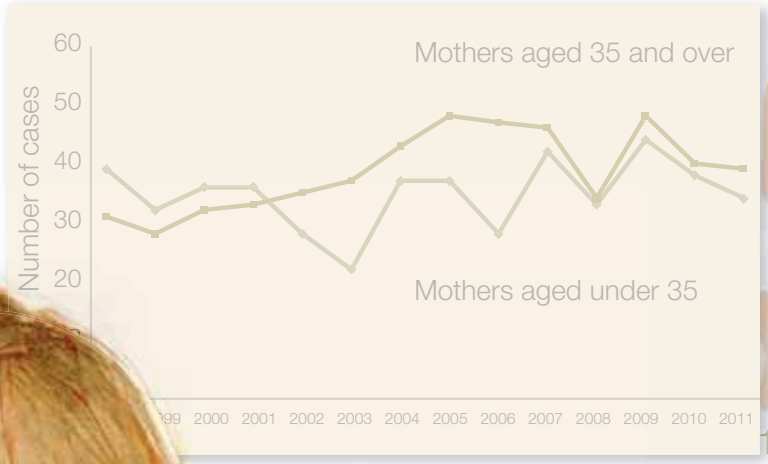
Congenital Anomaly Register & Information Service for Wales

caris review 2012

including data 1998 – 2011



GIG CYMRU NHS WALES

Iechyd Cyhoeddus Cymru
Public Health Wales

Contents

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Published by CARIS ISBN 978-0-9563807-3-9

Data analyses supplied by Public Health Wales Observatory, using CARIS and ADBE (ONS).

DESIGN: www.ridlerwebster.co.uk

Foreword

Welcome to the 2012 CARIS review. Based on data reported for pregnancies ending between 1st January 1998 and 31st December 2011, the review is intended primarily to inform health professionals with an interest in congenital anomalies. It should also be of value to public health professionals, health boards, the Welsh Government and interested lay individuals.

In addition to the annual overview of congenital anomalies in Wales and a summary of CARIS activity over the last year, this year we are focusing on chromosomal trisomies.

Once again we would like to thank all contributing health professionals for their ongoing support. We are very grateful to the following people for their contributions to this report:

- Rosemary Johnson for her article on Down screening (page 15).
- Rhian Hughes, Joanna Arthur, Tracy Price, Lloyd Evans, Bethan Patterson and Dee Hickey from the Public Health Wales Observatory Analytical Team for data analyses.
- Louise Richards from NWIS for additional birth data.
- Bethan Thomson for illustrations.

We always welcome feedback on our reports and our work in general. Please get in touch if you have any questions or suggestions.

Margery Morgan, Lead Clinician

Judith Greenacre, Director of Information

David Tucker, Manager

The CARIS team. We are (left to right) Helen Jenkins, David Tucker, Margery Morgan, Judith Greenacre and Val Vye.

Introduction

CARIS, the Congenital Anomaly Register and Information Service for Wales, aims to provide reliable data on congenital anomalies in Wales. These data are used to assess:

- patterns of anomalies;
- possible clusters of birth defects and their causes;
- antenatal screening and healthcare interventions; and
- health service provision for affected babies and children.

CARIS is part of Public Health Wales within the NHS in Wales. It is based at Singleton Hospital, Swansea.

As part of an agreement between Public Health Wales and the Welsh Government, CARIS produces a review every year which includes:

- an overview of congenital anomalies in Wales;
- a summary of CARIS activity during the previous year; and
- special reports with a detailed focus on specific anomalies.

This year the review covers data on pregnancies ending from 1998 to 2011, activity over the year 2011 and special reports with a detailed focus on chromosomal trisomies: Down syndrome (trisomy 21), Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13).

These anomalies are also being featured in the 2012 annual meetings.

Appendix A includes a list of the special reports published by CARIS in previous reviews.

More detailed information and data tables are available from the CARIS websites

www.wales.nhs.uk/caris (internet) and

www.howis.wales.nhs.uk/caris (intranet).

Overview of Congenital anomalies in Wales 1998 – 2011

For the years 1998 to 2011 there were 23,691 cases of congenital anomalies reported to CARIS (20,374 live born) against a background of 466,475 total (live and still) births in Wales.

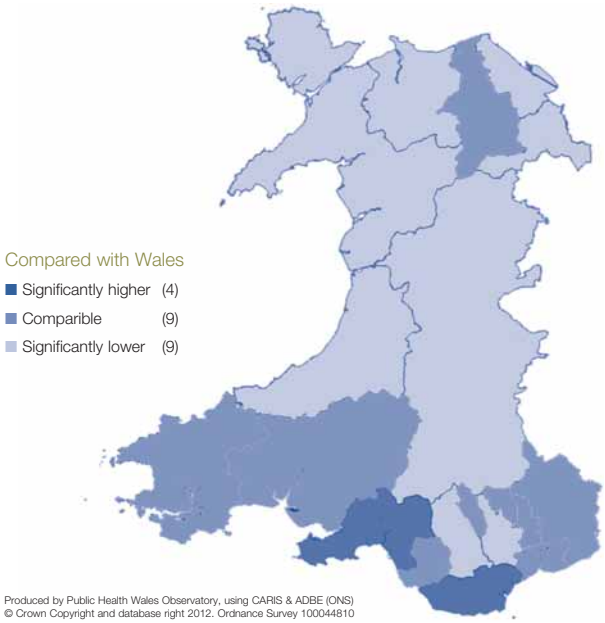
Patterns and clusters of anomalies

- The gross rate[1] of congenital anomalies reported is 5.1%.
- The rate of congenital anomalies in live born babies is 4.4%.
- 86% of cases are live born and 97% of these survive to the end of the first year. Survival is reduced with increasing complexity of anomalies.
- 60.6% of cases involve a single congenital anomaly. A further 10.7% of cases are associated with an underlying chromosome disorder.
- The above rates remain essentially unchanged from previous reviews.
- Congenital anomaly rates in Wales are often apparently higher than for other areas of Europe or Britain.
- Variations in rates are again seen around Wales (Figure 1). In part this is due to differences in reporting and CARIS continues to keep the situation under review. With improved reporting in South East Wales, previous lower rates of anomalies in Merthyr Tydfil and Newport Unitary Authority areas have increased to be comparable with Wales as a whole.
- Some specific anomalies continue to be monitored because of previously high rates in Wales. These include gastroschisis and isolated cleft palate. Further data collected since last year have not identified any change to previous patterns for these anomalies.
- Factors that affect anomaly rates include maternal risk factors such as age and smoking. There is also an association with socioeconomic deprivation, particularly for non chromosomal anomalies.
- Heart and circulatory defects are the largest single group reported, followed by anomalies of the limbs, musculoskeletal and the urinary system.
- For anomalies detected up to the first birthday, approximately one third of cases are detected antenatally, one third within the first week after the end of pregnancy and the remaining third later in infancy.
- Further study of trisomies 21, 18 and 13 this year has identified:
  - more babies with Down syndrome are now born to mothers aged 35 and over (page 11)
  - a gradual fall in rates of Patau syndrome (Trisomy 13) among mothers aged 35 years and over
  - the previous rise in prevalence of Edwards syndrome between 2000 and 2005 has not been sustained in following years, (the reasons for these changes are not clear).

Interventions and services for anomalies

- Rates of antenatal detection continue to improve in Wales, particularly for heart defects.
- Population level antenatal detection rates for Trisomies 21, 18 and 13 are 62%, 86% and 83% respectively. These rates are based on data for the years 1998 to 2011 and include all babies with these conditions, including those whose mothers were not offered formal screening in the past as well as those who preferred not to undergo screening.

Figure 1 Gross case rate per 10,000 total births based on data 1998 to 2012; Wales local authorities



1 The gross rate is the total number of cases of anomaly (regardless of whether the pregnancy ended in miscarriage, termination of pregnancy, live or still birth) divided by the total number of live and stillbirths.

TABLE 1: CARIS rates for some key anomalies 1998 – 2011

ANOMALY	ALL CASES		LIVEBORN CASES		PROPORTION
	Total number of cases	Rate per 10,000 total births	Number of liveborn cases	Rate per 10,000 live births	% cases liveborn
ALL CASES OF ANOMALY	23,691	507.9	20,374	439.0	86%
All neural tube defects	751	16.1	111	2.4	15%
Anencephaly	298	6.4	6	0.1	2%
Spina bifida	360	7.7	83	1.8	23%
Encephalocele	104	2.2	24	0.5	23%
Hydrocephaly	423	9.1	209	4.5	49%
Cataracts	193	4.1	193	4.2	100%
Sensorineural deafness	595	12.8	595	12.8	100%
Congenital cystic adenomatoid malformation of lung	83	1.8	75	1.6	90%
All cardiovascular	6,247	133.9	5,495	118.4	88%
Severe cardiac anomalies	1,393	29.9	1,065	22.9	76%
Hypoplastic left heart syndrome	149	3.2	69	1.5	46%
Transposition of great vessels	184	3.9	146	3.1	79%
Ventricular septal defects	2,426	52.0	2,231	48.1	92%
Cleft lip with / without cleft palate	526	11.3	422	9.1	80%
Isolated cleft palate	463	9.9	383	8.3	83%
Hypospadias	1,312	28.1	1,306	28.1	100%
Multicystic kidney	299	6.4	217	4.7	73%
Bilateral renal agenesis	71	1.5	3	0.1	4%
Gastroschisis	275	5.9	240	5.2	87%
Diaphragmatic hernia	186	4.0	128	2.8	69%
Craniosynostosis	295	6.3	275	5.9	93%
Limb reduction defects	462	9.9	281	6.1	61%
Dislocation / dyplasia of hip	974	20.9	968	20.9	99%
Cystic fibrosis	215	4.6	208	4.5	97%
Congenital hypothyroidism	289	6.2	289	6.2	100%
All chromosomal disorders	2,531	54.3	1,269	27.3	50%
Trisomy 21 (Down syndrome)	1,027	22.0	480	10.3	47%
Trisomy 18 (Edwards syndrome)	272	5.8	51	1.1	19%
45 X, (Turner syndrome)	191	4.1	50	1.1	26%

CARIS activity 2011

CARIS held annual meetings at the Princess of Wales Hospital, Bridgend and Wrexham Maelor Hospital, Wrexham in November. The focus was on respiratory anomalies and anomalies of the cardiac outflow tract. More than 170 people attended these meetings.

