

# caris review

## 10 years of reporting...

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**CARIS, the Congenital Anomaly Register and Information Service for Wales, is based at Singleton Hospital, Swansea. It is funded by the Welsh Assembly Government and is part of NHS Wales.**

## Foreword

Welcome to the 2007 CARIS annual review. This year we are able to report on a full ten years of CARIS data. In the report we use this information to illustrate how CARIS' aims are achieved.

This year three guest contributors from the world of screening explain their roles in Wales.

Detailed data tables are available from the CARIS website on [www.wales.nhs.uk/caris](http://www.wales.nhs.uk/caris)

Thank you very much to all contributing health professionals for their continuing support.

We would also like to thank the following who have helped with production of this report

- Tracy Price, Hugo Cosh and Gareth Davies of the Health Information and Analysis Team of the National Public Health Service for Wales who have undertaken the main annual data analysis
- Kerry Bailey who has prepared the work on anomalies and deprivation

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The CARIS team at the 2007 South Wales Annual Meeting. We are (left to right) David Tucker, Val Vye, Judith Greenacre, Margery Morgan and Helen Jenkins.

\* also accessible through the HOWIS (NHS Wales) website at [www.howis.wales.nhs.uk/caris](http://www.howis.wales.nhs.uk/caris)

## Summary

CARIS is the Welsh Congenital Anomaly Register and Information Service.

CARIS aims to provide reliable data on congenital anomalies in Wales. These data are used to assess –

- **Patterns of anomalies in Wales**
- **Possible clusters of birth defects and their causes**
- **Antenatal screening / interventions**
- **Health service provision for affected babies and children.**

Ten years of data are now available.

This year we have looked in greater detail at the patterns of anomalies in Wales.

Key points are –

- **The gross<sup>1\*</sup> rates of congenital anomalies reported is 4.9%.**
- **The rate of congenital anomalies in live born babies is 4.2%**
- **85% of cases are live born and 96% of these survive to the end of their first year. Survival is reduced with increasing complexity of anomalies**
- **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. In part this is due to differences in reporting**
- **Factors shown to 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 the urinary system and limb defects**
- **For anomalies detected up to the first birthday, approximately one third of cases are detected antenatally, one third within the first week after end of pregnancy, and the remaining third later in infancy**
- **Some specific anomalies continue to be investigated because of particularly high rates in Wales. These include gastroschisis and isolated cleft palate.**

We have assessed antenatal screening and looked at health provision to detect congenital anomalies. Key points are –

- **Rates of antenatal detection are improving in Wales**
- **Outcome data can be useful in planning services and for parent information.**

In our 2008 annual meetings we will be looking at future developments for mothers and babies affected by congenital anomalies. For the future of CARIS we will work towards achieving during the next ten years –

- **Better surveillance**
- **A maternity information system able to provide good denominator data.**

<sup>1\*</sup> The gross rate includes all cases of anomaly recorded as miscarriages, terminations of pregnancy, live and stillborn babies

## CARIS activity 2007

The team continued to be involved with projects in Wales, the United Kingdom and internationally.

### Wales

- The new RadIS II obstetric reporting module was piloted in Royal Glamorgan Hospital. This has enabled CARIS to have easy access to antenatal ultrasound data. When an ultrasonographer finds a suspicion of an abnormality the details are saved to be reported specifically to CARIS. We also have the opportunity to check postnatal scans in certain babies for example in those with dilated renal pelves. The plan in Wales is for all units to use the obstetric reporting module and this should improve case ascertainment for CARIS and the assessment of antenatal detection.
- The Welsh Paediatric Surveillance Unit agreed to investigate craniosynostosis for CARIS. This involves a regular reminder to paediatricians in Wales asking for details about the condition. CARIS chose to focus on craniosynostosis as this is a condition not normally detected antenatally. We were concerned that we were missing cases and unable to provide reliable data on prevalence rates and outcomes. The project is planned to run until the end of 2008.
- Data from the register was presented at the International Congress of Obstetrics and Gynaecology, London in July 2007 looking at the increased rates of hypospadias in mothers treated with clomiphene to induce ovulation.

- Annual meetings were held in University Hospital of Wales, Cardiff and Bodelwyddan Castle, Rhyl. The focus for these and the annual report was risk factors in the development of congenital anomalies.
- CARIS has been part of an assessment of Public Health functions in Wales organised by the Welsh Assembly Government, looking at different management arrangements.
- Improved access to inpatient (PEDW) and child health data from Health Solutions Wales has contributed to better and more timely case ascertainment. PEDW captures details of babies who may have not been diagnosed at birth but require admission for treatment or surgery later.

### United Kingdom

- CARIS continues to contribute to the British Isles Network of Congenital Anomaly Registers (BINOCAR) executive group.
- David Tucker chaired the BINOCAR clinical coding working group which has developed a coding framework to achieve consistency in coding of congenital anomalies across the UK.

## CARIS activity 2007

### International

- CARIS presented Welsh data on gastroschisis at the International Clearing House of Birth Defects Surveillance and Research (ICBDSR) conference in Italy.
- David Tucker joined the coding committee and a working group to advise on the International Clearing House annual report.
- As well as supplying annual anomaly data we continue to submit enhanced anonymised data to the ICBDSR rare diseases programme.
- CARIS presented data on the antenatal detection of congenital heart anomalies at the Naples meeting of the European Collaboration of Congenital Anomaly Registers (EUROCAT).
- We continued to contribute to a WHO worldwide study on orofacial clefting.

### Websites

[www.binocar.org](http://www.binocar.org)  
[www.eurocat.ulster.ac.uk](http://www.eurocat.ulster.ac.uk)  
[www.icbdsr.org](http://www.icbdsr.org)

### Publications in 2007 using CARIS data

Garne E, Loane M, Dolk H and a EUROCAT Working Group (2007), "Gastrointestinal Malformations: Impact of Prenatal Diagnosis on Gestational Age at Birth", *Paediatric and Perinatal Epidemiology*, Vol 21, pp 370-375.

Loane M, Dolk H, Bradbury and a EUROCAT Working Group (2007), "Increasing Prevalence of Gastroschisis in Europe 1980-2002: A Phenomenon Restricted to Younger Mothers?", *Paediatric and Perinatal Epidemiology*, Vol 21, pp 363-369.

## Ten years of CARIS data

CARIS began data collection on 1st January 1998. This report looks at the first ten years of information that CARIS has provided, to 31st December 2007.

The aims of CARIS are to provide reliable data on congenital anomalies in Wales.

These data are used to assess:

- **patterns of anomalies in Wales**
- **antenatal screening / interventions**
- **health service provision for affected babies and children**
- **possible clusters of birth defects and their causes.**

For this report, these uses of data have been grouped into two sections

- **Describing patterns of anomalies and identifying causes for concern such as high rates or clusters**
- **Using data to assess interventions and services, particularly antenatal screening for congenital anomalies.**

More details of the methods used by CARIS to collect, process and disseminate data and information are given in Appendix A.

# Patterns of anomalies in Wales

## Rates of congenital anomalies in Wales

### Overall rates

It is thought that about 30% of all conceptions are affected by some form of congenital anomaly. The vast majority of these miscarry spontaneously and may not come to the attention of health services.

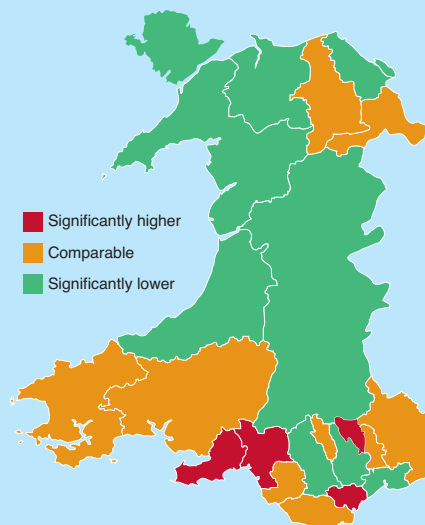
CARIS data (1998 - 2007) suggest that:

- About 5% of established pregnancies are affected by congenital anomaly. Some of these will result in miscarriage or termination of pregnancy following antenatal detection of defects.
- 4.2% of live born babies will have a congenital anomaly, although not all of these will be detected by the time of birth.

### Variations in rates around Wales

Across Wales, there are significant differences between Unitary Authorities in reported rates of anomalies (Figure 1). Swansea and Neath Port Talbot have traditionally shown higher rates than elsewhere in Wales and this reflects excellent reporting in these areas. Blaenau Gwent and Cardiff have also shown good reporting and have also had higher rates in recent years. The difficulty is in differentiating high rates due to good reporting from genuinely higher rates in the occurrence of anomalies. CARIS hopes to work with the NPHS in the coming year to find better ways to report variations in rates across Wales.

Figure 1: Comparison of gross rates of anomaly for Welsh Unitary Authorities with all Wales average.

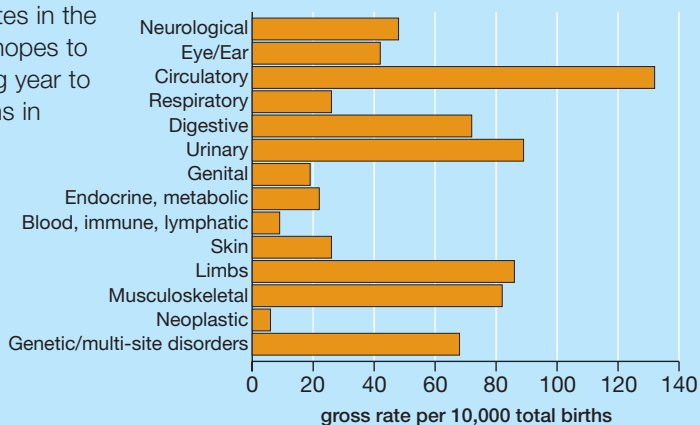


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## Types of congenital anomaly

CARIS classifies anomalies by the body system that is mainly affected. Rates for these anomaly groups are shown in Figure 2. Cardiovascular anomalies are the largest group, followed by anomalies of the urinary system and then limb defects.

