Prevalence and primary prevention of congenital anomalies in Northern Ireland

McCullough, N., & Dolk, H. (2017, Mar 9). Prevalence and primary prevention of congenital anomalies in Northern Ireland. Ulster University.

Link to publication record in Ulster University Research Portal

Publication Status:
Published (in print/issue): 09/03/2017

Document Version
Publisher's PDF, also known as Version of record

General rights
The copyright and moral rights to the output are retained by the output author(s), unless otherwise stated by the document licence.

Unless otherwise stated, users are permitted to download a copy of the output for personal study or non-commercial research and are permitted to freely distribute the URL of the output. They are not permitted to alter, reproduce, distribute or make any commercial use of the output without obtaining the permission of the author(s).

If the document is licenced under Creative Commons, the rights of users of the documents can be found at https://creativecommons.org/share-your-work/cclicenses/.

Take down policy
The Research Portal is Ulster University's institutional repository that provides access to Ulster's research outputs. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact pure-support@ulster.ac.uk

Download date: 23/05/2025

Prevalence and primary prevention of congenital anomalies in Northern Ireland

Dr Nichola McCullough and Prof Helen Dolk

Maternal, Fetal and Infant Research Centre
Ulster University

This Report has been published on 3 March 2017, to mark World Birth Defects Day

Acknowledgements

The work undertaken for this Report was funded by an HSCR&D Fellowship 2011-2014 and in association with the Public Health Programme 2008-2013 of the Executive Agency for Health and Consumers, European Commission, EUROCAT Joint Action (Grant Agreement 2010 22 04).

We thank the following people for supplying information Dr Carolyn Bailie, Fetal Medicine Department, Royal Jubilee Maternity Hospital; Belfast Health and Social Care Trust; Ms Rita Butler, Belfast Health and Social Care Trust; Ms Valerie Doyle, Southern Health and Social Care Trust; Mr Mervyn Humphreys Head of Regional Cytogenetic Laboratory; Ms Jacklyn Linton, Northern Health and Social Care Trust; Ms Emma McCall, NICORE, QUB; Ms Maria Monaghan, Belfast Health and Social Care Trust; Mr Isaac Philip, Paediatric Surgeon, Royal Belfast Hospital for Sick Children; Prof Mike Shields, Clinical Professor, QUB; Dr Domenica Taruscio, Instituto Superiore di Sanita, Rome; Mr Keith Trimble, Consultant Paediatric Otolaryngologist, Royal Belfast Hospital for Sick Children; The Hospital Information Branch, DHSSPSNI.

We are grateful for all those who participated in a stakeholder meeting in October 2013 to discuss the need for a register and surveillance system in Northern Ireland, and where the data in this Report were shown, in particular Dr Carolyn Bailie, Fetal Medicine Department at Royal Jubilee Maternity Hospital; Ms Christine Collins, Chair, Northern Ireland Rare Disease Partnership; Dr Inez Cook, Clinical Senior Lecturer, QUB; Dr Brid Farrell, Chair of the Regional User Advisory Group NI Child Health System; Dr Anna Gavin, Director of NICR, Centre for Public Health, QUB; Ms Ruth Greenlees, EUROCAT Central Registry, Institute of Nursing and Health Research, Ulster University; Dr Maria Loane, EUROCAT Central Registry, Institute of Nursing and Health Research, Ulster University; Prof Roy McClelland, Privacy Advisory Committee, Belfast Trust; Ms Fionnuala McCluskey, Lead Midwife, South Eastern Trust; Dr Shane McKee, Medical Geneticist, Belfast City Hospital, Belfast Health and Social Care Trust; Mrs Frances Murphy, Contact a Family; Dr Mary T O'Mahony, Specialist in Public Health Medicine, Health Service Executive, Ireland; Mr Isaac Philip, Paediatric Surgeon, Royal Belfast Hospital for Sick Children; Dr Heather Reid, Public Health Agency; Dr Claire Thornton, Regional Paediatric Pathologist, Royal Group of Hospitals; Mr David Tucker CARIS Manager, Public Health Wales.

Abbreviations

ASD	Atrial Septal Defect
AVSD	Atrioventricular Septal Defect
BUMPS	Best Use of Medicine in Pregnancy
CARIS	Congenital Anomaly Register and Information Service
CCAM	Congenital Cystic Adenomatoid Malformation
CEMACE	Centre for Maternal and Child Enquiries
CHD	Congenital Heart Defects
CHS	Child Health System
CMO	Chief Medical Officer
CRANE	Cleft Registry and Audit Network
DHSSPSNI	Department of Health, Social Services & Public Safety Northern Ireland
DQI	Data Quality Indicators
EPD	Enhanced Prescribing Database
EUROCAT	European Surveillance of Congenital Anomalies
EUROlinkCAT	Establishing a linked European Cohort of Children with Congenital Anomalies
EUROmediCAT	Medication Safety in Pregnancy
EUROPLAN	European Project for Rare Diseases National Plans Development
FAS	Fetal Alcohol Syndrome
FASD	Fetal Alcohol Spectrum Disorder
FD	Fetal Death
FMU	Fetal Medicine Unit
HES	Hospital Episode Statistics
HSC	Health and Social Care
HSCR&D	Health and Social Care Research & Development
ICD10	International Classification of Disease Version 10
LB	Livebirth
MFIR	Maternal, Fetal and Infant Research
MMR	Measles, Mumps and Rubella
NIC	Net Ingredient Cost
NICE	National Institute for Health & Care Excellence
NICORE	Neonatal Intensive Care Outcomes Research & Evaluation
NICR	Northern Ireland Cancer Registry
NIMACH	Northern Ireland Maternal and Child Health
NIMATS	Northern Ireland Maternity Information System
NIMI	Northern Ireland Maternal and Infant Loss
NTD	Neural Tube Defects
PDA	Patent Ductus Arteriousus
PFO	Patent Foramen Ovule
QUB	Queens University Belfast

RBHSC	Royal Belfast Hospital for Sick Children
RJM (FMU)	Royal Jubilee Maternity (Fetal Medicine Unit)
SD	Standard Deviation
TIS	Teratology Information Services
TOXBASE	National Poisons Information Service
UKTIS	UK Teratology Information Services
UU	Ulster University
VSD	Ventricular Septal Defect
WHO	World Health Organisation
WPW	Wolff-Parkinson-White Syndrome

Table of Contents

Proposal for a congenital anomaly registry in Northern Ireland 7
Executive summary 9
Part 1 Prevalence of congenital anomalies in Northern Ireland 12
Background 12
Methods 14
EUROCAT: European Surveillance of Congenital Anomalies 14
The Child Health System (CHS) 15
Hospital Episode Statistics (HES) 16
Neonatal Intensive Care Outcomes Research and Evaluation (NICORE) 16
Centre for Maternal and Child Enquiries (CEMACE)/Northern Ireland Maternal and Child Health (NIMACH) (now Northern Ireland Maternal and Infant Loss, NIMI) 16
HeartSuite 16
Regional Cytogenetic Records 17
Cleft Registry and Audit Network (CRANE) 17
Audits carried out in paediatric specialties, other clinical databases and other sources 17
Results 18
All congenital anomalies combined. 18
Prevalence by type of congenital anomaly 25
References 1 37
Part II Primary prevention of congenital anomalies in Northern Ireland 39
Aim and Background 39
Context of the primary prevention of congenital anomalies in NI. 39
Approaches to the prevention of congenital Anomalies 40
Methods: the survey 41
Results: Outcome of the Survey 41
Risk factors associated with maternal lifestyles and nutrition 41
Importance of planning for pregnancy 42
Folic Acid 42
Smoking 43

Alcohol consumption 44
Maternal weight before and during pregnancy 45
Drug use (prescribed medications and over the counter medications) 45
Recreational/illicit drug use 46
Correct hygienic behaviour in the home 46
Exposures to reprotoxic agents used at home or for hobbies 47
Screening and immunisation for Infectious diseases and chronic diseases 47
Infectious diseases 47
Chronic diseases 48
Information on and monitoring of medication use during pregnancy 49
References 2 53
Appendix 1 EUROCAT Subgroup definitions (http://www.eurocat-network.eu/aboutus/datacollection/guidelinesforregistration/guide1_4) 57

Proposal for a congenital anomaly registry in Northern Ireland

To mark World Birth Defects Day, March 3, 2017

- One third of Europe is covered by EUROCAT congenital anomaly registries, including all of England and Wales. ***Northern Ireland does not have a congenital anomaly registry.***

  A congenital anomaly registry in Northern Ireland was proposed as part of a Rare Diseases Registry in the NI Rare Diseases Implementation Plan in 2015 but no more details have been discussed since then.

- Why have a registry? Without a registry we cannot investigate clusters of birth defects, we cannot track new health threats such as the Zika virus, we cannot see how successful our public health recommendations to take folic acid to prevent spina bifida are, we cannot see how well our efforts to provide appropriate care to high risk mothers are working, we cannot see how successful our prenatal screening services are, we cannot plan our health services to help children and their families.

- Is Northern Ireland different? As termination of pregnancy for fetal anomaly is illegal in Northern Ireland, many more babies are born with severe congenital anomalies than in England and Wales. We need our own information here to help children and their families, and families of the future.

- Why now? The Health and Social Care (Control of Data Processing) Act (Northern Ireland) 2016 has made a register more feasible. Provisions for data linkage of de-identified patient information, for example through the Honest Broker Service and Administrative Data Research Centre mean that we have secure and accountable ways to use registry data for research. We have a concentration of skilled researchers in congenital anomaly epidemiology. The time is right.

The Maternal Fetal and Infant Research Centre (MFIR)* at Ulster University (UU) has internationally recognised expertise in congenital anomaly registers and surveillance. Here is how we propose a register could be organised in Northern Ireland:

- Co-ordinating centre in the Public Health Agency

- Electronic data transfer from clinical, civil registration, and public health databases to form a central confidential “registry spine” with HSC number of mother and infant, date of birth, birth outcome, congenital anomaly diagnoses.
  - Child Health System

  - Stillbirth records from Registrar General and perinatal and infant death records of NIMACH
  - Clinical Databases: Fetal Medicine Unit, Paediatric Cardiology (Heartsuite), Regional Cytogenetics Service, Neonatal Intensive Care (NICORE) and others.
  - HES data on hospital admissions

- Individual validation of diagnostic information for cases with complex, multiple or poorly specified diagnoses by trained staff, with medical geneticist supervision.

- Linkage with NIMATS and other databases via the Honest Broker Service to build up an extensive de-identified data file with information on maternal and baby factors and health service use

- An Annual Report

- Funding for an active research programme on a five yearly cycle

- Steering Committee of clinical and public health professionals, patient representatives and representatives of patient support groups.

- Information for parents, and opt-out mechanism for parents to withdraw their child from the Registry Spine. Newsletters to parents with details of new services, and information from the registry.

- North-South links with Irish EUROCAT registries

*UU MFIR is the co-ordinating centre of EUROmediCAT (www.euromedicat.eu), is a partner in EUROlinkCAT (www.eurolinkcat.eu) and is a member of the Steering Committee of EUROCAT (www.eurocat-network.eu). EUROCAT Central Registry resided at UU 2000-2014 until it was taken under the Rare Diseases Platform of the EU Joint Research Centre, Ispra, Italy.

Executive summary

Surveillance of congenital anomalies involves the regular collection and analysis of epidemiologic data on congenital anomalies to inform public health action. Surveillance data is needed to plan service provision (antenatally and postnatally), guide preventive actions by identifying risk and protective factors, and respond to emerging health threats (such as Zika or swine flu, or environmental pollution incidents). One third of Europe is covered by congenital anomaly registers, including all of England and Wales and nearly two thirds of Ireland. ***There is no congenital anomaly register in Northern Ireland.***

The aims of the first part of this Report are to provide a snapshot of the prevalence of congenital anomalies in Northern Ireland using available data sources, to assess the completeness and accessibility of different sources of information currently available, and to make recommendations for a surveillance system.

Northern Ireland has excellent sources of healthcare data on congenital anomalies. The geographical situation of Northern Ireland mean that affected women and babies are seen by services within Northern Ireland, whether or not they are also referred to specialist services elsewhere, making it relatively easy to collect population-based data. However, the data cannot be used in their current state for congenital anomaly surveillance. Different data sources need to be combined, coding needs to be verified to exclude minor anomalies and conditions which are suspected but not confirmed as congenital anomalies, and data need to be converted from healthcare episode-based data to baby/child-based data, avoiding duplication across sources.

In Northern Ireland in one year, among approximately 25,000 births:

- There were 16 stillbirths and 40 infant deaths with congenital anomaly in 2008. This was 14% of all stillbirths and 33% of all infant deaths[(1)].
- The Child Health System (CHS) recorded approximately 500 babies born with a major congenital anomaly in 2008.
- Neonatal Intensive Care Outcomes Research & Evaluation (NICORE) recorded 162 children admitted to neonatal units with major congenital anomalies in 2009, requiring 2850 days of neonatal unit care. This cost the health service approximately £2.35 million.
- Hospital Episode Statistics (HES) data recorded 5,411 children under 16 admitted to hospital in 2008 with diagnoses which included a Q code for a congenital anomaly, 6.9% of all admissions, although not all these codes represent true or major congenital anomalies;
- The Fetal Medicine Unit (FMU) in 2012 recorded 281 prenatal diagnoses of congenital anomaly
- Heartsuite data from the Royal Belfast Hospital for Sick Children (RBHSC) recorded 223 children with major congenital heart disease born in 2008, of whom only 40% were recorded in the CHS.

- CHS data and other sources in 2008 recorded 18 children born with spina bifida, 9 children with hydrocephalus, 24 children with cleft lip or cleft palate, 20 children with the severe abdominal wall defects gastroschisis or omphalocele, 75 boys with hypospadias (abnormal position of penile opening), 9 children born with a shortened or missing limb, and 30 children born with Down Syndrome.
- The Paediatric Surgery database recorded surgery in 2008 for 20 children with spina bifida, 13 with gastroschisis, 6 with exomphalos/omphalocele, 10 with Hirschprung's disease, 9 with tracheo-oesophageal fistula or atresia, 8 pyloric atresia or malrotation, 7 with posterior urethral valves, and 26 with other congenital conditions needing surgery.

The *aim of the second part of this Report* is to survey the policies in practices in Northern Ireland currently regarding primary prevention of congenital anomalies.

The work was conducted as part of a European survey that accompanied a set of European Surveillance of Congenital Anomalies (EUROCAT)/European Project for Rare Diseases National Plans Development (EUROPLAN) Recommendations for primary prevention of congenital anomalies for inclusion in National Plans for Rare Diseases.

We found that although there are policies and initiatives in relation to a number of relevant risk factors, which we document in detail, there is no overarching strategy for the prevention of congenital anomalies in Northern Ireland, nor any information source or monitoring of the effectiveness of the variety of guidelines and practices, nor any target relating to prevention of congenital anomalies.

We recommend that:

1. An overarching strategy for the prevention of congenital anomalies in Northern Ireland be developed.
2. An information hub be established for congenital anomalies, for surveillance of congenital anomalies and monitoring of risk factors.
3. That a congenital anomaly register be set up, which would routinely access: the CHS, the HeartSuite clinical database on congenital heart disease, the FMU clinical data on prenatal diagnoses, the Regional Cytogenetics Service on chromosomal and genetic diagnoses, NICORE data on neonatal care admissions, Registrar General and NIMACH data on perinatal and infant deaths, and HES data on hospital admissions.
4. That the congenital anomaly register should include a) a "spine" of identifiable well validated diagnostic information, kept securely b) provision for individual validation of diagnostic information for cases with complex, multiple or poorly specified diagnoses by trained staff, with medical geneticist supervision c) implementation of EUROCAT methodology to ensure comparability of data with the rest of UK/Ireland/Europe d) linkage of the "spine" with Northern Ireland Maternity Information System (NIMATS) and other

databases via the Honest Broker Service to build up an extensive de-identified dataset with information on maternal and baby factors and health service use for research and service planning e) provision for the minimal identified register to allow families to be contacted for the provision of services and information and for enrolment in special research studies.

5. That the operation of a congenital anomaly information hub or register for surveillance in Northern Ireland be designed and costed by a working group of stakeholders and that should take no more than 3 months from today.
6. That North-South links be pursued with the Irish EUROCAT registers.