CARIS continued to contribute to the British Isles Network of Congenital Anomaly Registers (BINOCAR). The first annual BINOCAR report combining data from England and Wales was published in December.[2] The report illustrated the benefit of collaborative working, and allows direct comparison between participating English regions and Wales.

EUROMedicat, a collaborative three year project led by EUROCAT (European Surveillance of Congenital Anomalies), began data collection. This involves CARIS and Swansea University. The project will study possible associations between prescription drugs taken during the 1st trimester and congenital anomalies. In addition to anonymised CARIS data, Swansea University will link data to GP prescriptions through the Secure Anonymised Information Linkage (SAIL).

The EUROCAT coding and classification committee began work advising the World Health Organisation (WHO) and Orphanet on the development of ICD11. This new coding system will replace ICD10. David Tucker is a member of the committee. This is an important task as it will set the framework for the coding of congenital anomalies in the future. The aim is to have a new classification ready for use in 2015.

The annual EUROCAT[3] registers' leaders meeting was held in Antwerp. New European Union (EU) funded work packages were presented and discussed. There was an update on EU rare diseases programme. Approximately 80% of rare diseases are found in children under the age of 5 years (most of them congenital).

Margery Morgan attended the International Clearing House[4] meeting in Geneva.

Publications and presentations

Posters presented at EUROCAT meeting, Antwerp, June 2011.

Association between raised Alpha Feto Protein (AFP) and congenital anomalies
Khan Z, Morgan M, Tucker D

Outcome of prenatal diagnosis of hypoplastic left heart syndrome in South Wales over a seven year period
Sinha A, Gopalakrishnan P N, Tucker D, Uzun O

Oral presentations: International Clearing House, Geneva, September 2011

Antenatally diagnosed nuchal transluscency and cystic hygroma – outcomes of live born infants
Goel N, Matthes J, Morgan M, Tucker D

Congenital anomalies profile in assisted conception vs. natural pregnancies
Younas K, Morgan M, Tucker D

Publications

Alessandra Lisi memorial prize for the best published paper using congenital anomaly register data – September 2011.

Outcome of fetuses with Turner syndrome: a 10 year congenital anomaly register based study Iyer N, Tucker D, Roberts S, Moselhi M, Morgan M Matthes M.

The Journal of Maternal-Fetal and Neonatal Medicine 2011

DOI: 10.3109/14767058.2011.564688

Drug safety in pregnancy - monitoring congenital anomalies.

Morgan M, De Jong-Van Den Berg L Jordan S Journal of Nursing Management, 2011, 19, 305–310

Additional publications in 2011 using CARIS data are given in Appendix B.

2 The Binocar report is available at http://www.binocar.org/Publications/Reports

3 www.eurocat-network.eu

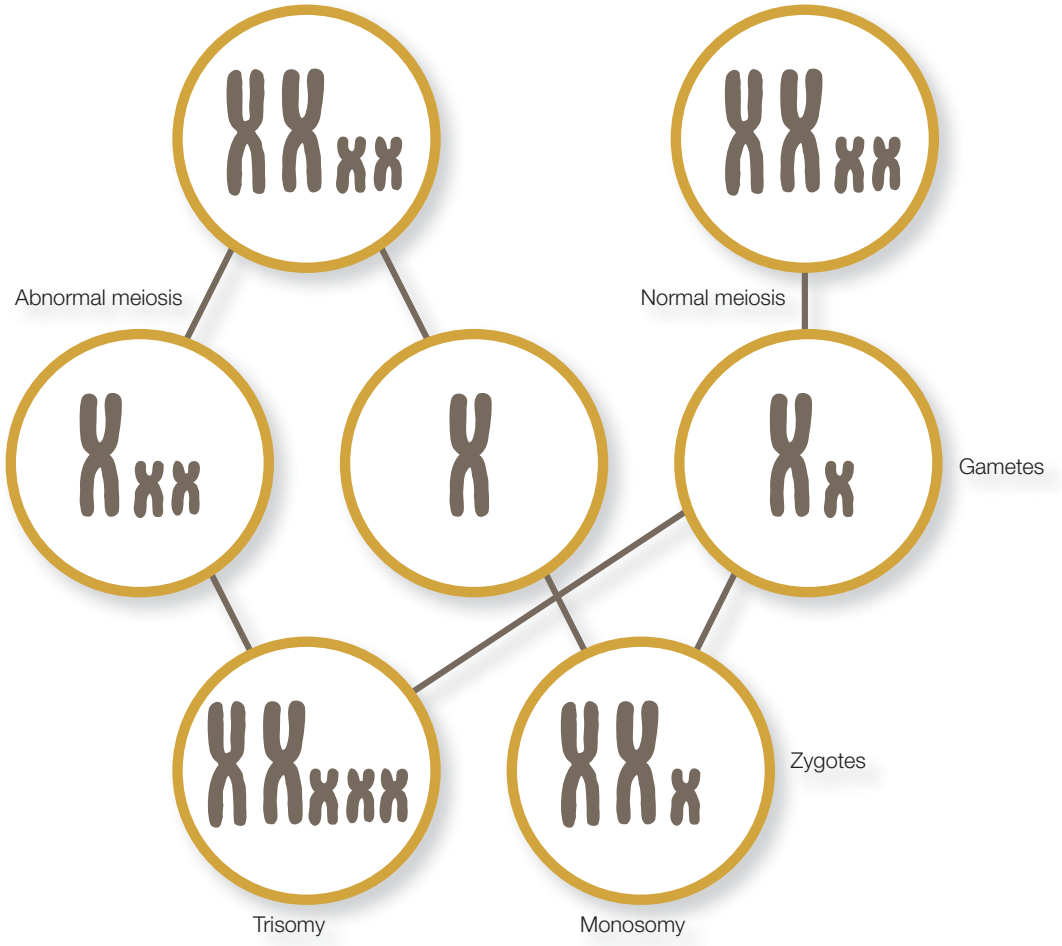
4 www.icbdsr.org

SPECIAL REPORTS:
Chromosomal trisomies

Introduction to trisomies[5,6]

A human normally has 46 chromosomes organized into 23 pairs (22 autosomal pairs and 1 pair of sex chromosomes). Meiosis is the process of cell division that is required to produce a gamete (egg or sperm) with only 23 chromosomes present. During this process genetic diversity is created through exchange of genetic material between homologous chromosomes and separation of chromosome pairs. When an egg is fertilized by a sperm to create a zygote, new pairs of chromosomes are formed in which each parent has contributed one chromosome to each pair. The random alignment of maternal and paternal chromosomes increases genetic variation. Sometimes an error in meiosis called non-disjunction occurs when there is failure of the parental chromosome pairs to separate, leading to an imbalance of chromosomes in the gamete (aneuploidy). A cell that has 'lost' a chromosome is called a monosomy and most monosomies are lethal (with the exception of Turner's syndrome, which is monosomic for the X or female chromosome). A cell with an extra chromosome is referred to as a trisomy. When fertilization occurs, the resultant zygote has 47 chromosomes instead of the usual 46, with three copies of a particular chromosome instead of the usual pair. These processes are illustrated in Figure 2.

Figure 2: Meiosis resulting in trisomy



5 Chromosome Abnormalities and Genetic Counselling, 2012 McKinlay Gardner et al, 4th edition, Oxford University Press

6 Core Concepts: Chromosome Aneuploidies, Neoreviews 2012;13;e30

Trisomies are the most common anomaly of chromosome number. Trisomy of any chromosome can occur (see Box 1 on page 19) but many trisomies are lethal and are rarely detected in established pregnancies. Trisomy 21 (Down syndrome) is the most common aneuploidy detected in established pregnancies, followed by trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome). Numbers and rates for these trisomies reported to CARIS are shown in Table 2.

The pregnancy outcome for trisomies reported to CARIS (1998 to 2011) is illustrated in Figure 3. All trisomies have high natural fetal loss rates and it has been estimated that more than 50% of embryos with a trisomy miscarry early[7]. Figure 3 shows that the greatest losses in established pregnancies are as a result of termination of pregnancy, associated with antenatal detection of anomalies. The percentage of fetuses live born with Down syndrome was 47%; the percentages for Edwards syndrome and Patau syndrome were 19% and 15% respectively.

The prevalence of trisomies rises with increasing maternal age (Figure 4) and this is the over-riding known risk factor for these anomalies.

Until the end of the 20th century, although prevalence rates for trisomies were higher among older mothers, the higher pregnancy rates among younger women meant that the actual number of pregnancies affected by trisomies was greater among younger mothers. With increasing pregnancy rates among older mothers this pattern has now changed with more affected pregnancies occurring among older mothers. These changes are illustrated in the sections on individual trisomies.