Figure 2: Main anomaly groups for cases reported to CARIS 1998-2007, rate per 10,000 total births. Source: CARIS, ONS



More data on individual types of anomaly are available from the CARIS website. Some information about the ‘top 25’ anomalies reported to CARIS are given in Appendix B. These have been chosen because they are common or of particular clinical or public health importance. In general, rates are at least as high as those reported from comparable registers elsewhere in Europe and the Western world. In many cases CARIS rates are higher. Some of this reflects differences in the way data is reported, together with the excellent reporting we enjoy in Wales.

Some anomalies are extremely rare and, even with ten years of data, numbers reported to CARIS are small. Examples of rare syndromes detected in liveborn babies are given in Appendix C.

### Patterns of anomalies

A baby may have a single anomaly or a complex pattern of defects affecting many different body systems. The pattern of anomalies, together with a thorough knowledge of embryology, can in some cases help point to possible causes for anomalies. For cases reported to CARIS:

- Over half of cases have a single anomaly
- Over a third have an anomaly affecting more than one body system or an underlying syndrome
- About 10% have a chromosomal anomaly

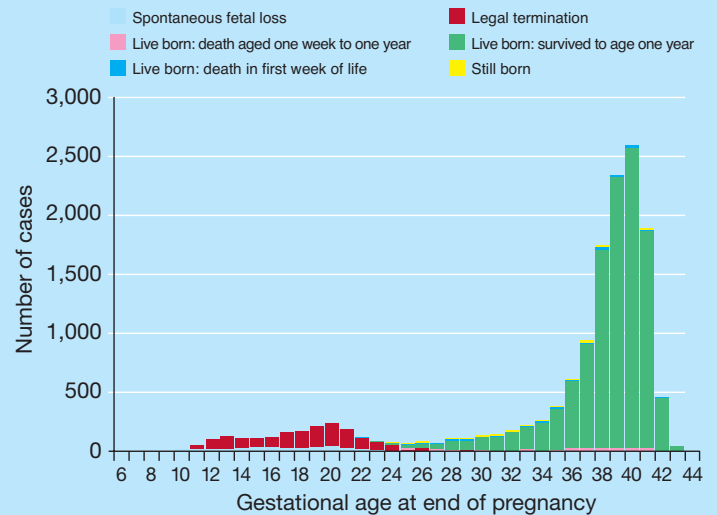
### Demographic features

#### Gestational age

Most babies reported to CARIS are live born at the end of a normal length pregnancy (Figure 3). However, there is a smaller peak of fetuses with pregnancy ending at 16-22 weeks gestation after termination of the pregnancy following antenatal detection of defects.

Figure 3: Congenital anomalies, outcome of pregnancy by gestational age, 1998-2007.

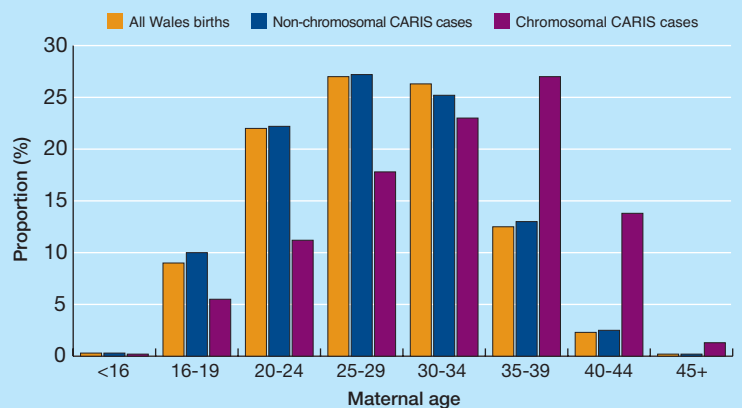
Source: CARIS



#### Maternal age

Maternal age plays a significant influence on the numbers and types of congenital anomaly that occur. CARIS data shows how maternal age distributions for babies with anomalies vary from those for babies without anomalies (Figure 4).

Figure 4: Rates of congenital anomalies reported by CARIS, by maternal age group, 1998-2007. Source: CARIS, ONS



## Patterns of anomalies in Wales

Greater proportions of mothers of babies with chromosomal syndromes are in the 35+ age groups compared to the general population of expectant mothers. This is due to the increasing incidence of chromosomal anomalies with advancing maternal age. In contrast, gastroschisis (a defect of the anterior abdominal wall) occurs more commonly in babies born to younger mothers. The reasons for this are unknown.

CARIS data has been used to calculate the maternal age related risk of having a baby with Down syndrome (Trisomy 21) in Wales (Figure 5). This shows how the risk of Down syndrome increases with maternal age. These risk values appear to be higher than those quoted in the Antenatal Screening leaflet.

Figure 5: Maternal age related risk in Wales of having a baby with Down syndrome (live and stillbirths) from CARIS data 1998 – 2007.

Maternal age group (years)	CARIS data
<20	1 in 1033
20-24	1 in 1297
25-29	1 in 916
30-34	1 in 558
35-39	1 in 170
40-44	1 in 58
45+	1 in 29

### Multiple pregnancy

Previous analysis of CARIS data shows that the relative risk of having a fetus affected by a congenital anomaly in a multiple pregnancy is 11.4%. This is 2.5 times higher than in a singleton pregnancy.

### Sex of fetus

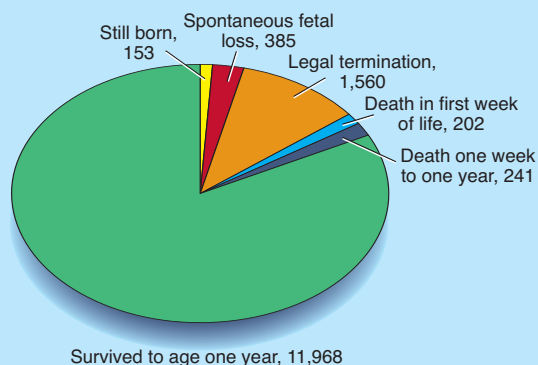
More male babies are born each year than female (ONS birth data shows 11 male babies born in Wales for every 10 females). CARIS data shows that this ratio is even greater for babies with congenital anomalies with 13 male babies for every 10 female. CARIS routinely looks at the male to female ratio for anomalies reported. This shows that the excess in male babies is mainly associated with defects of the urinary and genital systems, followed by anomalies of the digestive and musculoskeletal systems.

### Survival of babies with anomalies

CARIS records how each pregnancy ends and, if the baby is live born, whether he/she survives to the end of the first year of life. These data show that about 83% of babies with anomalies survive to their first birthday. Of the remainder, over half (11% of the total) result in termination of pregnancy with the rest associated with natural losses during pregnancy or post natal death (Figure 6).

Figure 6: Congenital anomalies by outcome of pregnancy, 1998-2006 (followed up to end 2007).

Source: CARIS

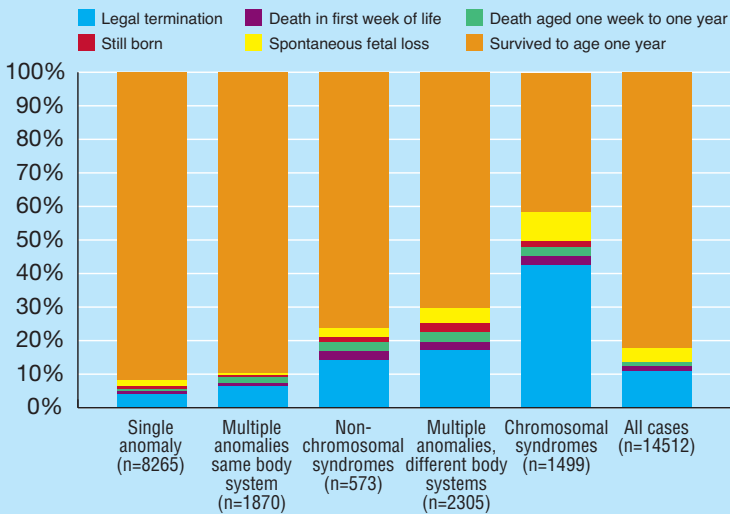




Survival outcome varies with the pattern of anomalies (Figure 7). As expected, survival rates are highest for babies with single anomalies. As the number and complexity of anomalies increases, survival reduces. Poorer survival is associated with increased rates of natural losses but also with termination of pregnancy following antenatal detection of anomalies.

Figure 7: Congenital anomalies, outcome of pregnancy by pattern of anomalies, 1998-2006 (followed up to end 2007).

Source: CARIS



The CARIS website shows survival outcome for individual anomalies. This shows, for example that:

- 90% of cases of anencephaly were terminated. In ten years there were less than ten live births with the condition, of which the majority did not survive for longer than 24 hours.
- Over 90% of babies with heart conditions were alive at one year of age.
- Hypoplastic left heart used to be universally fatal within a few weeks of life. With improved treatment, approximately half of liveborn babies with this condition are recorded as surviving at least to the end of their first year of life.

CARIS data can help give parents better information about how likely their babies are to survive. However, data is recorded historically and should be used cautiously in giving prospective predictions on risks to survival when the full picture of anomalies may not be known.

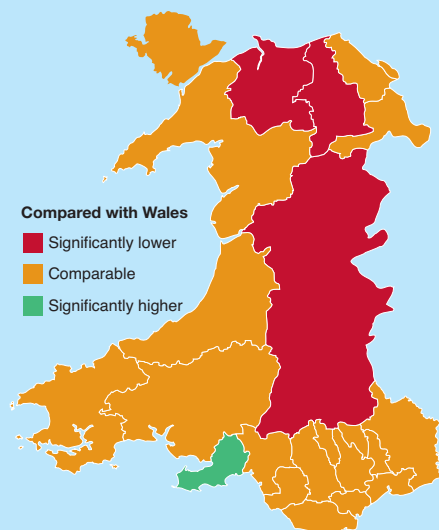
Also, survival is only one outcome of importance. CARIS does not collect equally important information to parents concerning other illness, intellect or quality of life.