Part 1 Prevalence of congenital anomalies in Northern Ireland

Background

Congenital anomalies are a major cause of fetal and infant mortality and childhood and lifelong morbidity and disability. The psychosocial and financial costs to the affected individual, their family and society can be high.

Data from EUROCAT Report 9[(2)] (the congenital anomaly surveillance system for Europe including parts of UK and Ireland) for the period 2004-8 (EUROCAT, 2011) show that:

- 2.3% of births have a major congenital anomaly
- 1.8% of livebirths have a major congenital anomaly of whom 97% survive the first week of life
- More than 1% of all liveborn babies have surgery for a congenital anomaly in the first few years of life
- 0.9% of babies have a major congenital anomaly prenatally diagnosed, including 0.4% which result in termination of pregnancy
- 1 per 1,000 births are perinatal deaths due to congenital anomaly (half of these stillbirths, half of these deaths in the first week).
- Congenital heart disease is the most numerous group of congenital anomalies (32%), with others including chromosomal anomalies (15%), NTD (5%), limb defects (18%), and orofacial clefts (7%).

An estimated 600 babies are born in Northern Ireland each year with congenital anomalies. Northern Ireland, in common with Ireland, is in an unusual situation in Europe in not providing access to termination of pregnancy in case of prenatally diagnosed severe congenital anomaly except where there is a risk of permanent and severe damage to the woman's mental and physical wellbeing. This means that in Northern Ireland more children are born and survive the first week of life with a congenital anomaly than other parts of the UK and Europe.

There are a number of primary preventive measures available that, if implemented effectively, have the potential to significantly reduce the prevalence of congenital anomalies. This includes vaccination against infectious diseases (the rubella vaccination programme has been extremely successful in reducing congenital rubella syndrome), raising folate status periconceptionally, reducing exposure to environmental and occupational pollutants, optimal care for women with chronic health conditions such as diabetes, epilepsy and depression where there are disease or medication-associated risks, and improving maternal lifestyle-related risk factors such as smoking, alcohol use and obesity. EUROCAT in collaboration with EUROPLAN has produced a set of recommendations for the inclusion of primary prevention of congenital anomalies in national Rare Disease plans across Europe[(3)].

Reducing the occurrence of congenital anomalies was identified as one of the key objectives of the World Health Organisation (WHO) millennium development goal four. Depending on the type, congenital anomalies may have a genetic, infectious or environmental origin; although in most of the cases it is difficult identify their cause[4]. Overall, multifactorial inheritance accounts for 20-25% of cases; chromosomal anomalies are present in approximately 13% of cases, with fewer than 2% of cases caused by single gene mutation and less than 1% diagnosed as teratogenic syndromes caused by maternal infections, drugs or alcohol[5].

The cost of congenital anomalies can be extensive for the individual, their families and society. Reduced health status and long term disability can have a negative effect on the individual's participation and quality of life, with families experiencing increased burden of care and financial strains related to direct costs and reduced working hours. At societal level, extensive efforts and funding are required to provide optimal health and social care for the individual across the life span.

In January 2014 The Centre for Disease Control reported that birth defects resulting in the hospitalisation of individuals in the United States costs over $2.6 billion per year and that after taking into consideration the financial and emotional burden of living with and caring for those with birth defects this figure rose significantly higher[6]. If we were to extrapolate to the Northern Ireland population size, in the absence of UK costings, this would be over £14 million per year. So a ten percent reduction in numbers through effective primary prevention costing £1 million per year could pay for itself.

Essential to the success of both reducing the prevalence of congenital anomalies and delivering optimal health care to individuals living with a congenital anomaly are surveillance systems that continuously and systematically monitor the epidemiologic data in order to take and evaluate public health action.

Surveillance of congenital anomalies is carried out by population-based congenital anomaly registries covering nearly one third of births in Europe (www.eurocat-network.eu). Sixty percent of the birth population of Ireland is covered by registries, all of Wales, all of England and a partial system is in place in Scotland. In Northern Ireland, there has been no registry or surveillance of congenital anomalies since 1995, though some information is produced by the CHS and is available through annual reports published by the Registrar General[1] and the Chief Medical Officer (CMO)[7].

The aims of the first part of this Report are to provide a snapshot of the prevalence of congenital anomalies and perinatal mortality due to congenital anomalies in Northern Ireland using available data sources, to assess the completeness and accessibility of different sources of information currently available, and to make recommendations for a surveillance system.

Methods

In the absence of a population based congenital anomaly register, a number of sources of information were used to ascertain the prevalence of congenital anomalies in Northern Ireland. For all of these, we requested numbers of cases with conditions belonging to the Q chapter of the International Classification of Disease version 10 (ICD10) (1992), and subdivided these into congenital anomaly subgroups as specified in EUROCAT Guide 1.3[8]. EUROCAT has a standard list of minor anomalies for exclusion, and we also excluded these in order to obtain rates comparable to those of EUROCAT registries[9].

A "total prevalence rate" is defined as the total number of congenital anomaly cases in livebirths, stillbirths and terminations of pregnancy for fetal anomaly, divided by the total number of births (live and still). This is expressed per 1,000 or per 10,000 births.

EUROCAT: European Surveillance of Congenital Anomalies

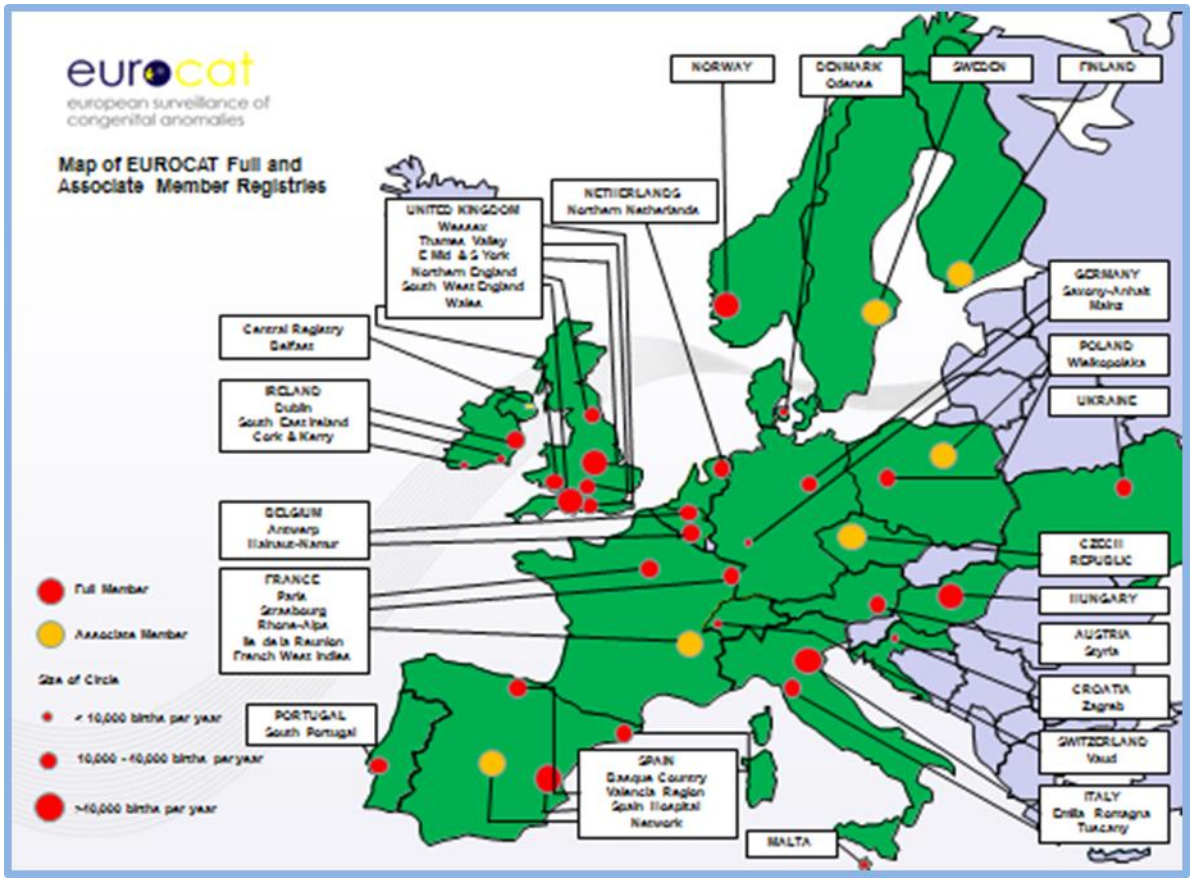
We extracted from the EUROCAT website the total prevalence rate for all full member EUROCAT registries (29 registries covering a total population of 796,513 births) for the birth year 2008[10] with which to compare the total prevalence as recorded by the various data sources in Northern Ireland. Where NI prevalence fell well below or well above the EUROCAT average, we looked for potential explanations; including consideration of the range of prevalence's reported by individual EUROCAT registries.

EUROCAT is a European network of population-based registries with the general objective of supporting the reduction of the public health burden of congenital anomalies by conducting coordinated epidemiological surveillance. Currently, the network has 43 registries in 23 countries. The network surveys more than 1.7 million births per year in Europe, with approximately 29% of the European birth population covered. EUROCAT collects data on congenital anomalies that occur in all cases of livebirths, stillbirths and late fetal deaths from 20 weeks gestational age, and terminations of pregnancy for fetal anomaly. The EUROCAT approach to coding and classification uses the ICD10 system to code anomalies, with additional application of the British Paediatric Association (BPA) one digit extension. EUROCAT methodology specifies standard subgroups (89 in EUROCAT Guide 1.3. 2005), and a standard list of minor anomalies for exclusion. EUROCAT makes available prevalence data on congenital anomalies (http://www.eurocat-network.eu/accessprevalencedata/prevalencetables). The prevalence rates and counts for subgroups are based on cases and not malformations, meaning that a baby with two distinct major anomalies will be counted in each of these subgroups, but never more than once in any one subgroup. A summary subgroup "All anomalies" provides a count of cases with one or more congenital anomalies.

Using the EUROCAT prevalence tables, a pan-Europe (across Europe) prevalence rate per 10,000 births, with 95% confidence intervals was calculated for the year 2008 based on data received from

the following registries: Hainaut (Belgium), Odense (Denmark), Paris (France), Tuscany (Italy), Dublin (Ireland), N Netherlands (Netherlands), Emilia Romagna (Italy), Vaud (Switzerland), Zagreb (Croatia), Malta, S Portugal, Antwerp (Belgium), Basque Country (Spain), Saxony-Anhalt (Germany), Mainz (Germany), Styria (Austria), Cork and Kerry (Ireland), SE Ireland, Wales (UK), Norway, Ukraine, Isle de la Reunion (France), Wielkopolska (Poland), Thames Valley (UK), Wessex (UK), East Midlands & South Yorkshire (UK), Northern England (UK), Hungary, and South West England (UK).

Prevalence rates were also calculated for the following EUROCAT registries in Ireland: Dublin, Cork and Kerry and SE Ireland; and for England and Wales: East Midlands & South Yorkshire, Northern England, South West England Thames Valley, Wales and Wessex.



The Child Health System (CHS)

The CHS is a patient centred community-based computer operational system that receives notifications from a range of professionals involved in the health care of children. The CHS has a number of modules that record general and specific health related information on children across all stages of development.

A frequency table ICD10 Q codes was requested for birth year 2008 from all four regional areas of the CHS, relating to live and stillbirths, resident in Northern Ireland, diagnosed and recorded at any

time following birth through to March 2012. The frequency count was a count of congenital anomalies, not a count of children, as one baby can have more than one anomaly. This was not ideal, but was very easy to produce and did not entail data confidentiality issues.

CHS figures were used in the CMO Report for births 2008, for Anencephalus and similar, Spina Bifida, Hydrocephaly and Down syndrome[7]. The advantage of the CHS data as reported by the CMO was that the CMO reported a count of affected babies, rather than a count of anomalies.

Hospital Episode Statistics (HES)

We requested the number of first admissions in 2008 where a Q code had been recorded for children less than 16 years of age, by age. "First admission" means first in that year (2008), not necessarily the first time in the child's life for the specified condition. One child may have more than one Q code, and thus be counted for several Q code categories, but only once for each Q code and once for the total Q code count. Q codes were given to Q+2 digits only, limiting the specificity with which major congenital anomalies could be selected for analysis.

Neonatal Intensive Care Outcomes Research and Evaluation (NICORE)

Many major congenital anomalies require immediate treatment/surgery upon birth, with the new-born baby being admitted to neonatal care units for special care. The Neonatal Intensive Care Outcomes Research and Evaluation (NICORE) is a neonatal data collection system that monitors performance in neonatal care units across Northern Ireland. It is a joint initiative between the Public Health Agency and QUB. Core information is collected on the care provided by each unit and includes: admission details, early outcomes up to 28 days, discharge details and diagnosis. Data on the number of admissions and survival rate of infants admitted to ICU with a congenital anomaly in 2009 were supplied by NICORE (2008 was not available)[11].

Centre for Maternal and Child Enquiries (CEMACE)/Northern Ireland Maternal and Child Health (NIMACH) (now Northern Ireland Maternal and Infant Loss, NIMI).

CEMACE supported by NIMACH collected data on maternal perinatal and infant deaths for Northern Ireland, including cause of death. A series of reports have been produced including a number on perinatal mortality including cause of death. Data on deaths associated with congenital anomalies for the year 2008 was collated from the July 2010 report[12].

HeartSuite

Heartsuite is a clinical database held at the RBHSC which collects data on all children diagnosed with congenital heart disease in Northern Ireland. Heartsuite provided data on the number of cases of congenital heart disease born in 2008, with diagnostic descriptions which we classified into EUROCAT congenital heart disease subgroups. A number of recent papers based on information extracted from the HeartSuite database were also identified. The aim of the papers ranged from

describing the prevalence of particular types of cardiac defects through to the evaluation of psychological interventions for children and their families.

Regional Cytogenetic Records

The diagnosis of chromosomal anomalies is undertaken by the Regional Cytogenetic Laboratory based within the NI Regional Genetics Service. A request was made to the Regional Cytogenetic Service for the most recent five years of available data for the following chromosomal anomalies in Northern Ireland: Down Syndrome; Patau syndrome; Edward syndrome and Turner syndrome

Cleft Registry and Audit Network (CRANE)

The CRANE database (https://www.crane-database.org.uk/) is a UK wide database of children that registers the number of births with a cleft lip and / or palate in England, Wales and Northern Ireland. Reports are published each year detailing the number of births per year for a 10 year period.

Audits carried out in paediatric specialties, other clinical databases and other sources.

The FMU supplied data for new diagnoses in the years 2008 and 2012. Information on the number of cases of congenital anomaly who were treated by surgery during 2008 was provided by a paediatric surgeon in the RBHSC.

Other sources included conference abstracts and papers referring to the NI population.

Results

All congenital anomalies combined.

Prevalence

In 2008, CHS recorded 25,792 live and stillbirths occurring to mothers resident in Northern Ireland. Within this cohort a total of 2055 congenital anomalies (major and minor) were diagnosed of which 156 were unique Q codes. Following exclusion of minor anomalies according to the standard EUROCAT list for exclusion[8], 583 (28%) major congenital anomalies were identified of which 132 were unique Q codes. We could not calculate the total number of *babies* with major congenital anomaly. However, if we assume that approximately 10%-15% of babies have more than one major congenital anomaly[13], then we can estimate approximately 495-525 affected babies, giving a total prevalence of 1.9-2.0%. This is somewhat below the EUROCAT total prevalence of 2.6% (Table 1). These figures nevertheless suggest that CHS is a good source of information on congenital anomalies, although incomplete.

For the year 2008, the FMU recorded at total of 343 cases of congenital anomaly prenatally diagnosed, for a prevalence rate of prenatally diagnosed cases of approximately 1.3%; for the year 2012, at total of 281 cases of congenital anomaly were prenatally diagnosed, for a prevalence rate of prenatally diagnosed cases of approximately 1.1%.

Table 1. Prevalence of major congenital anomalies in children born and resident in NI in 2008 based on CHS/other data sources (white) and Heartsuite (grey) data, compared to EUROCAT prevalence rates.

