino.

The registry follows the EUROCAT definition of population based II (includes all mothers delivering within the region of Emilia Romagna, irrespective of place of residence). In 2012, 93.7% of births were to resident mothers. Since 2006 the registry, in collaboration with the Regional births database (CeDAP) has reached a population coverage ~100% involving all 31 delivery units in the Region. In recent years immigration has created an important demographic change. The births to non-Italian citizens represented 30.5% of the total births in the region in 2012.

Sources of Ascertainment

Birth and death certificates do not include notification of CA. Emilia Romagna Registry has the following multiple sources of ascertainment:

1. **Voluntary hospital participation.** From 2011 reporting is on line using the IMER website. Data entry is password controlled with cases being entered by neonatologists, paediatricians and obstetricians during the first week of the infant’s life. We do not have specific notification from paediatric cardiology units, but from 2011 all complex CHD cases are reviewed by an expert Paediatric cardiologist. Paediatric cardiology centres supply diagnostic confirmation when requested by the registry for specific cases. Notification of a congenital anomaly is recorded up to 1 week.

2. **The Regional Births database (CeDAP).** This also provides the registry with a source of denominator and control data.

3. **The hospital discharge database (SDO)** provides a further source of ascertainment up to one year of life. An algorithm has been developed to identify and validate malformed cases according to the EUROCAT guidelines. Suspected cases are referred to the IMER reference person at the birth centre for confirmation

4. **The Regional TOPFA database** provides minimal data on TOPFA which reference centre clinicians integrate where possible.

5. **Rare Disease Registry** this provides about 1% of cases but these are complex recognised conditions and this source ensures a full description of the final diagnosis.

6. **Cytogenetics** From 2012 data cytogenetic test results and karyotypes where available will be provided to EUROCAT.

7. **Mortality database.** We intend from 2012 database to include data regarding deaths that occur in the 1st year of life rather than 1st week of life
**Termination of Pregnancy for Fetal Anomaly**

Termination of pregnancy became legal in Italy in 1978. Data for TOPFA first became available in 1982. The Italian law (L.N. 194/78) states that TOPFA is allowed in the case of diagnosis of serious fetal pathology which may detrimentally affect the woman's physical or psychological health. The upper gestational age limit for terminations is 23 weeks. TOPFA after prenatal diagnosis of birth defects are systematically included in IMER but data access is a current issue.

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

**Stillbirth Definition and Early Fetal Deaths**

The official definition of stillbirth in this Registry is now 180 gestational days in line with the Regional Births database (CeDAP). Fetal deaths of 20 weeks or more gestation are systematically included (with no lower weight limit exclusion criteria). The autopsy rate in 2011 was 37% overall. The post mortem rate was: 100% in stillbirths, 52% in induced abortions where information on PM was available, and 36% in neo natal deaths where information on PM was available.

**Exposure Data Availability**

Exposure information is obtained by interviews of the mothers of malformed infants. From 2003 data regarding maternal drugs in the first trimester is recorded as ATC codes and jobs are recorded using the ISCO work codes. Previously these data were recorded using internal codes. IMER Registry is participating in the EUROmediCAT project and holds data on maternal prescriptions from 2004-2011 in LDMP.

**Denominators and Controls Information**

Birth statistics are provided by the Regional births database (CeDAP) recorded by maternal age group and birth month. This source also provides information for control cases as every baby in the Emilia Romagna region has a certificate of assistance at delivery. General demographic information is available for all births in the area (e.g. mean maternal and paternal ages, percentage of mothers 35 years or older) making it a useful resource for population studies. In recent years immigration has created an important demographic change with an increase in births. As births to non-Italian citizens represented 30.6% of the total births in the Region in 2012 the citizenship of the mother is now coded for all births.

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

**Ethics & Consent**

The registry is recognised as part of the Health system information flow and regulated by Regional Laws. The parents have to agree to the inclusion of the child on the Register (opt-in).
Registry staff and computing
Dr. Amanda J Neville- EUROCAT Registry Leader (part time)
Dr Gianni Astolfi - Database management (full time)
Prof Elisa Calzolari – Genetic Expert

Address for Further Information
Registro IMER - IMER Registry (Emilia Romagna Registry of Birth Defects),
Centre for Clinical and Epidemiological Research, University of Ferrara
Azienda Ospedaliero- Universitaria di Ferrara
Corso Giovecca, 203
44121 Ferrara (Italy)

Tel. 00 39 0532 237384

Email: nvm@unife.it
Website: REGISTRO IMER
Profile of Medication Exposure

- In Emilia Romagna (IMER), for the period 1995-2014, 2.1% of all births resulted in a CA.
- Emilia Romagna recorded medication data since the registry began. However, only data from 1995 is used in the EUROmediCAT project.
- Medication exposure prevalence for CA cases is generally higher than all the other EUROmediCAT registries combined. Prevalence ranged from a low of 50 per 1,000 CA cases in 2013 to 465 per 1,000 CA cases in 2010 (see Figure 1). The low prevalence in 2013 is likely due to on-going ascertainment of medication exposures. Prevalence of medication in CA cases dropped significantly in the period 2003-2008. This decrease was due to the use of the healthcare database (cedap) for ascertaining cases, which improved the overall coverage and prevalence of CA cases, but at the cost of the quality of information. Medication data includes second and third trimester exposures.
- Between 1995 and 2004 the only source of medication exposure ascertainment used by the registry was direct reporting by the birth centre using the IMER form.
- On admission to the labour ward any medications that the mother was taking at the time were recorded.
- If a CA was identified the mother was then interviewed, using a registry form, to record any medications she took during pregnancy. The specific week of use during pregnancy was also recorded if possible.
- From 2004 IMER started moving to multi source ascertainment including surgery records (SDO) and assistance at birth certificates (Cedap). Only births notified directly on the IMER form to the Registry have maternal medication information.
- Medication exposure data are only available for a small number of TOPFA cases. The Ferrara TOPFA cases are ascertained directly by the registry in the obstetric and gynaecology wards. All available documentation is accessed. Occasionally one of the reference centres will send in a TOPFA completing the longer case report used for LB.
- Medication data relating to still births is taken directly from the clinical records for example obstetric records, records of hospital stays and any prenatal diagnostic checks.
- For specialist care, e.g. in cardiology or endocrinology clinics, the patient is responsible for their own medical records and keeps this information with their pregnancy records. This may or may not be added to the clinical file on admission.
- The code 8888888 is used where a medication is recorded on the case record but is undecipherable.
- The registry uses Z codes to denote herbal medications.
- Emilia Romagna participated in the EUROmediCAT FP7 prescription linkage study.
- The most frequent first trimester drugs recorded in Emilia Romagna are shown in Figure 2. The top 3 medications recorded are drugs for antibacterials for systemic use, other gynecologicals and analgesics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Emilia Romagna, 1995-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA Cases, Emilia Romagna, 1995-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Italy, Tuscany

History and Funding
The Registry started in 1979 in the province of Florence and from 1992 in the whole Tuscany region. The Registry is a surveillance programme included in the Regional Statistics System; it is formally recognised and supported by the Tuscany Region Health Authority. The Registry joined EUROCAT in 1979.