#### Variation in survival around Wales

Survival rates appear to vary between Unitary Authorities in Wales, with the best survival rates in Swansea, Monmouthshire and Neath Port Talbot (Figure 8). This may be because of the good reporting in these areas.

# Patterns of anomalies in Wales

Figure 8: Survival rates for CARIS cases by UNITARY Authorities in Wales 1998 – 2007.



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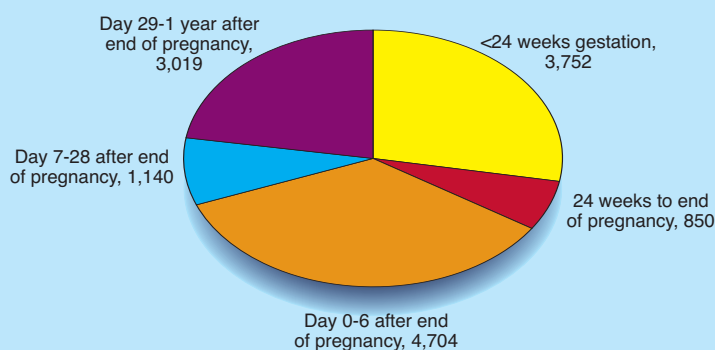
## Stage at which case of anomaly first suspected

CARIS collects data on when a fetus or baby is first suspected to have some form of anomaly. This is the earliest date known, regardless of how many anomalies may have been identified at a later stage.

Figure 9 shows that approximately one third of cases are first detected antenatally, one third detected in the first week of life and a final third later in infancy.

As CARIS only collects data on cases detected up to the end of the first year, detection rates later in childhood are not estimated.

Figure 9: Reported stage of pregnancy/infancy at which first suspected to have an anomaly, 1998-2007.



## Surveillance of congenital anomalies

CARIS data are used in various surveillance programmes that aim to detect a rise in congenital anomaly rates promptly. These systems look at the number of anomalies reported over a set period of time and compares to previous similar time periods to see if the number has changed beyond that which might be expected through chance variation.

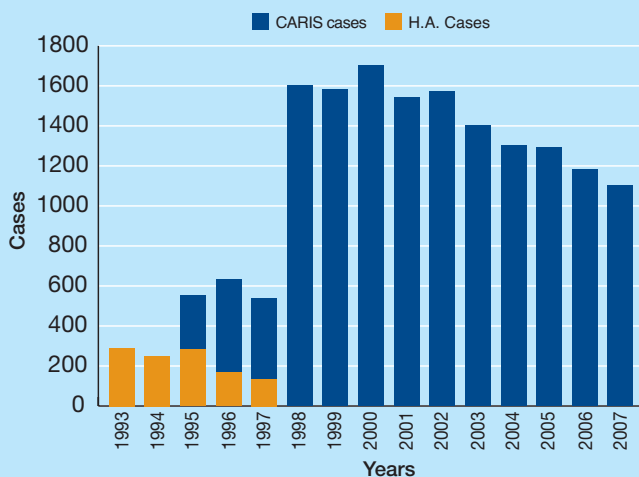
Two main systems use CARIS data:

- The Office for National Statistics operates the National Congenital Anomaly System (NCAS). The system compares numbers annually and for three month time periods. Before CARIS was established, reports to NCAS were paper based and were known to be incomplete. CARIS established electronic reporting and the presence of the regional register has greatly increased reporting to this system (Figure 10).

- EUROCAT operates a surveillance system using annual data supplied by CARIS. This system looks for changes in patterns of anomalies over time.

Both systems have their limitations. For example, both require pregnancy to have finished before cases are reported. A significant number of anomalies are now reported antenatally (see later) and may be known up to 6 months before reporting is due to take place. With the development of RadIS II, Wales will soon be in a strong position to develop antenatal surveillance of some key anomalies that are easily detected antenatally and where early investigation of a potential rise in rates would be important.

Figure 10: Numbers of cases reported to ONS Surveillance system, 1993 - 2007.



## Particular concerns

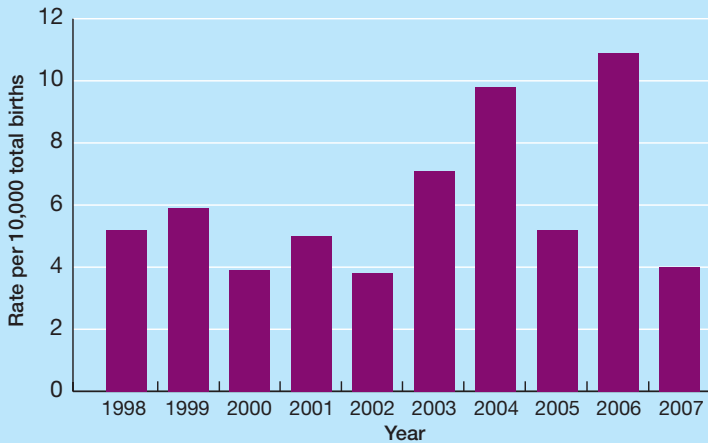
Over the past 10 years, CARIS data has highlighted a number of particular concerns about congenital anomalies in Wales.

### Gastroschisis

- Gastroschisis is a condition in which there is failure of normal development of the anterior abdominal wall. Abdominal organs may push out through the defect during fetal life and prompt surgery is required shortly after birth to return the organs into the abdomen and repair the defect. CARIS has reported extensively on gastroschisis in the past, in relation to the following.
  - The risk factors for the condition – the exact cause of the condition is not clear, however younger maternal age and smoking are significant risk factors for this condition. Low maternal weight and use of recreational drugs are also strongly associated with gastroschisis. CARIS data is able to describe many of these associations in Wales.
  - The prevalence of this condition is known to be rising, particularly in western countries. Wales has some of the highest rates in the world and this is not thought to be simply because of good reporting (Figure 11).
  - In 2004, CARIS and local clinicians noticed a marked rise in rates in Bridgend county. A cluster of up to 7 cases was identified and investigated by a multi-agency team. No obvious reason for the cluster could be identified. CARIS continues to actively monitor cases and to support further research into the condition.

# Patterns of anomalies in Wales

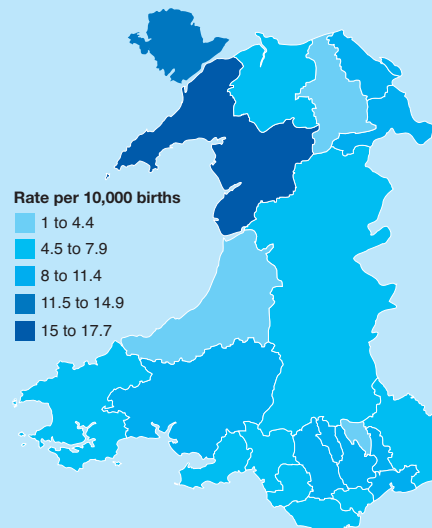
Figure 11: Gastroschisis in Wales, 1998 - 2007.



## Isolated cleft palate

Clefts or gaps in the lips or palate can occur if there is a failure of the processes by which different parts of the face fuse together during the period of 5 to 9 weeks after conception. Clefts of the lip and palate can occur either singly or in combination with each other. The CARIS review of 1998 – 2002 data first highlighted that rates for isolated cleft palate in Wales were significantly higher than rates for comparable areas in Europe. Analysis of Welsh data suggests that rates are particularly high in North West Wales (Figure 12). When previously reviewed, no obvious cause for this pattern could be found. With considerable additional data now available, CARIS hopes to work with the National Public Health Service for Wales to look at this again in the coming year.

Figure 12: Gross rates of isolated cleft palate by Welsh Local Authorities.



## Congenital anomalies and deprivation

Many studies have shown that people living in the most socioeconomically deprived areas have worse levels of health than those living in the most affluent areas. A wide variety of health outcomes have been noted to show this pattern, including life expectancy, diabetes, childhood pedestrian injuries and respiratory disease. Live born infants are more likely to die before the age of one in the most deprived areas<sup>2</sup>. Some of these differences are related to underlying differences in factors such as smoking rates, but this does not explain all the differences seen.

<sup>2</sup> Deprivation and Health, HIAT, NPHS 2004

### Socio economic deprivation and congenital anomalies

In 2000, Vrijheid et al<sup>3</sup> used Eurocat data to investigate the link between landfill sites and congenital anomalies. This also demonstrated an association between socioeconomic status and congenital anomalies in the UK (but not with other European countries).

- Risk of non-chromosomal anomalies increased with increasing socioeconomic deprivation. The risk for the most deprived quintile of the deprivation index was 40% higher than for the most affluent quintile. Some malformation subgroups also showed increasing risk with increasing deprivation: all cardiac defects, malformations of the cardiac septa, malformations of the digestive system, and multiple malformations. No evidence for socioeconomic variation was found for other non-chromosomal malformation groups, including neural tube defects and oral clefts.
- In analyses unadjusted for maternal age, the risk of chromosomal anomalies decreased with increasing levels of deprivation, mainly as a result of differences in the maternal age distribution between social classes.

### Congenital anomalies and deprivation in Wales

CARIS has long been interested in assessing whether congenital anomaly rates are associated with socioeconomic deprivation in Wales. Until now, this has not been feasible to study because of a number of challenges which we have now been able to address.