EUROCAT Subgroup*	NI: CHS data[a]/clinical sources[b]		EUROCAT[c]	
	Total	Prevalence per 10,000 total births [95% CI]	Total	Prevalence per 10,000 total births [95% CI]
Total Births	25792[a]	----------	796513	
All (major) anomalies	NA	----------	20661	259.39 [255.87 - 262.95]
Nervous system	47	18.22 [13.71 - 24.22]	1975	24.80 [23.71 - 25.91]
Neural Tube Defects	23	8.92 [5.94-13.38]	796	9.65 [8.98 - 10.36]
Spina bifida	18	6.98 [4.42-11.03]	395	4.96 [4.48 - 5.47]
Hydrocephalus	9	3.49 [1.84-6.63]	488	6.13 [5.60 - 6.69]
Microcephaly	8	3.10 [1.57-6.12]	197	2.48 [2.15 - 2.86]
Eye	6	2.33 [1.07 - 5.07]	349	4.38 [3.93 - 4.87]
Ear Face and Neck	3	1.16 [0.40 - 3.24]	168	2.11 [1.80 - 2.45]
Congenital Heart Defects (CHD)	223	86.46 [75.87 – 98.51]	6558	82.33 [80.35 - 84.35]
Severe CHD	56	21.71 [16.73 - 28.18]	1706	21.42 [20.41 - 22.46]
Transposition of great vessels	10	3.88 [2.11 - 7.14]	296	3.72 [3.31 – 4.16]
Ventricular Septal Defect (VSD)	76	29.47 [23.55 – 36.86]	1932	24.26 [23.20 – 25.36][a]
Atrial Septal Defect (ASD)	34	13.18 [9.44 – 18.41]	1357	17.04 [16.15 – 17.97][b]
Atrioventricular Septal Defect (AVSD)	11	4.26 [2.38 – 7.64]	312	3.92 [3.49 – 4.38]
Tetralogy of Fallot	8	3.10 [1.57 – 6.12]	283	3.55 [3.15 – 3.99]
Pulmonary valve stenosis	7	2.71 [1.31 – 5.60]	310	3.89 [3.47 – 4.35]
Aortic valve atresia/stenosis	5	1.94 [0.83 – 4.54]	121	1.52 [1.26 – 1.81]
Hypoplastic left heart	5	1.94 [0.83 – 4.54]	218	2.74 [2.39 – 3.13]
Coarctation of aorta	5	1.94 [0.83 – 4.54]	310	3.89 [3.47 – 4.35]
Respiratory	7	2.71 [1.31 - 5.60]	516	6.48 [5.93 - 7.06]
Oro-Facial clefts	28	9.31 [6.25 - 13.84]	1211	15.20 [14.36 - 16.08]
Cleft lip with or without palate	24	7.75 [5.02 - 11.98]	733	9.20 [8.55 - 9.89]
Digestive system	20	7.75 [5.02 - 11.98]	1392	17.48 [16.57 - 18.42]
Abdominal wall defects	20	7.75 [5.02 - 11.98]	537	6.74 [6.18 - 7.34]
Gastroschisis	12	4.65 [2.66-8.13]	244	3.06 [2.69 - 3.47]
Omphalocele	8	3.10 [1.57-6.12]	235	2.95 [2.59 - 3.35]
Urinary	98	38.00 [31.19 - 46.28]	2709	34.01 [32.74 - 35.32]
Congenital hydronephrosis	73	28.30 [22.52-35.57]	841	10.56 [9.86 - 11.30]
Genital	81	31.41 [25.28 - 39.01]	1814	22.77 [21.74 - 23.85]
Hypospadias	75	29.80 [23.21-36.43]	1456	18.28[17.35 - 19.24]
Limb	116	44.98 [37.51 - 53.91]	3416	42.89 [41.46 - 44.35]
Limb reduction	9	3.49 [1.84-6.63]	421	5.29 [4.79 - 5.82]
Upper limb reduction	6	2.33 [1.07-5.07]	304	3.82 [3.40 - 4.27]
Club foot –Talipes equinovarus	5	1.94 [0.83- 4.54]	930	11.68 [10.94 - 12.45]
Hip dislocation and/or dysplasia	16	6.20 [3.82 -10.08]	621	7.80 [7.20 - 8.43]
Polydactyly	22	8.53 [5.63-12.91]	721	9.05 [8.40 - 9.74]
Syndactyly	30	11.63 [8.15-16.60]	428	5.37 [4.88 - 5.91]
Musculoskeletal*	14	5.43 [3.23 - 9.11]	776	9.74 [9.08-10.45]
Other malformations*	6	2.33 [1.07 - 5.07]	925	11.61 [10.89-12.39]
Teratogenic syndromes with malformations*	<5	1.16 [0.40 - 3.42]	68	1.19 [0.10-1.46]
Genetic syndromes and microdeletions*	5	1.94 [0.83 - 4.45]	442	5.55 [5.06-6.09]
Chromosomal	45	17.45 [13.04 - 23.34]	2953	37.07 [35.75 – 38.44]
Down syndrome	30	11.63 [8.15-16.60]	1706	21.42 (20.41 - 22.46)
Edwards syndrome/trisomy 18	5	1.94 [0.83-4.54]	404	5.07 (4.59 - 5.59)

A: CHS data based on number of codes, not number of cases.
B: Heartsuite data (for CHD) and CRANE data (for orofacial clefts) based on number of cases with one or more codes within subgroup. Total CHS and Heartsuite figures include livebirths and stillbirths only, CRANE livebirths only.
C:EUROCAT data based on number of cases with one or more codes within subgroup. Total prevalence in EUROCAT figures includes livebirths, stillbirths and terminations of pregnancy for fetal anomaly. EUROCAT cases with VSD as only type of CHD 7 EUROCAT cases with ASD as only type of CHD. Coded by pre 2012 EUROCAT subgroup coding. EUROCAT has a total of 89 subgroups. The above table includes a selection of these where at least 5 cases were recorded by CHS.

Perinatal and infant mortality due to congenital anomalies

According to the Registrar General Report 2010, 16 stillbirths (from 24 weeks) and 40 infant deaths due to congenital anomaly were registered in 2008. This was 14% of all stillbirths and 33% of all infant deaths[1]. The prevalence of stillbirths with congenital anomaly in NI in 2008 according to Registrar General figures was 0.58 per 1,000 births, and infant deaths with congenital anomaly was 1.55 per 1,000 births. CEMACE reported congenital anomalies as the primary cause of death for 13 stillbirths (i.e. 0.5 per 1,000 births) and 23 neonatal (first month) deaths (i.e. 0.9 per 1,000 births) that occurred in NI during 2008, a total extended perinatal mortality of 1.4 per 1,000 births[12]. Perinatal and infant death rates vary slightly by source according to whether it is by year of registration, year of death, or year of birth, and whether it is for all occurring in Northern Ireland, or all to residents of Northern Ireland.

For the period 2008-2012 EUROCAT reported a perinatal mortality rate for late fetal death (from 20 weeks) and stillbirths with congenital anomalies of 0.46 per 1,000, with deaths in the first week 0.47 per 1,000 resulting in an overall perinatal mortality rate of 0.93 per 1,000. The rates varied by country. Of note are the rates for England and Wales EUROCAT registries of 1.09 per 1,000 and Ireland of 2.06 per 1,000 (http://www.eurocat-network.eu/content/EUROCAT-Perinatal-Mortality-Table-2.pdf)[14]. Countries where there are high proportions of terminations of pregnancy for fetal anomaly tend to have lower perinatal death rates due to congenital anomaly, and high rates in Ireland and Northern Ireland compared to the average European rates and UK rates can therefore be expected, and congenital anomalies can be expected to account for a higher proportion of all perinatal deaths in Ireland/Northern Ireland. Published statistics for 2007/2008 record 76 medical abortions as being performed in Northern Ireland, of which 47 were terminations of pregnancy. In 2008/2009 71 medical abortions were recorded of which 44 were terminations of pregnancy. The number with congenital anomaly is not known[15]. Statistics are not collected for women leaving Northern Ireland to terminate a pregnancy following prenatal diagnosis of a severe congenital anomaly. The law with regard to termination of pregnancy for fatal anomaly is under review.

Perinatal and infant mortality by type of congenital anomaly is shown in Table 2. It should be noted that NI (Registrar General) data are for first year deaths compared to EUROCAT data for first week deaths, and NI data are based on very small numbers. An unpublished analysis of RG data for 2001-2010 by Dolk found chromosomal anomalies to account for 23% of stillbirths and 27% of neonatal deaths with congenital anomaly; NTDs to account 15% of stillbirths and 8% of neonatal deaths with congenital anomaly; and CHD to account for 10% of stillbirths and 20% of neonatal deaths with congenital anomaly.

Cause of death registration is limited by the take up of autopsies by parents of stillbirths and infant deaths, particularly for the diagnosis of internal anomalies; however, excellent sources of information are available for congenital anomaly diagnoses in stillbirths and infant deaths, which can be used in future for congenital anomaly surveillance.

Table 2. Perinatal and infant mortality rates for congenital anomalies in NI during 2008 compared to EUROCAT five year perinatal mortality rates (2008-2012)

	EUROCAT perinatal mortality in EUROCAT Full Member Registries (28 registries in 16 countries), 2008- 2012, by type of congenital anomaly					Stillbirth and infant mortality rates for Northern Ireland as reported in the Registrar General 2010 report, 2008 by type of congenital anomaly			
Description	Breakdown by anomaly subgroup (as a % of all FDs)	Breakdown by anomaly subgroup (as a % of all LBs with death in 1st week)	Prevalence of FD due to CA per **1,000** births	Prevalence of 1st week deaths due to CA per **1,000** births		Breakdown by anomaly subgroup (as a % of all stillbirths with CA)	Breakdown by anomaly subgroup (as a % of all infant deaths with CA)	Stillbirth due to CA per 1,000 births	Infant mortality due to CA per 1,000 births
All Anomalies	100%	100%	0.46	0.47		100% (n=16)	100% (n=40)	0.58	1.55
All Anomalies Excluding Chromosomal Anomalies	66.5	85.0	0.31	0.40		--------	--------	--------	--------
Nervous system (EUROCAT: Q00-Q07)	18.1	15.9	0.08	0.07		12.5	22.5	0.08	0.35
Congenital heart defects (EUROCAT: Q20-Q26)a	16.2	29.5	0.07	0.14		12.5	15.0	0.08	0.23
Respiratory (EUROCAT: Q30-Q34)	5.3	13.0	0.02	0.06		--------	5.0	--------	0.08
Digestive system (EUROCAT: Q38-Q45; Q79.0)b	6.4	16.9	0.03	0.08		--------	2.5	--------	0.04
Urinary (EUROCAT: Q60-Q64; Q79.4)c	9.5	18.0	0.04	0.08		31.2	5.0	0.19	0.08
Limb (EUROCAT: Q69-Q74)d	10.4	9.5	0.05	0.04		6.2	7.5	0.04	0.12
Chromosomal	33.5	15.0	0.15	0.07		31.2	37.5	0.19	0.58
Other congenital malformations e	--------	--------	--------	--------		6.2	5.0	0.03	0.08

a:Northern Ireland rate is based on Q20-Q28
b:Northern Ireland is based on Q35-Q45
c:Northern Ireland rate is based on Q50-Q64; EUROCAT categorises Q50-Q52, Q54-Q56 as genital anomalies only
d:Northern Ireland rate is based on Q65-Q79. EUROCAT categorises Q 74.02-Q79 as other anomalies/ syndromes.
e:Northern Ireland only rate

Neonatal care admissions for babies with congenital anomalies in 2009

Many major congenital anomalies require immediate treatment/surgery upon birth, with the newborn baby being admitted to neonatal care units for special/intensive care. The cost of providing neonatal care to the health service is substantial. In 2010/2011 the average daily cost of neonatal intensive care provided by Trusts in Northern Ireland was estimated to be £825 per day (based on a total cost of £18,058k and 21,877 bed-days).

In the year 2009, NICORE data recorded that a total of 1769 of the 25206 (6.9%) babies liveborn in NI (resident or not) were admitted to neonatal care, with 1166 (4.6%) of these requiring intensive and/or high dependency care. 162 (9%) of the admissions to neonatal units were infants that had at least one congenital malformation, with 88% surviving to discharge (Table 3). The average length of stay was 17.59 days (SD 31.97). The sum total of neonatal care days for infants with congenital anomalies in 2009 was 2850[(11)]. This cost the health service approximately £2.35 million (at an average cost of NIC of £825 per day).

Hospital Admissions for children (aged up to and including 16 years) with a diagnosis of a congenital anomaly during 2008

In the year 2008, HES data show that there were 77,315 first admissions of children aged 16 years and under to a HSC hospital in NI, of which 6.9% (n=5411) had a diagnosis of congenital anomaly (Q code). We were not able to distinguish major and minor congenital anomaly cases. While HES data are a good source of notification data on children with congenital anomalies admitted to hospital if further checking with other records is performed, experience of congenital anomaly registers using HES data (eg. the Congenital Anomaly Register & Information Service [CARIS] register in Wales) has shown that many HES Q codes are not eligible for registration, and HES data tends to vastly overestimate the prevalence of major congenital anomalies.

During this period the total stay duration for all children admitted to hospital was 156,387 days. The average stay duration stay in hospital for children with a Q code was 3.8 days, and was twice as high as that of children without a Q code diagnosis who on average spent only 1.9 days. A costing of health service care for children with congenital anomalies is not at present available.
Admissions by anomaly category are shown in Table 4.

In 2008, the Paediatric Surgery at RBHSC database recorded surgery in 2008 for a total of 99 children with spina bifida or mainly gastrointestinal conditions (assuming that each child had one condition only), which equates to approximately 0.4% of births. Other conditions such as congenital heart disease are not included in these data.

EUROCAT estimates that 1% of liveborn babies require surgery for a major congenital anomaly[(2)].

Table 3. Number of neonatal admissions and duration of stay for infants with congenital anomalies in survivors and non survivors* for the year 2009, NICORE data[11]

	Infants (n)		Mean (SD) Days spent in NNU			Total sum of days		
	Survivors	Non-Survivors*	Survivors	Non-Survivors	Total	Survivors	Non-Survivors	Total
Recognised trisomy/chromosomal syndromes	37		18.35 (23.36)	2.5 (0.70)	17.54 (23.01)	679	5	684
Respiratory system	3		5.67 (5.03)	1.2 (0.44)	2.88 (3.56)	17	6	23
Cardiovascular system	40		22.6 (46.09)	2.5 (0.707)	21.64 (45.16)	904	5	909
Central nervous system	17		16.59 (30.02)	23 (28.28)	17.26 (29.15)	282	46	328
Gastrointestinal	27		11.37 (22.92)	36.50 (40.30)	13.10 (24.25)	307	73	380
Recognised Malf. Syndrome	6		10.83 (4.7)	1.33 (0.57)	7.67 (6.04)	65	4	69
Genito-Urinary	3		6.33 (1.15)	1.25 (0.50)	3.43 (2.82)	19	5	24
Musculo-Skeletal	8		27.50 (46.9)	-	27.50 (46.9)	220	-	220
Undiagnosed Dysmorphic syndromes	6		31 (34.82)	7.5 (11.67)	21.60 (29.43)	186	30	216
Other CLP, IEM	8		15.75 (18.62)	-	15.75 (18.62)	126	-	126
TOTAL	143	19				2850	167	2979

Non Survivor profile: Of the 19 infants with congenital anomaly that did not survive to discharge n=5 (26%) had one recorded defect n= 6 (32%) had two recorded defects, n=3 (16%) had three recorded defects, n=2 (10%) had four recorded defects and n=3 (16%) had five recorded defects.

**Individual numbers suppressed due to small numbers*

Table 4. Number of first admissions to HSC hospitals in NI during 2008 of children aged 0-16 years (inclusive) with a diagnosis of congenital anomalies (Q00-Q99).

	N (%) by Age group (years)					
Anomaly subgroup *	**0**	**1**	**2-5**	**6-9**	**10-16**	**Total**
Nervous system (Q00-Q07)	47	21	58	32	39	197
Eye (Q10-Q15)	18	9	23	6	6	62
Ear, Face and neck (Q16-Q18)	21	16	21	48	66	172
CHD (Q20-Q26)	284	68	107	65	61	585
Respiratory (Q30-Q34)	62	15	23	5	<5	109
Orofacial clefts (Q35-Q37)	42	8	8	6	10	74
Digestive system (Q38-Q45)	227	33	66	17	25	368
Genital (Q50-Q56, excl Q53)[a]	60	59	87	43	47	296
Urinary (Q60-64)	89	19	30	13	21	172
Limb (Q65-Q74)[b]	599	44	77	28	78	826
Musculoskeletal (Q75-Q79)	59	8	17	17	20	121
Teratogenic syndromes with malformations (Q86) [b]	6	<5	6	<5	<5	19
Other Malformations (Q27, Q28, Q80-Q85, Q89)	154	18	33	24	59	288
Genetic syndromes and microdeletions	9	11	16	12	14	62
Chromosomal (Q90-Q93,Q96-Q99)	51	25	55	23	35	189

a:This excludes undescended testes (Q53)

b: Includes minor anomalies.