Population Coverage
The programme is population-based which includes all mothers resident in the Region of Tuscany. It involves all the regional hospitals and the coverage is around 95% of all births in the Tuscany region (approximately 3.5 million inhabitants and 30,000 births per year).

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

Maximum Age at Diagnosis
Up to 1 year of age

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

Stillbirth Definition and Early Fetal Deaths The official definition of stillbirth in this Registry is: 180 gestational days. Fetal deaths of 20 weeks or more gestation are systematically included.

Exposure Data Availability Maternal and paternal occupation, lifestyle and socio-economic characteristics are obtained by interviews of mothers of malformed infants.
Denominators and Controls Information

Vital statistics and other epidemiological information are obtained by the Certificate of Delivery Assistance (Certificato di Assistenza al Parto - CAP) collected by the Regional Bureau of Statistics.

Ethics & Consent

The registry does not require ethics committee approval in order to collect and store data. At the moment informed consent is not required by national legislation, but the registry asks for oral authorization from the mother. The parents have to agree to the inclusion of the child on the Register (opt-in).

Address for Further Information
Dr Anna Pierini, Registry Leader
Unit of Epidemiology, CNR Institute of Clinical Physiology,
Via Moruzzi 1, I-56124 Pisa, Italy
Tel: +39 050 3152102
Fax: +39 050 3152570
Email: apier@ifc.cnr.it

Profile of Medication Exposure

- Reporting of CA cases in Tuscany is based on multiple sources of ascertainment. For the period 1995-2014, 2.2% of all births were born with a CA.
- Medication exposure data is available from 1995.
- Medication exposure prevalence ranges from a low point of 75 per 1,000 CA cases in 2011 to 179 per 1,000 CA cases in 2014 (see Figure 1).
- Data sources include an interview with the mother administered by a gynecologist, neonatologist or paediatrician after birth.
- Interview records are available for 100% of LB, FD and TOPFA recorded in the registry.
- The most frequent first trimester drugs recorded in Tuscany are shown in Figure 2. The top 3 medications recorded are drugs for other gynecologicals, thyroid therapy and antibacterials for systemic use.
Figure 1: Prevalence of medication exposure* in the first trimester per 1,000 CA cases, Tuscany, 1995-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Tuscany, 1995-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Malta

History and Funding
The Registry started in 1985 as a research project of the University of Malta. It started as a hospital-based register collecting data regarding congenital anomalies diagnosed in babies born at the main general hospital. It became a member of EUROCAT in 1986. Funding for the research project was stopped in 1995 and in January 1997 the Department of Health Information resumed the functions of the Registry increasing coverage to all hospitals on the islands making it a national population-based register. The Registry is now run and funded by the Government Directorate for Health Information and Research. The aim of the registry is to provide accurate epidemiological information regarding the occurrence of congenital anomalies in Malta and Gozo.

Population Coverage
The Registry is population-based covering all resident mothers in Malta, Gozo and Comino and presently covers about 4,000 births per year. The number of resident mothers giving birth in a hospital outside the area is considered to be negligible as Malta is an island and population movement is limited. It is unlikely that mothers will go abroad to give birth. The registry is considered to cover close to 100% of births occurring on the Islands.

Sources of Ascertainment
Reporting is voluntary. Several sources of information have been used since 1997 and the Registry has back-dated its information to include these sources of information from 1993. For this reason data since 1993 may be considered most complete and reliable. The Registry employs active data collection from multiple sources including: delivery and obstetric file notes, paediatric file notes, paediatric echo cardiology records, genetic clinics records, National Mortality Register, National Obstetric System database, Hospital Activity Analysis database, National Cancer Register and the hypothyroid screening programme. Voluntary reporting by doctors is also available. These sources cover the whole population of the Maltese Islands.

Babies with a congenital anomaly may be diagnosed and registered up to 1 year of age. Minor anomalies (as defined by EUROCAT) are not registered unless in combination with other major defects. There is no legal requirement for notification of congenital anomalies without parental consent.

Maximum Age at Diagnosis
Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy is illegal in Malta.

Stillbirth Definition and Early Fetal Deaths
The official definition of stillbirth is: a baby born with no signs of life at gestational age of 22 weeks or more, or a birth weight equal to or greater than 500g. Stillbirths are registered. All early fetal deaths of 20 weeks gestation and over which have been diagnosed as having a congenital anomaly are included. Autopsy rates for 2013 were 58% in stillbirths and 26% for infant deaths.
Exposure Data Availability
Information regarding maternal disease and exposure to medicinal drugs, smoking, alcohol and drug abuse as well as parental occupation are collected for all malformed infants.

Denominators and Controls Information
Epidemiology background data on all births are available from the National Obstetric Information Systems (NOIS) database and the National Statistics Office (NSO).

Registry Description References

Ethics & Consent
The Superintendent of Public Health, within his legal responsibility, requires that a Malta Congenital Anomalies Register is kept in the interests of Public Health (DH circular 36/09). Ethics approval is needed prior to case based data being released for individual studies, projects or theses.

Malta became an EU member in 2004 and complies with directive EC95/46. There is no national legislation requiring informed consent in order to register a baby with a congenital anomaly.

Address for Further Information
Dr Miriam Gatt, Malta Congenital Anomalies Registry, Directorate for Health Information and Research, 95 Guardamangia Hill, Guardamangia PTA 1313, Malta
Tel: +356 25599000
Fax: +356 25599385
Email: miriam.gatt@gov.mt

Profile of Medication Exposure
• In Malta, for the period 1996-2013, 3.2% of all births were born with a CA. Prevalence rates in the more recent years are subject to change as the Registry updates its data with any new CA cases reported.
• Malta began registering medication data in 1996.
• The prevalence of medication exposures ranged from 119 per 1,000 CA cases in 1996 to 396 per 1,000 CA cases in 2012 (see Figure 1). A new ante-natal reporting form was introduced in 2008, resulting in an increase in reporting of drug exposure cases.
• The registry has invested increased effort into recording medication exposures in pregnancy and this may explain the increase in prevalence of medication use in more recent years.
• Medication exposures are prospectively recorded in the registry and should not be influenced by maternal recall bias.
• Data sources include obstetric/midwife medical records and paediatric medical records.
• Medication data are not available for TOPFA as TOPFA are illegal in Malta.
The most frequent first trimester drugs recorded in Malta are shown in Figure 2. The top 3 medications recorded are sex hormones, antithrombotic agents and drugs for obstructive airway disease.

Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Malta, 1996-2013 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Malta, 1996-2013*

*Only includes medications with prevalence >1 per 1,000 CA
Netherlands, North

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

Population Coverage
The registry is population-based, including all mothers resident in the registration area. In the beginning, the program covered 7,500 births annually in the province of Groningen and the northern part of the province of Drenthe. From 1989 onwards, coverage was gradually increased to 20,000 births annually in the provinces of Groningen, Friesland and Drenthe. In the recent years the number of births in the region decreased to 18,500, approximately 10% of all births in the Netherlands. Home deliveries (35% of births per year) are included and it is estimated that only a few percent of resident mothers would give birth outside the defined registry area.

Sources of Ascertainment
Children and foetuses with congenital anomalies diagnosed before or after birth are eligible for registration at the Eurocat NNL registry, if the mother lived in the region at the time of birth and the child is not older than 10 at notification. There is no lower limit for gestational age, spontaneous and induced abortions are included. Notification of children and foetuses with congenital anomalies is voluntary. Registry personnel are actively involved in case ascertainment, using multiple sources such as obstetric records, hospital administration data, pathology records, etc. Cytogenetic lab results are electronically downloaded from the Genetics department and include all abnormal karyotype reports, both from prenatal and postnatal samples. For cases reported to the registry it is verified whether any genetic tests were performed and test results are registered in the database. The only pediatric cardiology centre in the registration area, also part of the UMCG, supplies systematic case lists and diagnostic details to the registry. A number of frequently occurring mild anomalies is not registered, unless they occur in combination with other serious congenital anomalies. If new information becomes available for registered children before 10 years of age, the files are updated.

Maximum Age at Diagnosis
Up to 10 years of age.

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

Stillbirth Definition and Early Fetal Deaths
A stillbirth is defined as a fetus of at least 24 weeks gestation that died in uterus or during birth. There are no age or weight limits for inclusion of early fetal deaths/spontaneous abortions. Autopsy rates per year are not available.
**Exposure Data Availability**
Since 1997 parents have been asked to fill out a questionnaire including questions on occupational activities, smoking habits, alcohol consumption and recreational drug use and socioeconomic status. In addition, data from community pharmacies are used to collect data on medication dispensed in the period from 3 months before and during pregnancy. After the information of the pharmacy is received, a telephone interview with the mother is done, to verify whether she has actually taken the medication dispensed from the pharmacy and if she has taken any over-the-counter medication. The response rate to the questionnaire is 80%.

**Denominators and Controls Information**
General statistics are available from the Central Bureau of Statistics (CBS). No information on non-malformed infants is collected.

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

**Address for Further Information**
Hermien de Walle, registry leader
Marian Bakker, epidemiologist
Eurocat Northern Netherlands
Department of Genetics, University Medical Center Groningen
PO Box 30.001, 9700 RB Groningen, The Netherlands
tel: +31 50 361 7115
fax: +31 50 361 7232
email: eurocat@umcg.nl
website: www.eurocatnederland.nl
www.geneticsgroningen.nl

**Profile of Medication Exposure**
- Reporting of CA cases in N Netherlands is based on active case finding. For the period 1995-2014, 2.7% of all births were born with a CA.
- Medication exposure data is available from 1995 for the Northern Netherlands.
- Medication exposure prevalence is high in N Netherlands compared to other centres, ranging from 137 per 1,000 CA cases in 1995 to 462 per 1,000 CA cases in 2008 (see Figure 1), due to the extensive data collection methodology. Medication exposure is lower in recent birth years, because it takes some time to collect all the information.
- Data sources include obstetric, midwife, paediatric, and maternal pharmacy medical records which are recorded irrespective of pregnancy status.
- From 1997, the registry obtained data from community pharmacies on medication dispensed in the period from 3 months before and during pregnancy. This was followed up with a telephone interview with the mother to verify whether she actually took the medication dispensed from the pharmacy and if she has taken any OTC medication. The
change in registry recording methods coincided with the sharp increase in reported cases of medication exposure in 1997. Repeat prescriptions have only been reported in recent years, compared to earlier years of registration. A questionnaire was also sent to mothers after the birth and included questions relating to use of specific drugs (folic acid, multivitamins, vaccinations anaesthetics, insulin and other medications in relation to Diabetes Mellitus). The questionnaire had an 80% response rate,

- Medication data are available for LB, FD and TOPFA.
- The registry uses Z codes to denote herbal medications
- The most frequent first trimester drugs recorded in N Netherlands are shown in Figure 2. The top 3 medications recorded are analgesics, sex hormones, and antibacterials.

**Figure 1:** Prevalence of medication exposure* in the first trimester per 1,000 CA cases, N Netherlands, 1995-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, N Netherlands, 1995-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Norway

History and Funding
The Medical Birth Registry of Norway (MBRN), initiated in 1967, is managed and funded by the Norwegian National Institute of Public Health. The Registry joined EUROCAT in 1998.

Population Coverage
The MBRN is population based and covers all births in Norway, irrespective of place of residence of the mothers. Approximately 60,000 births are registered annually. Births by non-resident mothers delivering in Norway account for approximately 0.2% of all births.

Sources of Ascertainment
Reporting to the Registry is compulsory. The Registry is based on the notification of births from the delivery units, and since 1999 also from the neonatal units for infants transferred to such units after birth. Congenital anomalies are most often registered at birth, but may be registered up to 1 year of age. Autopsy reports are collected for stillbirths with birth weight ≥500g, and for termination of pregnancy for fetal anomalies (TOPFAs) where an autopsy has been conducted, which is the case for the majority of TOPFAs.

The MBRN does not receive direct notification from cytogenetic laboratories or specific notification from pediatric cardiology departments.

Maximum Age at Diagnosis
Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy is legal and is the mother's decision up to gestational age of 12 weeks. After gestational age of 12 weeks, permission is required from the commission and these have been recorded from 1999 onwards. If a congenital anomaly is diagnosed, the upper limit is 18 weeks gestation (with exemptions). Since Dec. 1998, all TOPFAs are registered in the MBRN.

Stillbirth Definition and Early Fetal Deaths
The official definition of a stillbirth for perinatal mortality statistical purposes is a fetal death before or during labour with a gestational age of ≥22 weeks or with a birth weight of ≥500g. Early fetal deaths/spontaneous abortions of fetuses with a gestational age of ≥16 weeks were included in the definition during the period 1967 to 2001, whereas those occurring with a gestational age of ≥12 weeks have been included from 2002 onwards.