- Being a new register, the numbers of cases reported to CARIS and available for study were initially small, making it difficult to detect differences between areas with different levels of deprivation. With ten years of data and over 15,000 cases reported, this is no longer such a serious issue.
- In order to calculate rates, CARIS needed a special download of birth data including maternal age and the level of socioeconomic deprivation occurring in the area of mother's residence. This is not normally available from the Office for National Statistics without special permission. This year we have been able to obtain suitable anonymised data from the National Community Child Health Database.
- Differences in reporting across Wales may influence the results if better reporting hospitals are located in particularly affluent or deprived areas. In order to counter this, we have used deprivation scores for very local areas (Lower Super Output Areas or LSOAs) and aggregated them up across Wales into 5 groups from most deprived to most affluent. Each group does not therefore relate to any easily defined geographic area of Wales.
- It is always difficult to know exactly how to measure deprivation. The Welsh Index of Multiple Deprivation (WIMD) is now available and is used increasingly in analyses of Welsh data. The factors used in the index are shown in Figure 13.

<sup>3</sup>M Vrijheid, H Dolk, D Stone, L Abramsky, E Alberman, J E S Scott; Socioeconomic inequalities in risk of congenital anomaly Arch Dis Child 2000;82:349-352 (May)

# Patterns of anomalies in Wales

Figure 13: Welsh Index of Multiple Deprivation (WIMD).

The Welsh Index of Multiple Deprivation 2005 is based on the idea of distinct 'domains' of deprivation which can be recognised and measured separately. These are:

- Income**
- Employment**
- Health**
- Education, Skills and Training**
- Geographical access to services**
- Housing**
- Physical Environment**

A version of WIMD 2005 with the health domain removed was used, in order to prevent a circular analysis where health is a factor in both the independent and outcome variables. WIMD 2005 was chosen since, as the independent variable, it relates to the period of outcomes under study more closely than WIMD 2008.

### Chromosomal disorders

It is known that mothers in more affluent areas tend to have their babies at older ages than mothers in more deprived areas. As the prevalence of fetal chromosomal disorders is known to increase with maternal age, there is a natural tendency for rates of fetal chromosomal disorders to be higher in mothers from more affluent areas. This is demonstrated for Wales by CARIS data (Figures 14 & 15).

Figure 14: Congenital anomalies, median maternal age by WIMD fifth, 1998-2007.

Source: CARIS/WIMD 2005

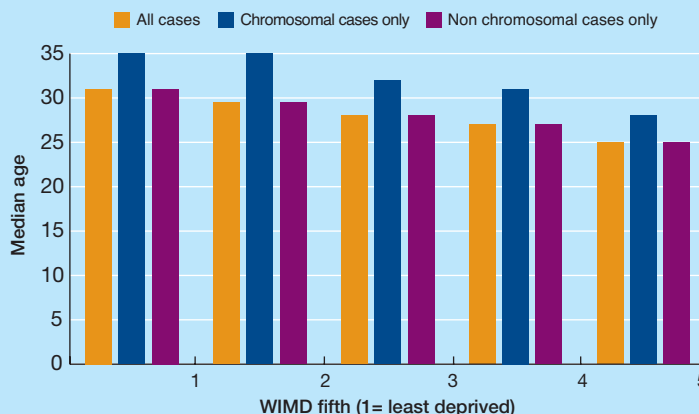
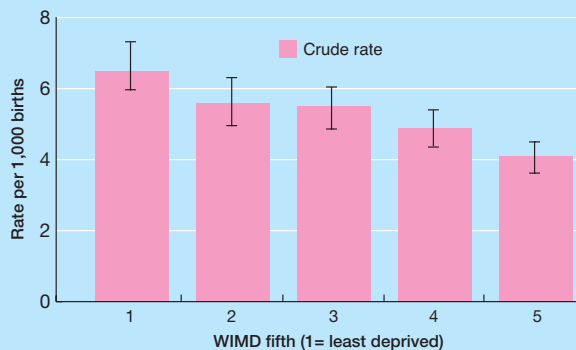


Figure 15: Congenital anomalies (chromosomal only), rate per 1,000 births by WIMD fifth, 1998-2007

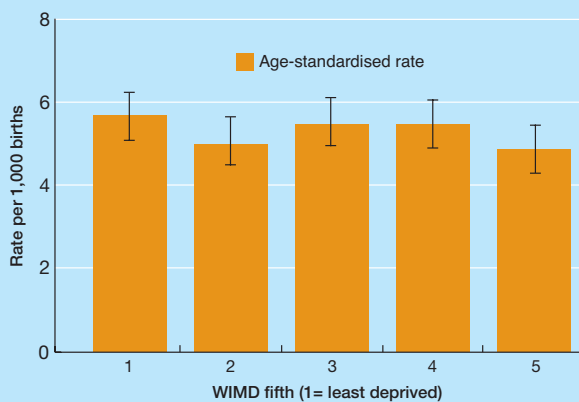
Source: CARIS/HSW (NCCHD) / WIMD 2005



When these rates are adjusted for maternal age, the pattern seen using crude rates is no longer apparent and differences between deprivation 5ths are not significant (Figure 16).

Figure 16: Congenital anomalies (chromosomal only), rate per 1,000 births by WIMD fifth, 1998-2007.

Source: CARIS/HSW (NCCHD) / WIMD 2005



### Non Chromosomal cases

For both crude (Figure 17) and maternal age adjusted data (Figure 18), rates of cases of non chromosomal anomalies drop between the 1st (least deprived) and 2nd deprivation quintiles then rise with increasing levels of deprivation. The most deprived quintile has a significantly higher rate of non-chromosomal anomalies. The other quintiles are not significantly different.

Babies born in the fifth most deprived areas are 13% more likely to have a non-chromosomal anomaly than those in the fifth most affluent areas and 20% more likely than the second quintile of affluence and this is significant. This pattern is quite similar to that observed by Vrijheid et al.

Many of the causes of congenital anomalies are not known. Suggested associations of non-chromosomal congenital anomalies include proximity to landfills, diet, including reduced intake of folic acid and obesity. All of these have been found to be more common in deprived areas.

Figure 17: Congenital anomalies (non-chromosomal only), rate per 1,000 births by WIMD fifth, 1998-2007.

Source: CARIS/HSW (NCCHD) / WIMD 2005

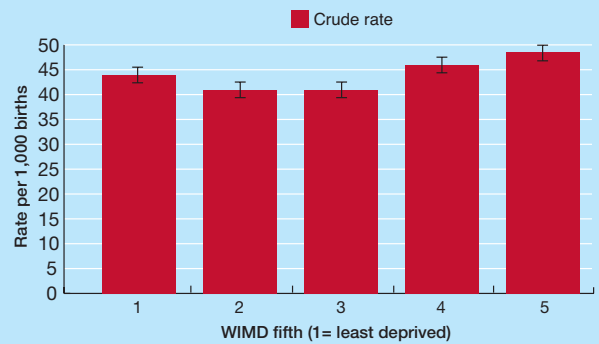
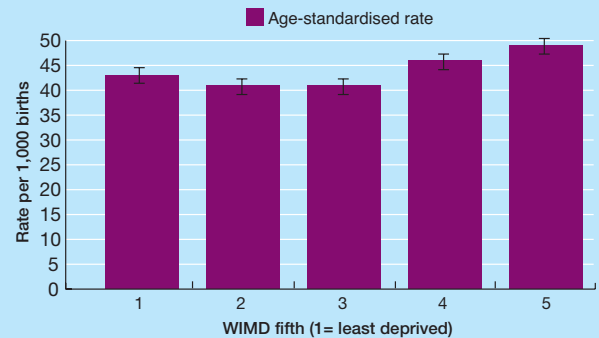


Figure 18: Congenital anomalies (non-chromosomal only), rate per 1,000 births by WIMD fifth, 1998-2007.

Source: CARIS/HSW (NCCHD) / WIMD 2005



### Summary

The prevalence of non-chromosomal anomalies appears to be associated with living in deprived areas, although this relationship is not a simple one. Chromosomal anomalies are known to be associated with increased maternal age and so crude rates are higher in more affluent areas. When rates are adjusted for age this pattern disappears. Rates of non chromosomal anomalies are higher in more deprived areas.

There are a number of areas for further study arising from this initial work on congenital anomalies and deprivation in Wales, including looking at some key individual anomalies. CARIS will work with the NPHS to look at this in greater detail over the coming year.

## Antenatal detection in Wales

### Antenatal Screening and Interventions

One of the significant moments in a pregnancy for parents is the ultrasound anomaly scan. Today this comes with the option of photographs, the chance of discovering the baby's sex and making the experience a shared family event.

On a more serious note the 20 week scan has become the mainstay of antenatal screening.

The objectives for screening include reassurance that the baby is normal and identification of

- non viable abnormalities
- abnormalities associated with high morbidity and long term handicap
- fetal conditions with the potential for intrauterine therapy
- fetal conditions which will require postnatal investigation/ treatment and
- parental preparation.

CARIS aims to collect data to inform clinicians and Antenatal Screening Wales on the effectiveness of antenatal screening throughout the delivery units in Wales. Since CARIS started, screening techniques have changed, improved and become more uniformly available to Welsh mothers.

An antenatal anomaly is normally reported to CARIS by the ultrasonographer at the time of detection. This has enabled us to estimate the detection rate in certain conditions. Changes to the RadIS reporting module will streamline reporting when available throughout Wales. A report to the register will be generated at every ultrasound scan where an anomaly is detected. Most units should be equipped for this by 2009.

Antenatal Screening Wales produces literature to help women navigate the experience of ultrasound and screening. An information leaflet is produced by Antenatal Screening Wales and, in the absence of more robust or Wales specific data, the leaflet quotes the RCOG indicative detection rates. For this report we have compared the quoted antenatal detection rates with the actual reports that CARIS receives.