*Based on EUROCAT Guide 1.3

Prevalence by type of congenital anomaly

Nervous System Anomalies (Q00-Q07)

The EUROCAT subgroup Nervous System includes major disorders that affect regions of the brain and spinal cord. Nervous System anomalies includes Neural tube defects (NTD), a group that includes Anencephaly which is lethal, Encephalocele and Spina bifida), Hydrocephaly, Microcephaly and Arhinencephaly/ holoprosencephaly.

The CHS recorded a total of 47 diagnoses for major types of nervous system disorders with a max prevalence rate of 18.22 per 10,000 births (95% CI 13.7-24.2) (Table 1) if one assumes that all babies had no more than one nervous system code recorded. During 2008 HES recorded a total of 197 first admissions for children aged 16 years or less who had received a diagnosis for nervous system anomalies, of which 47 (24%) were admissions for children aged less than one year old.

EUROCAT recorded a higher average rate for nervous system disorders (24.8 per 10,000 births; 95% CI 23.7-25.9) (Table 1) but the Northern Ireland rate recorded by CHS lies between England and Wales EUROCAT (25.5 per 10,000 births; CI 23.6-27.5) and Ireland EUROCAT (17.1 per 10,000 births; CI 13.5-21.3).

NICORE[11] recorded 19 neonatal care admissions with central nervous system disorders in 2009 (Table 3), 12% of all neonatal care admissions with congenital anomaly.

Of the 47 nervous system codes in CHS data, 23 were NTD and 18 spina bifida. The NTD rate in NI was lower than the EUROCAT average (Table 1), and the ratio of spina bifida to other types of NTD was much higher in NI (Table 1 shows a roughly 1:1 ratio in EUROCAT between spina bifida and other types of anencephaly compared to 18:5 in CHS data). According to EUROCAT Data Quality Indicators (DQI), low NTD rates combined with a high proportion of spina bifida usually indicates poor recording to terminations of pregnancy by the registry, since a higher proportion of anencephaly than spina bifida result in termination of pregnancy (Loane, DQI in EUROCAT Report 9)[2]. In 2012, the FMU recorded 21 prenatal diagnoses of spina bifida.

A published conference abstract by local clinicians noted that the total prevalence rate for NTD in NI was 10.24 per 10,000, with a birth prevalence rate of 4.66 per 10,000 births with "Eighty four percent cases of NTDs were diagnosed antenatally leading to termination of pregnancy in 30% and 83% cases of spina bifida and anencephaly respectively"[16].

A rate of hydrocephaly of 3.5 per 10,000 births from CHS data, also as reported by the CMO[7], is lower than the EUROCAT average, despite the inclusion of hydrocephaly associated with spina bifida in the CHS numbers which are excluded from EUROCAT.

Eye Anomalies (Q10-Q15)

The EUROCAT subgroup *Eye anomalies* includes disorders that affect the visual system. All cases with a Q code diagnosis Q10-Q15 are counted once in this subgroup. Exclusions for minor anomalies

include: Q10.1-Q10.3, Q10.5, and Q13.5. Specific types of severe ocular defects for which separate prevalence rates are also calculated in EUROCAT include: Anophthalmos/Microphthalmos, Anophthalmos, Congenital cataracts and Congenital glaucoma.

Information on the rates of eye anomalies was available from two main sources, the CHS and HES Department of Health, Social Services & Public Safety Northern Ireland (DHSSPSNI), and a paper which examined "the changing visual profile of children attending a regional specialist school for the visually impaired in Northern Ireland" which provided non-population-based rates of specific types of eye anomalies[17].

The CHS recorded a total of 6 diagnoses for major types of eye disorder according to the EUROCAT codes for inclusion, with a prevalence rate of 2.33 per 10,000 births (95% CI 1.07-5.07). The EUROCAT average rate for eye anomalies for 2008 was 4.38 per 10,000 births (95% CI 3.93-4.87), nearly twice as high as the CHS NI rate. The combined rate for the England and Wales EUROCAT registries (3.85 per 10,000 births; CI 3.13-4.69) and Irish EUROCAT registries (6.43 per 10,000 births; CI 4.30-9.23) were higher than the NI rate.

HES indicated a total of 62 first admissions recorded as having a diagnosis for Eye anomalies, of which 18 were under one year of age, but HES Q codes were accurate to two digits (Q+2 digits) only rather than the three digits needed to exclude minor anomalies.

Congenital cataract was the most frequent specific diagnosis recorded by CHS, but all numbers for individual anomalies were below 5.

McClelland et al[17] indicated that over a period of 30 years (1975-2004), among children in introductory years of a local school for the visually impaired (n=266) 4% were recorded as having congenital glaucoma, with 13% having disorders of the lens including congenital cataract.

Ear face and neck anomalies (Q16-Q18)

The EUROCAT subgroup *Ear, Face and Neck* include major disorders that affect these three anatomical areas. All cases with a diagnosis of Q16-Q18 are counted once in this subgroup. Exclusions for minor anomalies include the following codes: Q17.0-17.5; Q17.9, Q18.0-Q18.2, Q18.4-Q18.7, Q18.80 and Q18.9. EUROCAT also calculates a separate prevalence rate for the specific defect Anotia.

The CHS recorded 11 codes Q16-18 but after exclusion of minor anomalies, there were less than 5. HES indicated a total of n=172 of which n=21 were under the age of one year, but it was not possible to exclude the minor anomaly codes.

The EUROCAT average rate (2.15 per 10,000 births; 95% CI 1.84-2.49), was nearly twice as high as the NI CHS rate, but similar rates to NI CHS were recorded by the England and Wales EUROCAT

registries (1.26 per 10,000 births; 95% CI 0.86-1.78) and Irish EUROCAT registries (1.11 per 10,000 births; 95% CI 0.35-2.59).

Congenital Heart Defects (CHD) (Q20-26)

The EUROCAT subgroup CHD includes 17 subgroups of major cardiac defects. Patent ductus arteriosus is excluded if gestational age is less than 37 weeks, since this is a manifestation of immaturity at birth and usually resolves spontaneously. "Severe" CHD consists of all the subgroups combined excluding VSD, ASD or pulmonary valve stenosis.

The HeartSuite database indicated that of the total number of individuals (n=1071) who had been referred to the regional paediatric cardiology department for investigation, diagnosis and treatment of cardiac anomalies, a total of 232 were considered to have a normal heart and 336 had only an innocent functional murmur. Of the remaining cases, 224 met the EUROCAT inclusion criteria for CHD. Exclusions were cases recorded as having resolved (spontaneous closure) (ASD n=7; VSD n=46; Patent Ductus Arteriousus (PDA) n=24 and Patent Foramen Ovule (PFO) n=11); cases excluded by EUROCAT (41 PDA which we assumed to be preterm in the absence of gestational age information, 49 PFO, 3 peripheral pulmonary arterial stenosis); Other conditions included Long QT syndrome, Kawasaki disease and (Wolff-Parkinson-White Syndrome (WPW); 32 cases were recorded as undergoing screening for heart conditions mostly due to family history of heart conditions, or for some if they had presented with symptoms associated with a heart condition.

The prevalence rate for the 224 confirmed Heartsuite cases was 86.5 per 10,000 births (95% CI 75.9-98.5). In comparison, the CHS recorded a total of n=90 diagnoses for CHD, or 40% of all cases recorded by Heartsuite. HES data indicated that there had been a total of 585 first admissions recorded as having a diagnosis of CHD of which 284 were under the age of one, but including conditions EUROCAT would exclude.

In 2012, the FMU recorded 40 cases of CHD prenatally diagnosed, suggesting a prenatal detection rate of one fifth or less of all CHD.

The EUROCAT average rate for CHD (82.3 per 10,000 births; 95% CI 80.4-84.4) was marginally lower than the NI Heartsuite rate. The combined rate for the England and Wales EUROCAT registries (63.4 per 10,000 births; 95% CI 60.3-66.5) was lower, as was the combined rate for Ireland EUROCAT registries (66.0 per 10,000 births; 95% CI 58.7-74.0). NI is in the unique situation of having a clinical database for the entire geographical population, and this may well mean a better reporting than in many EUROCAT registries. However, not having full individual case data for this Report means that the Heartsuite data were less well verified than EUROCAT registry data.

In NI the most common type of heart defect diagnosed according to Heartsuite data was Ventricular sepal defect (VSD) with 77 cases, followed by ASD with 34. The rates per 10,000 births for these two

usually less severe types of CHD in NI were similar to the EUROCAT rates (Table 1). The Heartsuite rate of Severe CHD was 21.71 per 10,000, very similar to the EUROCAT rate (Table 1).

NICORE [11] recorded 42 neonatal care admissions with cardiovascular system anomalies in 2009 (Table 3), 26% of all neonatal care admissions with congenital anomaly and the most numerous category.

The NI Baby Hearts Study, funded by Chest Heart and Stroke, a collaboration between University of Ulster and the RBHSC, is a three year study ending in October 2017 which should provide detailed information on prevalence and risk factors for congenital heart disease.

Respiratory anomalies (Q30-Q34)

The EUROCAT subgroup *Respiratory anomalies* records major anomalies of the nose, larynx, trachea and bronchus and the lung. All cases with a Q code diagnosis Q30-Q34 are counted once in this subgroup. Exclusions are Q31.4; Q31.5; Q32.0 and Q33.1. EUROCAT also produces separate prevalence rates for Choanal atresia and Cystic adenomatous malformation of the lung.

The CHS recorded a total of 7 diagnoses for major types of respiratory anomalies (after exclusion of 3 minor codes), with a prevalence rate of 2.71 per 10,000 births (95% CI 1.31 – 5.60). The EUROCAT average rate for respiratory anomalies (6.48 per 10,000 births; 95% CI 5.93-7.06) was more than twice the NI rate. The combined rate for the England and Wales EUROCAT registries (7.59 per 10,000 births; 95% CI 6.55-8.73) and Irish EUROCAT registries (5.76 per 10,000 births; 95% CI 3.76-8.44) were also more than twice the NI CHS rate.

HES indicated a total of 62 first admissions for children under the age of one who were recorded as having a diagnosis of a respiratory anomaly, with 13 having a code for a malformation of the lung (Q33) of which many would be excluded by a congenital anomaly registry, and may be secondary to prematurity.

NICORE[11] recorded 8 neonatal care admissions with respiratory system anomalies in 2009 (Table 3), 5% of all neonatal care admissions with congenital anomaly.

The most common type of major respiratory anomaly diagnosed in NI CHS were for malformations of the lung (n=6), with 5 recorded as having congenital cystic lung (Q33.0).

Data on the occurrence of specific types of respiratory anomalies in NI was also provided by two consultants, based on information contained within clinical audits. Choanal atresia is a congenital anomaly whereby either one or both of the nasal airway passages are blocked or narrowed with excess tissue, making it difficult for babies to breathe through their nose. Eight cases were recorded during the four year period of time April 2008 and April 2012 (Dr Keith Trimble, personal

communication on 07/07/2012). On average this would indicate a rate of 0.78 per 10,000 births. The EUROCAT rate for this anomaly was 1.02 per 10,000 births.

Cystic adenomatous malformation of the lung (CCAM) is a rare condition in which a benign mass of abnormal lung tissue is present on a section of the lung. Over a 10.5 year period (January 1999-June 2009) a total of 51 cases were reported as being detected with an estimated minimum incidence of 1 in 4,800, or 1.94 per 10,000 births (Prof Mike Shields, personal communication 26/04/2012). The EUROCAT rate for this anomaly for the year 2008 was 0.87 per 10,000 births, suggesting a higher rate in NI. An increasing prevalence has been recorded by EUROCAT over the last ten years[18]. The FMU in 2012 recorded 28 prenatal diagnoses of CCAM, possibly another indication of a rising trend.

Orofacial Clefts (Q35-Q37)

The EUROCAT subgroup *Orofacial clefts* includes cleft palate, cleft lip, and cleft lip with cleft palate. All cases with a Q code diagnosis of Q35-Q37 are counted once in this subgroup. EUROCAT have a further two subdivisions of this anomaly that i: cases with cleft lip with or without cleft palate and ii: cases with cleft palate only. Cases are excluded if there is an association with holoprosencephaly or anencephaly subgroups.

The CHS recorded a total of 24 diagnoses of orofacial clefts, with a prevalence rate of 9.31 per 10,000 births (95% CI 6.25 – 13.84). The CRANE 2010 annual report[19] indicated that during the year 2008 a total of 28 babies were born in NI with cleft lip and/or palate (10.86 per 10,000 births, 95% CI 7.51-15.69). HES indicated a total of 74 first admissions with this diagnosis, 42 of which were for children under one year of age.

The EUROCAT average rate (15.20 per 10,000; 95% CI 14.36-16.08) was more than 50% higher than the NI CHS and CRANE rates. The combined rate the England and Wales EUROCAT registries was 16.32 per 10,000 births (95% CI 14.71-17.88) and Irish EUROCAT registries 14.84 per 10,000 births (95% CI 11.51-18.85), both also higher than the CHS and CRANE rates. This, together with a higher rate estimated by HES for this well-defined congenital anomaly, suggests some under recording on both CHS and CRANE.

Digestive system (Q38-Q45, Q79.0)

The EUROCAT subgroup of *Digestive anomalies* records major digestive defects that affect the tongue, mouth and pharynx, diaphragm, oesophagus, upper alimentary tract, intestine and gallbladder, bile ducts and liver. All cases with a Q code diagnosis of Q38-Q45 and Q79.0 are counted once in this subgroup. Exclusions for minor anomalies and conditions that may not be congenital (eg pyloric stenosis) include the following codes Q38.1, Q38.2, Q38.50, Q40.0, Q40.1, Q40.21, Q43.0, Q43.20, Q43.81 and Q43.82. EUROCAT also produces separate prevalence rates for the following specific subtypes of digestive anomalies: Oesophageal atresia, Duodenal atresia or stenosis, Atresia

or stenosis of other parts of the small intestine, Ano-rectal atresia and stenosis, Hirschsprung's disease, Atresia of bile ducts, Annular pancreas and Diaphragmatic hernia.

CHS recorded a total of 20 diagnoses for major types of digestive anomalies, following exclusion of 223 minor anomaly codes, giving a prevalence rate of 7.8 per 10,000 (95% CI 5.0-12.0). HES indicated that there was a total number of n=368 first admissions, the majority of which were for children aged under one year (n=227), including minor codes.

The EUROCAT average rate for digestive anomalies was 17.4 per 10,000 (95% CI 16.5-18.4), more than twice the NI CHS rate. The combined rate for the England and Wales EUROCAT registries (17.3 per 10,000 births; 95% CI 12.3-15.2) and Irish EUROCAT registries (17.3 per 10,000 births; 95% CI 13.7-21.6) were close to the EUROCAT average, confirming under ascertainment by CHS.

Specific subgroups of digestive system anomalies were recorded for less than 5 cases each in CHS data for 2008. The FMU in 2012 recorded 10 prenatal diagnoses for diaphragmatic hernia, and 11 gastrointestinal atresias.

NICORE[11] recorded 29 neonatal care admissions with gastrointestinal anomalies in 2009 (Table 3), 18% of all neonatal care admissions with congenital anomaly, also including abdominal wall defects below.

Abdominal Wall Defects (Q79.2, Q79.3, Q79.5)

The EUROCAT subgroup *Abdominal wall defects* includes omphalocele/exomphalos and gastroschisis. All cases with a Q code diagnoses Q79.2, Q79.3, Q79.5 are counted once in this subgroup. EUROCAT also produces separate prevalence rates for Gastroschisis and Omphalocele. The CHS recorded a total of 20 diagnoses for abdominal wall defects, giving a prevalence rate of 7.75 per 10,000 (95% CI 5.02-11.98). HES indicated that a total of n=40 first admissions had a diagnosis of Q79. However this level of information did not allow us to identify the number of cases with the codes specific to this EUROCAT subgroup.