Exposure Data Availability
Descriptive information, such as maternal history of disease and, since 1999, voluntary information of smoking habits and occupation, is also registered.

Denominator and Controls Information
Information available for malformations are available for the total population of births.
Registry Description References

Ethics & Consent
All research projects requiring the use of person identifiable information from the MBRN must have approval from the Regional Committees for Medical and Health Research Ethics (REC). Research using anonymised data from the MBRN are exempt from institutional review board approval in Norway.

Address for Further Information
Director Marta Ebbing, Medical Birth Registry of Norway, Kalfarveien 31, N-5018 Bergen, Norway; Tel: +47 5320 4035; Fax: +47 5320 4001
Email: marta.ebbing@fhi.no

Chief physician Kari Klungsøyr, Medical Birth Registry of Norway, Kalfarveien 31, N-5018 Bergen, Norway; Tel: +47 5320 4023; Fax: +47 5320 4001
Email: kari.klungsoyr@fhi.no

Profile of Medication Exposure
- In Norway, for the period 2005-2010, 3% of all births were born with a CA.
- In the EUROmediCAT project, Norway's medication exposure data is based on the Norwegian prescription database established in 2004 which was linked to the CA data in the Norwegian CA registry (MBRN). Data was restricted to births from 2005 to ensure that first trimester exposures were available for all CA cases.
- Medication exposure prevalence is high ranging from 340 per 1,000 CA cases in 2005 to 388 per 1,000 CA cases in 2007 (see Figure 1). All medications are confirmed first trimester exposed only.
- In the prescription database all medications that are prescribed and collected at a pharmacy are recorded. This includes women that get pregnant and those who terminate their pregnancy.
- Norway is participating in the EUROmediCAT prescription linkage study.
- The most frequent drugs recorded in Norway are shown in Figure 2. The top 3 medications recorded are drugs for antibacterials for systemic use, sex hormones and antihistamines.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Norway, 2005-2010 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC Drug Group out of All CA Cases, Norway, 2005-2010*

*Only includes medications with prevalence >1 per 1,000 CA.
Poland

History and Funding
The Polish Registry of Congenital Malformations (PRCM) has been in operation since 1997. It was founded as a scientific project ordered by the Polish Ministry of Health and financed by the State Committee for Scientific Research. Since 1 July 2000 it has been part of the Government Programme of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland, financed by the Polish Ministry of Health. As part of this Programme the Registry provides the Polish Ministry of Health with important information needed in health care management. In 2003 it was decided that data for the Wielkopolska Region, which is part of the territory covered by the PRCM, would be transferred to EUROCAT separately and treated as full member registry data.

Population Coverage
The PRCM is a population-based registry of Type I (all mothers resident in defined geographic area). For years 1998-2000 data for Poland (Associate registry) comes from 9 provinces of Poland: Pomorskie, Zachodniopomorskie, Warminsko-Mazurskie, Kujawsko-Pomorskie, Wielkopolskie, Lubuskie, Lodzkie, Dolnoslaskie and Opolskie. In 2001 the Slaskie Province (Silesia) was added, in 2002 the Lubelskie and Podkarpackie Regions joined the Registry and in 2004 - Mazowieckie. In 2006 next two Provinces joined the PRCM – Swietokrzyskie and Podlaskie. In 2007 Malopolskie Province joined the PRCM. Since year 2007 the whole Poland has been covered by the Polish Registry and in 2010 data for 15 provinces has been transferred to the EUROCAT (the data for the 16th province - Wielkopolska - is sent separately). In 2008 in these 15 provinces 375 304 live- and stillbirths occurred which corresponds to 90.12% of all births in Poland.

Sources of Ascertainment
Notification was recommended by the Ministry of Health until 4th December 2014 (as an official Government Programme, however notification was not obligatory). From 5th December 2014 notification has became mandatory and consists of multi-source reporting. The sources include: delivery unit staff, ultrasound staff, postnatal ward staff, paediatric intensive care unit staff, fetal medicine unit staff, paediatricians, post-mortem reports, regional genetic and cytogenetic services and paediatric cardiology referral centres. The main source of information is a double-sided notifications form filled out by a physician responsible for diagnosing the malformations. The notification forms are sent immediately to the PRCM Central Working Group. Additionally all birth records in Wielkopolska are reviewed and abstracted by trained staff with the aim of ascertainment of cases. Birth certificates do not record congenital anomaly. Death certificates allow for notification of congenital anomaly as a cause of death and they are therefore used as a source. Electronic and Web-based data capture has been implemented (about 20% of all notifications). Well visited web site www.rejestrwad.pl
In the last 5 years (2005-2009), the total prevalence of ALL ANOMALIES is about 1.5%, indicating that there are ascertainment issues.

**Maximum Age at Diagnosis**
Up to 2 years of age.

**Termination of Pregnancy for Fetal Anomaly**
Although termination of pregnancy is legal, it can only be performed by a physician when: 1) a pregnancy poses danger to health or life of the pregnant women; 2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease; 3) there is a plausible suspicion the pregnancy has arisen from a prohibited act. The upper gestational age limit for termination of a severe congenital anomaly affected pregnancy is 24 weeks. Although the termination of pregnancy is legal, in Poland there is public pressure not to perform such a procedure and that is why the data on pregnancy terminations might be underestimated. Hence, the registry currently does not register terminations of pregnancy following prenatal diagnosis.

**Stillbirth Definition and Early Fetal Deaths**
The official stillbirth definition is as follows: fetal death (stillbirth) is a death prior to the complete expulsion or extraction of a product of conception from a mother, irrespective of pregnancy duration; the death is indicated by the fact that after separation the fetus does not breathe, or shows no other evidence of life, such as heart beating, pulsation of the umbilical cord, or definite movement of voluntary muscles. For statistical purposes we include all fetuses weighing at least 500g at the moment of birth, having reached the 22nd week of gestational age, if the weight is unknown, or reaching 25cm of the body length (crown-heel). We do not include early fetal deaths or spontaneous abortions. Autopsy rates vary between regions or even between health care units, the ranges for performance are as follows: stillbirths 10-30%, early neonatal deaths 20-30%, later deaths 1 week to 1 year 10-20% and deaths with congenital anomaly 30-40%.

**Data Availability**
The following data is gathered by way of registration forms, although its availability may be limited, depending on the source of registration: chronic illness in mother, pregnancy induced conditions in mother, acute maternal illness during pregnancy, therapeutic and recreational drugs taken during pregnancy, invasive tests in pregnancy, folic acid use in pregnancy, smoking habits, alcohol use, mother’s obstetric history as well as the country of residence, family history of congenital malformations, and genetic conditions in family members, father’s and mother’s occupational and environmental hazards, father's and mother's education.
Denominators and Controls Information
Information on all births (live and stillbirths) is available from birth certificates, gathered by the Central Statistical Office for Poland. Since 2005 information on controls has been gathered by the Registry.