### Neural tube defects

These are the most common central nervous system abnormalities likely to be diagnosed by an ultrasonographer. The defects include spina bifida, anencephaly and encephalocele and relate to a problem with development of the spine leaving the brain or spinal cord exposed. In Wales the prevalence is 1.7/1000 total births.

The Antenatal Screening Wales information leaflet suggests a 90% chance of spina bifida being seen at the 18-20 week anomaly scan and a 99% chance for anencephaly.

#### Risk Factors for Neural Tube Defects

Geography	- high in Wales compared to Western Europe
Family history	- previous affected child or mother, maternal diabetes
Diet	- folate poor nutrition or metabolism
Teratogenic drugs	- antiepileptic drugs, methotrexate, retinoic acid
Chromosomal anomalies	- particularly trisomy 13 and trisomy 18

As ultrasound expertise and technology have improved, the detection potential has increased for antenatal screening. This has meant that the dependence on maternal serum alphafetoprotein has greatly diminished. It also has reduced the need for confirmatory amniocentesis to estimate acetylcholinesterase and alphafetoprotein in the liquor.

**Key Ultrasound Pointers for Neural Tube Defects**

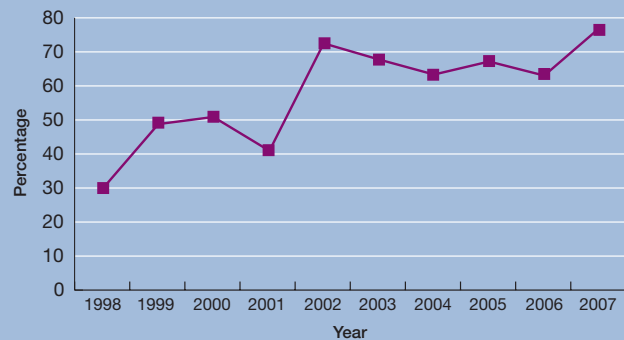
- splaying of spine ossification centres
- defect in the skin line at the lesion
- cystic meningeal sac
- loss of normal spinal curvature
- absence of the skull vault
- lemon shaped skull
- banana/boomerang shaped cerebellum
- third ventricular enlargement
- microcephaly/enlarging ventricles



Figure 19: Ultrasound showing anencephaly.

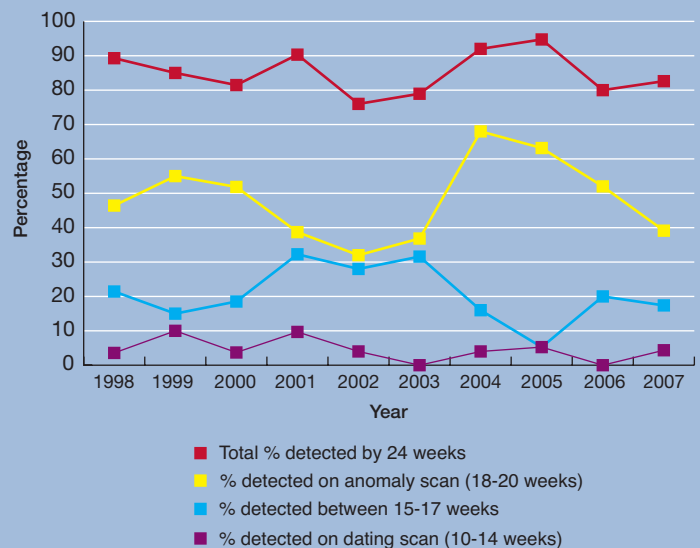
CARIS data shows that the detection of anencephaly before 24 weeks gestation over the 10 year period 1998-2007 was 97.2%. Increasingly anencephaly is being detected on the 10-14 week dating scan (Figures 19 & 20). In 2007 early detection on the dating scan accounted for 76.9% of cases.

Figure 20: Proportion of cases of non-chromosomal anencephaly detected at dating scan (10-14 weeks gestation).



Overall antenatal detection of spina bifida in Wales before 24 weeks gestation between 1998-2007 is 85.1%. This is a little below the 90% figure used by Antenatal Screening Wales. Figure 21 shows detection at various gestational ages and the overall detection rate before 24 weeks.

Figure 21: Proportion of cases of non-chromosomal spina bifida detected at differing stages of gestation.



## Antenatal detection in Wales

### Hydrocephaly

Hydrocephaly is caused by the accumulation of cerebrospinal fluid within the ventricular system. Usually an obstruction of the aqueduct or posterior fossa is responsible. In spina bifida it can be caused by the Arnold Chiari malformation.

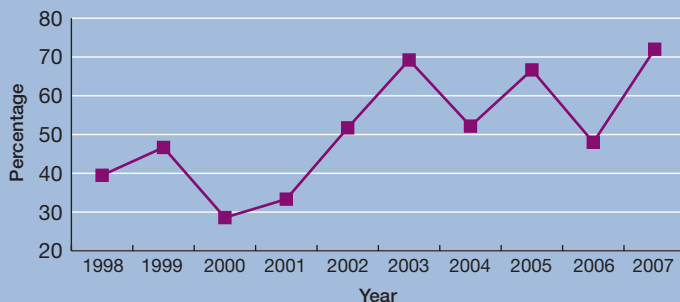
Ventriculomegaly is a descriptive term which records increased ventricle size above 10mm and not implying any signs of increased pressure.

#### Ultrasound Plan for Hydrocephaly

- inspect brain for any structural abnormality
- look for other system anomalies
- exclude infection
- offer karyotype

Over the last 10 years 312 cases of hydrocephaly have been reported. Of these 250 were non-chromosomal. For these, overall antenatal detection before 24 weeks was 50.4%, although detection is much better in more recent years as shown in Figure 22. Detection is now reasonably close to the Antenatal Screening Wales leaflet figure of 60% by 24 weeks gestation.

Figure 22: Antenatal detection of non-chromosomal hydrocephaly before 24 weeks gestation (1998-2007).



### Major Heart Problems

Cardiac congenital anomalies are the most common seen and account for significant morbidity and mortality. Antenatal detection is challenging and is based on securing a four chamber view and assessment of the outflow tracts. This will include the six cardiac connections.

#### Right side of the Heart

- inferior and superior venae cavae drain to right atrium
- right atrium connects through tricuspid valve to right ventricle
- right ventricle connects to pulmonary artery



Figure 23: Fetal heart - normal 4 chamber view

#### Left side of the Heart

- pulmonary veins drain into left atrium
- left atrium connects through mitral valve to left ventricle
- left ventricle connects to the aorta

Babies with major heart problems are those that will require specialist help when born. Antenatal detection is very important in planning delivery and sometimes immediate postnatal care.

CARIS data shows that the detection rate of many heart anomalies is improving. The ASW information leaflet gives a 25% chance of having a major heart anomaly diagnosed at the anomaly scan. Overall detection of hypoplastic left heart syndrome by 24 weeks gestation is 68.7% but in 2007 this was as high as 83.3%. Detection rates are much lower for other conditions including transposition of great arteries. The 10 year antenatal detection rate for transposition is just 16.0% by 24 weeks gestation.



### Diaphragmatic hernia

If abdominal contents are able to pass into the thoracic cavity, lung development can be compromised. The earlier this happens the more likely it is that pulmonary hypoplasia will occur and jeopardise survival.

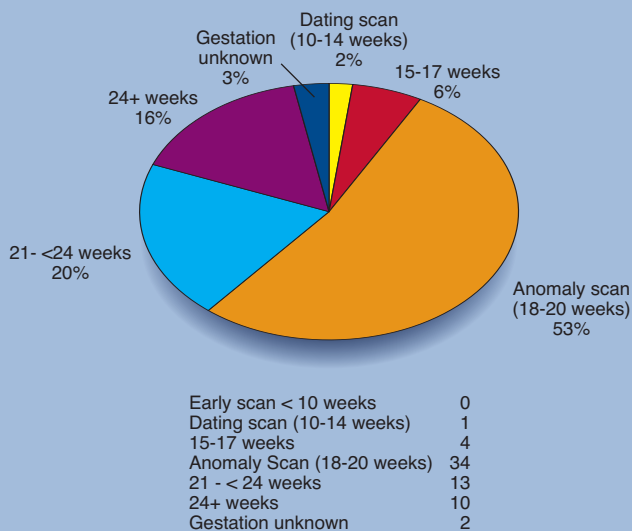
The finding of a diaphragmatic hernia at an ultrasound scan presents a difficult dilemma in predicting outcome.

#### Poor prognostic signs for diaphragmatic hernia

- other abnormalities, commonest being cardiac and chromosomal
- diagnosis before 24 weeks
- polyhydramnios
- hydrops fetalis
- intrauterine growth retardation

Antenatal detection rates seem quite variable for this condition with detection varying across the years from 11.1% in 2004 to 83.3% in 2006 (Figure 24). The overall 10 year detection rate is 47.3%. ASW leaflet gives a 60% chance of detection at the anomaly scan.

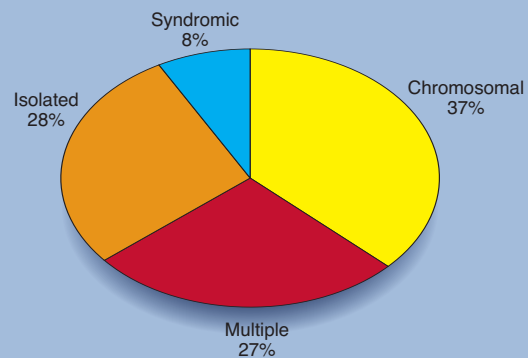
Figure 24: Time of diagnosis in antenatally detected diaphragmatic hernia (1998-2007).