The EUROCAT average rate (6.74 per 10,000; 95% CI 6.18-7.34) was lower than the NI rate. The combined rate for the England and Wales registries (9.94 per 10,000 births; 95% CI 8.76-11.25) was higher than the NI rate, while the combined rate for the Irish EUROCAT registries (3.77 per 10,000 births; 95% CI 2.19-6.03) was lower than the NI rate.

In the NI CHS data, the most common type of type of abdominal wall defect was gastroschisis with 12 cases. The remaining 8 cases were Omphalocele. In 2012, the FMU (RJM) recorded 9 gastroschisis and 8 exomphalos diagnosed prenatally. Rates of gastroschisis in the UK have been considerably higher than the EUROCAT average for the last decade and more[18] and these rates suggest NI is similar to the rest of the UK.

Genital Anomalies (Q50-Q52, Q54-Q56)

The EUROCAT subgroup *Genital anomalies* records major defects that occur in the genitalia of both males and females. All cases with a Q code diagnosis Q50-Q52, Q54-Q56 are counted once in this subgroup. Exclusions for minor anomalies include the following Q code: Q52.3, Q52.5, Q53, Q55.20, and Q55.21. EUROCAT also produces separate prevalence rates for the specific subgroups Hypospadias and Indeterminate sex.

After excluding 277 cases of undescended testicles (Q53), the CHS recorded a total of 81 major genital anomalies, giving a prevalence rate of 31.4 per 10,000 (95% CI 25.3-39.0). HES indicated that 672 first admissions had a diagnosis of genital anomalies, with the majority of admissions aged less than one year old (n=224). A significant proportion (56%) of the genital anomalies associated with admissions was for undescended testicle (Q53), excluded from EUROCAT rates.

The EUROCAT average rate (22.8 per 10,000; 95% CI 21.7-23.9) was lower that the NI rate. The combined rate for the England and Wales EUROCAT registries (22.4 per 10,000 births; 95% CI 20.66-24.4) and Irish EUROCAT registries (17.1 per 10,000 births; 95% CI 13.5-21.3) were lower than the NI CHS rate.

In NI the most common type of genital anomaly recorded by CHS was hypospadias (Q54), with 75 cases, giving a rate higher than that recorded by EUROCAT (Table 1). HES recorded 44 admissions aged less than one year old with a diagnosis of Hypospadias which suggests that some of the hypospadias cases recorded by CHS were either minor (glanular) not requiring surgery or would require surgery later than the first year of life.

Urinary Anomalies (Q60-Q64, Q79.4)

The EUROCAT subgroup *Urinary Anomalies* records major defects that affect the urinary system: kidney, ureter and bladder. All cases with a diagnosis of Q60-Q64, Q79.4 are counted once in this subgroup. Excluded minor anomaly Q codes are Q61.1, Q62.7 and Q63.3. EUROCAT also produces separate prevalence rates for the following specific types of defects: Bilateral renal agenesis, Renal dysplasia, Congenital hydronephrosis, Bladder exstrophy and/or epispadia and Posterior urethral valve and /or prune belly.

The CHS recorded a total of n=98 diagnoses of urinary anomalies (after exclusion of 5 cases of Q62.7) giving a prevalence rate for this anomaly of 38.0 per 10,000 (95% CI 31.2-46.3). HES indicated a total of 89 first admissions with a diagnosis of urinary anomalies in children aged less than one year. The EUROCAT average rate (31.04 per 10,000; 95% CI 32.74-35.32) was lower than the NI rate (Table 1). The combined rate for the England and Wales EUROCAT registries (32.43 per 10,000 births; 95% CI 32.45-34.71) and Irish EUROCAT registries (15.95 per 10,000 births; 95% CI 12.48-20.09) were also lower than the NI CHS rate. However in this subgroup it is likely that a significant proportion of cases may have more than one code which would lead to overestimation of the CHS rate.

In NI the most common type of urinary anomaly recorded by CHS was congenital hydronephrosis (Q 62.0), with 73 cases identified (74% of the total). However it needs to be noted that there was evidence of discrepancies between the four areas of the CHS in the rates of diagnosis, with one area in particular diagnosing significantly higher rates compared to the other three. The experience of EUROCAT has been that it is difficult to standardise the definition and inclusion criteria for congenital hydronephrosis. Congenital hydronephrosis accounted for only 31% of total EUROCAT urinary cases. Thus, it is likely that NI CHS rates may be overestimated due to over diagnosis of this anomaly, as well as duplicate counting of cases with more than one diagnosis coded within the urinary category.

The FMU in 2012 recorded 28 prenatal diagnoses of renal anomalies.

NICORE[11] recorded 7 neonatal care admissions with genitorurinary system anomalies in 2009 (Table 3), 4% of all neonatal care admissions with congenital anomaly, and this also includes the genital anomaly category above.

Limb Anomalies (Q65-Q74)

The EUROCAT subgroup *limb anomalies* records major defects that occur as a consequence of the partial or complete failure of the limb to develop. All cases with a Q code diagnoses Q 65-Q74 are counted once in this subgroup. Exclusions for minor anomalies are the Q codes Q65.3-Q65.5, Q66.2-Q66.9, Q67.0-Q67.8, Q68.0, Q68.21, Q68.3-Q68.5 and Q74.00 EUROCAT also produces separate prevalence rates for Limb reduction, Upper limb reduction, Lower limb reduction, Complete absence of a limb, Club-foot, Hip dislocation and/or dysplasia, Polydactyly and Syndactyly.

The CHS recorded a total of 116 major limb defects, following exclusion of 679 minor diagnoses (most of which were for deformities of the foot) giving a prevalence rate of 45.0 per 10,000 births (95% CI 37.5-53.9). HES indicated that a total of n=826 first admissions had a diagnosis of limb anomalies, the majority of which were for children under the age of one (n=599). 68% of the first admissions with limb anomalies were recorded as having congenital deformities of the feet (Q66), some of which would be for exclusion (Q66.2-Q66.9).

The EUROCAT average rate (42.9 per 10,000; 95% CI 41.5-44.4) was similar to the NI CHS rate. The combined rate for the England and Wales registries (40.1 per 10,000 births; 95% CI 37.7-42.7) was somewhat lower than the NI rate, but the combined rate for the Irish EUROCAT registries (51.6 per 10,000 births; 95% CI 45.2-58.7) was similar or higher than the NI rate.

In NI the most common type of limb anomaly recorded was for congenital anomalies of the feet (Q 66 excluding the minor forms) with 28 cases recorded, followed by 22 cases of part of syndactyly - webbed toes (Q 70.3). In general syndactyly was probably overestimated by CHS as minor forms cannot be recognised from their codes alone.

Clubfoot was under-recorded by CHS (see Table 1). Following enquiries to the regional paediatric orthopaedic consultants, we were informed that an audit of clubfoot cases in NI was to be undertaken. Rates of limb reduction recorded by CHS were also lower than expected (Table 1).

Musculoskeletal Anomalies (Q75.0-75.1, Q75.4-Q75.9, Q76.1-Q76.4, Q76.6-Q76.9, Q77, Q78, Q79.6-Q79.9)

Prior to 2012, EUROCAT subgroups included the subgroup *Musculoskeletal Anomalies*. All cases with the following Q code diagnoses were counted one in this subgroup: Q75.0-75.1, Q75.4-Q75.9, Q76.1-Q76.4, Q76.6-Q76.9, Q77, Q78, and Q79.6-Q79.9. Exclusions for minor anomalies are Q codes: Q75.2, Q75.3, Q76.71, Q76.0, Q76.5, Q76.61, Q76.62 and Q76.43. EUROCAT also produced separate prevalence rates for Thanatophoric dwarfism, Jeunes syndrome, Achondroplasia, Craniosynostosis and Congenital constriction of the bands/amniotic band. The subgroup classification system of EUROCAT has now changed (see EUROCAT Guide 1.4, 2016)[9].

CHS recorded a total of 14 musculoskeletal anomalies, following exclusion of 3 minor codes, giving a prevalence rate of 5.43 per 10,000 births (95% CI 3.23 - 9.11). HES indicated a total of 121 first admissions with musculoskeletal anomalies, of which 48% were for children under the age of one year old, but exclusion of minor anomalies could not be applied.

The EUROCAT average rate for this subgroup of anomalies was 9.74 per 10,000 births (95% CI 9.08-10.45), higher than the NI rate.

In NI the subgroup identified with the most cases was Craniosynostosis, with 5 cases giving a prevalence of 1.94 per 10,000 (95% CI 0.83 - 4.45).

A published paper reported on rates of Thanatophoric Dysplasia and Achondroplasia in NI[20]. Over an 11 year period (1995-2006) they identified “22 cases of thanatophoric dysplasia, four cases of osteogenesis imperfecta type II and two cases (5%) of achondroplasia”.

There were 8 Neonatal Care admissions for musculoskeletal conditions in 2009 (Table 3), 4% of all neonatal are admissions for congenital anomaly, including also limb anomalies above.

Other Malformations (Q27, Q28, Q80-85, Q89)

Six cases were identified by CHS as having an “other malformation”, according to the pre-2012 EUROCAT subgroup including Q27, Q28, Q28, Q80-85 and Q89 and excluding Q27.0, Q82.5, Q82.80, Q83.3, Q84.5 and Q89.9. This subgroup included asplenia, Situs inversus, Conjoined twins and Disorders of the skin. The EUROCAT average rate was five times higher than that of NI CHS (Table 1).

Teratogenic syndromes with malformations (Q86, P35.0,P35.1, P37.1)*

The EUROCAT subgroup *Teratogenic syndromes with malformations* records major anomalies that are known to have occurred as a consequence of exposure to teratogenic factors, for example fetal alcohol spectrum disorder (FASD), fetal valproate syndrome and maternal infection syndromes.

Maternal infection syndromes have P codes that were not included in the CHS dataset requested. The CHS recorded a total of 3 Q coded teratogenic syndromes with malformations with a prevalence rate of 1.16 per 10,000 (95% CI 0.04-3.24). HES for the year 2008 indicate that there was a total 19 first admissions with a diagnosis of teratogenic syndromes with malformations, of which 32% (n=6) were for children aged under 1 year.

The EUROCAT average rate (1.19 per 10,000; 95% CI 0.097-1.46) was similar to the NI rate although including a wider range of codes. The combined rate for the England and Wales EUROCAT registries (0.98 per 10,000 births; 95% CI 0.64-1.45) and Irish EUROCAT registries (1.55 per 10,000 births; 95% CI 0.62-3.20) are difficult to compare due to small numbers of cases.

Genetic syndromes (Q87).

Five cases were recorded of genetic syndromes by CHS, about half as many as expected on the basis of EUROCAT rates.

NICORE[(11)] recorded 9 neonatal care admissions with recognised malformation syndromes in 2009 (Table 3), 6% of all neonatal care admissions with congenital anomaly. There were 10 Neonatal Care admissions for undiagnosed dysmporphic syndromes in 2009 (Table 3), 6% of all neonatal are admissions for congenital anomaly.

Chromosomal anomalies (Q90-92, Q93, Q96-Q99)

The EUROCAT subgroup *Chromosomal anomalies* records chromosomal abnormalities which are usually associated with structural malformations: Q code Q90-92, Q93 and Q96-Q99 are counted once in this subgroup. The Q code 93.6 relating to microdeletions is excluded. EUROCAT also produces separate prevalence rates for Down syndrome (trisomy 21), Patau syndrome (trisomy 13), Edward syndrome (trisomy 18), Turner syndrome and Klinefelter syndrome.

CHS recorded a total of 45 diagnoses for chromosomal anomalies giving a prevalence rate of 17.4 per 10,000 (95% CI 13.0-23.3), including 28 Down Syndrome. HES for 2008 indicate 189 first admissions with a diagnosis of chromosomal anomalies, of which 51 (27%) were under the age of one. Diagnostic tests to confirm chromosomal anomalies are carried out by the Regional Cytogenetic Laboratory. Karyotyping can be performed prenatally or postnatally. The Regional Cytogenetic Laboratory reported that they had performed a total of 71 positive tests for the following specific types of chromosomal anomalies: Down syndrome (n=43), Patau syndrome (n=6), Edward syndrome (n=16) and Turner syndrome (n=6). However, some pre and postnatal tests may refer to the same

case. Some prenatal diagnoses may have been followed by termination of pregnancy outside NI and would not be recorded in CHS numbers. The FMU in 2012 recorded 23 prenatal diagnoses of chromosomal abnormality.

The EUROCAT average rate for chromosomal anomalies (37.1 per 10,000; 95% CI 35.8-38.4) was more than twice as high as the NI CHS rate, and also higher than the rate recorded by the Regional Cytogenetic Laboratory. The combined rate for the England and Wales EUROCAT registries (44.6 per 10,000 births; 95% CI 42.0-42.2) and Irish EUROCAT registries (43.2 per 10,000 births; 95% CI 37.2-49.7) were also more than twice the NI CHS rate for 2008.

The CMO Report[7] cited 30 cases of Down syndrome born to mothers resident in Northern Ireland in 2008, giving a rate of 12 per 10,000 total registered births to mothers resident in NI. The rates reported for the year 2008 were lower than for the previous 2 years (2006, 2007) and the following year (2009) which had rates of 20, 20 and 21 per 1,000 respectively. These rates were closer to the average for EUROCAT (22 per 10,000).

Maternal age is strongly associated to risk of Down Syndrome and other chromosomal anomalies and any assessment of differences in prevalence between populations needs to take this into account[21]. Table 5 shows that in 2008, 53 cases of Down Syndrome cases were expected on the basis of EUROCAT maternal age specific cases (by indirect standardisation), although the CMO report[7] recorded only 30, or an average of 43 per year.

There were 39 Neonatal Care admissions for chromosomal syndromes in 2009 (Table 3), 24% of all neonatal are admissions for congenital anomaly.

Table 5. Expected number of Down Syndrome cases in Northern Ireland in 2008, by maternal age, based on EUROCAT maternal-age specific rates, and CMO maternal age-specific rates for 2005-9.

Maternal Age group	Births registered in Northern Ireland 2008	EUROCAT Total prevalence rate per 1000	Expected number of Down syndrome cases in NI, 2008	Number of Down Syndrome cases for NI 2005-9, CMO Report 2010[10]	Rate per 1000 for NI 2005-9, CMO Report 2010[10]
<20	1426	0.7	0.95		0.9
20-24	4264	0.7	3.17		0.4
25-29	7335	0.9	6.26		0.8
30-34	7486	1.5	11.37		1.2
35+	5120	6.1	31.26		(4.1, 12.2, 6.4)*
Total	25,631		53.01	214 (average 42.8/year)**	

*age groups 35-39, 40-44, 45-49

** 35 in 2005, 46 in 2006, 50 in 2007, 30 in 2008, 53 in 2009

References 1

1. Annual Report of the Registrar General for NI 2010. Available from http://www.nisra.gov.uk/demography/default.asp132.htm
2. EUROCAT (2011). EUROCAT Report 9. *Birth Defects Research Part A Clinical and Molecular Teratology*. 91: (S1). S1-S100.
3. EUROCAT and EUROPLAN (2013). Primary Prevention of Congenital Anomalies: Recommendations on Policies to be considered for the Primary Prevention of Congenital Anomalies in National Plans and Strategies on Rare Diseases. EUROCAT Central Registry, University of Ulster. Available from http://www.eurocat-network.eu/content/EUROCAT-EUROPLAN-Primary-Preventions-Reccomendations.pdf
4. http://www.who.int/mediacentre/factsheets/fs370/en/ (http://www.who.int/mediacentre/factsheets/fs370/en/ Accessed 16/06/2014).
5. EUROCAT (2013). EUROCAT Special Report: Primary Prevention of Congenital Anomalies in European Countries. EUROCAT Central Registry, University of Ulster. Available from http://www.eurocat-network.eu/content/Special-Report-Primary-Preventions-of-CA.pdf
6. http://www.cdc.gov/features/birthdefectscostly/ (http://www.cdc.gov/features/birthdefectscostly/ Accessed 16/06/2014).
7. Department of Health, Social Services and Public Safety. (2011) CMO Annual Report 2010 (PDF 4.43 MB) [Online]. Available from: http://www.thehealthwell.info/node/799665
8. EUROCAT (2005). EUROCAT Guide 1.3: Instructions for the registration of congenital anomalies. EUROCAT Central Registry, University of Ulster. Available from http://www.eurocat-network.eu/aboutus/publications/publications.
9. EUROCAT (2013). EUROCAT Guide 1.4: Instructions for the registration of congenital anomalies. EUROCAT Central Registry, University of Ulster. Available from http://www.eurocat-network.eu/aboutus/publications/publications
10. www.eurocat-network.eu/accessprevalencedata/prevalencetables. Available at http://www.eurocat-network.eu/accessprevalencedata/prevalencetables accessed 4/12/2012
11. Neonatal Intensive Care Outcomes Research and Evaluation Database (NICORE). Queens University Belfast (accessed 2012)
12. Centre for Maternal and Child Enquiries (CMACE) Perinatal Mortality 2008:United Kingdom. CMACE: London, 2010.