Registry Description References

Ethics & Consent
The Registry doesn’t require ethics committee approval for all studies based on the Registry data solely, but requires an approval for other projects (using Registry data but focusing on f.e. genetic or clinical studies.
Until December 2014 parents had to agree to the inclusion of the child on the Register. They signed the notification form and were informed that they could also remove the child from the Register. In case of refusal, the information on the child was included in the Register as ‘NN’, without name and exact address.

Until the notification is mandatory (since December 2014) a physician responsible for diagnosing the malformations is obligated to report the malformation to the Registry with all the information on the child.

Address for Further Information
Prof Anna Latos-Bielenska, Registry Director; Dr. Anna Materna-Kiryluk, Organizing Co-ordinator Polish Registry of Congenital Malformations
Department of Medical Genetics, ul. Rokietnicka 8, 60-806 Poznan, Poland
Tel: + 4861 854 73 49; mobile +48 601561407
Fax: + 4861 854 76 13
Email: alatos@ump.edu.pl

Profile of Medication Exposure
• Reporting of CA cases in Poland (excluding Wielkopolska) is based on multiple sources of ascertainment. For the period 1999-2010, 1.6% of all births were born with a CA. Poland is an Associate registry.
• Medication exposures in pregnancy are available from 1999.
• Prevalence ranged from 30 per 1,000 CA cases in 2000 to 71 per 1,000 CA cases in 2010 (see Figure 1). Timing of medication exposure is unknown for a large proportion of these CA cases.
- Data sources include obstetric/midwife medical records and paediatric medical records. Maternal interviews were also conducted after birth.
- Medication exposure data are only available for LB and FD.
- The most frequent first trimester drugs recorded in Poland are shown in Figure 2. The top 3 medications recorded are sex hormones, antibacterials for systemic use and drugs for functional gastrointestinal disorders.

Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Poland, 1999-2010 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Poland 1999-2010*

*Only includes medications with prevalence >1 per 1,000 CA
Poland, Wielkopolska

History and Funding
The Polish Registry of Congenital Malformations (PRCM) has been in operation since 1997. It was founded as a scientific project ordered by the Polish Ministry of Health and financed by the State Committee for Scientific Research. Since 1 July 2000 it has been part of the Government Programme of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland, financed by the Polish Ministry of Health. As part of this Programme the Registry provides the Polish Ministry of Health with important information needed in health care management. In 2003 it was decided that data for the Wielkopolska region, which is part of the territory covered by the PRCM, would be transferred to EUROCAT separately and treated as full member registry data.

Population Coverage
The PRCM is a population-based registry of Type I (all mothers resident in defined geographic area). In year 2009 Wielkopolska region had a population of 3408,3 thousand people (8.93% of Poland) spread over area of 29 827 square kilometers (9.54% of the Poland territory) with 41 043 births per year (live and stillbirths), corresponding to 9.79% of total births in Poland).

Sources of Ascertainment
Notification was recommended by the Ministry of Health until 4th December 2014 (as an official Government Programme, however notification was not obligatory). From 5th December 2014 notification has became mandatory and consists of multi-source reporting. The sources include: delivery unit staff, ultrasound staff, postnatal ward staff, paediatric intensive care unit staff, fetal medicine unit staff, paediatricians, post-mortem reports, regional genetic and cytogenetic services and paediatric cardiology referral centres. The main source of information is a double-sided notifications form filled out by a physician responsible for diagnosing the malformations. The notification forms are sent immediately to the PRCM Central Working Group. Additionally all birth records in Wielkopolska are reviewed and abstracted by trained staff with the aim of ascertainment of cases. Birth certificates do not record congenital anomaly. Death certificates allow for notification of congenital anomaly as a cause of death and they are therefore used as a source. Electronic and Web-based data capture has been implemented (about 20% of all notifications). Well visited web site www.rejestrwad.pl

Maximum Age at Diagnosis
Up to 2 years of age.
Termination of Pregnancy for Fetal Anomaly

Although termination of pregnancy is legal, it can only be performed by a physician when: 1) a pregnancy poses danger to health or life of the pregnant women; 2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease; 3) there is a plausible suspicion the pregnancy has arisen from a prohibited act. The upper gestational age limit for termination of a severe congenital anomaly affected pregnancy is 24 weeks. Although the termination of pregnancy is legal, in Poland there is public pressure not to perform such a procedure and that is why the data on pregnancy terminations might be underestimated. Hence, the registry currently does not register terminations of pregnancy following prenatal diagnosis.

Stillbirth Definition and Early Fetal Deaths

The official stillbirth definition is as follows: fetal death (stillbirth) is a death prior to the complete expulsion or extraction of a product of conception from a mother, irrespective of pregnancy duration; the death is indicated by the fact that after separation the fetus does not breathe, or shows no other evidence of life, such as heart beating, pulsation of the umbilical cord, or definite movement of voluntary muscles. For statistical purposes we include all fetuses weighing at least 500g at the moment of birth, having reached the 22nd week of gestational age, if the weight is unknown, or reaching 25cm of the body length (crown-heel). We do not include early fetal deaths or spontaneous abortions. Autopsy rates vary between regions or even between health care units, the ranges for performance are as follows: stillbirths 10-30%, early neonatal deaths 20-30%, later deaths 1 week to 1 year 10-20% and deaths with congenital anomaly 30-40%.

Data Availability

The following data is gathered by way of registration forms, although its availability may be limited, depending on the source of registration: chronic illness in mother, pregnancy induced conditions in mother, acute maternal illness during pregnancy, therapeutic and recreational drugs taken during pregnancy, invasive tests in pregnancy, folic acid use in pregnancy, smoking habits, alcohol use, mother's obstetric history as well as the country of residence, family history of congenital malformations, and genetic conditions in family members, father's and mother's occupational and environmental hazards, father's and mother's education.

Denominators and Controls Information

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

Registry Description References

Ethics & Consent
The Registry doesn’t require ethics committee approval for all studies based on the Registry data solely, but requires an approval for other projects (using Registry data but focusing on f.e. genetic or clinical studies.

Until December 2014 parents had to agree to the inclusion of the child on the Register. They signed the notification form and were informed that they could also remove the child from the Register. In case of refusal, the information on the child was included in the Register as ‘NN’, without name and exact address.

Until the notification is mandatory (since December 2014) a physician responsible for diagnosing the malformations is obligated to report the malformation to the Registry with all the information on the child.