### Exomphalos

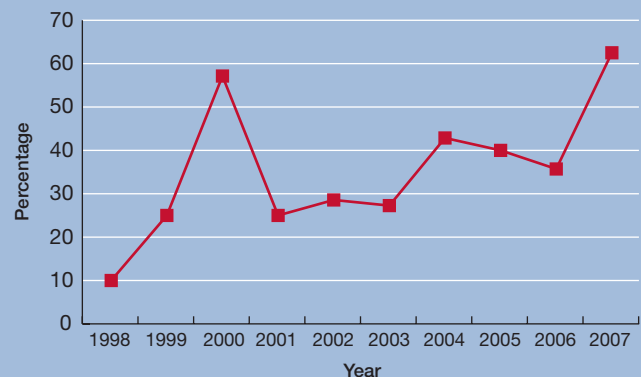
This is an incomplete return of the abdominal contents to the abdominal cavity in early pregnancy. Bowel is usually present as can be stomach, liver or spleen, held within a relatively thick membrane. It is frequently associated with other abnormalities, and in over a third of cases, is associated with chromosomal disorders (Figure 25).

Figure 25: Aetiological description of cases of exomphalos (1998-2007).



The detection rate by 24 weeks gestation is 77.8% over the last 10 years. Increasingly more cases are being detected at the 10-14 week dating scan.

Figure 26: Proportion of non-chromosomal cases of exomphalos detected at dating scan (10-14 weeks) 1998-2007.



# Antenatal detection in Wales

## Gastroschisis

Gastroschisis has a high prevalence in Wales. It consists of a hernia of abdominal contents through the abdominal wall usually to the right of the umbilical cord insertion. Bowel floats freely in the amniotic fluid and this contact may be responsible for complications affecting the bowel.

As with exomphalos, antenatal detection is increasingly occurring earlier in pregnancy. Many cases reported to CARIS are detected at the 10-14 week dating scan. The overall detection rate by 24 weeks gestation is 86.9%. (See Figure 27 for more detailed breakdown of when antenatally detected cases were identified). The ASW leaflet gives a 90% chance of detection of gastroschisis or exomphalos at the anomaly scan.

Figure 27: Time of diagnosis in antenatally detected non-chromosomal cases of gastroschisis (1998-2007).

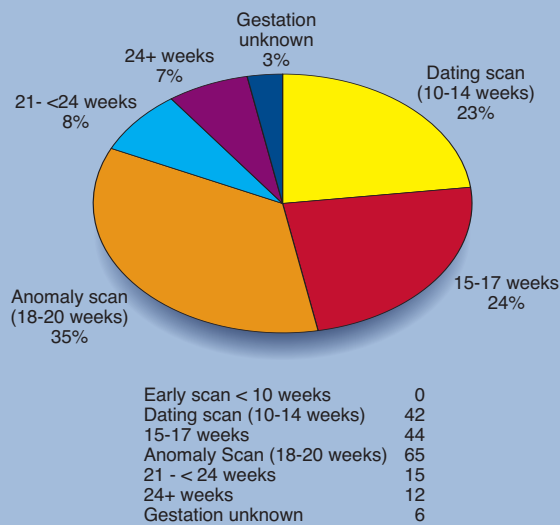
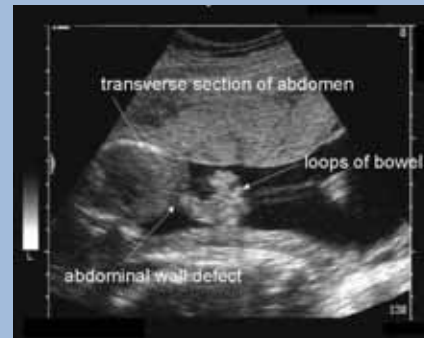


Figure 28: Antenatal scan showing gastroschisis.



## Major renal problems

Renal agenesis and multicystic kidneys account for the majority of serious kidney problems.

Bilateral renal agenesis is associated with oligohydramnios giving the characteristic Potter's syndrome of low set ears, wide set eyes, micrognathia, limb contractures, talipes and pulmonary hypoplasia. Liquor volume can be normal before 17 weeks. After this, oligohydramnios can make the demonstration of absent kidneys and bladder difficult. Changes in the shape of the adrenal glands and absence of the renal arteries shown by colour Doppler may be helpful.

Multicystic kidneys are easier to detect as the kidneys are enlarged and echogenic despite associated oligohydramnios. It may not be possible to detect these until 24 weeks gestation. Earlier subtle increases in size may be detectable as may early hyperechogenicity.

CARIS data shows that 83.7% of cases of renal agenesis and 63.9% of multicystic dysplastic kidneys are detected by 24 weeks gestation. The ASW leaflet suggests a figure of 85% for the antenatal detection of major kidney problems.

### Missing bones or very short arms or legs

At the 18 to 20 week scan a survey is made of bony structures and measurements taken. These include the biparietal diameter, head circumference and femur length. Morphology of the bones including cranial vault and ribs is assessed at the same time.

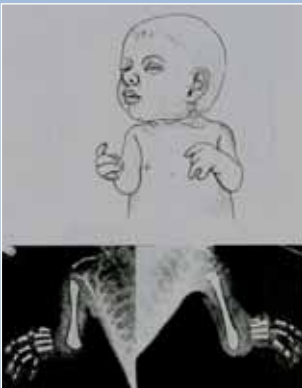


Figure 29: Xray showing bilateral agenesis of radius and ulna.

Amniotic bands are thought to be responsible for about half of limb deficiencies and amputations. In these there is usually a transverse defect only. Most reductions of the upper limbs are isolated events, those involving the lower limbs are often part of more complex problems. Although the ASW leaflet suggests a 90% chance of these being diagnosed at the anomaly scan, CARIS data shows that this is a very heterogenous group.

Diagnosis takes place at various times so it is difficult to give an overall detection rate.

### Heart and Bowel Problems connected with Downs Syndrome

#### Soft markers

Ultrasound soft markers for chromosomal abnormalities remain a controversial area. Scans of many normal fetuses may demonstrate soft markers which are specific appearances on the scan without an underlying structural anomaly. Drawing attention to this may cause parental anxiety and result in unnecessary amniocenteses and potential fetal loss.

At present there is not enough evidence to support karyotyping fetuses with soft markers in a low risk population.

#### Specific anomalies

Duodenal atresia and atrioventricular septal defect are common abnormalities with Down syndrome. Increased nuchal thickening can be a useful sign to suggest a karyotype should be offered to the mother.

Of the 709 cases of Down syndrome reported to CARIS, 87 (12%) had an atrioventricular septal defect and 5 (0.7%) were reported to have duodenal atresia. The ASW leaflet suggests a 40% chance of picking up heart and bowel problems connected with Down syndrome.

# Antenatal detection in Wales

## Health Service Provision

The importance of collecting accurate congenital anomaly data can affect the way the health service works for the population of Wales.

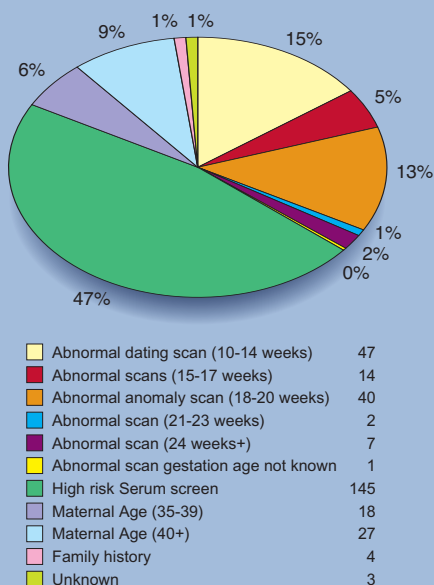
### Describing patterns of services

CARIS can increasingly give an insight into the ways that different services and interventions interact to assist with patient care.

The NHS in Wales has used CARIS data relating to cardiac anomalies and cleft lip and palate to plan services.

We have a close relationship with Antenatal Screening Wales and help with details of antenatal detection and outcomes. For example, Figure 30 shows the different pathways taken for amniocentesis to be performed for cases of Down syndrome.

Figure 30: Reason for amniocentesis in cases of trisomy 21 (1998-2007).



One of the advantages of good antenatal screening and detection is the ability to plan delivery in a suitable unit with appropriate paediatric resources.

Diaphragmatic herniae and severe cardiac anomalies are examples of conditions that benefit from delivery in a tertiary centre and CARIS can record the appropriateness of place of delivery. Figure 31 illustrates how babies, who are live born following antenatal detection of diaphragmatic hernia in Wales, are over eight times more likely to be delivered in a tertiary centre than those not detected before birth.

Figure 31: Diaphragmatic hernia - antenatal detection and delivery for live born babies (1998-2007).

	Tertiary delivery	Non-tertiary delivery
Antenatally detected	41	3
Not antenatally detected	5	35
<b>Total</b>	<b>46</b>	<b>38</b>

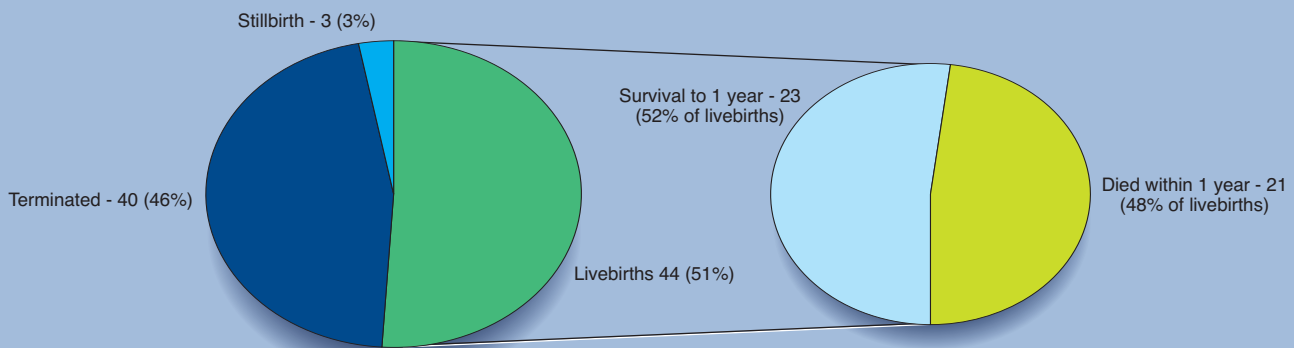
## Information for parents

Expectant mothers can find out about CARIS through Antenatal Screening Wales or from wall posters distributed through most antenatal clinics.