13. Garne E, Dolk H, Loane M, Wellesley D, Barisic I, Calzolari E and Densem J (2011). Paper 5: Surveillance of multiple congenital anomalies: implementation of a computer algorithm in European registers for classification of cases. Birth Defects Research (Part A). 91: S44-S50.

14. http://www.eurocat-network.eu/content/EUROCAT-Perinatal-Mortality-Table-2.pdf)

15. https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/hs-termination-of-pregnancy-stats-14-15.pdf (https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/hs-termination-of-pregnancy-stats-14-15.pdf Accessed 22/02/2017)

16. Dabir T, Stewart F, Hill N (2009). Neural tube defects in 21st century: is Northern Ireland changing? Cerebrospinal Fluid Research 6 (Suppl 2):S2

17. McClelland J, Saunders K J, Hill N, Magee, A, Shannon M, Jackson, A J (2007). The changing visual profile of children attending a regional specialist school for the visually impaired in Northern Ireland. Ophthalmic and Physiological Optics, 27: 556–560. doi:10.1111/j.1475-1313.2007.00523.

18. EUROCAT (2012). EUROCAT Statistical Monitoring Report 2009. *EUROCAT Central Registry, University of Ulster*. Available from http://www.eurocat-network.eu/aboutus/publications/publications

19. CRANE Annual Report October 2010. Available from https://www.crane-database.org.uk.

20. Donnelly DE, McConnell V, Paterson A, Morrison PJ (2010). The prevalence of thanatophoric dysplasia and lethal osteogenesis imperfecta type II in Northern Ireland – a complete population study Ulster Med J; 79(3):114-118

21. Loane M, Morris J, Addor M-C, Arriola L, Budd J, Doray B, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, Latos- Bielenska A, McDonnell R, Mullaney C, O'Mahony M, Queisser-Wahrendorf A, Rankin J, Rissmann A, Rounding C, Salvador J, Tucker D, Wellesley D, Yevtushok L Dolk H (2013). Twenty-year trends in the prevalence of Down syndrome and other trisomies in Europe: impact of maternal age and prenatal screening. *European Journal of Human Genetics*. 21: 27-33.

Part II Primary prevention of congenital anomalies in Northern Ireland

Aim and Background

The *aim of the second part of this Report* is to survey the policies, recommendations, guidelines and practices in Northern Ireland that may directly or indirectly prevent or reduce the occurrence of congenital anomalies.

In 2012, a survey on the existence of primary prevention-related policies and public health actions for congenital anomalies in Member States was conducted as part of the EUROCAT Joint Action 2011-2014, designed by a working group led by the Instituto Superiore di Sante in Rome and including Ulster University. The multinational results are available at http://www.eurocat-network.eu/content/Special-Report-Primary-Preventions-of-CA.pdf[1]. This work was designed to complement an associated objective of the EUROCAT Joint Action: the development of recommendations on primary prevention of congenital anomalies for inclusion in National Plans for Rare Diseases. These recommendations and the papers derived from it[2, 3] are available at http://www.eurocat-network.eu/.

Context of the primary prevention of congenital anomalies in NI.

In Northern Ireland the responsibility for setting policy on health and social care including public health and maternal health and wellbeing is within the remit of the Department of Health and Social Services and Public Safety for Northern Ireland (DHSSPSNI), recently renamed Department of Health. The department works alongside the Public Health Agency, the Health and Social Care (HSC) Board and the five HSC Trusts in implementing policy and delivering. Other departments that may have input into primary prevention of congenital anomalies include those with a responsibility for setting policy on environmental health and the regulation of consumer products. These departments in turn may commission Non-Departmental Public Bodies to implement and deliver policies. For example the Health and Safety Executive Northern Ireland is the independent regulator of health and safety in the workplace.

The most effective time to implement primary prevention strategies is in the preconception period, before women have conceived. This is because the period of organogenesis when the fetus is vulnerable to teratogenic agents is very early in pregnancy, before many women may recognise their pregnancy, and because changing exposures may be a lengthy process. The Strategy for Maternity Care in Northern Ireland 2012-2018[4] defines preconception care as 'any advice or management that occurs before a pregnancy' and have identified the outcome of preconception care to be healthier women at the start of pregnancy.

Approaches to the prevention of congenital Anomalies

Preventive approaches may also be categorised as **primary, secondary or tertiary**:

Primary prevention

Primary prevention strategies are interventions that begin before the disease (or malformation) process has begun and thus lead to the baby being born without a congenital anomaly. Strategies are directed at removing or reducing the influence of factors that are known to increase the risk of the congenital anomalies. Approximately half of all pregnancies are estimated to be unplanned, emphasising the need for preconceptional measures. Prevention of congenital anomalies can be universal - directed at a population level as part of a public health initiative, or targeted at high risk individuals who are at high risk due to complex health or social factors.

There is a wide range of potential primary prevention measures. This includes universal strategies such as maternal infection control through coordinated vaccination programmes that protect women against the infections such as rubella and influenza; improvement of women's nutritional status and periconceptional folic acid supplementation; encouraging the cessation of maternal lifestyle behaviours that have been associated with congenital defects eg smoking, alcohol consumption and recreational drug use. Individual strategies that target higher risk women include directed clinical care for those women with chronic illness who may wish to start a family and will need to be carefully monitored, including their medication use (eg women with diabetes, epilepsy or obesity); provision of genetic counselling for individuals known to have a high risk for genetic disorders to help affected families make informed choices when planning a family; avoiding high levels of exposure in women at occupational risk; avoiding high community exposures to environmental pollutants.

Preventing congenital anomalies can only partly be achieved through women's own choices. Potentially more important is to create environments where the fetus, as one of the most vulnerable members of the community, is protected - environmental pollution, unnecessary medication and infection exposures, poor quality food, tobacco advertising, poverty, education are all factors to be addressed at a societal level rather than an individual level.

Secondary prevention

Secondary prevention encompasses early detection of the anomaly to allow for more effective treatment and care, including clinical care and support to families. This may be by prenatal or neonatal screening. Termination of pregnancy is not included in the definition of secondary prevention.

Tertiary prevention

Tertiary prevention strategies use medical and surgical interventions that will cure, control or prevent further complications arising from the congenital anomaly.

Methods: the survey

In 2012, a survey on the existence of primary prevention-related policies and public health actions for congenital anomalies in Member States was administered to one respondent in each European Member States, including Northern Ireland, who was asked to gather the information from their country.

In Northern Ireland a scoping exercise was undertaken to identify current policies, guidelines and recommendations. This included reviewing information published on health websites both lay and professional, governmental reports and academic literature. Where information was not readily available local government departments and education/training institutions were contacted for assistance. This included the following: Department of Environmental Heath; HCS Public Health Agency; the Health and Safety Executive Northern Ireland; A representative local council; Toxicology; local University departments and independent bodies responsible for providing education and training to health care professionals in Northern Ireland.

Section one of the questionnaire was designed to obtain an overview of public health actions and guidelines for maternal lifestyle factors. Areas of focus in this section included planning a pregnancy and also the following maternal factors: smoking, alcohol use, obesity, medication use, recreational drug use and exposure to reprotoxic agents used in the home. The second section of the questionnaire covered policies and guidelines on infectious diseases, chronic diseases and medication use in pregnancy. The third section considered policies and guidelines on genetic counselling services that were available, how they were accessed and if they were any initiatives aimed at specific at risk groups. The fourth section enquired about policies and guidelines that informed women and men about the congenital anomaly risks that were posed by environmental and occupational exposure to toxic agents. This included chemicals, chemotherapeutic agents, pesticides, organic solvents, cleaning products, metals, industrial products and radiation. It also considered whether there were identified industrial areas or waste landfills that were considered to be a risk.

Results: Outcome of the Survey

We found that although there are policies and initiatives in relation to a number of relevant risk factors, which we document in detail below, there is no overarching strategy for the prevention of congenital anomalies in Northern Ireland, nor any information source or monitoring of the effectiveness of the variety of guidelines and practices, nor any target relating to prevention of congenital anomalies.

Risk factors associated with maternal lifestyles and nutrition

This section asked about recommendations and guidelines on maternal lifestyles and nutrition (excluding folic acid/folate recommendations). A number of recommendations and guidelines aimed at modifying maternal lifestyles were identified, many of which were applicable to both pregnant

women and/or women planning a pregnancy. Areas of focus in this section included planning for pregnancy and the following maternal factors: smoking, alcohol use, obesity, medication use, recreational drug use and exposure to reprotoxic agents used in the home.

Importance of planning for pregnancy

Within the Strategy for Maternity Care[4] one of the objectives identified for the preconception period is the universal promotion of key public health messages for **ALL** females of childbearing age. This includes advising and supporting prospective parents in the following areas: developing a healthy lifestyle; achieving or maintaining optimal weight status; recognition of the benefits of folic acid; decreasing the risk of infection by promoting immunisation against infectious diseases such as Rubella and by promoting safe sex to prevent infection by hepatitis, HIV and other sexually transmitted diseases. The strategy also recognises that in addition to receiving advice and support those with pre-existing familial and/or clinical conditions should have access to specialist services, and that preconception support should be available to women with prior poor obstetric outcomes and as well as those women with complex social factors.

For women resident in Northern Ireland advice on planning for a pregnancy is widely available on the internet through a number of endorsed and unendorsed websites. For example the NHS Choices website[5] offers general advice for women trying to get pregnant. The Patient.co.uk website has a comprehensive leaflet providing advice and guidance to women who are planning to become pregnant or have just become pregnant[6]. Information includes similar factors identified by the NI maternity strategy. Two of the local Trust websites also provide information on planning a pregnancy for the general public - the Northern Trust[7] and the Southern Trust[8]. The Human Fertilisation and Embryology Centre: Regional Fertility Centre has a web page that offers advice on planning pregnancy on their page "Improve your chances of getting pregnant" and includes advice on smoking cessation, alcohol consumption and obesity[9].

Folic Acid

Folic acid is well established to protect against NTDs such as spina bifida, and possibly a number of other congenital anomalies where evidence remains inconclusive. In the UK, unlike the United States and Australia and a number of other countries, there is no programme of mandatory food fortification with folic acid, and instead women are advised to take folic acid supplements and eat food rich in folates or fortified with folic acid. Research suggests that the majority of women leave it too late to start folic acid supplementation, starting after they find out they are pregnant or have seen a health professional.

Information on folic acid can be found in the Pregnancy Book and in most information materials given to pregnant women. Since the time of the survey, folic acid campaigns have been organised by the GoFolic campaign of the Shine Charity for Spina Bifida and Hydrocephalus (https://www.shinecharity.org.uk/equality/campaigns/gofolic, accessed Feb 2017)[10] and SafeFood

(http://www.safefood.eu/Healthy-Eating/Food,-Diet-and-Health/Life-Stages/Pregnancy/Folic-Acid.aspx, accessed Feb 2017)[11].

Information on the NI government website https://www.nidirect.gov.uk/folic-acid (accessed Feb 2017)[12] advises "An unborn baby's spinal cord develops early, so it's important women take a daily supplement of folic acid when:

- trying to conceive
- likely to conceive
- during the first 12 weeks of pregnancy

….If you are pregnant or planning to become pregnant, take a daily 0.4mg (400 microgram) folic acid supplement until the twelfth week of your pregnancy". The site also specifies folate rich foods. The "preparing for pregnancy" pages of the site advises that a higher dose (5 mg) should be prescribed by the GP if the mother already has a baby with spina bifida, or the mother has coeliac disease, diabetes, obesity, or is taking anti-epileptic medicines. The specific folic acid page advises 0.5 mg in error for women who have a previous child with spina bifida and does not mention other conditions. Recent guidelines released by The Public Health Agency/HSCB NI advises that those women who: have diabetes; are taking ante-epileptic drugs; have a BMI>30; have coeliac disease or thalassaemia should be prescribed the higher dose of 5mg daily from 12 weeks before conception to 12 weeks pregnant http://www.publichealth.hscni.net/publications/folic-acid-and-vitamin-d-guidelines-health-professionals (Accessed 21/02/2017)[13].

Smoking

Smoking has been identified as a risk factor for a number of congenital anomalies including heart defects, musculoskeletal defects, orofacial defects and gastrointestinal defects[14]. Despite the known risks a significant number of women in Northern Ireland are recorded as smoking during pregnancy. A recent report by the Public Health Agency indicated that in 2011 smoking was a maternal risk factor for 16.30% of the births in NI[15]. Information extracted from NIMATS for the period November 2011-November 2012 showing that 15.79% of pregnant women were recorded as smokers at booking, with 26.74% recorded as having partners that smoked Business Services Organisation, personal communication, 28/11/2012) .

Antenatal advice from the National Institute for Health and Clinical Excellence (NICE) recommend that women who are pregnant and are currently smoking should be advised to stop, should offered personalised information and advice on how to stop smoking, and that smoking behaviour should be monitored throughout the pregnancy[16, 17]. The risk of second-hand smoke is also identified. It should be noted that whilst the guidelines identify the risks and benefits to the health of both the mother and unborn child this is not specifically in relation to congenital anomalies.

The Pregnancy Book[18], developed by the Department of Health (with a local version) is a free publication given to all women in the early stages of pregnancy. This guide provides women with information for all stages of pregnancy and recommendations on how to be healthy during pregnancy. The book provides women with a "stop smoking action plan" and specifies that advice and guidance on local smoking cessation services can be sought from their GP; midwife, health visitor, practice nurse or pharmacist.

The statistical bulletin Statistics on Smoking Cessation Services in Northern Ireland: 2008/2009 reported that of the 21,272 people who set a quit date through the smoking cessation services a total of 285 were pregnant. When followed up 4 weeks after setting the quit date, 68% of the 285 women self-reported to have successfully quit[19].

Alcohol consumption

Alcohol use during pregnancy can result in FASD; a condition particularly characterised by neurodevelopmental problems, but also associated with dysmorphic features and some major congenital anomalies. There is evidence that alcohol consumption in the periconceptional period may increase the risk for NTDs, specific types of CHD and orofacial clefts[20]. Alcohol was reported as a maternal risk factor for less than 1% of births that were registered in 2011[15].

Antenatal advice from National Institute for Health & Care Excellence (NICE) advocates that women should avoid alcohol in the first three months in particular, as this could increase the risk of miscarriage[16]. There is also specific guidance for the management of pregnancy in women with complex social factors including alcohol abuse[21]. The Public Health Agency of Northern Ireland recommends that women who are pregnant or planning to become pregnant should avoid alcohol and have published an online resource for guidance[22]. The leaflet, which is embedded with the Agency's general section on alcohol use, informs women of the risk of miscarriage, having a baby with fetal alcohol syndrome (FAS) and of the potential health and learning problems for the baby at birth and beyond.

The Pregnancy Book[18] informs women that they should avoid alcohol, but should they chose to drink that they limit this to 1 to 2 units of alcohol once or twice a week, and that intoxication should be avoided. The Pregnancy Book also identifies the risks of alcohol consumption to the unborn baby with reference to FAS. Guidance on alcohol consumption in social situations is also provided as are sources of help and support. Women are recommended to talk to their doctor, midwife, pharmacist or other healthcare professional.

Note that since January 2016, after the 2012 survey was completed, the UK CMO's have put out new unified guidelines[23]. The report advises that "If you are pregnant or think you could become pregnant, the safest approach is not to drink alcohol at all, to keep risks to your baby to a minimum; Drinking in pregnancy can lead to long-term harm to the baby, with the more you drink the greater the risk; The risk of harm to the baby is likely to be low if you have drunk only small amounts of

alcohol before you knew you were pregnant or during pregnancy; If you find out you are pregnant after you have drunk alcohol during early pregnancy, you should avoid further drinking. You should be aware that it is unlikely in most cases that your baby has been affected. If you are worried about alcohol use during pregnancy do talk to your doctor or midwife."

