

Final October 2015

CONGENITAL ANOMALY SURVEILLANCE

2014-2015

Dr. James Robins

Review of data relating to Congenital Anomalies detected in NHS Greater Glasgow & Clyde between 1st April 2014 and 31st March 2015.

Source data provided by Hilary Jordan of Information Services.

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CONGENITAL ANOMALY SURVEILLANCE

Congenital Anomaly Surveillance

CONGENITAL ABNORMALITY

Congenital anomalies comprise a wide range of abnormalities of body structure or function that are present at birth and are of prenatal origin. The focus of this report is on major structural anomalies. These are the structural changes that have significant medical, social or cosmetic consequences for the affected individual and will typically require medical intervention.

A congenital disorder, or congenital disease, is a condition existing at birth. The disorder may be the result of genetic abnormality, errors of morphogenesis, the intrauterine environment, infection or chromosomal abnormality.

Congenital anomalies are of four clinically significant types.

- **Malformations:** the development of a structure is arrested delayed or misdirected early in embryonic life and the effect is permanent
- **Deformations:** distinct from malformations in both timing and impact. They are conditions that arise from the application of mechanical stress to normally formed tissues. They may occur later in pregnancy and can be temporary
- **Disruptions:** complete breakdown of normal tissues
- **Dysplasias:** Cellular abnormality of the originating tissue e.g. expansion of immature cells with a corresponding decrease in the number and location of mature cells.

Congenital disorders may consist of more than one abnormality. When multiple effects occur in a specified order the disorder is known as a **sequence**. When the order is not known it is called a **syndrome**.

Congenital anomalies may be classified in a variety of ways e.g. with regard to onset, morphogenesis or aetiology during organogenesis. The cause of congenital anomaly can be reliably determined in only a small percentage of cases.

POPULATION-BASED CONGENITAL ANOMALIES SURVEILLANCE

A population-based congenital abnormality surveillance programme has a defined source population, (typically defined by maternal residence), and all identified congenital anomalies occurring within that source population are ascertained and included regardless of delivery site.

This review includes all fetuses and neonates with a congenital anomaly born to mothers living within the catchment area of Greater Glasgow & Clyde Health Board during 2014 - 2015.

The denominator used to calculate prevalence consists of all births to resident mothers. The corresponding numerator consists of fetuses or neonates with congenital anomalies born to resident mothers, (see below for explanation of prevalence calculations).

CONGENITAL ANOMALY SURVEILLANCE

Data sources include all health facilities within the catchment area where the births occur, birth and stillbirth registries, referral treatment centres for individuals with congenital anomalies, administrative databases and any identifiable fetus or neonate with a congenital anomaly. Using multiple sources improves the completeness of the case ascertainment.

Experienced information analysts and health board staff conduct core data abstraction. They have electronic access to participating institutions and actively review multiple data sources to identify cases. This type of case ascertainment requires considerable resources and personnel. Active case ascertainment seeks to enhance case detection and case reporting and improves data quality because more extensive clinical details are collected.

PURPOSE

In general terms Public Health Surveillance is the ongoing systematic collection, analysis and interpretation of health data for the purpose of planning, implementation and evaluation of health strategies. The primary users of surveillance information are usually public health professionals and healthcare providers.

The objectives of this particular surveillance programme are to:-

- Measure the prevalence of congenital anomalies within the community
- Monitor trends in the prevalence of different types of anomaly within the defined population
- Improve management to minimize complications and adverse outcomes amongst those who are affected by congenital abnormality
- Allow evaluation of screening and prevention programmes
- Assess the effect of prenatal screening and diagnosis on birth prevalence
- Disseminate findings and interpretations to health care partners and appropriate organizations
- Provide a basis for epidemiologic research and prevention programmes

WHY PREVALENCE?

All congenital anomaly registers report the number of babies with anomalies born during a calendar year. Perhaps this should mean that they would all report incidence rates. However in practice the majority of congenital anomaly registers actually report prevalence estimates. In birth defects epidemiology the terms live birth prevalence, birth prevalence and total prevalence are commonly used. It is worth considering why this is the case.

The incidence is the rate of occurrence of new cases of a disease or condition over a specified period of time expressed as a ratio or percentage.

Incidence = number of new cases over specified period of time/size of population under consideration

The appropriate denominator for calculation of the incidence, (the size of the population under consideration who are initially disease free), is debatable. In the circumstances of this review it would be the

CONGENITAL ANOMALY SURVEILLANCE

number of maternities booked through antenatal services over the year 1st April 2014 and 31st March 2015, (Appendix 1).