Address for Further Information
Prof Anna Latos-Bielenska, Registry Director; Dr. Anna Materna-Kiryuk, Organizing Co-ordinator
Polish Registry of Congenital Malformations
Department of Medical Genetics, ul. Rokietnicka 8, 60-806 Poznan, Poland
Tel: + 4861 854 73 49; mobile +48 601561407
Fax: + 4861 854 76 13
Email: alatos@ump.edu.pl
Profile of Medication Exposure

- Reporting of CA cases in Wielkopolska is based on multiple sources of ascertainment. For the period 1999-2013, 2.5% of all births were born with a CA.
- Medication exposures in pregnancy are available from 1999.
- Medication exposure prevalence ranged from 28 per 1,000 CA cases in 2000 to 64 per 1,000 CA cases in 2002 (see Figure 1). Timing of medication exposure is unknown for a large proportion of these CA cases.
- Data sources include obstetric/midwife medical records and paediatric medical records. Maternal interviews were also conducted after birth.
- Medication exposure data are only available for LB and FD.
- The most frequent first trimester drugs recorded in Wielkopolska are shown in Figure 2. The top 3 medications recorded are sex hormones, antibacterials and thyroid therapy drugs.

Figure 1: Prevalence of medication exposure* in the first trimester per 1,000 CA cases, Wielkopolska, 1999-2013, compared to all other EUROMediCAT registries combined

*Excludes vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Wielkopolska, 1999-2013*

*Only includes medications with prevalence >1 per 1,000 CA
Spain, Basque Country

History and Funding
Registration of congenital anomalies in the Basque Country started on 1 January 1990. The Registry became a EUROCAT member in September 1990. The Registry is financially supported by the Health Department of the Basque Government.

Population Coverage
The Registry is located in the Basque Country region, in northern Spain, covering a geographic area of 7,260 km\(^2\) and a population of 2,162,944 inhabitants. It is a population based registry which therefore includes all mothers delivering in the Basque Country excluding any non-residents. The average number of annual births 2008-2012 is 21093 It is estimated that 1-2% of outside resident mothers deliver in the covered hospitals.

Sources of Ascertainment
Reporting is voluntary, although the capture of data is now systematic for 80% of cases using the automated hospital database. There is an active search for cases (livebirths, stillbirths and induced abortions), through multiple sources of information: Hospital discharge records, Hospital automated data, Neonatal Units, Specialist Paediatric Department, Cytogenetics and Pathology laboratories and private maternity hospitals.

Paediatric cardiology centres supply diagnostic confirmation when requested by the registry for specific cases.

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

Maximum Age at Diagnosis
Routinely reported to the Registry up to 1 year of age

Termination of Pregnancy for Fetal Anomaly
Since March 2010 “Sexual and reproductive health and abortion” in Spain is governed by a new law. Termination of pregnancy is now legal for certain indications, including prenatal diagnosis of severe anomaly, at any time on pregnancy. Data about techniques of prenatal screening and diagnosis are systematically collected.

Stillbirth Definition and Early Fetal Deaths
The official definition of stillbirth in the Basque Country and Spain too, is: a gestational age of 22 weeks or a birth weight of 500G. Post-mortem examination rates are highly variable in the region. About 90% of autopsies in stillbirths and neonatal deaths were performed in the public maternity hospitals (the remaining 10% of parents did not give permission). The autopsy rate following TOP is high (70%), but the quality varies, depending on hospitals.

Exposure Data Availability
Information on maternal drug use, maternal and paternal diseases, outcome of previous
pregnancies and assisted conception is available.

Denominators and Controls Information
Statistics are provided by the Basque Statistics Institute (EUSTAT).

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

Legislation complies with EC95/46 Directive with respect to disease registers and surveillance since 1999. There is not national legislation requiring informed consent to register a baby with a congenital anomaly.

Address for Further Information
Larriat Arriola
Registro Anomalías Congénitas CAV
Subdirección de Salud Pública
Av. Navarra 4
20013 SAN SEBASTIAN
Spain
Tel: +34 943-022770
Fax: +34 943-022750
Email: l-arriola@euskadi.eus

Profile of Medication Exposure
- Although drug data is available from 1995, ATC coding is only available in the EUROmediCAT central database from 2005 onwards.
- For the period 2005-2013, 2.6% of all births were born with a CA in Basque Country.
- Medication exposure prevalence ranged from 42 per 1,000 cases in 2005 to 294 per 1,000 CA cases in 2013 (see Figure 1)
- Sources of medication exposures include prospectively recorded maternity records. From 2011, the registry also had direct access to maternal prescription data.
- The most frequent first trimester drugs recorded in Basque Country are shown in Figure 2. The top 3 medications recorded are drugs for thyroid therapy, analgesics and antibacterials for systemic use.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Basque Country, 2005-2013 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Basque Country, 2005-2013*  

*Only includes medications with prevalence >1 per 1,000 CA.
Spain, Valencia Region

History and Funding
The Congenital Anomalies Registry of Valencia Region started a pilot study of feasibility of establishing a population-based registry in 2010. Data were collected retrospectively since 2007. The registry is included in the Valencian Rare Diseases Information System (SIER) and it is funded by the Regional Health Authority (Conselleria de Sanitat).

Population Coverage
The registry covers the whole Valencia Region (ComunitatValenciana). All major congenital anomalies are registered that occur in pregnancies of mothers residing in this region of Spain. The population of the current area is approximately 5 million. The annual number of births for the registry area is about 55,000. Minor anomalies are excluded according to EUROCAT criteria.

Sources of Ascertainment
Reporting is compulsory (Act published in the Official Bulletin) and multi-source. The main information sources for case identification are:
- Public and private hospital discharges records.
- Perinatal Mortality Registry Valencia Region.
- Induced Abortion Registry of Valencia Region.
Complementary information is obtained from Metabolic Disorder Registry and clinical records are reviewed for the majority of cases obtained from hospital discharge register.

Maximum Age at Diagnosis
Up to 1 year.

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

Stillbirth Definition and Early Fetal Deaths
Stillbirths of 22 weeks after the last menstrual period or more are registered. Early fetal deaths/spontaneous abortions are not included.

Exposure Data Availability
Information on maternal drug use, maternal and paternal diseases and occupations, outcome of previous pregnancies, is collected from the clinical records.