Table 2 Cases, proportions and rates of trisomies per 10,000 total births, Wales, 1998-2011

	Cases	% of chromosomal anomalies	% of all anomalies	Rate per 10,000 births
T21 (Down syndrome)	1,027	40.6	4.3	22.0
T18 (Edwards syndrome)	272	10.7	1.1	5.8
T13 (Patau syndrome)	113	4.5	0.5	2.4
Other trisomies	18	0.7	0.1	0.4
All chromosomal anomalies	2,531	-	10.7	54.3
All anomalies	23,691	-	-	507.9

Produced by Public Health Wales Observatory, using CARIS & ADBE (ONS)

Figure 3: Trisomy 21, 18 and 13 by outcome of pregnancy, numbers and proportions, Wales, 1998-2011

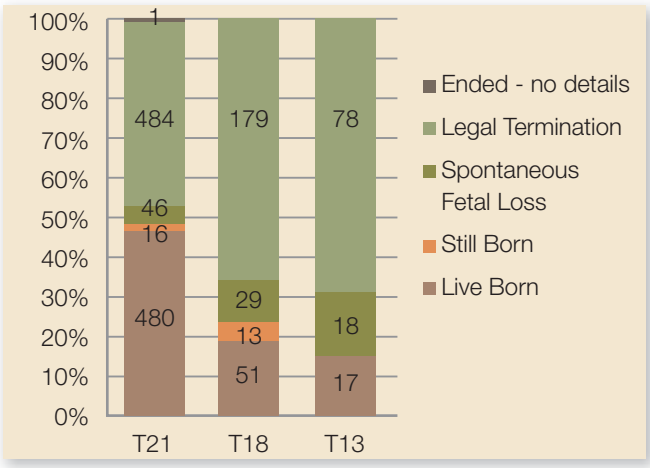
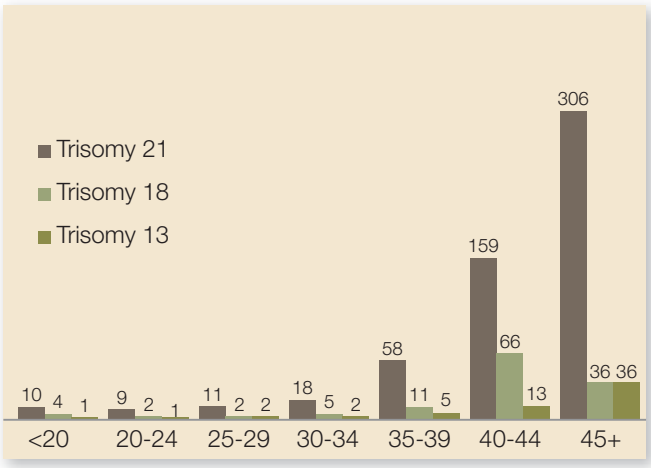


Figure 4: Trisomy 21, 18 and 13, rate per 10,000 total births by maternal age group, Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS)

7 The Developing Human, 9th edition, 2013, Elsevier

SPECIAL REPORTS:
Chromosomal trisomies

Reviews undertaken for the common autosomal trisomies have identifed some common features:[8]

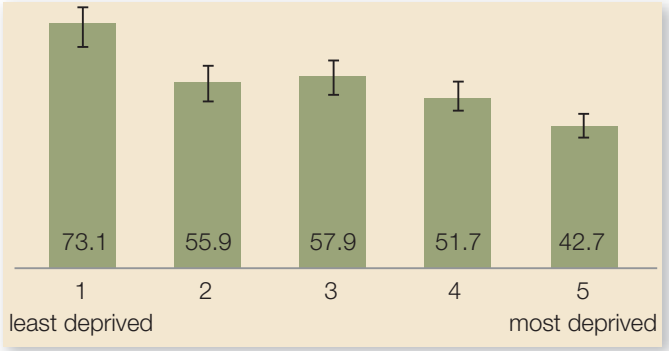
- Different approaches to prenatal testing, termination of pregnancy, registration and data collection can make detailed study of the epidemiology of trisomies difficult.
- Ionizing radiation is the only environmental risk factor to show non-dysjunction in experimental animals. In studies following significant human exposure to radiation (Hiroshima, Nagasaki; Chernobyl), results are inconsistent regarding increased prevalence of trisomies, often because of a lack of good quality baseline data as well as issues above.
- Advancing paternal age has been implicated as a risk factor for all three common trisomies although the effect appears small[9]. Again, evidence is inconsistent and is often confounded by associated increased maternal age.
- Crude rates suggest chromosomal anomalies (including trisomies) are more common among babies born to mothers living in more affluent socioeconomic areas. This is again related to maternal age as mothers in more affluent areas tend to delay childbearing until later years. If rates are adjusted for maternal age, the association with increasing affluence is greatly reduced. This is illustrated in Figure 5a & 5b.

EUROCAT publishes data from congenital anomaly registries across Europe, allowing comparisons to be made with regional registries and against European averages. Average data for full EUROCAT member registries and Wales are given in Table 3 (2006 to 2010).[10]

These suggest that figures for Wales are comparable to European average rates, although rates for trisomy 13 are slightly lower. However, comparisons have to be treated with caution. EUROCAT does not adjust for factors such as maternal age or national policies on termination of pregnancy.

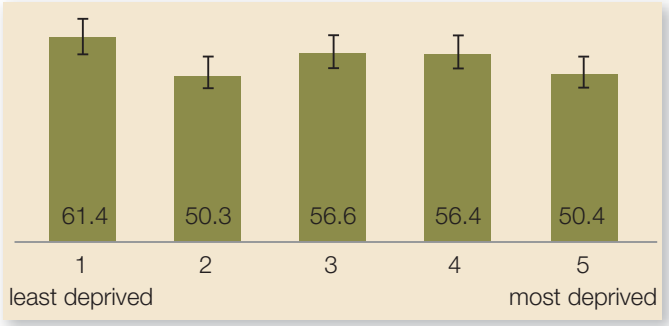
Figure 5 Chromosomal anomalies by Welsh Index of Multiple Deprivation fifth

a) Crude rate per 10,000 births by WIMD fifth, Wales 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS) & WIMD 2011 (WG)

b) Age-standardised rate per 10,000 births by WIMD fifth, Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS) & WIMD

Table 3 Comparison of EUROCAT rates for Wales and Europe for Trisomies 21, 18 & 13: 2006 to 2010

Rates per 10000 births 2006 to 2010	EUROCAT (all full member registries)		EUROCAT data for Wales (from CARIS)	
	All*	Live births	All*	Live births
Down syndrome (T21)	21.38	9.79	21.43	10.60
Edwards syndrome (T18)	5.11	0.84	5.87	1.20
Patau syndrome (T13)	2.09	0.17	1.77	0.40

*live births, fetal losses and terminations for congenital anomaly

8 State of Texas DSHS. Birth defects risk factor series. Accessed from www//dshs.state.tx.us/birthdefects/risk (September 2012)
9 De Sousa E, Morris JK. (2010) *Case-control analysis of paternal age and trisomic anomalies.* Archives of disease in childhood, 95 (11), 893-897.
10 Available from EUROCAT website various tables accessed at www.eurocat-network.eu (September 2012)

TRISOMY 21
Down syndrome

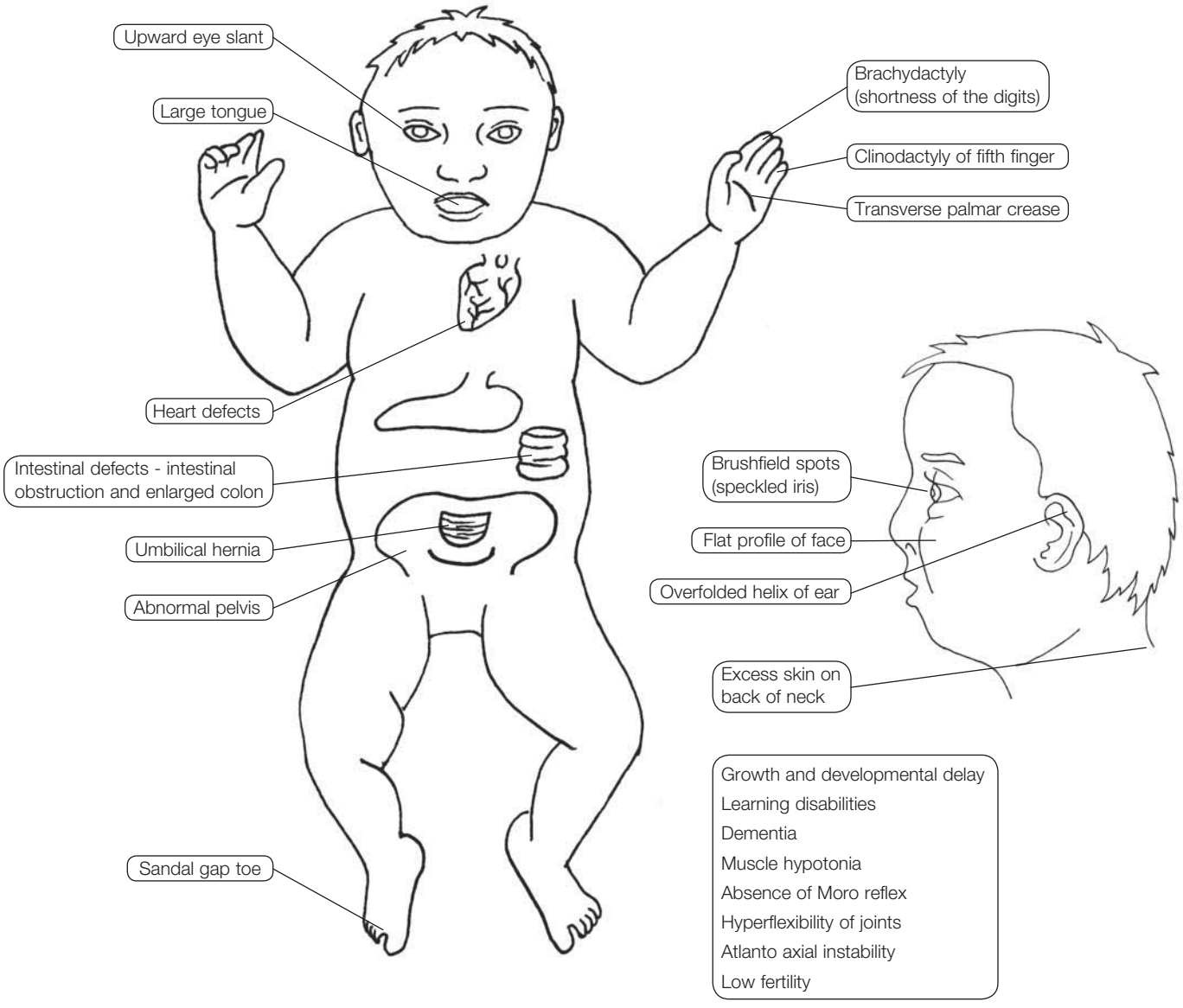
Definition and natural history

Trisomy 21 was first described by John Langdon Down in 1866. He described a group of children with similar features that were distinct from other children with mental impairment. In 1959 Jerome Lejeune and Patricia Jacobs, working independently, determined the cause to be a trisomy of chromosome 21. The presence of this additional part or whole of chromosome 21, normally originates from the mother.