The reason given for the use of prevalence rates is that it is not possible to ascertain all 'new' cases of any particular anomaly as a proportion of pregnancies affected with an anomaly will miscarry spontaneously before being diagnosed. Indeed, although 16,397 women booked with NHS GG&C between 1st April 2014 and 31st March 2015, a total of 18,011 appointed referrals were made during the same time period. This means that at least 1,614 pregnancies were 'lost' from time of referral to booking, (Appendix 1).

As a consequence congenital anomaly registers, such as EUROCAT and BINOCAR, report prevalence estimates per 1,000 or 10,000 total births, (live and stillbirths). These are referred to as **birth prevalence** estimates even though the pregnancy may not result in a 'birth' because of late miscarriage or termination of pregnancy for fetal anomaly, (fetal loss less than 20 weeks gestation is excluded from prevalence data).

For completeness it is worth mentioning live birth prevalence and total prevalence. **Live birth prevalence** measures the number of cases with congenital anomalies among live births. Simply all live births with any congenital anomaly divided by all live births during the defined period.

Total prevalence figures measure the number of cases with congenital anomalies in live births, fetal deaths (stillbirths), and elective terminations for fetal anomaly. Total prevalence is hence defined as the number of cases of live birth, fetal death and termination for fetal anomaly (numerator) among a defined cohort of live births, stillbirths and elective terminations, (denominator).

October 2015

Jim Robins, with grateful thanks due to Hilary Jordan & Paul Burton.

LINKS TO PREVIOUS REPORTS

Links to previous reports

Previous reports are available on-line for download through the GG&C Public Health Screening website.

GG&C CONGENITAL ANOMALY REPORT FOR 2013-2014

http://library.nhsggc.org.uk/mediaAssets/Public%20Health%20Screening/CongenitalAnomaly2013-2014_Final.pdf

GG&C CONGENITAL ANOMALY REPORT FOR 2012-2013

http://library.nhsggc.org.uk/mediaAssets/Public%20Health%20Screening/CongenitalAnomaly2012-2013_FinalDraft.pdf

GG&C CONGENITAL ANOMALY REPORT FOR 2011-2012

<http://library.nhsggc.org.uk/mediaAssets/Public%20Health%20Screening/Review%20of%20Congenital%20Anomalies%20I%20Robins%202013.pdf>

The report for 2010-2011 is no longer available on-line.

Core Data

This report considers all live-births, stillbirths, fetal losses and terminations of pregnancy between 1st April 2014 and 31st March 2015 that were associated with one or more congenital abnormalities.

The congenital anomaly data used to compile this report are collected from a number of different sources. The contents of this report are merely a 'snapshot' taken from the database held within Public Health Screening on 28th August 2015. The data set is evolving and constantly updated as further abnormalities are recognized within this birth cohort.

An essential aspect of the congenital anomalies surveillance programme is the precise and accurate coding of the recorded malformation. The ICD 10 system is considered to be the international standard diagnostic classification system for all general epidemiological purposes. However, ICD 10 lacks specificity for coding some congenital abnormalities and most genetic syndromes. The Royal College of Paediatrics & Child Health (RCPCH - formerly the British Paediatric Association), developed an adaptation of the ICD 10 system by adding an extra digit to the code in order to allow more detailed coding. These extensions are used where they exist in order to improve data quality.

CASE BASED REVIEW

A total of 346 cases were identified from 345 pregnancies.¹ This is slightly more than the data reported for 2013-2014 but similar to the numbers described in 2012-2013. The case rate is calculated at 260/10,000 live and stillbirths.² The numbers are dependent on the date of data extraction and the degree of case ascertainment, (proportion of notifications reported out of all cases of congenital abnormality in the population), rather than any real change in congenital anomaly.

The majority of cases were live births, (n= 249, 72%). There were 7 stillbirth and 2 fetal losses. Termination of pregnancy following prenatal diagnosis of abnormality accounted for 88 cases, (25%), (Figure 1.1).

Overall a total of 551 abnormalities were classified in these 346 cases using the ICD 10 system, the primary abnormality and a variable number of associated abnormalities, (Figure 1.2).