Denominators and Controls Information
Background data on births are available from the Metabolic Disorder Registry (population based birth registry). The data of the National Statistics Institute (INE) are used too.
Ethics & Consent

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

Address for Further Information

Clara Cavero Carbonell (cavero_cla@gva.es)
Congenital Anomalies Registry of the Valencia Region
Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunidad Valenciana
Conselleria de Sanitat. Generalitat Valenciana.
Avenida de Catalunya, 21
46020 Valencia (Spain)
Tel : +3496 1925724
Fax: +3496 1925703

Profile of Medication Exposure

- Medication exposure data is available in the EUROmediCAT central database from 2007.
- For the period 2007-2013, 2.3% of all births were born with a CA.
- Medication exposure prevalence ranged from 90 per 1,000 CA cases in 2007 to 200 per 1,000 CA cases in 2012 (see Figure 1).
- Medication exposure data are only available for LB only.
- Sources of medication exposures include prospectively recorded maternity records. In addition, the Integral Management of Pharmaceutical Services (known as GAIA) which registers the prescription and dispensing of drugs in ambulatory (outpatient) care is available after a request.
- The most frequent first trimester drugs recorded in Valencia Region are shown in Figure 2. The top 3 medications recorded are corticosteroids, antibacterials and gynecological antiinfectives & antiseptics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Valencia Region, 2007-2013 compared to all other EUROMedCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Valencia Region, 2007-2013*

*Only includes medications with prevalence >1 per 1,000 CA.
Switzerland, Vaud

History and Funding
The Registry of Switzerland was originally set up in 1988, and also became a member of EUROCAT in 1988. Different cantonal registries sent their data to the Central Registry in Lausanne. The aim at the beginning was to cover the whole country (80,000 births/year). In the first years of activity 30-81% of births were surveyed. For financial reasons, many cantons had to stop this activity and in 1993 the Swiss Registry covered 50% of all births in Switzerland. In 1998, the following cantons were included in the programme: Zurich, Fribourg, Argovie, Tessin, Vaud, Valais, Neuchatel and Jura. The Registry is located in the Division of Medical Genetics in the University Hospital of Lausanne. The Registry has formerly been associated with members from the Swiss Academy of Medical Sciences and from the Swiss Society of Paediatrics. The system was financed by the Swiss Federal Agency for Statistics for the Central registry and by the cantonal health department for some cantonal registries. As the level of ascertainment was quite heterogeneous between the local cantonal registries and their activities fluctuating according to the years (cf prevalence rate <200 per 10,000), it was decided in January 2002 to restrict the registration to canton of Vaud only and to change the name of the registry: Registry of Vaud (Switzerland).

Population Coverage
The Registry is population-based and as such it covers all mothers resident in the canton of Vaud. The percentage of mothers delivering in a hospital outside the Registry area is not known precisely although it is thought to be very low. The Registry covers about 9% of all births in Switzerland (approximately 7,500 births annually). The changing coverage is detailed above.

Sources of Ascertainment
Reporting is voluntary. Active case finding and multiple sources of information are used: delivery units, paediatric departments, cytogenetic and genetic counseling and pathology units. Data about different methods of prenatal diagnosis are collected (ultrasound, serum markers, cytogenetic and molecular). Paediatric cardiology centres supply systematic case lists and diagnostic details to the registry. The registry is situated in the Department of Medical Genetics and we thus have direct access to the cytogenetic and DNA laboratories; they systematically supply the registry with abnormal karyotypes and molecular studies prenatally and postnatally diagnosed. Twice a year we contact the other laboratories covering the residual population of the canton to check for anomalies. There is no upper age limit for registration of a child with a malformation.

Maximum Age at Diagnosis
There is no upper age limit.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy is legal up to 12 weeks gestation under most circumstances but this limit is extended to 24 gestational weeks if a congenital anomaly is diagnosed. In the latter circumstance, additional permission must be granted by two further physicians. Induced abortions following prenatal diagnosis are included in the Register.
Stillbirth Definition and Early Fetal Deaths
The official stillbirth definition is: a gestation age of >=27 weeks or length >=30cm and these are included in the register. Early fetal deaths/spontaneous abortions are included if they are 20 gestational weeks or more with no weight restrictions. Autopsy statistics were not available.

Exposure Data Availability
Information on maternal occupations and diseases, maternal drug use, outcome of previous pregnancies is available for the malformed infants.

Denominators and Controls Information
Background data on births are available from the Service Cantonal de Recherche et d’Information Statistique (SCRIS).

Ethics & Consent
The registry does not require ethics committee approval in order to collect and store data.

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

Address for Further Information
Dr Marie-Claude Addor, Registre Vaudois des Anomalies Congenitales and Swiss Registry for EUROCAT, Division of Medical Genetics, Maternite, CH-1011 CHUV-Lausanne, Switzerland
Tel: +41 21 3143391
Fax: +41 21 3143392
Email: marie-claude.addor@chuv.ch
monique.devolz@chuv.ch
Web: www.hospvd.ch/public/chuv/genmol/eurocat/euro-home.htm (username: eurocat, password: tropic)

Profile of Medication Exposure
• In Vaud, for the period 1997-2014, 3.9% of all births were born with a CA.
• Medication exposure data is available from 1997 for Vaud.
• The prevalence of medication exposures ranged from 36 per 1,000 CA cases in 2000 to 188 per 1,000 CA cases in 2013 (see Figure 1).
• Data sources include obstetric/midwife records, medical geneticist records and paediatrician records.
• Medication data are available for LB, FD and TOPFA. Obstetric/midwife records are available for approximately 90% of LB, 60% of FD and 70% of TOPFA cases recorded in the registry.
• The most frequent first trimester drugs recorded in Vaud are shown in Figure 2. The top 3 medications recorded are drugs for thyroid therapy, antibacterials for systemic use, and analgesics.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Vaud, 1997-2014 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Vaud, 1997-2014*

*Only includes medications with prevalence >1 per 1,000 CA
Ukraine

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

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

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

Population Coverage
BD surveillance annually covers about 28000 births in two oblasts (provinces) of Western Ukraine – Rivne and Khmelnytsky, representing approximately 6% of births in Ukraine. The population is relatively homogeneous and stable (data is pooled from these two oblasts). The Registry is of Type III (all mothers delivering in the defined geographic area excluding non-residents of that area).

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

Maximum Age at Diagnosis
Up to 1 year of age.

Termination of Pregnancy for Fetal Anomaly
Termination of pregnancy is legal and performed by a physician when: 1) a pregnancy poses danger to health or life of a pregnant woman; 2) prenatal diagnosis or other medical evidence indicates high probability of serious and irreversible damage to a fetus or it is an untreatable life-threatening disease; 3) there is a plausible suspicion the pregnancy has arisen from a prohibited act.
Up until 31 December 2005, the upper gestational age limit for termination of pregnancy in Ukraine was 28 weeks AND/OR 1000 g.
From 1 January 2006, Ukraine redefined the definition and the current upper gestational age limit for termination of pregnancy is 22 weeks AND/OR 500 g.