Most Down syndrome (90%) are due to simple trisomy with the presence of an extra chromosome. A small proportion can be due to a Robertsonian translocation in which the additional chromosomal material is attached to one of the usual chromosome pairs. This condition may then be inherited and suggests the need for parental genetic studies.

Physical features vary between individuals with trisomy 21. Such features were important before the advent of cytogenetics as they were pointers to the diagnosis (Figure 6).

Figure 6: key features of trisomy 21 / Down syndrome



TRISOMY 21
Down syndrome

Affected babies are often small for gestational age. All babies show delayed development and subsequent moderate to severe learning disability so that children and adults with Down syndrome require lifetime support (this is the most common genetic cause of learning disabilities in children).

Children with Down syndrome tend to have frequent colds and ear infections, as well as bronchitis and pneumonia (some prevention is possible through routine childhood immunisations). Up to 1% of children with Down syndrome develop leukaemia, often successfully treated with chemotherapy. Adult females can have fertility problems although pregnancies are known. Adult males are usually infertile.

As individuals with Down syndrome are surviving longer, it is becoming apparent that the trisomy is associated with increased frequency and earlier onset of Alzheimer's disease, characterized by progressive loss of memory, cognitive function and by personality changes.

Despite all these challenges, with more active management of the complications the long term outlook for a baby with Down syndrome has greatly improved both in terms of survival and in quality of life and achievement.

CARIS has reports of 481 live born babies with Down syndrome (1998 to 2011), of which 467 have survived to the end of the first year of life. Thirty four babies died in infancy, giving a 1 year survival rate of 93%.

A five year survival rate of 86% has also been estimated, based on data up to 2006. Nine deaths occurred among 263 children between their first and fifth birthdays. Loss to follow up of children moving outside Wales is difficult to assess but could affect quoted survival rates.

Life expectancy for adults with Down syndrome has improved so that many now live into their sixties. Survival appears poorer for those babies with additional anomalies (particularly cardiac) and low birth weight. Poorer survival in the USA has also been found in Afro-Caribbean groups[11].

The Public Health Wales Observatory is currently working in collaboration with Swansea University and Cardiff University to study in greater detail what happens to live born babies with Down Syndrome in Wales. Swansea University has developed the Secure Anonymised Information Linkage (SAIL) system that collects and links anonymised data from a number of sources. These can then be used by researchers to investigate the population's contact with the NHS, social care, education system and other areas. Within this Cardiff University has created the Welsh Electronic Cohort of Children (WECC), which collects data on children born in Wales. By using these sources it is hoped to report in greater detail on the survival of those born with Down Syndrome and the impact on survival of additional major anomalies. Further analyses on educational attainment and health service usage are also planned.

Epidemiology, trends and risk factors

Down syndrome is the most common chromosomal anomaly. Over one thousand cases have been reported to CARIS (1998 to 2011). The overall gross prevalence of 22 per 10,000 births suggests that around 1 in 450 fetuses coming to the attention of maternity services during this time have been affected by this trisomy. Maternal age related rates are given in Table 4 for 1998 to 2010. The overall recurrence risk of Down syndrome is estimated at about 1% following an affected pregnancy.

Table 4: Maternal age related rates per 10,000 total births and frequency of babies affected by Down syndrome; CARIS data, 1998-2011

Maternal age group (yrs)	Number of cases	Gross rate	Frequency based on CARIS gross rates
<20	42	9.8	1 in 1024
20 to 24	91	8.8	1 in 1133
25 to 29	136	10.5	1 in 949
30 to 34	217	18.1	1 in 551
35 to 39	343	57.9	1 in 173
40 to 44	181	158.6	1 in 63
45+	17	306.3	1 in 33
<35	486	12.3	1 in 812
35+	541	132	1 in 132

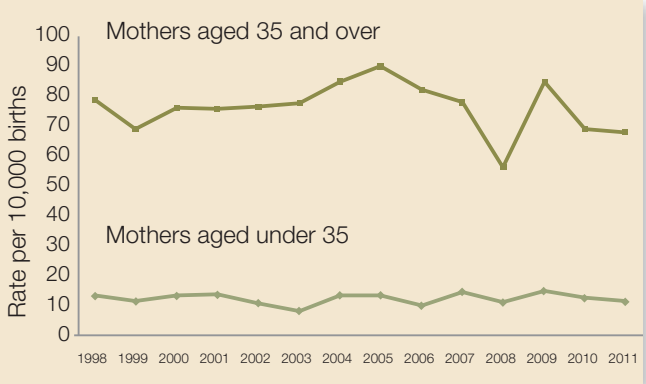
Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS)

Down syndrome rates for the babies of mothers under 35 years and 35 years and above have remained fairly constant over the years of CARIS data collection (Figure 7a). There is however a general upward trend in the actual number of babies reported to CARIS, particularly for older

11 State of Texas DSHS. Birth defects risk factor series. Accessed from www//dshs.state.tx.us/birthdefects/risk (September 2012)

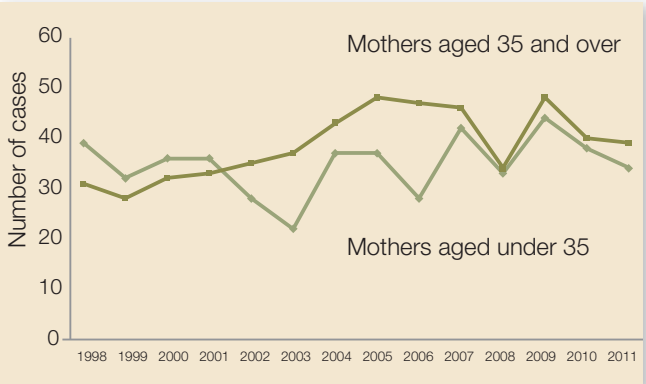
mothers (Figure 7b). This is due to increasing pregnancy rates in this maternal age group. From 2002, there have been more babies with Down syndrome born to older mothers than younger mothers, despite younger mothers having much higher pregnancy rates. Apart from the general risk factors already discussed for trisomies, there are no confirmed additional specific risk factors for Down syndrome.

Figure 7a: Down syndrome cases by maternal age, rate per 10,000 births, Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS)

Figure 7b: Down syndrome cases by maternal age, number of cases, Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS

Antenatal findings

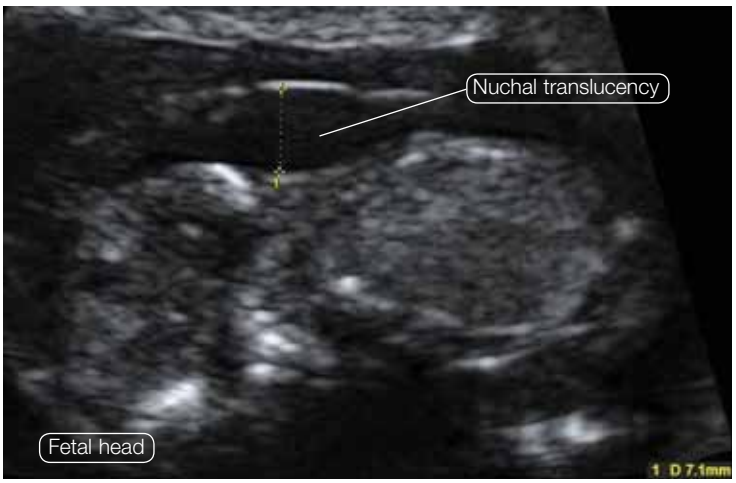
This can be a difficult chromosomal anomaly to detect on ultrasound. As a result, serum screening has developed to aid antenatal diagnosis.

Increased nuchal translucency (how much the skin of the neck is separated from the underlying tissue by fluid – see Figure 8) and an absent nasal bone are the most useful findings in the first trimester scan. Abnormal ductus venosus flow and tricuspid regurgitation have also been reported.

Atrioventricular septal defects and an increased nuchal fold are key findings of Down syndrome in the 20 week anomaly scan. Duodenal atresia is rare but also strongly suggestive of the trisomy.

From CARIS data 62% of fetuses with Down syndrome were detected antenatally (1998-2011). This includes all mothers regardless of whether they took up antenatal testing. These rates may rise now that Down syndrome screening is offered routinely to all mothers across Wales. One third of cases were detected at birth or within the first year of life and 4% were detected later in infancy or childhood.

Figure 8: Antenatal ultrasound scan showing nuchal translucency



TRISOMY 21
Down syndrome

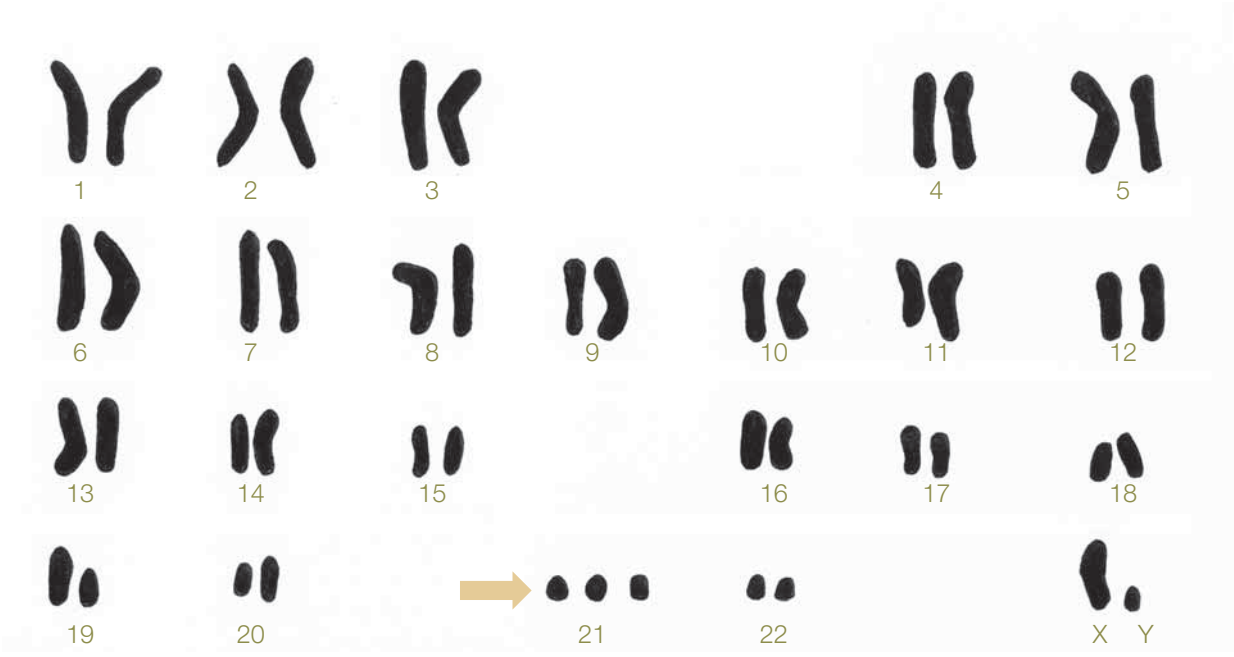
Associated anomalies

Down syndrome can be associated with additional congenital anomalies although the severity and extent is very variable[12]. Significant associated anomalies include the following:

- **Heart defects:** These are extremely common among babies with Down syndrome and CARIS records cardiac anomalies (excluding minor septal defects) in over two thirds of cases. It is recommended that all babies with trisomy 21 should be assessed for these conditions.
- **Intestinal defects:** Those requiring surgery are reported to occur in about 12% of babies with Down syndrome. CARIS reports intestinal anomalies in 10% of live born cases but the number requiring surgery is not always clear. Duodenal atresia is a well known but very rare complication.
- **Other physical defects:** These include cleft lip with or without cleft palate, and polydactyly. Instability of the atlanto-axial joint occurs in approximately 15% of people with Down syndrome and may lead to spinal cord compression. Some anomalies are less common e.g. neural tube defects.
- **Vision problems:** More than 60% of children with Down syndrome have vision problems and should have their vision tested regularly.
- **Hearing loss:** About three quarters of children with Down syndrome have some form of hearing loss, highlighting the importance of newborn screening and regular hearing tests. CARIS reports sensori-neural hearing loss in 3.3% of cases but the frequency of conductive hearing loss is not known as this information is not routinely collected.
- **Hypothyroidism:** About 1% of babies with Down syndrome are born with congenital hypothyroidism which, if untreated, can affect growth and brain development. Congenital hypothyroidism can be detected with routine newborn screening tests and treated with oral doses of thyroid hormone. Children with Down syndrome are also at increased risk of acquiring thyroid problems and should be tested annually for this condition. CARIS reports about 7% of live born babies with Down syndrome having either congenital or acquired hypothyroidism.

It is not possible to determine an accurate prevalence of these anomalies as affected pregnancies may be terminated without recording associated anomalies or reporting them to CARIS.

Trisomy 21 karyotype



12 Centers for Disease Control and Prevention (CDC). Down Syndrome. www.cdc.gov Accessed September 2012

New thoughts on screening

by Rosemary Johnson, All Wales Screening Coordinator, Public Health Wales

There are a number of different antenatal screening tests for Down syndrome, all of which give a risk based on maternal age and adjusted for the individual pregnancy. The detection rate of potential cases is up to 90% for some tests. The risk calculation is complex and involves a number of maternal factors and fetal measurements from an ultrasound scan. The result is calculated by the laboratory and expressed as a risk ratio, for example 1 in 500.

The Down syndrome screening test currently offered in Wales is the quadruple test.
The current uptake of screening is about 50% and the detection rate is around 75% of cases. The screening test requires an ultrasound scan in early pregnancy and a blood test taken at 15-18 weeks of pregnancy. The biochemical markers AFP (alphafetoprotein, hCG (human chorionic gonadotrophin), uE3 (unconjugated oestriol) and Inhibin A are assessed. If the risk of an affected pregnancy is greater than 1 in150 (occurs in about 3 to 4% of pregnancies), the result is described as 'screen positive' and the woman will be offered a diagnostic test (amniocentesis).

Following recommendations from the UK National Screening Committee[13], the Minister has asked that first trimester screening for Down syndrome screening be introduced in Wales. This test uses a measurement of the nuchal translucency (NT) and crown rump length (CRL) obtained on the early pregnancy scan (between 11 and 14 weeks) and a blood test for free beta hCG and PAPP-A (pregnancy associated protein A). It is anticipated that this test will have a higher detection rate (up to 90%) and a lower screen positive rate. As with the quadruple test, if a woman has a chance of Down syndrome of more than 1 in 150, she will be offered a diagnostic test. A formal project has been established by Antenatal Screening Wales to coordinate implementation.

A number of activities have formed part of the project, including a training needs analysis developed to inform the project about health professionals' knowledge of Down syndrome and antenatal screening. The questionnaire included questions about people living with Down syndrome, knowledge of the combined and quadruple test and knowledge of invasive procedures. The responses from 320 health professionals involved in the antenatal screening programme indicated that they had a good level of knowledge about the current screening programme but were less well informed about the long term issues that affect people living with Down syndrome. The review has informed the development of an e-learning resource, which will support the implementation of combined screening and the provision of information to women to support informed decision making.

The project has also undertaken an audit of 84 cases of Down syndrome identified by CARIS (from Jan 2010 to March 2011). The aim of the audit was to establish the current situation prior to the implementation of first trimester Down syndrome screening, with particular regard to the diagnostic pathway and decisions made by women. A data collection proforma was developed by Antenatal Screening Wales. The proforma was coded by CARIS to ensure anonymity and sent to the screening coordinator for completion.
The completed proforma were returned to Antenatal Screening Wales for analysis.
The return rate was 86% (72/84).

The audit demonstrated the complexity of the antenatal screening pathway. The potential that the pregnancy is affected by Down syndrome can be raised by early pregnancy scan findings, result of the Down syndrome screening programme and by the fetal anomaly scan. The audit showed that women were provided with information, advice and counselling when a diagnostic test was offered. The audit indicated that when offered, the uptake of invasive testing was around 50%, irrespective of whether the indication for offering the invasive test was following a Down syndrome screening result or an ultrasound finding.

Looking to the future, it is possible that screening for more major and minor fetal anomalies in the first trimester will be considered by ultrasound and serum screening. The possibilities of measuring cell free fetal DNA in a sample of maternal blood to aid diagnosis as well as cell free fetal RNA to analyse fetal gene expression are now being explored[14].

13 UK NSC Policy recommendations 2007-2010: Model of Best Practice
14 First Trimester Screening for Aneuploidy Neoreviews 2012;13;e4 Trisomy 18 and Trisomy 13: Treatment and Management Decisions. T. Allen Merritt, Anita Catlin, Charlotte Wool, Ricardo Peverini, Mitchell Goldstein, Bryan Oshiro. Neoreviews 2012;13;e40

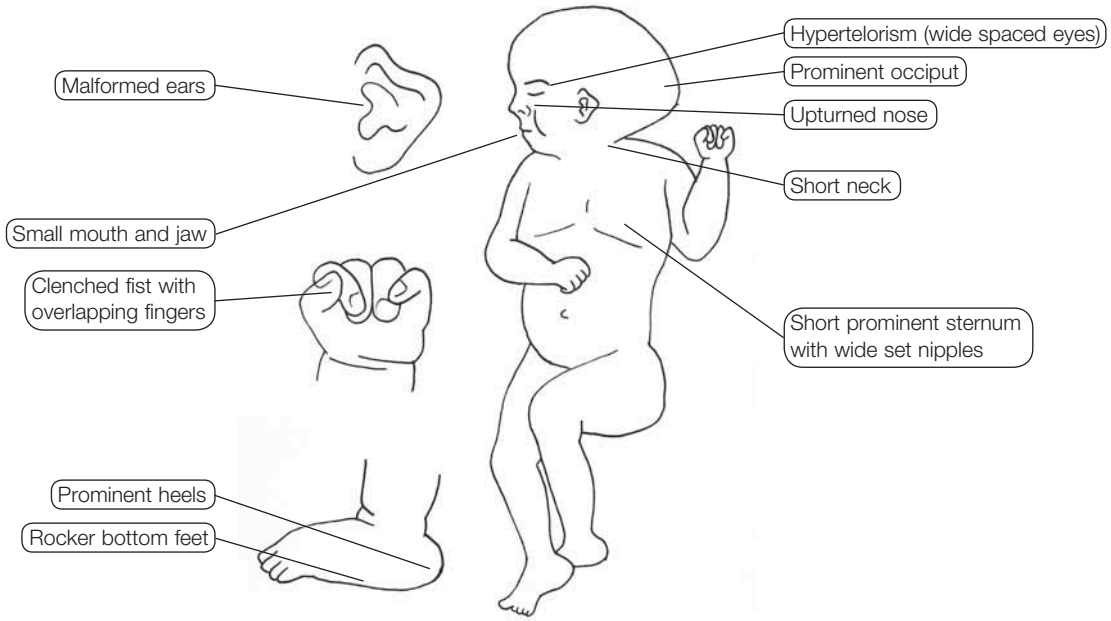
TRISOMY 18
Edwards syndrome

Definition, natural history and findings

This trisomy occurs with an extra chromosome 18 and is the second most common trisomy. This syndrome was first described in 1960 by John H Edwards[13]. The non disjunction error at meiosis is thought to be maternal in 90% of cases. Genetic support should be arranged when the diagnosis of trisomy 18 is made.

If an antenatal diagnosis has not been made, suspicion at birth will be raised by the presence of typical features of the condition, including low birth weight, microcephaly, short sternum and narrow pelvis. The face is characteristic with a small jaw (micrognathia) and low set malformed ears. There are flexed digits with overlapping fingers, hypoplastic nails and rocker bottom feet (Figure 9).

Figure 9: typical features of trisomy 18 / Edwards syndrome



Trisomy 18 karyotype

13 Edwards J H, Harnden DG, Cameron AH, Crosse VM, Wolff OH: *A new trisomic syndrome.* The Lancet, London, 1960, 1: 787-790

The outlook is poor as the baby is often affected by multiple anomalies. Most babies who survive to term only live for a few weeks. Less than one in ten survive the first year of life although some have survived considerably longer. Survivors have significant feeding difficulties, growth and developmental delays and marked intellectual impairment.