If an anomaly is detected antenatally, the register can help by providing outcome data to inform and help with decision making.

For example, Figure 32 illustrates recorded survival outcomes for hypoplastic left heart.

Figure 32: Outcomes in non-chromosomal hypoplastic left heart syndrome (1998-2006).



Health professionals who are aware of CARIS may find that this helps the counselling process when faced with a woman who has delivered a baby with a congenital anomaly. It can be reassuring to parents that there is a system for recording, analysing and making sense of what has happened.

To help with this we have developed a parent information leaflet to explain the register in detail.



## Screening services in Wales

CARIS works very closely with the screening services in Wales. We are delighted to hear details of the services offered.

### Antenatal Screening Wales –



*Rosemary Johnson  
Director of Antenatal  
Screening Wales*

#### When and why were you set up?

In 2001 there was no national system for managing and monitoring antenatal screening in Wales and variable access to some screening tests.

Antenatal Screening Wales was set up to ensure pregnant women were offered a uniform screening service with careful maintenance of standards.

We have worked closely with NHS Trusts and key stakeholders, including CARIS, establishing a framework for the antenatal screening programme in Wales.

#### How do you compare with England?

The Department of Health has established a different structure in England. This includes commissioning Programme Centres to lead specific antenatal screening programmes, for example the Fetal Anomaly and Down's syndrome Screening Programme Centre.

#### What would you reckon is the greatest achievement of Antenatal Screening Wales?

I think this is the close collaboration we have developed with different specialities and stakeholders across Wales.

This lively debate has resulted in consensus about best practice and evidence based antenatal screening services for women.

#### What about the most difficult obstacle – what was that?

This has been prioritising issues and deciding which ones we take forward in any given year. Antenatal screening is complex with multiple screening tests and many ethical issues to address within our current budget. The lack of an all-Wales Information Management & Technology (IM&T) strategy for maternity services continues to make service development, planning and monitoring particularly difficult.

*(Margery Morgan) I agree. With no uniform maternity database in Wales, comparison of pregnancies with normal babies and those with congenital anomalies is impossible.*

#### How are things going to change in the next 10 years?

I would expect to see major improvements in the Down's syndrome screening programme leading to a higher detection rate with a lower false positive rate.

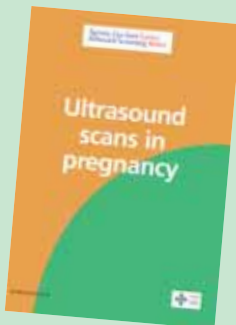
The RadIS II obstetric reporting module, currently being introduced to units around Wales, should provide us with audit data to analyse the performance of ultrasound and detection of structural fetal anomalies.

Above all we hope to have an all-Wales IM&T strategy for maternity services which includes antenatal screening to make service development, planning and monitoring easier and in line with the requirements of other screening programmes.

### Where does CARIS fit in?

CARIS is vital to the work of ASW because it provides high quality information about pregnancy outcomes and the performance of many aspects of the antenatal screening programme. Without CARIS we would be unable to assess the effectiveness of a number of the screening tests.

*Thank you Rosemary*



### Newborn Screening Wales



*Don Bradley  
Director of Neonatal  
Screening*

### When and why was Newborn screening Wales set up?

#### Phenylketonuria

Newborn screening was originally introduced to detect phenylketonuria (PKU), an inborn error of metabolism of the amino acid phenylalanine, first described in 1934.

Greatly elevated levels of phenylalanine are present in the blood in the first week of life and this leads to profound learning difficulties if untreated. Work in the 1950s led to the idea that if the disease could be detected pre-symptomatically and a diet low in phenylalanine introduced, then normal development was possible. This led the eponymous Robert Guthrie to invent his technique of collecting whole blood from newborns onto filter paper from a heel-prick and measuring the phenylalanine by his bacterial inhibition assay. In the 21st century virtually all PKU screening is undertaken by tandem mass spectrometry. The birth prevalence of PKU in Wales is approx. 1:10,000.

Screening started in Wales during 1970 and currently we screen over 34,000 newborns each year.

#### Congenital hypothyroidism

With the introduction of radio-immuno assays in the 1970s an assay for thyroid stimulating hormone (TSH) became available leading to the introduction of screening for congenital hypothyroidism (CHT) in 1982. CHT is generally due to either agenesis or ectopic development of the thyroid gland leading to elevated TSH levels, reduced levels of thyroxine and consequent learning difficulties. Identification in the first week of life followed by life-long treatment with thyroxine leads to normal development. The birth prevalence of CHT in Wales is 1:2,600.

# Screening questions and answers

## Cystic Fibrosis

It has been possible to screen newborns for cystic fibrosis since the late 1970s by measuring immuno-reactive trypsin (IRT) in a heel-prick blood spot. The test had poor specificity leading to large numbers of false positive tests which then required a sweat test to confirm or refute the screening test.

In 1989 the gene for cystic fibrosis was isolated and the most common gene defect ( $\Delta F508$ ) identified. At the same time evidence suggested that outcome was better in those diagnosed early. False positive tests are rare these days with limited molecular analysis as a second tier check. Screening started in Wales in December 1996. The birth prevalence of CF in Wales is approximately 1:2,500.

### *CARIS data on Cystic Fibrosis in Wales*

- 125 infants were born between 1998-2006.
- 5 terminated pregnancies.
- Prevalence rate of 1:2200
- 14 with echogenic bowel detected antenatally.
- 23 born with meconium ileus - 6 with antenatal echogenic bowel.
- 2 with chromosomal anomalies
- 6 with gut anomalies

## Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is an untreatable, lethal, X-linked disease affecting about 1:4,500 males with a third of cases arising from new mutations. Boys are normal at birth, with clinical symptoms of muscle weakness becoming evident between 3 and 4 years. Muscle deterioration continues and those affected rarely live beyond 20-25 years.

The traditional diagnostic process is often prolonged and further affected siblings may be born before the first has been diagnosed. Again, newborn screening has been possible since the 1970s by measuring creatine kinase (a marker of muscle disease) in the heel-prick blood spot, but it was the isolation of the dystrophin gene in the 1980s and the subsequent ability to recognise gene deletions in affected individuals which led us to consider newborn screening for DMD. This was clearly not on the usual grounds of enabling early medical intervention but rather to avoid the distressing diagnostic delay. It also enabled families to plan for the future in practical ways including reproductive choice in further pregnancies. Screening has been available since the late 90's.

## How do you compare with England?

Currently there are 14 laboratories in England offering newborn screening for PKU and CHT.

Those labs covering populations with a high prevalence of sickle cell disorder have offered screening since the 1990s. The disease primarily affects those from sub-Saharan Africa, the Caribbean, the Mediterranean and the Middle East.

There are plans (2009) to screen for medium chain acyl-CoA dehydrogenase deficiency, the most common disorder of fatty acid oxidation. Affected individuals are unable to create energy from fat during periods of fasting, intercurrent illness with fever, or surgery. The birth prevalence of MCADD is about 1:12,000.

At present screening for these two disorders is not available in Wales but discussions are underway with a view to introducing it.

### What would you say the screening programme has achieved?

The Wales programme has achieved a great deal with minimal resources.

We were:

- the first laboratory to design a computerised recording and reporting system in the 1970s
- the first to design and implement two-tier CF screening.

We also introduced screening for Duchenne Muscular Dystrophy, a disease which challenges conventional screening principles. This involved gaining parental informed consent, again a first in newborn screening. We have published widely on the psychosocial and other aspects of newborn screening.

### What would you say were obstacles to the programme?

Information technology is a major issue because only through an integrated system can we ensure that every newborn is not only tested, but tested during the first week of life. The NHS number which is allocated shortly after birth should become the main identifier for all newborns but this is not yet the case in Wales.

Also there is a lack of governance of the programme which makes some issues difficult to address.

### What about missed cases and false positives?

In Wales we have not seen either false negatives or false positives for PKU; we would expect to miss about 7% of cases of CF and 10% of cases of DMD but with very few false positives. CHT Screening is complicated since mild transient elevations of TSH are common in neonates and the disorder may develop later in life.

### How are things going to develop in the next 10 years?

Newborn screening in the UK is rather conservative and probably rightly so. It is not uncommon for more than 20 disorders to be included in the screening panel in many countries. Many of these are rare, where there is little known of their natural history and where treatment may be problematic. There will be modest, hopefully evidence-based, additions in the next 10 years.

### Where does CARIS fit in?

All affected individuals identified by screening are reported to CARIS. This enables these disorders to be placed into the context of all congenital anomalies in Wales.

*Thank you Don*

# Screening services in Wales

## Newborn Hearing Screening Wales



*Sally Minchom  
Director of Neonatal  
Hearing Screening Wales*

### What is the story about newborn hearing screening in Wales – when and why were you set up?

This is a national programme that screens babies' hearing shortly after birth. It was fully implemented in Wales in October 2004.

The effect on the child and family of undiagnosed deafness can be significant. It can cause impaired language development, communication, family functioning, literacy, social and emotional well being and affect employment prospects. Early identification and intervention (before 6 months) have been found to reduce these deficits.

Distraction tests done by health visitors before this were not effective.

### What type of hearing loss do you record?

We record permanent bilateral hearing loss greater than 40 dBHL. We also keep information on mild hearing loss, unilateral hearing loss and auditory neuropathy spectrum.

### How do you compare with England?

We work closely and compare very well with England doing slightly better in terms of screens offered and coverage.