Stillbirth Definition and Early Fetal Deaths
The stillbirth definition is as follows: fetal death (stillbirth) is a death prior to the complete expulsion or extraction of a product of conception. Till January, 1, 2006 for statistical purposes we include all fetuses weighing 1000g or more at the moment of birth or/and gestational age above 28 weeks; Spontaneous abortions include fetuses weighing less than 1000g and gestational age less than 28 weeks.
From January 1, 2006, Ukraine redefined stillbirth definition as all fetuses weighing 500g or more at the moment of birth or/and gestational age above 22 weeks.
In Ukraine Certificates of Neonatal Death are NOT medical documents, they are issued by civil authorities.

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

Denominators and Controls Information
Information on all births (live and stillbirths) is available from birth certificates, gathered by the Regional Vital Statistics. There are 2 controls for each CA case. Controls are newborns without CA, of the same gestational age, same sex, same weight, same area of residence, born in the same medical institution within a week (before or after) of the birth of the CA case. The initial source of information for all newborns is a double-sided ‘Child Birth and Examination Notification/CA Registration Form’ filled out by a neonatologist.

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

Ethics & Consent
Registration of birth defects and follow-up is an integral part of health care protocols. The registry does not require ethics committee approval in order to collect and store data. National legislation does not require informed consent in order to register a baby with a congenital anomaly.

Addresses for further information:
International Coordinator:
Dr. Wertelecki W,
“OMNI-Net for Children”,
9, Oakdrive,
Mobile, Al, USA 36608
Phone/Fax: 1 251 343 69 19
E-mail: omninetukr@gmail.com

Medical Coordinator:
Dr. Yevtushok L,
“OMNI-Net for Children”,
36, 16 Lypnya Str., Room 709,
Rivne, Ukraine 33028
Phone/Fax: 38 036 262 3447
E-mail: yevtushokl@gmail.com
Profile of Medication Exposure

- For the period 2009-2013, 2.4% of all births were born with a CA.
- Medication exposure data is available from 2009.
- Medication exposure prevalence ranges from 42 per 1,000 CA cases in 2013, to 79 per 1,000 CA cases in 2011 (see Figure 1).
- Data sources include follow-up medical records for the pregnancy (filled in by district obstetrician and/or geneticist) and/or notification of birth submitted to the regional Newborn registry (filled in by a neonatologist, who also uses the obstetrician’s records to fill in chapters regarding risk factors, medications and complications). The information is collected in two ways: prospectively to birth for obstetrician’s records, retrospectively for neonatologist’s notification of birth and both prospectively (i.e. detected prenatally and followed up till birth and further on) and retrospectively (if detected at birth or after birth) for geneticist’s records.
- Availability of chronic medications exposure data - the main source is neonatal records (‘Child Birth and Examination Notification/CA Registration Form’ for the Neonatal Registry) with limited access to obstetrician data.

- The most frequent first trimester drugs recorded in Ukraine are shown in Figure 2. The top 3 medications recorded are drugs for functional gastrointestinal disorders, sex hormones and cough & cold preparations.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Ukraine, 2009-2013 compared to all other EUROmediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Ukraine, 2009-2013*

*Only includes medications with prevalence >1 per 1,000 CA
UK, Wales

History and Funding
The Congenital Anomaly Register and Information Service (CARIS) collect data on all cases of congenital anomaly born to mothers normally resident in Wales. Data collection commenced on 1st January 1998 and includes any baby where pregnancy ended on or after this date. The Wales register joined EUROCAT in 1998. The register is based at Singleton Hospital, Swansea and since 1st October 2009 became part of Public Health Wales NHS trust. The register aims to collect data which can be used to describe the pattern of congenital anomalies across Wales. This should help:

- Build up and monitor the picture of congenital anomalies in Wales
- Assess interventions intended to help prevent or detect congenital anomalies
- Plan and co-ordinate provision of health services for affected babies and children
- Assess possible clusters of birth defects and their causes

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

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

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

Sources of Ascertainment:
Reporting is voluntary. The Register relies upon multi-source reporting including: antenatal clinics, delivery units, paediatric departments, ophthalmology, cytogenetics, pathology, orthopaedics, maxillo-facial and regional centres of paediatric surgery. Each delivery unit has a nominated coordinator to help ensure good reporting. Register staff also visit units to help with data collection. Registration covers all fetuses with prenatally diagnosed anomalies. There is no lower age limit so fetal losses and early terminations with anomalies are registered. All live born babies with structural anomalies are registered if diagnosed before their 1st birthday, but all chromosomal anomalies and syndromes are registered, even if diagnosed later.

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

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

**Maximum Age at Diagnosis**

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

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

**Termination of Pregnancy for Fetal Anomaly**

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

**Stillbirth Definition and Early Fetal Deaths**

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

**Exposure Data Availability**

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

**Denominators and Controls Information**

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

**Registry Description References**

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

**Ethics & Consent**

The registry requires ethics committee approval in order to collect and store data and this comes from Leicester Regional MREC committee, under the auspices of the British Network of Congenital Anomaly Registers (BINOCAR). Approval is renewed every 5 years, next due in 2014.
National legislation requires informed consent but the registry is exempt from this. The register has been granted exemption under section 251 of the Health Service Act 2006. Parents have to ask for the removal of the child from the Register (opt-out).

Information governance standards, policies and protocols are agreed and set by a committee within Public Health Wales.

Address for Further Information
Mr David Tucker, Public Health Wales. Congenital Anomaly Register and Information Service for Wales (CARIS), Level 3 - West Wing, Singleton Hospital, Sketty Lane, Swansea, SA2 8QA
Tel: +44 1792 285241
Fax: +44 1792 285242
Email: david.tucker2@wales.nhs.uk

Profile of Medication Exposure
- In Wales, for the period 1998-2013, 3.8% of all births were born with a CA.
- Medication exposure data is available from 1998.
- Reporting of medication exposure prevalence is generally good in Wales. Prevalence ranges from a low point of 125 per 1,000 CA cases in 2013, possibly reflecting on-going ascertainment of medications, to 192 per 1,000 CA cases in 2004 (see Figure 1). Prevalence was generally high in the early years and decreased after 2004. From 2004, increasing pressure on the midwifery service resulted in fewer data collection forms being completed/returned to the registry. The data collection form includes information on medications taken in pregnancy.
- Data sources include obstetric/midwife medical records and paediatric medical records.
- Medication data are available for LB, FD and TOPFA.
- The most frequent first trimester drugs recorded in Wales are shown in Figure 2. The top 3 medications recorded are drugs for obstructive airway diseases, analgesics and antibacterials for systemic use.
Figure 1: Prevalence of medication exposure* in first trimester per 1,000 CA cases, Wales, 1998-2013 compared to all other EUROMediCAT registries combined

*Excludes Vitamins, minerals and folic acid
Figure 2: Prevalence of most frequent first trimester drug exposure by ATC drug group out of all CA cases, Wales, 1998-2013*

*Only includes medications with prevalence >1 per 1,000 CA