CARIS has data on 51 babies with Edwards syndrome who were live born. Of these, 46 died during infancy, suggesting a 1 year survival rate of 9.8%. So far, only three cases have survived to the age of five (2 translocations and 1 mosaic).

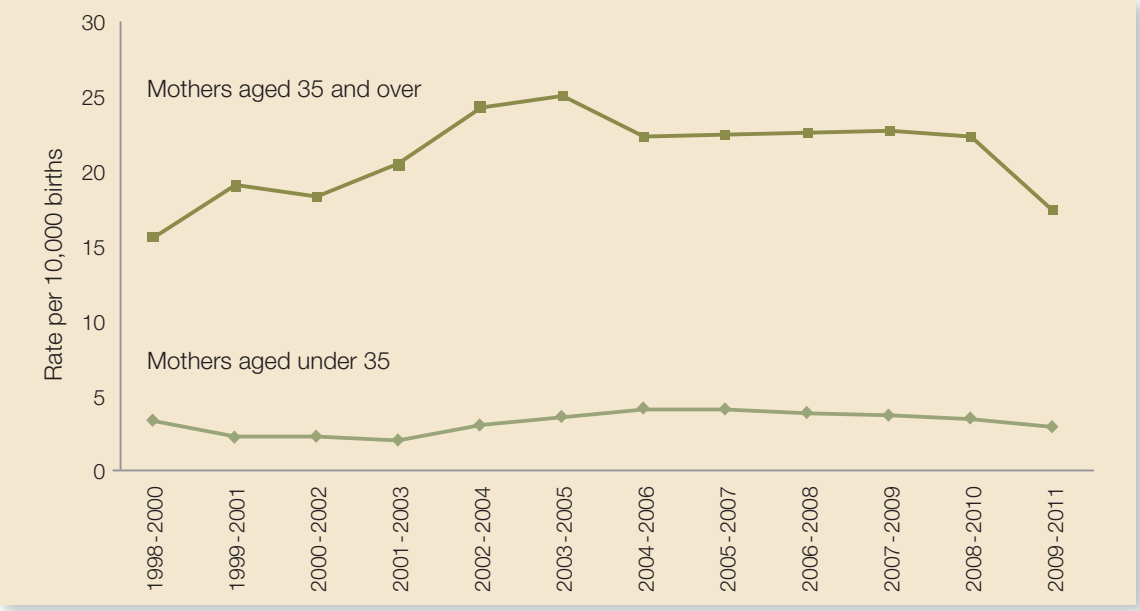
Perinatal palliative care is a concept designed to help families with making choices about pregnancy management, birth decisions and end of life care for babies with this condition. Paediatric involvement in the antenatal period is important for those parents who choose to continue the pregnancy and consensus is important when deciding the intensity of medical interventions to be given.

Epidemiology, trends and risk factors

Edwards syndrome is much less common than Down syndrome. For Wales the overall gross prevalence of 5.8 per 10,000 births, suggests that about 1 in 1700 fetuses coming to the attention of maternity services have been affected by this trisomy. Rates for Wales are comparable to those for Europe. Females are thought to be affected more frequently than males.

As for other trisomies there is a strong association with increasing maternal age. Recent work by EUROCAT has suggested an upward trend in prevalence for several European countries that cannot be explained by maternal age factors alone. This upward trend also occurred in Wales during 2000 to 2005 particularly among older mothers but has not been sustained in recent years (Figure 10). CARIS will continue to keep the situation under review. The State of Texas[14] review of risk factors for Edwards syndrome found no clear association with other risk factors independent of maternal age, including ethnicity, lifestyle or environmental factors. As for Down syndrome, the overall recurrence risk is estimated at about 1% following an affected pregnancy. Potential associations have been suggested with urban living and assisted reproductive technology but these associations are not proven and are complicated by problems of case ascertainment and the confounding effect of maternal age.

Figure 10: Edwards syndrome cases by maternal age, 3-year rolling rates per 10,000 births, Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS)

14 State of Texas DSHS. Birth defects risk factor series. Accessed from www//dshs.state.tx.us/birthdefects/risk (September 2012)

TRISOMY 18
Edwards syndrome

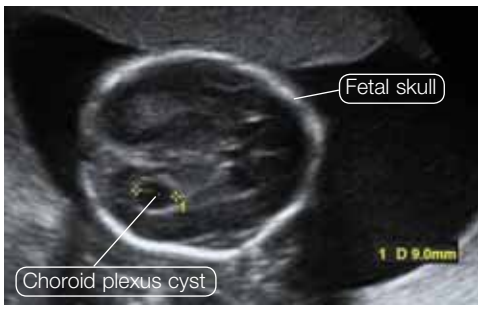
Antenatal findings

Trisomy 18 is usually suspected antenatally because of the multiple associated anomalies detectable through antenatal ultrasound.

Ultrasound Findings (in order of frequency)

- Flexed/Overlapping fingers
- Septal defects
- Micrognathia
- Growth restriction
- Strawberry skull
- Low set ears
- Choroid plexus cysts (Figure 11)
- Renal anomalies
- Exomphalos
- Diaphragmatic hernia

Figure 11: Antenatal ultrasound scan showing a choroid plexus cyst



If a fetus has multiple anomalies an amniocentesis will be offered to confirm the karyotype. If trisomy 18 is not diagnosed until the third trimester the ultrasound appearance may be that of growth restriction with associated polyhydramnios.

Women carrying a fetus affected by trisomy 18 often have altered serum markers of AFP (alphafetoprotein, hCG (human chorionic gonadotrophin) and oestriol. These findings are not yet sufficiently constant to act as a screening test but are similar to the marker pattern used in screening for trisomy 21. Some cases of Edwards syndrome are picked up through karyotyping following a positive serum screening test for Down syndrome.

CARIS data suggest that 86% of cases were diagnosed antenatally and only about 10% of babies were diagnosed at birth or later. The remainder are accounted for by spontaneous fetal loss.

Associated anomalies

Significant additional anomalies associated with trisomy 18 include:

- **Central nervous system:** holoprosencephaly (failure of the forebrain to divide properly); neural tube defects
- **Facial clefting:** cleft lip and / or cleft palate
- **Heart defects:** septal or outflow cardiac defects.
- **Urogenital defects:** horseshoe kidney, hydronephrosis

Babies with Trisomy 18 should have an echocardiogram and abdominal ultrasound to assess cardiac and renal/genital anomalies.

Among babies reported to CARIS with Edwards syndrome, there were a variety of renal defects, notably 21 cases with horseshoe kidneys, 20 cases of facial clefting and 2 babies with holoprosencephaly. The prevalence of these anomalies is difficult to determine as affected pregnancies may be terminated without reporting associated anomalies to CARIS.