In 236 (68.2%) cases only one abnormality is listed. However in the remaining 110 cases, (31.8%), two or more abnormalities are classified. Generally accepted figures from WHO and other organizations suggest that approximately 75% of fetuses will have just one anomaly. It is uncertain as to why the collected figures in this report suggest a higher incidence of associated abnormality.

¹ One set of twins, each co-twin exhibiting an abnormality.

² This is calculated from the number of live and stillbirths for residents of NHS GG&C from 1st April 2014 to 31st March 2015, total 13,295, (Appendix 1).

CORE DATA

It could represent a 'thorough' diagnostic assessment but may simply be due to the process of active data collection from multiple sources as well as the inclusion of what may be considered by some as more 'minor' abnormalities.

Figure 1.1: Pregnancy outcome, (n=346)

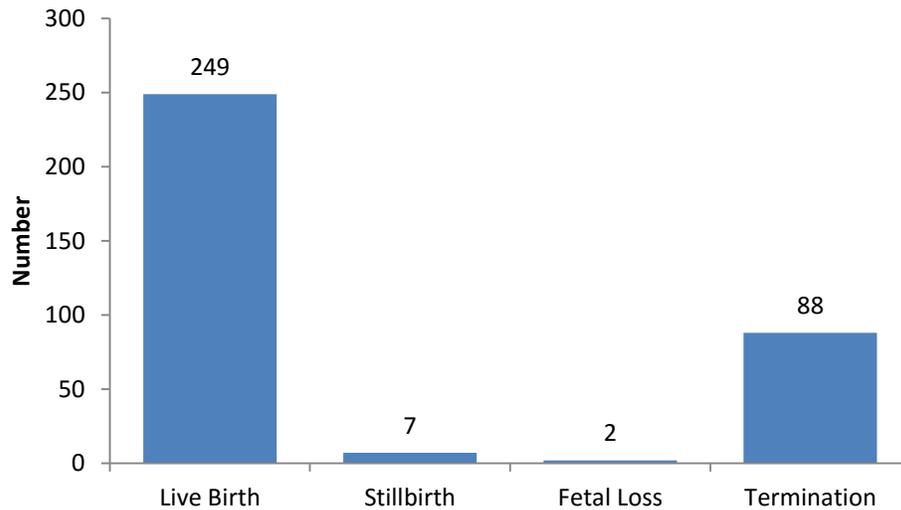
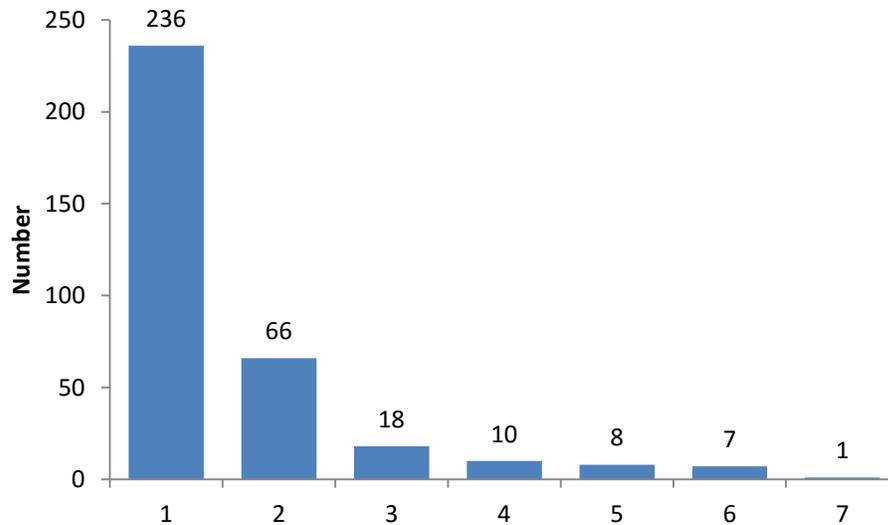


Figure 1.2: Abnormalities per case, (n=346)



The principle data set on the 346 cases, including associated abnormalities, is provided as a list ordered on the basis of the primary abnormality as defined under ICD 10. It includes pregnancy outcome and 'point of diagnosis' data. Additional information has also been collected on gestational age at time of birth or termination, gestational age at 'point of diagnosis' if prenatal, maternal age, birth order for multiple

CORE DATA

pregnancy and gender. Further supporting data has been made available from the NHS GG&C Pregnancy & Newborn Screening (PNBS) database.

The basic data set can be summarized as a table listed by Congenital Malformation Category as coded under ICD 10, (Table 1.1).