### What would you say the screening programme has achieved?

The screening programme performs to a high standard.

- 99.9% of eligible babies are offered screening and 99.3% of babies are tested
- 79.1% of babies are tested within 7 days
- 100% of high risk babies and 97% of well babies complete the screen in 4 weeks
- 1.3% babies screened are referred for assessment
- Of those assessed, about half (0.6% of all babies screened) have normal hearing
- 86.5% of babies referred have been assessed by 3 months of age

Since the introduction of universal newborn hearing screening, 1.3 per 1000 babies have been identified as having permanent significant bilateral hearing loss (defined as greater than 40 dBnHL). The mean age of hearing aid fitting was 30 weeks (median 18 weeks). This figure includes babies where the original decision not to fit hearing aids was altered after further information was gained about the hearing loss or parents reviewed their initial decision. 62% had hearing aids fitted within 4 weeks of confirmation of hearing loss.

The bottom line is that the programme has identified more than the predicted number of babies which had been thought to be 1.1 per 1000 babies from previously collected UK figures. Hearing aids and support services have been introduced to families at a significantly earlier time.

The programme has also succeeded by working closely with audiologists and paediatricians and as a result local trusts have improved services for children. Networking teams have been established across Wales with audit and training.

### What would you say were obstacles to the programme?

The information system! We use the Child Health system of which there are 12 in Wales with potential inaccuracies with data transfer.

Agenda for change was a disappointment to many of our staff especially the screeners who received a lower banding compared to screeners in the rest of the UK.

We would appreciate it if midwives could distribute leaflets more effectively to give mothers time to think about screening before delivery.

### What about missed cases and false negatives?

We collect information about all children diagnosed with hearing loss in Wales. Included in these cases will be children who have not been diagnosed by the screening programme. Some of these will be true missed cases either missed by screening with a false screen pass or a very small number who do not receive a screening test. Some babies identified as needing an assessment do not attend.

Some children have progressive or acquired hearing loss which makes interpreting the data difficult. We rely on children not picked up by the programme being identified by health visitors and other professionals.

The programme has only been running for 5 years and so we are only just beginning to collect this data.

### What associated congenital anomalies do you see?

Sensorineural hearing loss can occur in isolation or as part of a syndrome. Hearing loss can run in the family or occur with no family history. The commonest associated abnormalities are of the head and neck. Babies needing Special Care are high risk

and follow a different screening pathway from well babies.

### How are things going to develop in the next 10 years?

In the next 10 years, I would like to see a more combined approach to antenatal and neonatal screening programmes. Parents need to have timely information to make choices about screening tests.

I look forward to the development of assessment of neonates for hearing loss which so far has proved to be exacting and challenging.

Being able to provide more information about the nature of hearing loss shortly after birth will allow better hearing aid fitting and where appropriate earlier cochlear implants. This should help communication development in young children.

### Where does CARIS fit in?

Paediatricians should notify CARIS of significant congenital hearing loss and so CARIS should have information about all the children held on the NBHSW hearing impaired database. In the longer term we would hope to work with CARIS to analyse our data on hearing loss and additional congenital anomalies.

More information about Newborn Hearing Screening Wales can be obtained on our website [www.screeningservices.org/nbhsw](http://www.screeningservices.org/nbhsw)

*Thank you Sally but I fear that paediatricians do not let us know of all cases.*

*CARIS data is thought to be incomplete. 215 cases have been reported in the 10 year period (1998-2007) giving a prevalence of 6.6 per 10,000 live births.*

## Appendix A: How CARIS operates

We collect data on any baby or fetus, for whom pregnancy ended after 1st January 1998, where the mother is normally resident in Wales at the end of pregnancy.

CARIS uses a multiple source reporting system and, at present, over 100 individuals or agencies regularly send us information.

Data from clinical and laboratory sources are reported via warning cards, reporting forms and data exchanges. CARIS co-ordinators in each trust are responsible for much of the clinical reporting (details available from our website).

In the CARIS office, data are collated; information is coded and quality carefully checked. The data are then available for feedback to clinicians – paediatricians, ultrasonographers, midwives, etc. We also supply information to the National Assembly for Wales, EUROCAT, International Clearing House for Birth Defects and the Office for National Statistics (NCAS) for surveillance.

We cannot overemphasise the importance we give to data confidentiality. We operate a strict security and confidentiality policy and have gained support under Section 60 of the Health and Social Care Act 2001. This is renewed annually. This means that the register can continue collecting and analysing data.

CARIS has set up an Expert Advisory Group to advise on future developments and monitor progress of the register.

Over 37,000 recorded pregnancies occur in Wales each year. Of these, about three quarters are registered as live or still births, the rest ending in termination or spontaneous loss of the fetus before the 24th week of pregnancy. About 3% of births take place at home. Wales has 13 consultant obstetric units

and 13 midwifery led units. The majority of births take place in these units. However, a significant number of births to Welsh mothers occur in English hospitals. Good links with congenital anomaly registers that border Wales (Mersey, West Midlands and the South West of England) remain important. Clinical reporting is invaluable in identifying cases to CARIS, particularly those babies who:

- die but do not have a post mortem
- survive and have anomalies not requiring immediate specialist help.

Clinical reporting also gives details such as expected date of delivery that can be difficult to obtain from other sources.

Diagnostic services, particularly ultra sound and pathology, can alert us to a case or give valuable further information. Regional specialist services, including cytogenetics, can help by providing more details of the anomalies involved. We also link to other databases, such as PROTOS (Cardiff), RadIS (Radiology information system), the All Wales Perinatal Survey and the Standard Child Health Computer System.

## Appendix B: 'Top 25' conditions: prevalence rate 1998-2007

ANOMALY	ALL CASES		LIVE BORN CASES		
	Total number of cases	Rate per 10,000 total births	Number of live born cases	Rate per 10,000 live births	% cases live born
<b>Central Nervous System</b>					
Anencephaly	220	6.8	6	0.2	3%
Encephalocele	69	2.1	18	0.6	26%
Spina Bifida	256	7.9	48	1.5	19%
Hydrocephaly	310	9.6	143	4.4	46%
Cataracts	114	3.5	114	3.5	100%
Sensorineural deafness	215	6.6	215	6.7	100%
<b>Pulmonary</b>					
Congenital cystic adenomatoid malformation of lung	41	1.3	34	1.1	83%
<b>Cardiovascular</b>					
Hypoplastic left heart syndrome	112	3.5	51	1.6	46%
Transposition of great vessels	130	4.0	104	3.2	80%
Ventricular septal defects	1,640	50.7	1,490	46.3	91%
<b>Gastrointestinal</b>					
Cleft lip with / without cleft palate	360	11.1	286	8.9	79%
Cleft palate	317	9.8	252	7.8	79%
<b>Genitourinary</b>					
Hypospadias	840	26.0	835	25.9	99%
Multicystic kidney	196	6.1	137	4.3	70%
Bilateral renal agenesis	51	1.6	0	0.0	0%
<b>Musculoskeletal / limbs</b>					
Gastroschisis	195	6.0	173	5.4	89%
Diaphragmatic hernia	126	3.9	86	2.7	68%
Craniosynostosis	198	6.1	179	5.6	90%
Limb reduction defects	335	10.4	203	6.3	61%
Dislocation / dysplasia of hip	703	21.7	698	21.7	99%
<b>Endocrine / metabolic</b>					
Cystic fibrosis	152	4.7	146	4.5	96%
Congenital hypothyroidism	179	5.5	179	5.6	100%
<b>Chromosomal</b>					
Trisomy 21 (Down syndrome)	709	21.9	326	10.1	46%
Trisomy 18 (Edwards syndrome)	193	6.0	41	1.3	21%
45 X, (Turner syndrome)	138	4.3	40	1.2	29%

## Appendix C: CARIS data on selected rare conditions

Condition	Number	10 year live birth prevalence Rate per 10,000 live births	Birth ratio
<b>Autosomal dominant conditions</b>			
Neurofibromatosis	68	2.11	1:4735
Hereditary spherocytosis	17	0.53	1:18940
Tuberous sclerosis	14	0.43	1:23000
Achondroplasia	12	0.37	1:26830
Hereditary motor and sensory neuropathy (Charcot-Marie-Tooth)	9	0.28	1:35770
Myotonic dystrophy	6	0.19	1:53660
Multiple congenital exostoses	5	0.16	1:64390
<b>Autosomal recessive conditions</b>			
Cystic fibrosis	146	4.5	1:2205
Phenylketonuria	33	1.02	1:9755
Spinal muscular atrophy	17	0.53	1:18940
<b>Microdeletion conditions</b>			
22q deletion / Di George syndrome	46	1.43	1:7000
William's syndrome	14	0.43	1:23000
Prader Willi Syndrome	13	0.40	1:24765
Angelman's syndrome	11	0.34	1:29270
Smith-Magenis syndrome	3	0.09	1:107320
<b>Syndromes</b>			
Noonan syndrome	22	0.68	1:14635
Marfan's syndrome	20	0.62	1:16100
Beckwith-Wiedemann Syndrome	19	0.59	1:16945
Goldenhar syndrome	14	0.43	1:23000
Sotos syndrome	7	0.22	1:45990
Saethre-Chotzen syndrome - (Acrocephalosyndactyly type III)	6	0.19	1:53660
Smith-Lemli-Opitz syndrome	6	0.19	1:53660
CHARGE	5	0.16	1:64390
Cornelia de Lange syndrome	5	0.16	1:64390
Kabuki make-up syndrome	4	0.12	1:80490
Moebius syndrome	4	0.12	1:80490
Pfeiffer syndrome	4	0.12	1:80490
Aperts syndrome	3	0.09	1:107320
Klippel-Trenaunay-Weber syndrome	3	0.09	1:107320
Zellweger Syndrome	3	0.09	1:107320