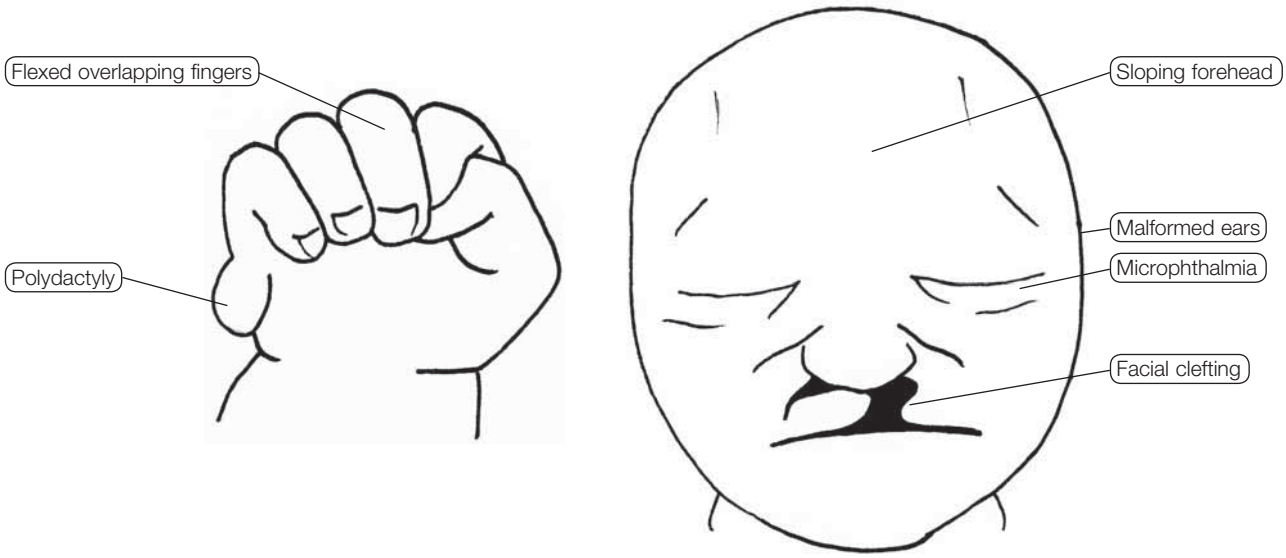
TRISOMY 13
Patau syndrome

Definition, natural history and findings

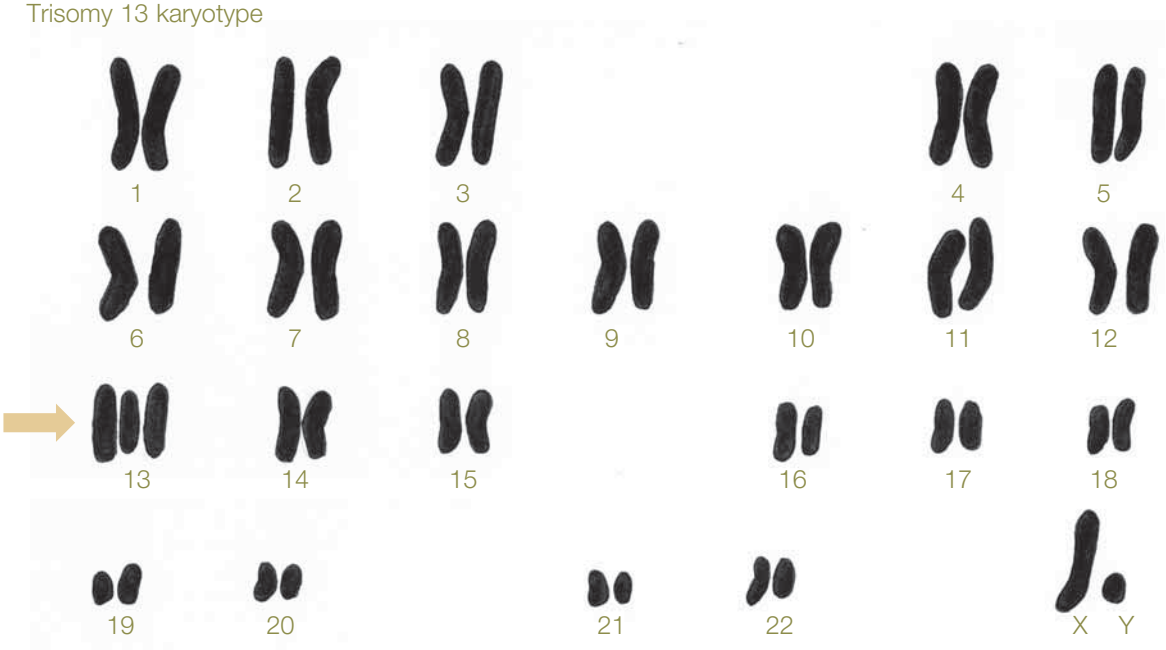
This syndrome was first observed by Thomas Bartholin in 1657. It wasn't until 1960 that Klaus Patau[15] discovered that the chromosomal basis of the disease was caused by trisomy of chromosome 13. This occurs at meiosis. The additional chromosome 13 derives from the mother in 90% of cases. One in five cases have a Robertsonian translocation. As this can be inherited, parental studies are important to look for a balanced translocation. If this is the case then there would be an increased recurrence risk with future pregnancies. Otherwise the recurrence risk following an affected pregnancy is less than 1%.

Patau syndrome is commonly associated with typical physical features and serious additional anomalies. Typical features of Patau's syndrome are illustrated in Figure 12 and include low set malformed ears, sloping forehead, microphthalmia, scalp defects (cutis aplasia), foot deformities and polydactyly. A single umbilical artery is often present. The presence of these and the associated serious anomalies, holoprosencephaly, orofacial clefting, congenital heart defects, renal anomalies, exomphalos and cutis aplasia should raise a suspicion of trisomy 13.

Figure 12: typical features of trisomy 13/Patau's syndrome



Trisomy 13 karyotype



15 Patau K, Smith DW, Therman E, Inhorn SL, Wagner HP: *Multiple congenital anomaly caused by an extra autosome.* The Lancet, 1960 1 : 790-3

TRISOMY 13
Patau syndrome

In CARIS cases 69% of the 113 reported cases resulted in termination of the pregnancy and a further 16% were spontaneous fetal losses. Only 17 cases (15%) were live born.

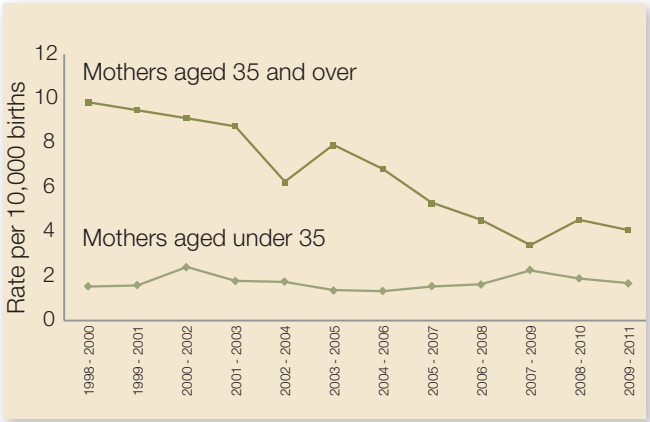
The outcome is poor and CARIS data gives a one year survival rate among live born babies of 29% (5 of 17 live born cases survived infancy). Survival has been reported to childhood and late teens and this is also supported by CARIS data.

Survivors with trisomy 13 have significant intellectual disability requiring extensive support. Decisions about investigation and treatment are made carefully and involve parents at every stage.

Epidemiology, trends and risk factors

Patau syndrome is less common than Down and Edwards syndrome. For Wales the overall gross prevalence of 2.4 per 10,000 births (Table 2) suggests that around 1 in 4200 fetuses coming to the attention of maternity services have been affected by this trisomy. Rates for Wales are slightly lower than those for Europe. In contrast to Edwards syndrome, males are thought to be affected more frequently than females. As is the case for other trisomies, there is a strong association with increasing maternal age, although Welsh data shows the gross rate is falling among mothers aged 35 years and over (Figure13). The reasons for this trend are not clear. No other risk factors have been clearly linked independently to this condition.

Figure 13: Patau syndrome cases by maternal age, 3-year rolling rates per 10,000 births,Wales, 1998-2011



Produced by Public Health Wales Observatory, using CARIS & NCCHD (NWIS)

Antenatal findings

There is no clear association between maternal serum markers and Patau syndrome. Antenatal detection depends mainly on relatively straightforward antenatal ultrasound detection of typical features and associated anomalies (see below). As with trisomy 18, growth restriction and polyhydramnios are common.

CARIS data show antenatal detection of the trisomy in 83% of cases with a diagnosis at birth of only 5.3%.

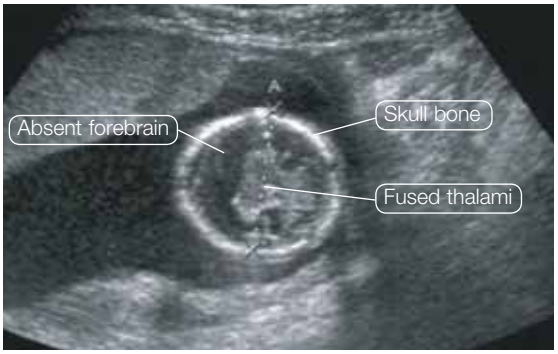
Associated anomalies

- **Central nervous system:** microcephaly; holoprosencephaly (Figure 14); neural tube defects
- **Facial clefting:** cleft lip and / or cleft palate
- **Eye defects:** microphthalmia, cataract, coloboma, retinal dysplasia or retinal detachment, sensory nystagmus, cortical visual loss, and optic nerve hypoplasia
- **Heart defects:** ventricular septal defects, hypoplastic left heart
- **Urogenital defects:** abnormal genitalia; kidney defects
- **Other anomalies:** exomphalos

Following confirmation of the diagnosis at birth, investigation in terms of echocardiogram and renal ultrasound are usually done. A referral to a geneticist is also made for the parents.

CARIS reporting includes cleft lip and or palate in 43% of cases of trisomy 13 and holoprosencephaly in 17%.

Figure 14: Antenatal ultrasound showing holoprosencephaly



Other trisomies and mosaics

Trisomies account for about 60% of all cytogenetic abnormalities identified in spontaneous fetal losses. The most commonly seen abnormal karyotypes at the time of miscarriage are trisomy 16, monosomy X and triploidy.

Box 1: Trisomies[16]

Trisomy 1	almost unknown in an established pregnancy
Trisomy 2	rare and lethal, observed as an acardiac fetus in monozygous twins
Trisomy 3	extremely rare, acardiac fetus in monozygous twins
Trisomy 4	very rare finding as a mosaic at CVS or amniocentesis
Trisomy 5	rare and only recorded as mosaic
Trisomy 6	rare and again only recorded as mosaic, with a benign outcome
Trisomy 7 & 8	survival reported in literature, few reports only
Trisomy 9	survival reported with heart and central nervous system anomalies
Trisomy 10	survival only seen in mosaics and with multiple anomalies
Trisomy 11	survival only seen in mosaics with a benign outcome
Trisomy 12	one of the most frequently described mosaics who have a variable outcome
Trisomy 13	Patau syndrome
Trisomy 14	rare reports of survival
Trisomy 15	only seen as mosaic with poor outcome
Trisomy 16	associated with spontaneous fetal loss, and could account for 1% of all conceptions. Mosaics have a high risk of poor outcome including fetal growth restriction and an association with maternal pre eclampsia
Trisomy 17	thought to be lethal early in pregnancy, mosaics have variable outcome with a higher risk of cerebellar malformations
Trisomy 18	Edwards syndrome
Trisomy 19	very rare, only one case reported in literature (normal live birth)
Trisomy 20	rare with poor outcome, a common mosaic seen at amniocentesis with variable outcome
Trisomy 21	Down syndrome
Trisomy 22	associated with high beta HCG levels in 1st trimester and later fetal growth restriction, this trisomy has a chance of term pregnancy with limited survival. Mosaics have a high risk of anomalies

16 Chromosome Abnormalities and Genetic Counselling, 2012 McKinlay Gardner et al, 4th edition, Oxford University Press

Other trisomies and mosaics

Triploidy

This is a rare condition where a baby has three full haploid sets of chromosomes. This means that the karyotype will show 69 chromosomes with XXX, XXY or XYY sex chromosome complements. There are usually significant anomalies with growth restriction, hypotonia, hydrops, poly or oligo hydramnios and multiple congenital anomalies.

True triploidy is a lethal condition but life expectancy may be longer if there is a diploid (normal)/triploid mosaicism.

CARIS has reports of 90 cases of triploidy and a further 5 cases of other forms of polyploidy. The outcome for polyploidy cases reported to CARIS confirms the lethal nature of this condition.

Mosaicism

If a chromosome pair fails to separate (nondisjunction) during an early division of the zygote, an embryo can be produced with two or more cell lines, each with different chromosome complements. Individuals with these differing numbers of chromosomes are called mosaics. So a mosaic with trisomy 21 could have been produced at an early stage – a zygote may have an additional chromosome 21 which is then lost with further division, meaning that some cells of the embryo have a normal chromosome complement and others have the additional chromosome 21. The earlier in embryogenesis that an error occurs in cell division the greater likelihood the embryo has a significant proportion of the abnormal cell line meaning an increased risk for problems in the fetus.