Table 1.1: Classification according to primary abnormality, (ICD1 10), (n=346)

CONGENITAL MALFORMATION CATEGORY	ICD 10 Code	Total	Rate³
SPINA BIFIDA	Q05	12	9.0
OTHER NEURAL TUBE DEFECTS	Q00-Q01	8	6.0
OTHER CENTRAL NERVOUS SYSTEM	Q02-Q04; Q06-Q07	13	9.8
EYE, EAR, FACE & NECK	Q10-Q18	3	2.3
HEART/CIRCULATORY SYSTEM	Q20-Q28	26	19.6
RESPIRATORY SYSTEM	Q30-Q34	9	6.8
CLEFT LIP & CLEFT PALATE	Q35-Q37	16	12.0
OTHER DIGESTIVE	Q38-Q45	16	12.0
GENITAL ORGANS	Q50-Q56	12	9.0
URINARY SYSTEM	Q60-Q64	30	22.6
CONGENITAL DEFORMITIES OF HIP	Q65	14	10.5
CONGENITAL DEFORMITIES OF FEET	Q66	20	15.0
LIMB REDUCTION DEFECTS	Q71-Q73	4	3.0
EXOMPHALOS	Q792	1	0.8
GASTROSCHISIS	Q793	7	5.3
OTHER LIMB & MUSCULOSKELETAL SYSTEM	Q67-Q70; Q74-Q791; Q794-Q799	28	21.1
OTHER ANOMALIES	Q80-Q89	24	18.1
DOWNS SYNDROME	Q90	36	27.1
OTHER CHROMOSOMAL	Q91-Q99	23	17.3
CONGENITAL NEOPLASMS	C00-D48	8	6.0
BLOOD, BLOOD-FORMING ORGANS & IMMUNE	D50-D89	3	2.3
CONGENITAL HYPOTHYROIDISM	E03	6	4.5
PKU	E700-E701	3	2.3
CYSTIC FIBROSIS	E84	5	3.8
OTHER ENDOCRINE, NUTRITIONAL & METABOLIC	E16-E90 (excl. E700-E701 & E84)	6	4.5
NERVOUS SYSTEM	G11-G71	4	3.0
BLINDNESS, DEAFNESS	H50-H919	1	0.8
OTHER CIRCULATORY	I40-I82	0	0.0
DENTOFACIAL ANOMALIES	K070-K071	0	0.0
CONGENITAL INFECTION	P230-P378	8	6.0
TOTAL ANOMALIES		346	260.2

³ Rate per 10,000 live and stillbirths. The surveillance tool used to compile the data within this report is restricted to mothers' resident within the geographically defined area of NHS GG&C at time of delivery. The denominator for the prevalence data is therefore the total live births and stillbirths for that area from 1st April 2014 to 31st March 2015: total 13,295. (Appendix 1). Source: Child Health Universe Extract run 28 August 2015.