Maternal weight before and during pregnancy

Maternal obesity has become a major public health concern within the UK, with one in five pregnant women classified as being obese[24]. There is evidence to indicate that maternal obesity increases the risk of having a baby born with congenital anomalies including NTDs, spina bifida (cardiovascular anomalies, septal anomalies cleft palate cleft lip and palate, anorectal atresia, hydrocephaly and limb reduction anomalies[25].

NICE provides guidelines on how to advise women on achieving and maintaining a healthy weight in the preconceptional, prenatal and postnatal stages[26]. "A Fitter Future for All" is a framework for preventing and addressing the public health concern of overweight and obesity in Northern Ireland 2012-2022. This strategy identified that obesity could increase the chances of complications, including fetal abnormalities. The strategy also identifies the importance of the preconceptional stage and recommends that women trying to become pregnant and those that are pregnant should receive information and guidance on nutrition. Those women who are overweight/obese and are pregnant should be given the opportunity to participate in weight management programs that are specific to this stage of life[27]. The Pregnancy Book gives advice on how to eat healthily and that eating too much of certain types of food can lead to weight gain. The book emphasizes the balance between eating healthily and not putting on weight. It advises women that if they are concerned about their weight they should talk to their GP or other health care professional. Women are advised not to diet but to try and stay active by keeping up normal activity or exercise, and also advise that this should be done for as long as they feel comfortable[18].

Drug use (prescribed medications and over the counter medications)

Medication use during pregnancy is common http://www.eurocat-network.eu/preventionandriskfactors/medicationduringpregnancy/medicationintroduction[28]. However, the safety of most medications for use by pregnant women has not been established as pregnant women are not included in clinical trials, and postmarketing surveillance takes time to build evidence, particularly for rare outcomes like specific congenital anomalies. It is a particular concern for women with chronic health conditions where medication is essential to maintain the health of both the mother and the unborn baby. Several types of prescribed medications have been shown to be associated with an increased risk congenital anomalies. The anti-epileptic drug valproic acid is associated with spina bifida and a variety of other malformations[29] and the antiepileptic drug Carbamazepine is also associated with spina bifida but with a lower risk than valproic acid[30]. A number of studies (but not all) show evidence of an association between antidepressant use and the increased risk of congenital anomalies such as congenital heart disease[31]. It is important that

clear advice and guidelines are available for women who are pregnant or planning to become pregnant and those responsible for delivery of care.

There are a number of NICE guideline recommendations on drug use during pregnancy for women with specific chronic illnesses that necessitate the use of medication. NICE provide guidelines to cover a range of conditions including: mental health, Antenatal and postnatal mental health[32] and hypertension[33].

The Pregnancy Book advises women that whilst some medicine can harm their unborn baby, many are safe. Women who are pregnant are advised to always check with their doctor, midwife or pharmacist before taking any medicine, and that all health professionals know that they are pregnant before they prescribe medication or treat them (eg dentist, x-ray). For women with complex health care needs that necessitate the use of medication they are advised to discuss this with their doctor, ideally before they become pregnant or as soon as they find out they are pregnant. Women are advised to limit their use of over the counter medication as much as possible. Information on medicines for minor ailments are provided, with preferred choices and contraindicated medicines identified. Safe medications are identified[18].

Recreational/illicit drug use

There is some evidence to indicate that use of recreational drugs can increase the risk of congenital anomalies including CHD[34] and gastroschisis[35].

The NICE guidelines Pregnancy and complex social factors[21] provide guidance on the management of pregnant women who misuse substances, recommending that women who use recreational drugs need additional care and that women should be provided with information about the potential effects of drug misuse on their unborn baby, which services are available and offered a referral to these services.

The Pregnancy Book advises women that recreational/illicit drugs can harm the baby. Women are advised to speak to their GP or midwife if they use these drugs and are provided with a national helpline number[18].

Correct hygienic behaviour in the home

The consumption and preparation of certain types of foods or contact with animals in the home may increase the risk of harming the health of both the pregnant woman and also the unborn baby. NICE recommend that pregnant women should be supplied with information on food hygiene and how to reduce the risk of infection. It also recommends practicing hygienic behaviours that will help prevent against toxoplasmosis infection which can result in eye and nervous system anomalies in babies. Pregnant women are advised to avoid raw and undercooked meats as well as cat faeces, another source of toxoplasmosis[16]. The Pregnancy Book advises on which types of foods to avoid, eg cheese,

pate and certain types of fish; Women are advised on the preparation of food including the washing of vegetables; all utensils and working area; not to eat raw food and to ensure that all food is thoroughly cooked; and provides guidance on the storage and use of leftover food[18].

Exposures to reprotoxic agents used at home or for hobbies

At the time of the survey there was no available advice and guidance for exposures to reprotoxic agents used at home or for hobbies. Since the survey has been completed the Royal College of Obstetrics and Gynecologists have published a scientific impact paper designed to provide guidance to pregnant and breastfeeding women on the sources and routes of chemical exposures. The paper, which acknowledges that there are NO official antenatal guidelines on chemical exposures, advocates a safety first approach to women whereby they assume that a risk may be present, thus taking a precautionary approach. Advice and information is provided on exposures to chemicals through the consumption of food such as oily fish which may contain heavy metals and fruit and vegetables which may have residual traces of pesticide. The report also highlights that certain materials used to package food and beverages such as plastics and cans may also contain chemicals which could increase the risk of harm. The report also identified personal care products and household chemicals as sources of chemical exposure. Personal care products included "moisturisers, sunscreens, cosmetics, fragrances, shower gels and hairsprays". Household products identified as increasing the risk of chemical exposures included cleaning products, air fresheners, furniture, carpets, fabrics and paint and glue. The report also highlighted the need for caution regarding over the counter medication and herbal remedies as many of these products were coated in substances containing pthalates. Endocrine disrupting chemicals are addressed as needing particular caution[36].

Screening and immunisation for Infectious diseases and chronic diseases

The aim of this section was to assess the availability and implementation of screening and immunisation programmes for Infectious diseases and chronic diseases associated with the risk of congenital anomalies in the PRECONCEPTION and/or PRENATAL period. The section also records details of the presence/absence of systems designed specifically to monitor medication use during pregnancy.

Infectious diseases

A range of infectious diseases contracted by women during pregnancy have been found to increase the risk of congenital anomalies. The survey asked about systematic screening of the following infectious diseases: Toxplasmosis; Rubella; Cytomegalovirus; Syphillis; Varicella-Zoster Virus; Hepatitis B and HIV/AIDS. The following questions on screening and prevention during the PRECONCEPTION (1&2) and PRENATAL (3) stages were asked:

1. Are women planning pregnancy offered laboratory tests to evaluate immunization status for the following infectious diseases: **Toxplasmosis; Rubella; Cytomegalovirus; Syphillis; Varicella-Zoster Virus; Hepatitis B and HIV/AIDS.**
2. Are women planning pregnancy offered immunization/vaccination about the following infectious diseases, as part of preventive care program: **Rubella; Varicella-Zoster Virus; and Hepatitis B**
3. Is the immunization status of non immune pregnant women regularly monitored (eg monthly) during pregnancy for the following infectious diseases: **Toxplasmosis; Rubella; Cytomegalovirus; Syphillis; Varicella-Zoster Virus; Hepatitis B and HIV/AIDS.**

At the time of the survey Northern Ireland did not have a preconception care strategy in place. The NHS choices website informs women that if they are thinking of becoming pregnant and are uncertain of their immunity to rubella those women should ask their GP to check. If they were not immune they would then be offered this vaccine. A local trust page[7] (Accessed 03/10/2013) also advises women if they are planning a pregnancy to talk to their GP about HIV infection or any other sexually transmitted disease. In Northern Ireland there is a universal policy to vaccinate all children with MMR (2 doses) by the age of five years. This includes rubella. Between the years 2001-2011 vaccination coverage (by second dose) for all children under the ages of five years ranged from 84% in the early part of the decade through to 92% in the later years. Whilst the universal programme has the potential to reduce the risk of women developing rubella in their child bearing years it does not cover all women. In particular in recent years there has been an increase in the number of births that have occurred among women who have moved into the province from countries that may not have such a universal vaccination programme. It is important that these women are screened for rubella status if pregnant or planning to become pregnant along with those women born in NI that may be unsure of their status.

The Infectious Diseases in Pregnancy Screening in Northern Ireland performs screening tests at the first ANTENATAL appointment for the following four infections: Rubella; Syphillis; Hepatitis B and HIV/AIDS[37]. If women test positive for the infection it is recommended that they are then referred to specialist services for further assessment[38]. The immunisation status of non-immune pregnant women is not regularly monitored throughout pregnancy unless an infection is suspected. All tests and treatments are free of charge.

The UK National Screening Committee makes recommendations on all aspects of population screening, including infectious diseases in pregnancy – in Feb 2017 these were HIV, Hepatitis and Syphilis. Rubella screening in pregnancy was no longer advised from April 2016[39].

Chronic diseases

Maternal chronic conditions and/or the medications used to treat them may increase the risk of a range of congenital anomalies. In a recently published cohort study the following conditions led to an increased risk of congenital heart disease (CHD) in babies: diabetes; hypertension; thyroid

disorders; maternal CHD; connective tissue disorders; epilepsy and mood disorders[40]. The following questions on screening and care during the PRECONCEPTION (1) and PRENATAL (2) stages were asked.

1. Is there a preconception consultation/visit program to investigate if a woman planning pregnancy has – or is at risk of developing – the following chronic diseases that might affect the pregnancy: Epilepsy/seizures; Diabetes mellitus; Thyroid disorders; Hyperphenyalaninemia (Phenylalanine Hydroxylase Deficiency); Pathologies of malabsorption (colitis ulcerosa; morbus Crohn's; coeliac disease; etc) and Asthma
2. Is there a PRENATAL SPECIAL CARE PROGRAM* for pregnant women suffering from the following diseases illnesses: Epilepsy/seizures; Diabetes mellitus; Thyroid disorders; Hyperphenyalaninemia (Phenylalanine Hydroxylase Deficiency); Pathologies of malabsorption (colitis ulcerosa; morbus Crohn's; celiac disease; etc) and Asthma

It was difficult to access full information on the preconceptional and prenatal care offered to women with chronic diseases, as they tended not to form part of an NI wide recognised programme. At the time of the survey, the seizure clinic at the Belfast Trust offered specialist preconception consultations to NI women with epilepsy but this was not a separate clinic. During 2016, the Public Health Agency has been developing a new programme of pre-pregnancy and prenatal care for women with epilepsy. An EU funded "Coperation and Working Together" programme was developing pre-pregnancy services for women with diabetes (http://www.cawt.com/default.aspx?CATID=4245, accessed Feb 2017)[41] and since the 2012 survey, these services have developed (http://www.publichealth.hscni.net/news/diabetes-services-proving-be-great-success-northern-ireland)[42] and a resource has been made available for women with diabetes (http://www.womenwithdiabetes.net/HealthcareProfessionalWebsite/)[43]. Specialist prenatal care is known to be also available for women with Thyroid disorders and Hyperphenyalaninemia.

Information on and monitoring of medication use during pregnancy

Given the uncertainty surrounding the safety of numerous types of medications during pregnancy (both prescribed and non-prescribed) it is important that clear advice and guidelines on are available for those providing care for pregnant women. The survey asked the following questions:

1. Are there Teratology Information Services (TIS) in your country/region?
2. Is there systematic monitoring available on medication use in pregnancy in your country?

The Regional Medicines and Poisons Information Service is a regional service that is based at the Royal Victoria Hospital. It is described as a pharmacy based service that operates to provide support and information for healthcare professionals who are based in both the community and also in hospitals. If members of the public contact the service then they are referred to their own GP or other health care professional for advice. This service also operates an enquiry answer service for

cases of poisoning including non-medicine poisoning. This includes "household products, petrol or oil products, agricultural, industrial or garden chemicals and plants"[44].

Other sources of information available for health professionals in Northern Ireland include National Poisons Information Service) TOXBASE, the primary clinical toxicology database of the National Poisons Information Service and the United Kingdom Teratology Information Services (UKTIS), a national service that provides information, by telephone, on the toxicity of drugs and chemicals in pregnancy. This system is aligned with TOXBASE, and information is available on the regional variation of pregnancy related calls to the UKTIS[45].

Note that subsequent to the survey in 2012, the UK Teratology Information Service have launched the Best Use of Medicine in Pregnancy (BUMPS) information service (http://www.medicinesinpregnancy.org/) which provides information leaflets for pregnancy on a range of medicines and other services[46].

Currently Northern Ireland does not systematically monitor the use of medication during pregnancy. NIMATS is a system completed by midwives during all stages of pregnancy. During booking appointments women are asked to self-report their present medication use. Data linkage between information systems such as the enhanced prescribing database (EPD) and Northern Ireland Longitudinal Study does provide a methodology by which to assess the prevalence of pregnant women who may be using prescribed medication, and the Honest Broker Service should soon facilitate linkage of the EPD to NIMATS [47]. It is thus feasible for the future to provide routine monitoring of prescription medication in pregnancy.

Genetic risks for congenital anomalies

The survey asked if there were genetic counselling services available in the region and if they were based on national and or regional policies. In Northern Ireland genetic counselling services are available through the Regional Genetic Services. Access to the genetic counselling services, which are not based on national or regional policy, can be accessed through a number of routes.

Environment, home and workplace risks for congenital anomalies

Information in this area was not collected, and it was difficult to identify where the responsibilities lay, for example in relation to pollutant levels and pregnancy.

The Health and Safety Executive are responsible for the workplace and implement the Health and Safety at Work (Northern Ireland) Order 1978. Information for women can be found at https://www.nidirect.gov.uk/articles/working-when-pregnant (Accessed Feb 2017)[48] which states "Some workplace hazards can affect pregnancy at a very early stage or even before conception, so employers must think of the health of women of child bearing age, not just wait until you tell your employer that you're pregnant……Your employer, as part of their normal risk assessment must

consider if any work is likely to present a particular risk to women of child bearing age. You should tell your employer that you are pregnant as early as possible so that they can identify if any further actions are needed. When you tell your employer that you are pregnant your employer should review their risk assessment for your specific work and identify any changes that are necessary to protect you and your unborn baby's health. Your employer should involve you in the process and continue to review the assessment as your pregnancy progresses to see if any adjustments are necessary.

These risks might be caused by:

- lifting or carrying heavy loads
- standing or sitting for long periods
- exposure to toxic substances
- long working hours

Your employer must then either remove the risk or remove you from being exposed to it (for example, by offering you suitable alternative work). If neither of these is possible, your employer should suspend you from work on full pay."

No information was identified regarding the implementation of these health and safety regulations for pregnancy eg the number of women offered alternative work, or the extent to which the provisions for risk assessment of the environment for women of childbearing age are being implemented.

Surveillance and monitoring of the implementation of public health actions and their effectiveness on reducing the risk of congenital anomalies

The last section of the survey asked if information on the risk factors identified within the survey was specifically recorded for congenital anomalies. Northern Ireland, as highlighted in Part 1 of this report, does not have a Congenital Anomaly Register or Surveillance programme.

For example, the effectiveness of policy regarding folic acid supplementation in reducing the prevalence of NTDs is not monitored. Nor are risk factor prevalences in pregnancy monitored, although NIMATS has been trying to improve the collection of information on risk factors such as folic acid and smoking. There is no monitoring of serum folate levels in women of childbearing age, which could be an effective way of assessing the combined effects of folate rich foods, supplementation, and consumption of fortified foods.

Provision of training activities for healthcare professionals and the availability of educational and promotional materials

The survey asked about the provision of training activities for healthcare professionals that would enable them to provide information on the risks associated with chronic and infective maternal

conditions. A number of organisations are responsible for delivering training to healthcare professionals most likely to provide preconception and prenatal healthcare, but an overview of content related to prevention of congenital anomalies could not be provided.

There is a range of educational and/or promotional materials available to inform women, for example the Pregnancy Book[18], but again no overview available of these materials in relation to congenital anomaly prevention.

It is not clear what is taught in the schools curriculum in relation to healthy pregnancy or congenital anomaly prevention. Some material is taught as part of Biology, but not all students take Biology past the age of 14. Key messages, such as the importance of planning a pregnancy and the importance of the very early pregnancy stage to the health of the baby, should be considered as part of the core curriculum.