Those who are mosaic for a given trisomy are usually less severely affected than those with the non-mosaic condition.

Antenatal cytogenetic testing is done using chorionic villi and amniocytes obtained at CVS or amniocentesis.

The mosaic form of Down syndrome is thought to account for about 2% of all cases diagnosed. In Wales 14 cases (1.4%) have been reported to CARIS.

APPENDIX A:
Previous CARIS reports

Subject of special reports	Report year	Data
Neural tube defects Gastroschisis	1999	1998

Cleft lip & palate Down syndrome update	2000	1998-1999
Antenatal detection Limb reduction defects	2001	1998-2000

Congenital heart disease Trisomies 13 & 18	2002	1998-2001
Update on clefts Sex chromosome anomalies	2003	1998-2002

Urinary tract anomalies Update on gastroschisis	2004	1998-2003
Congenital causes of intestinal obstruction Congenital defects of the diaphragm and abdominal wall	2005	1998-2004

Neural tube defects Disorders of the central nervous system	2006	1998-2005
Congenital anomalies – causes and mechanisms Risk factors for congenital anomalies	2007	1998-2006

Antenatal detection Screening services in Wales	2008	1998-2007
Skeletal anomalies NHS fetal anomaly screening programme	2009	1998-2008

Eye anomalies Facial anomalies	2010	1998-2009
Respiratory anomalies Anomalies of the cardiac outflow vessels	2011	1998-2010

APPENDIX B: Additional publications in 2011 using CARIS data

- Prevalence at birth of cleft lip with or without cleft palate: Data from the International Perinatal Database of Typical Oral Clefts (IPDTOC). Cleft Palate Craniofac J. 2011 Jan;48(1):66-81
- Botto L, Feldkamp M, Amar E, Carey J, Castilla E, Clementi M, Cocchi G, de Walle H, Halliday J, Leoncini E, Li Z, Lowry B, Marengo L, Martinez-Frias M-L, Merlob P, Morgan M, Luna-Munoz L, Rissmann A, Ritvanen A, Scarano G and Mastroiacovo P (2011). Acardia: Epidemiologic findings and literature review from the International Clearinghouse for Birth Defects Surveillance and Research. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: (262). 273.
- Boyd P, Barisic I, Haeusler M, Loane M, Garne E and Dolk H (2011). Paper 1: The EUROCAT network: organization and processes. Birth Defects Research (Part A). 91: 2-15.
- Boyd P, Haeusler M and Barisic I (2011). EUROCAT Report 9: Surveillance of congenital anomalies in Europe 1980-2008. *Birth Defects Research (Part A).* 91: S1.
- Boyd P, Loane M, Garne E, Khoshnood B, Dolk H and EUROCAT Working Group (2011). Sex chromosome trisomies in Europe: prevalence, prenatal detection and outcome of pregnancy. *European Journal of Human Genetics.* 19: 231-234.
- EUROCAT (2011). EUROCAT Report 9. *Birth Defects Research Part A Clinical and Molecular Teratology.* 91: (S1). S1-S100.
- Feldkamp M, Botto L, Amar E, Bakker M, Bermejo E, Bianca S, Canfield M, Castilla E, Clementi M, Csaky-Szunyogh M, Leoncini E, Li Z, Lowry B, Mastroiacovo P, Merlob P, Morgan M, Mutchinick O, Rissmann A, Ritvanen A, Siffel C and Carey J (2011). Cloacal exstrophy: An epidemiologic study from the International Clearinghouse for Birth Defects Surveillance and Research. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: 333-343.
- Greenlees R, Neville A, Addor M-C, Amar E, Arriola L, Bakker M, Boyd P, Calzolari E, Doray B, Draper E, Vollset S E, Garne E, Gatt M, Haeusler M, Kallen K, Khoshnood B, Latos- Bielenska A, Martinez-Frias M-L, Materna-Kiryluk A, Dias C M, McDonnell R, Mullaney C, Nelen V, O'Mahony M, Pierini A, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rankin J, Rissmann A, Ritvanen A, Salvador J, Sipek A, Tucker D, Verellen-Dumoulin C, Wellesley D and Wertelecki W (2011). Paper 6: EUROCAT member registries: organization and activities. *Birth Defects Research (Part A).* 91: S51-S100.
- Mutchinick O, Luna-Munoz L, Amar E, Bakker M, Clementi M, Cocchi G, Da Graca Dutra M, Feldkamp M, Landau D, Leoncini E, Li Z, Lowry B, Marengo L, Martinez-Frias M-L, Mastroiacovo P, Metneki J, Morgan M, Pierini A, Rissmann A, Ritvanen A, Scarano G, Siffel C, Szabova E and Arteaga-Vazquez J (2011). Conjoined twins: A worldwide collaborative epidemiologic study of the International Clearinghouse for Birth Defects Surveillance and Research. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: 274-287.
- Orioli I, Amar E, Arteaga-Vazquez J, Bakker M, Bianca S, Botto L, Clementi M, Correa A, Csaky-Szunyogh M, Leoncini E, Li Z, Lopez-Camelo J, Lowry B, Marengo L, Martinez-Frias M-L, Mastroiacovo P, Morgan M, Pierini A, Ritvanen A, Scarano G, Szabova E and Castilla E (2011). Sirenomelia: An epidemiologic study in a large dataset from the International Clearinghouse for Birth Defects Surveillance and Research, and literature review. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: 358-373.
- Orioli I, Amar E, Bakker M, Bermejo E, Bianchi F, Canfield M, Clementi M, Correa A, Csaky-Szunyogh M, Feldkamp M, Landau D, Leoncini E, Li Z, Lowry B, Mastroiacovo P, Morgan M, Mutchinick O, Rissmann A, Ritvanen A, Scarano G, Szabova E and Castilla E (2011). Cyclopia: A epidemiologic study in a large dataset from the International Clearinghouse of Birth Defects Surveillance and Research. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: 344-357.
- Siffel C, Correa A, Amar E, Bakker M, Bermejo E, Bianca S, Castilla E, Clementi M, Cocchi G, Csaky-Szunyogh M, Feldkamp M, Landau D, Leoncini E, Li Z, Lowry B, Marengo L, Mastroiacovo P, Morgan M, Mutchinick O, Pierini A, Rissmann A, Ritvanen A, Scarano G, Szabova E and Olney R (2011). Bladder Exstrophy: An epidemiologic study from the International Clearinghouse for Birth Defects Surveillance and Research, and an overview of the literature. *American Journal of Medical Genetics Part C (Seminars in Medical Genetics).* 157: 321-332.

APPENDIX C:
Champions and coordinators

CARIS co-ordinators

Welsh delivery units have a co-ordinator, experienced in advising about reporting to CARIS. They can supply warning cards, forms and help with filling these in. They can retrieve notes to record the best data about mother and baby. In many units the initial warning card is sent to the co-ordinator before being sent to the CARIS office so that the co-ordinator is aware of the suspicion of an anomaly.

CARIS champions

All units have an obstetrician and paediatrician with a particular interest in congenital anomalies. They have kindly agreed to act as champions for CARIS, keeping the profile high in the unit. They also are available if there are local reporting problems.

Hospital	CARIS champion in paediatrics	CARIS champion in obstetrics	CARIS co-ordinators
Bronglais	John Williams	Angela Hamon	Jo Mylum / Helen James
Glangwili	Gwyneth Owen	Roopam Goel	Anya Evans
Neath Port Talbot / Princess of Wales	Katherine Creese	Sushama Hemmadi	Elaine Griffiths & Diane Evans
Nevill Hall	Tom Williams	Delyth Rich	Tim Watkins
Powys	(to be confirmed)	(not applicable)	Val Hester & Sue Tudor (Welshpool) Carole Stanley & Pat Mason (Newtown)
Prince Charles	David Deekollu	Jonathan Rogers	Kindry Dennett
Royal Glamorgan	Jay Natarajan	Jonathan Pembridge	Nicola Ralph
Royal Gwent	Vera Antao	Anju Kumar	Tim Watkins
Singleton	Geraint Morris	Marsham Moselhi	Helen Jenkins / Valerie Vye
UHW	Jenny Calvert	Christine Connor	Danielle Richards
Withybush	Devasettihalli Appana	Chris Overton	Amanda Taylor / Camilla Cooke
Wrexham	Praveen Jauhari	Bid Kumar	Sue Yorwerth
Ysbyty Glan Clwyd	Ian Barnard	Maggie Armstrong	Jenny Roberts
Ysbyty Gwynedd	Mair Parry	David Gatongi	Jackie Stockton & Linda Williams

APPENDIX D:
Ways to report to CARIS

Reporting forms

This represents all the clinical data collected by CARIS on any baby or fetus. It is normally completed once the pregnancy has ended and there is reasonable evidence of at least one congenital anomaly.

Reporting support

The CARIS staff offer support to units to facilitate data collection.

Specialist sources

Information from specialist sources usually involves detailed diagnostic data and is extremely useful to CARIS, both in improving the quality of information on known cases and discovering new ones.

Useful sources include:

- PEDW – (Patient Episode Database for Wales) – records inpatient activity including any paediatric surgery;
- NCCHD – (National Community Child Health Database) – all children born in Wales should be recorded;
- Paediatric cardiology databases,
  - University Hospital of Wales
  - Alder Hey Hospital, Liverpool;
- New born blood test results;
- Cytogenetics; and
- SHIRE medical genetics register.

Warning cards/e-alerts

Warning cards can be used to let CARIS know about results of an anomaly scan or other concerns in the antenatal period. This lets CARIS know of potential cases to follow-up.
Web-based reporting has been developed to make this quicker and easier.

The e-alert[17] can be found on the CARIS website.

The e-alert or warning card can be used when there is an antenatal suspicion of an anomaly or to alert postnatally. This may be a particularly useful way for staff to notify the register of cases when time is pressing.

CARIS is keen to hear of any possible cases:

- to contribute to the evaluation of antenatal screening; and
- to improve the number of confirmed cases subsequently identified.

17 http://nww2.nphs.wales.nhs.uk:8080/CARIS WarningCard.nsf/WarningCardForm?OpenForm