CORE DATA

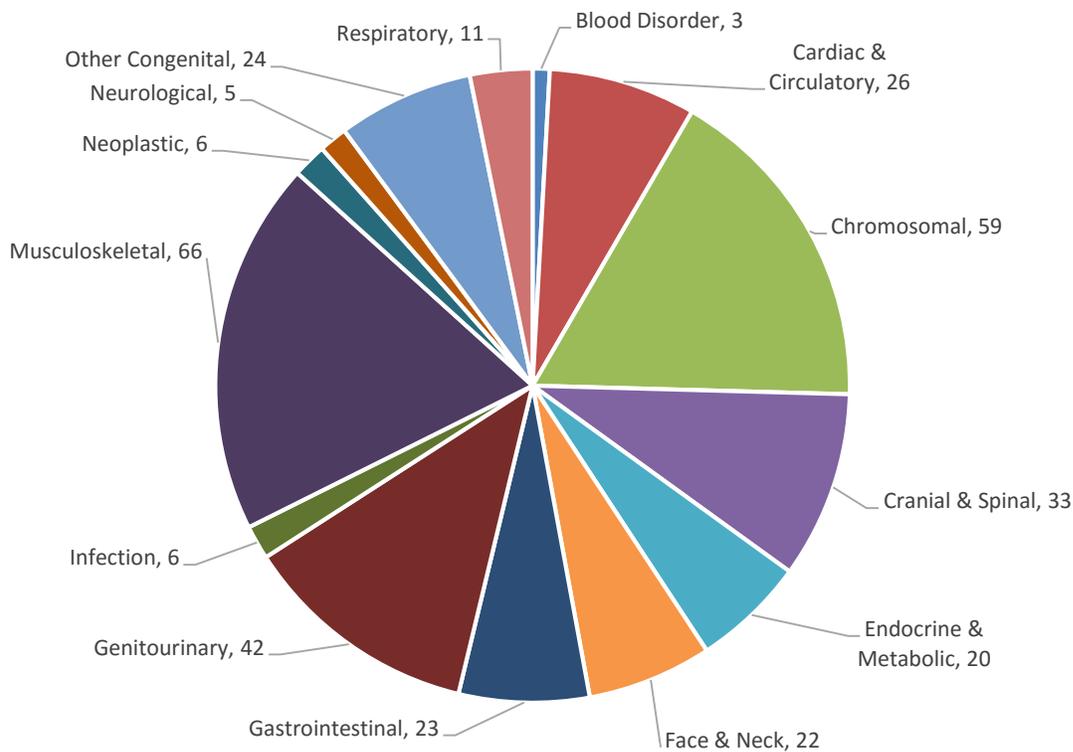
However, it is easier to consider this data if some of these categories are grouped together. Therefore, abnormalities of the musculoskeletal system, comprising 'Congenital Deformities of Hip', 'Congenital Deformities of Feet', 'Limb Reduction Defects' and 'Other Limb & Musculoskeletal System', are the commonest primary classification, (n=66, 19%).

Chromosomal abnormality, ('Down Syndrome' and 'Other Chromosomal Disorders'), is the next largest grouping, (n=59, 17%), with primary abnormalities of the genitourinary system, ('Genital Organs' and 'Urinary System'), accounting for forty-two of the cases.

Cranial & spinal abnormalities, ('Spina Bifida', 'Other Neural Tube Defects' and 'Other Central Nervous System'), is the preferred primary classification in 33, (9.5%). Cardiac and circulatory disorders, 'Heart/Circulatory System' and 'Other Circulatory', account for 26 of the primary abnormalities, (7.5%).

Clearly even with the this regrouping of primary malformation category some disorders, as classified and ordered under ICD 10, are more typically reviewed under other 'systems' and hence an aggregated and simplified classification has been used in these reports in order to aid case presentation. Thus exomphalos and gastroschisis are included as abnormalities of the gastrointestinal tract rather than musculoskeletal system, (although the latter is technically correct). This simplification also attempts to correct some errors inherent in ICD 10, (e.g. 'Congenital Lobar Emphysema' (P250) is listed as a 'Congenital Infection' under ICD 10 rather than as a primary disruption of broncho-pulmonary development). An aggregated and simplified chart based on primary abnormality is presented in Figure 1.3.

Figure 1.3: Simplified classification by primary abnormality, (n=346)



CORE DATA

ABNORMALITY BASED REVIEW

The data are a little more complex when all 551 abnormalities, as defined under ICD 10, are considered, (Table 1.2).

Abnormalities of the musculoskeletal system, comprising 'Congenital Deformities of Hip', 'Congenital Deformities of Feet', 'Limb Reduction Defects' and 'Other Limb & Musculoskeletal System', remain the largest grouping, (n=107, 19.4%). Thereafter cardiac & circulatory abnormalities form the second most common grouping, (n=75, 13.6%).

Table 1.2: Anomalies in any diagnostic position by ICD 10 grouping, (non-exclusive), (n=551)