References 2

1. http://www.eurocat-network.eu/content/Special-Report-Primary-Preventions-of-CA.pdf
2. Taruscio D, Mantovani A, Carbone P, Barisic I, Bianchi F, Garne E, Nelen V, Neville A, Wellesley D and Dolk H (2015). Primary Prevention of Congenital Anomalies: Recommendable, Feasible and Achievable. Public Health Genomics. [Abstract]
3. Taruscio D, Arriola L, Baldi F, Barisic I, Bermejo E, Bianchi F, Calzolari E, Carbone P, Curran R, Garne E, Gatt M, Latos- Bielenska A, Khoshnood B, Irgens L, Mantovani A, Martinez-Frias M-L, Neville A, Rissmann A, Ruggeri S, Wellesley D and Dolk H (2014). European Recommendations for Primary Prevention of Congenital Anomalies: A joined Effort of EUROCAT and EUROPLAN Projects to Facilitate Inclusion of This Topic in the National Rare Diseases Plans. Public Health Genomics. 17: 115-123. [Abstract]
4. https://www.health-ni.gov.uk/sites/default/files/publications/dhssps/maternitystrategy.pdf
5. http://www.nhs.uk/pages/home.aspx (http://www.nhs.uk/pages/home.aspx)
6. http://www.patient.co.uk/health/planning-to-become-pregnant
7. http://www.northerntrust.hscni.net/livewell/1341
8. http://www.southerntrust.hscni.net/pdf/Greatreasonsnottosmokewhenyouarepregnant.pdf
9. http://www.hfea.gov.uk/getting-pregnant.html.
10. https://www.shinecharity.org.uk/equality/campaigns/gofolic
11. http://www.safefood.eu/Healthy-Eating/Food,-Diet-and-Health/Life-Stages/Pregnancy/Folic-Acid.aspx
12. https://www.nidirect.gov.uk/folic-acid (https://www.nidirect.gov.uk/folic-acid)
13. http://www.publichealth.hscni.net/publications/folic-acid-and-vitamin-d-guidelines-health-professionals.
14. Hackshaw A, Rodeck C, Boniface S (2011). Maternal smoking in pregnancy and birth defects: a systematic review based on 173,687 malformed cases and 11.7 million controls. Human Reproduction Update 17(5): 589-604.
15. Children's Health in Northern Ireland. A statistical profile of births using data drawn from the NI Child Health System September 2012.
16. Routine care for the healthy pregnant woman' NICE clinical guideline 62. Available from https://www.nice.org.uk/guidance/cg62 (Accessed 12/12/2012)

17. NICE guidelines Quitting smoking in pregnancy and following childbirth NICE Public Health 26. Available from http://www.nice.org.uk/ph26 (Accessed 12/12/2012)

18. http://www.publichealth.hscni.net/publications/pregnancy-book (Accessed 12/12/2012).

19. Statistical Bulletin PHIRB 4/2009 Statistics on Smoking Cessation Services in Northern Ireland, 2008/09.

20. Grewal J, Carmichael SL, Ma C, Lammer EJ, Shaw GM (2008) Maternal periconceptional smoking and alcohol consumption and risk for select congenital anomalies. Birth Defects Res A Clin Mol Teratol. 2008 Jul;82(7):519-26. doi: 10.1002/bdra.20461.

21. NICE guidelines Pregnancy and complex social factors: A model for service provision for pregnant women with complex social factors NICE clinical guidelines 110. Available from http://publications.nice.org.uk/pregnancy-and-complex-social-factors-cg110 (Accessed 12/12/2012)

22. http://www.knowyourlimits.info/AboutConceptionAndPregnancy.aspx (Accessed 12/12/2012)

23. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/545937/UK_CMOs__report.pdf (Accessed 21/02/2017)

24. Centre for Maternal and Child Enquiries (CMACE). Maternal obesity in the UK: Findings from a national project. London: CMACE, 2010

25. Stothard, KJ Tennant, PWG Bell, Rankin, J (2009) Maternal Overweight and Obesity and the Risk of Congenital Anomalies A Systematic Review and Meta-analysis JAMA, February 11, 2009—Vol 301, No. 6

26. Weight management before, during and after pregnancy NICE Public Health guide guidance 27 . Available from http://publications.nice.org.uk/weight-management-before-during-and-after-pregnancy-ph27 (Accessed 12/12/2012)

27. http://www.dhsspsni.gov.uk/framework-preventing-addressing-overweight-obesity-ni-2012-2022.pdf (Accessed 12/12/2012)

28. http://www.eurocat-network.eu/preventionandriskfactors/medicationduringpregnancy/medicationintroduction.

29. Jentink J, Loane M, Dolk H, Barisic I, Garne E, Morris JK, de Jong-van den Berg, LTW and EUROCAT Antiepileptic Working Group (2010). Valproic acid monotherapy in pregnancy and major congenital malformations. The New England Journal of Medicine 362(23): 2185-2193.

30. Jentink J, Dolk H, Loane M, Morris J, Wellesley D, Garne E, de Jong-van den Berg L and EUROCAT Antiepileptic Study Working Group (2010). Intrauterine exposure to

carbamazepine and specific congenital malformations: systematic review and case-control study. British Medical Journal. 341: C6581.

31. Malm H, Artama M, Gissler M, Ritvanen A (2011). Selective serotonin reuptake inhibitors and risk for major congenital anomalies. Obstet Gynecol, 118(1): 111-20.

32. Antenatal and postnatal mental health: Clinical management and service guidance (CG45). Available from http://www.nice.org.uk/CG45.

33. Hypertension in pregnancy: diagnosis and management. Available from http://www.nice.org.uk/cg107

34. Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, Elixson M, Warnes CA, Webb CL and the American Heart Association Council on Cardiovascular Disease in the Young (2007). Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation, 115 (23): 2995-3014.

35. Draper E, Rankin J, Tonks A, Abrams KR, Field DJ, Clarke M and Kurinczuk J (2008). Recreational drug use: a major risk factor for gastroschisis?. American Journal of Epidemiology. 167: (4). 485-491.

36. Chemical Exposures During Pregnancy: Dealing with Potential, but Unproven, Risks to Child Health Scientific Impact Paper No. 37 May 2013)

37. http://www.dhsspsni.gov.uk/antenatal_leaflet.pdf (accessed 03/10/13)

38. http://infectiousdiseases.screening.nhs.uk/screeningresults (accessed 03/10/13)

39. https://www.gov.uk/guidance/infectious-diseases-in-pregnancy-screening-programme-overview (Accessed Feb 2017)

40. Liu S, Joseph, KS, Lisonkova S, Rouleau J, Van den Hof, M Sauve R, Kramer MS and for the Canadian Perinatal Surveillance System (Public Health Agency of Canada) (2013). Association Between Maternal Chronic Conditions and Congenital Heart Defects Clinical Perspective A Population-Based Cohort Study. Circulation. 2013;128:583-589

41. http://www.cawt.com/default.aspx?CATID=4245 (accessed Feb 2017)

42. http://www.publichealth.hscni.net/news/diabetes-services-proving-be-great-success-northern-ireland (Accessed Feb 2017)

43. http://www.womenwithdiabetes.net/HealthcareProfessionalWebsite

44. http://www.belfasttrust.hscni.net/Pharmacy.htm (Accessed 12/12/2012)

45. http://www.uktis.org/docs/Annual%20Report%20(FINAL%2009-10-2012) (Accessed 19/12/12)

46. http://www.medicinesinpregnancy.org/

47. Wemakor, A, Dolk H, Casson K and de Jong-van den Berg L (2012). Prevalance and patterns of antidepressant use among women of reproductive age in Northern Ireland (NI). Pharmacoepidemiology and Drug Safety. 21: (3). 426 [Abstract]

48. https://www.nidirect.gov.uk/articles/working-when-pregnant (Accessed Feb 2017)

Appendix 1 EUROCAT Subgroup definitions (http://www.eurocat-network.eu/aboutus/datacollection/guidelinesforregistration/guide1_4)

EUROCAT Subgroup	Description	Often diagnosed after one week of age
Nervous System		
Neural Tube Defects:	Neural tube defects inlcude anencephalus, encephalocele, spina bifida and iniencephalus	no
Anencephalus and similar	Total or partial absence of brain tissue and the cranial vault.The face and eyes are present. (incompatible with life)	no
Encephalocele	Cystic expansion of meninges and brain tissue outside the cranium. Covered by normal or atrophic skin.	no
Spina Bifida	Midline defect of the osseous spine usually affecting the posterior arches resulting in a herniation or exposure of the spinal cord and/or meninges	no
Hydrocephaly	Dilatation of ventricular system, not due to primary atrophy of the brain, with or without enlargement of the skull	no
Microcephaly	A reduction in the size of the brain with a skull circumference less than three standard deviations below the mean for sex, age and ethnic origin. Definitions known to vary between clinicians and regions.	yes
Arhinencephaly / holoprosencephaly	Absence of the first cranial (olfactory) nerve tract. There is a spectrum of anomalies from a normal brain, except for the first cranial nerve tract, to a single ventricle (holoprosencephaly)	yes
Eye		
Anophthalmos / microphthalmos	-	
Anophthalmos	Unilateral or bilateral absence of the eye tissue. Clinical diagnosis	no
Microphthalmos	Small eye/eyes with smaller than normal axial length. Clinical diagnosis	yes
Cataract	Alteration in the transparency of the crystalline lens	yes
Congenital glaucoma	Large ocular globe as a result of increased ocular pressure in fetal life	yes
Ear		
Anotia	Absent pinna, with or without atresia of ear canal	no

Congenital heart defects (CHD)		
Severe CHD	13 subgroups of severe CHD as defined below	yes
Common arterial truncus	Presence of a large single arterial vessel at the base of the heart (from which the aortic arch, pulmonary and coronary arteries originate), always accompanied by a large subvulvar septal defect.	yes
Transposition of great vessels, complete	Total separation of circulation with the aorta arising from the right ventricle and the pulmonary artery from the left ventricle	no
Single ventricle	Only one complete ventricle with an inlet valve and an outlet portion even though the outlet valve is atretic	no
VSD	Defect in the ventricular septum	yes
ASD	Defect in the atrial septum	yes
AVSD	Central defect of the cardiac septa and a common atrioventricular valve, includes primum ASD defects	yes
Tetralogy of Fallot	VSD close to the aortic valves, infundibular and pulmonary valve stenosis and over-riding aorta across the VSD	yes
Tricuspid atresia and stenosis	Obstruction of the tricuspid valve and hypoplasia of the right ventricle	no
Ebstein's anomaly	Tricuspid valve displaced with large right atrium and small right ventricle	no
Pulmonary valve stenosis	Obstruction or narrowing of the pulmonary valves which may impair blood flow through the valves	yes
Pulmonary valve atresia	Lack of patency or failure of formation altogether of the pulmonary valve, resulting in obstruction of the blood flow from the right ventricle to the pulmonary artery	no
Aortic valve atresia/stenosis	Occlusion of aortic valve or stenosis of varying degree, often associated with bicuspid valves	yes for stenosis
Hypoplastic left heart	Hypoplasia of the left ventricle, outflow tract and ascending aorta resulting from an obstructive lesion of the left side of the heart	no
Hypoplastic right heart	Hypoplasia of the right ventricle, always associated with other cardiac malformations	no
Coarctation of aorta	Constriction in the region of aorta where the ductus joins aorta	yes
Total anomalous pulmonary venous return	All four pulmonary veins drain to right atrium or one of the venous tributaries	No
PDA as only CHD in term infants	Open duct in infancy or later and requiring invasive treatment	yes
Respiratory		
Choanal atresia	Bony or membraneous choanae with no passage from nose to pharynx	Yes for unilateral
Cystic adenomatous malf of lung	Cystic structures of the lung, usually unilateral	No

Orofacial clefts		
Cleft lip with and without cleft palate	Clefting of the upper lip with or without clefting of the maxillary alveolar process and hard and soft palate	
Cleft palate	Fissure defect of the soft and/or hard palate(s) or submucous cleft without cleft lip	No
Digestive system		
Oesophageal atresia with or without tracheo-oesophageal fistula	Occlusion or narrowing of the oesophagus with or without tracheo-oesophagael fistula	no
Duodenal atresia and stenosis	Occlusion or narrowing of duodenum	no
Atresia and stenosis of other parts of small intestine	Occlusion or narrowing of other parts of small intestine	no
Ano-rectal atresia and stenosis	Imperforate anus or absence or narrowing of the communication canal between the rectum and anus with or without fistula to neighbouring organs	no
Hirschsprung's disease	Absence of the parasympatic ganglion nerve cells (aganglionosis) of the wall of the colon or rectum. May result in cong megacolon	yes
Atresia of bile ducts	Congenital absence of the lumen of the extrahepatic bile ducts	yes
Annular pancreas	pancreas surrounds the duodenum causing stenosis	yes
Diaphragmatic hernia	Defect in the diaphragm with protrusion of abdominal content into the thoracic cavity. Various degree of lung hypoplasia on the affected side	no
Abdominal wall defects		
Gastroschisis	Protrusion of abdominal contents through an abdominal wall defect lateral to an intact umbilical cord and not covered by a membrane	No
Omphalocele	Herniation of abdominal content through the umbilical ring, the contents being covered by a membrane sometimes ruptured at the time of delivery	No
Urinary		
Bilateral renal agenesis including Potter syndrome	Bilateral absence, agenesis, dysplasia or hypoplasia of kidneys including Potter's syndrome. Incompatible with life	no
Renal dysplasia	Maldevelopment of kidney tissue	yes
Congenital hydronephrosis	Obstruction of the urinary flow from kidney to bladder. Only if renal pelvis is 10 mm or more after birth	yes

Bladder extrophy	Defect in the closure of the bladder and lower abdominal wall	no
Posterior urethral valve and/or prune belly	Urethral obstruction with dilatation of bladder and hydronephrosis. In severe cases also distended abdomen	no
Genital		
Hypospadias	The urethral meatus is abnormally located and is displaced proximally on the ventral surface of the penis	Yes
Indeterminate sex	Includes true and pseudohermaphroditism male or female	No
Limb		
Limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the limbs	no
Upper limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the upper limb(s)	no
Lower limb reduction	Total or partial absence or severe hypoplasia of skeletal structure of the lower limb(s)	no
Complete absence of a limb	Complete absence of a limb	no
Club foot - talipes equinovarus	Foot anomaly with equinus of the heel, varus of the hindfoot and adductus of the forefoot	no
Hip dislocation and/or dysplasia	Location of the head of the femur outside its normal position	no
Polydactyly	Extra digit or extra toe	no
Syndactyly	Partial or total webbing between 2 or more digits includes minor forms	yes
Other anomalies / syndromes		
Skeletal dysplasia	A large group of genetic diseases with developmental disorders of chondro-osseous tissue	Yes
Craniosynostosis	Premature closure of cranial sutures	Yes
Congenital constriction bands / Amniotic bands	Bands in the amniotic fluid that causes constriction of part of the brain, body or limbs, including limb-body-wall complex	No
Situs inversus	Inverse position of thoracic or abdominal organs or both	Yes
Conjoined twins	Siamese twins	No
Congenital skin disorders	A group of mainly genetic skin disorders in the newborn	No
Teratogenic syndromes with malformations	Congenital anomalies in pregnancies with known teratogenic exposure	Yes
Fetal alcohol syndrome	Fetal exposure to alcohol during pregnancy with following impact on fetal growth, facial appearance and development	Yes

Valproate syndrome	Fetal exposure to valproate during pregnancy with impact on fetal growth, facial appearance and development. Often associated with spina bifida	Yes
Maternal infections resulting in malformation	Specific maternal viral infections during pregnancy resulting in congenital anomalies in the fetus or infant	Yes
Genetic syndromes and microdeletions	Clinically or genetically diagnosed syndromes with dysmorphic features or congenital anomalies with or without a microdeletion	Yes
Sequences	Pattern of multiple anomalies derived from a single known or presumed prior anomaly or mechanical factor.	No
Chromosomal		
Down syndrome	karyotype 47,XX +21 or 47,XY +21 and translocations/mosaicism	no
Patau syndrome/trisomy 13	karyotype 47,XX +13 or 47,XY +13 and translocations/mosaicism	No
Edwards syndrome/trisomy 18	karyotype 47,XX +18 or 47,XY +18 and translocations/mosaicism	No
Turner syndrome	karyotype 45,X or structural anomalies of X chromosome	Yes
Klinefelter syndrome	karyotype 47,XXY or additional X-chromosomes	yes