CONGENITAL MALFORMATION CATEGORY	ICD 10 Code	Total	Rate
SPINA BIFIDA	Q05	12	9.0
OTHER NEURAL TUBE DEFECTS	Q00-Q01	8	6.0
OTHER CENTRAL NERVOUS SYSTEM	Q02-Q04; Q06-Q07	40	30.1
EYE, EAR, FACE & NECK	Q10-Q18	10	7.5
HEART/CIRCULATORY SYSTEM	Q20-Q28	74	55.7
RESPIRATORY SYSTEM	Q30-Q34	13	9.8
CLEFT LIP & CLEFT PALATE	Q35-Q37	23	17.3
OTHER DIGESTIVE	Q38-Q45	27	20.3
GENITAL ORGANS	Q50-Q56	23	17.3
URINARY SYSTEM	Q60-Q64	46	34.6
CONGENITAL DEFORMITIES OF HIP	Q65	14	10.5
CONGENITAL DEFORMITIES OF FEET	Q66	24	18.1
LIMB REDUCTION DEFECTS	Q71-Q73	15	11.3
EXOMPHALOS	Q792	5	3.8
GASTROSCHISIS	Q793	7	5.3
OTHER LIMB & MUSCULOSKELETAL SYSTEM	Q67-Q70; Q74-Q791; Q794-Q799	54	40.6
OTHER ANOMALIES	Q80-Q89	28	21.1
DOWNS SYNDROME	Q90	36	27.1
OTHER CHROMOSOMAL	Q91-Q99	28	21.1
CONGENITAL NEOPLASMS	C00-D48	16	12.0
BLOOD, BLOOD-FORMING ORGANS & IMMUNE	D50-D89	3	2.3
CONGENITAL HYPOTHYROIDISM	E03	6	4.5
PKU	E700-E701	3	2.3
CYSTIC FIBROSIS	E84	5	3.8
OTHER ENDOCRINE, NUTRITIONAL & METABOLIC	E16-E90 (excl. E700-E701 & E84)	7	5.3
NERVOUS SYSTEM	G11-G71	5	3.8
BLINDNESS, DEAFNESS	H50-H919	2	1.5
OTHER CIRCULATORY	I40-I82	1	0.8
DENTOFACIAL ANOMALIES	K070-K071	8	6.0
CONGENITAL INFECTION	P230-P378	8	6.0
TOTAL ANOMALIES		551	414.4

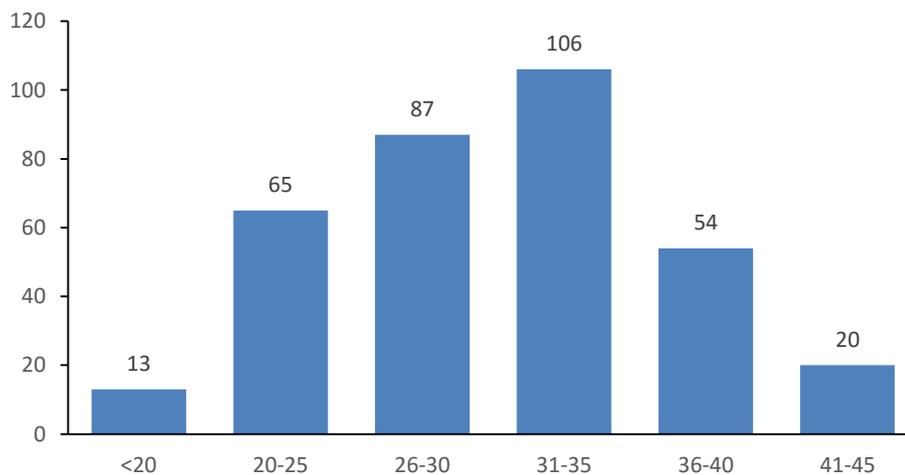
CORE DATA

The single most commonly defined, (coded), abnormality was trisomy 21, (Down syndrome), which was listed on 36 occasions. The next most common abnormality was talipes equinovarus, (n=24), followed by VSD, hypospadias and developmental dysplasia of the hip, (n= 16, 15 & 14 respectively).

MATERNAL AGE

Overall 345 pregnancies accounted for the 346 classified cases of abnormality.⁴ Maternal age at time of delivery, miscarriage or termination ranged from 16 to 44 years, (Figure 1.3). The mean age was 30.5 years. Although maternal age is recorded in the register, no information is held on the father.

Figure 1.3: Maternal age at delivery or loss, (n=345)



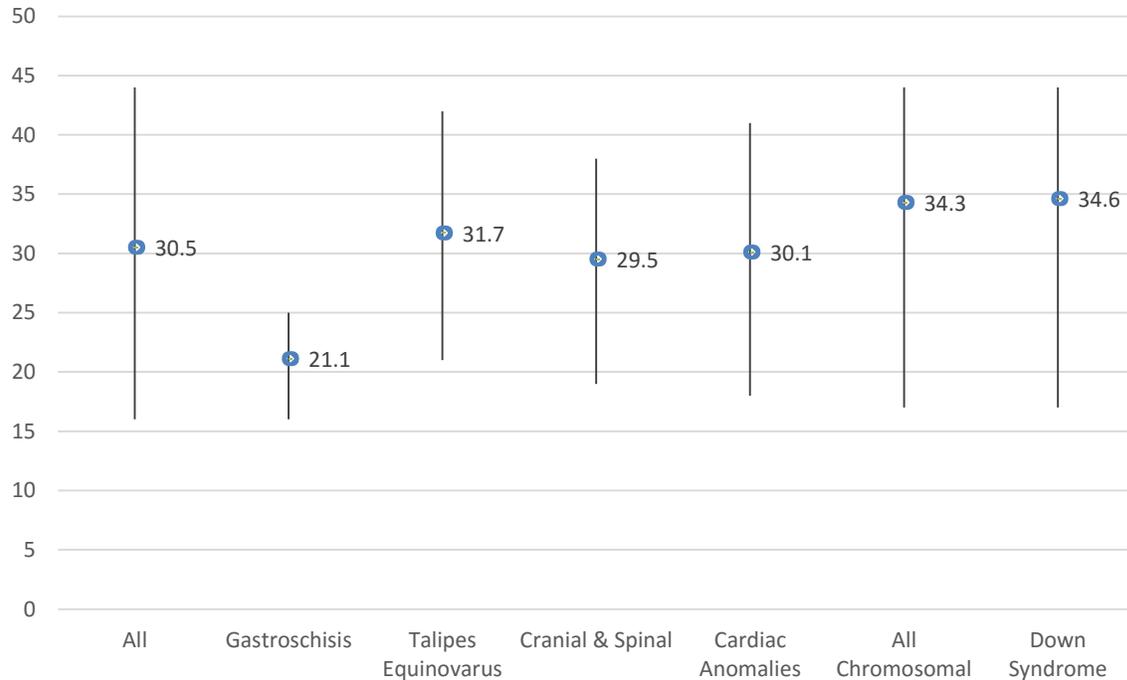
Data from WHO, EUROCAT, BINOCAR and other surveillance programmes suggest that mothers under the age of 20 years have the highest prevalence of non-chromosomal anomalies when compared with older mothers, whereas the birth prevalence of chromosomal anomalies increases with age.

A very cursory analysis of the data, (Figure 1.4), suggests some age related trends. It is difficult to draw too many conclusions from such a small data set but clearly gastroschisis is particularly associated with younger mothers.

⁴ One mother delivered twins where each co-twin had a significant abnormality.

CORE DATA

Figure 1.4: Mean & range of maternal age (years) at time of delivery or loss by primary abnormality or abnormality group



GENDER

It has been long recognized that overall males are at greater risk than females but gender differences in the prevalence of specific birth defects are common e.g. developmental dysplasia of the hip is much more common in female infants.

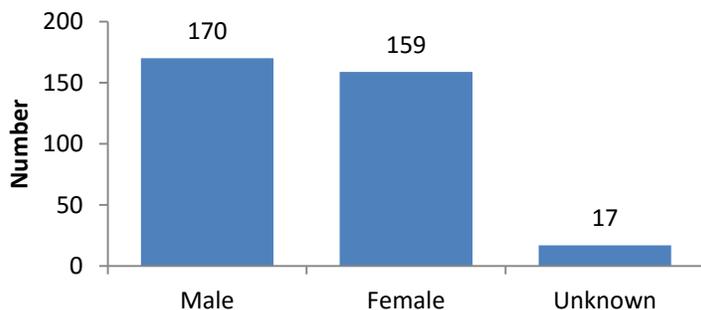
Gender is recorded for 329 cases. Congenital abnormality was slightly more prevalent in males than females. In 17 cases gender is recorded as 'unknown', (Figure 1.5).

All but two of the major categories of birth defect, abnormalities of the Cranial & Spinal and Endocrine systems, had a higher prevalence amongst males. Even so congenital hypothyroidism was more common in female infants.

The mean gestation at delivery for the unknown group was 15.47 weeks, (range 10-21 weeks). The majority were terminations of pregnancy, (n=16), with one spontaneous fetal loss. In all but one case a prenatal diagnosis of abnormality had been made. One pregnancy accounts for two cases of unknown fetal gender.

CORE DATA

Figure 1.5: Fetal & infant gender, (n=346)



MULTIPLE PREGNANCY

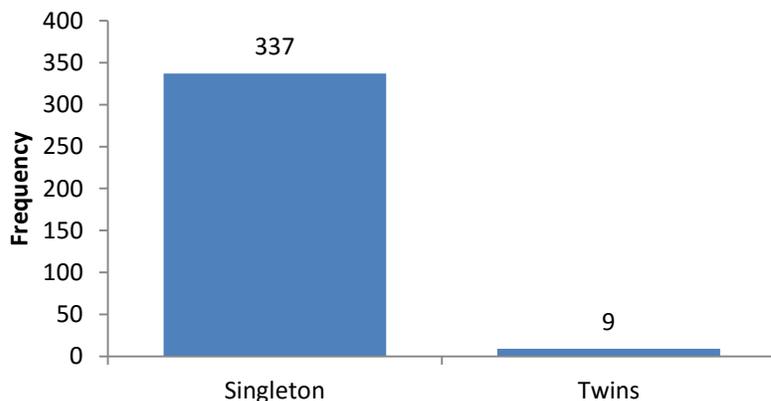
There were 180 twin pregnancies resulting in either live-birth or stillbirth in NHS GG&C during 2014-2015. This is lower than 2013-2014 and reflects boundary changes occurring in 2014. Three hundred and fifty-eight babies were live born with two stillbirths: two pregnancies resulted in the birth of both live born and stillborn co-twins.

The incidence of congenital anomalies in twin pregnancies is generally higher than in singletons. All anomalies that occur in singletons can also occur in dizygotic twins. There are specific anomalies that occur with monozygotic twins. These fall into two main groups: asymmetrical free twins and conjoined twins, (Schwalbe).

Nine cases are recorded from twin pregnancies, (Figure 1.6).

Figure 1.6: Cases with a defined primary abnormality by fetal number

*346 cases but 345 pregnancies



One case of diastematomyelia with tethered cord was diagnosed at birth in a female first twin delivered at term. Her co-twin showed no evidence of abnormality.

CORE DATA

Cardiac abnormalities were seen in two male second twins without abnormality of their co-twins. In one of these cases tetralogy of Fallot had been diagnosed prenatally at the routine 20 week anomaly scan. The pregnancy continued to 36 weeks. An AVSD, without associated abnormality, was diagnosed between one and 12 months in the other case.

Q062	DIASTEMATOMYELIA & TETHERED CORD	No abnormality of co-twin
Q212	AVSD	No abnormality of co-twin
Q213	TETRALOGY OF FALLOT	No abnormality of co-twin
Q914	TRISOMY 13	Stillbirth; No abnormality of co-twin

Selective reductions were performed in three cases. One of these, relates to the acardiac twin described below. In the other cases selective reduction was performed at 21 weeks gestation for multiple limb abnormalities, (bilateral absence of forearms associated with abnormalities of the lower limbs), and at 16 weeks for a second twin diagnosed with trisomy 18 at 13 weeks gestation. In both of these cases there was no abnormality of the co-twin and the pregnancies progressed to live birth of the remaining twin.

Q712	ABSENT FOREARM - BILAT	Selective reduction; No abnormality of co-twin
Q898	ACARDIAC TWIN SEQUENCE	}Twin 1 Acardiac twin
Q899	CONGENITAL ANOMS NOS	}Twin 2 Pump-twin
Q910	TRISOMY 18	Selective reduction; No abnormality of co-twin

Conjoined twins, (Q894)

Symmetrical conjoined twins are complete same sex twins joined at certain body sites. Conjoined twins occur in 1:50,000 births. The most common type is thoracophagus. Ultrasound diagnosis is based on a lack of separation, synchronicity of movement, and shared body organs. Prognosis depends on the extent of fusion

Q894	CONJOINED TWINS	Only one diagnosis/form for conjoined twin
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In the above case termination of pregnancy was performed following early ultrasound diagnosis at nine weeks gestation.

Acardiac Twin Sequence/TRAP Sequence, (Q898)⁵

Often considered to be the most severe form of early twin-to-twin transfusion syndrome. Acardius is anatomically misleading term in that the majority of supposedly acardiac foetuses have at least a rudimentary, although non-functioning, heart. Ultrasound diagnosis is based on the detection of a 2nd twin

⁵ The coding of TRAP sequence should really include P023 'TRAP sequence' as the primary malformation with Q249 'Acardia' and Q000 'Anencephaly' as an essential minimum. Other common malformations such as absent upper limbs, rudimentary alimentary tract etc. should also be coded. The database has now been updated accordingly.

CORE DATA

with absent or rudimentary heart, the detection of reversed arterial perfusion and signs of cardiac failure in the pump twin.

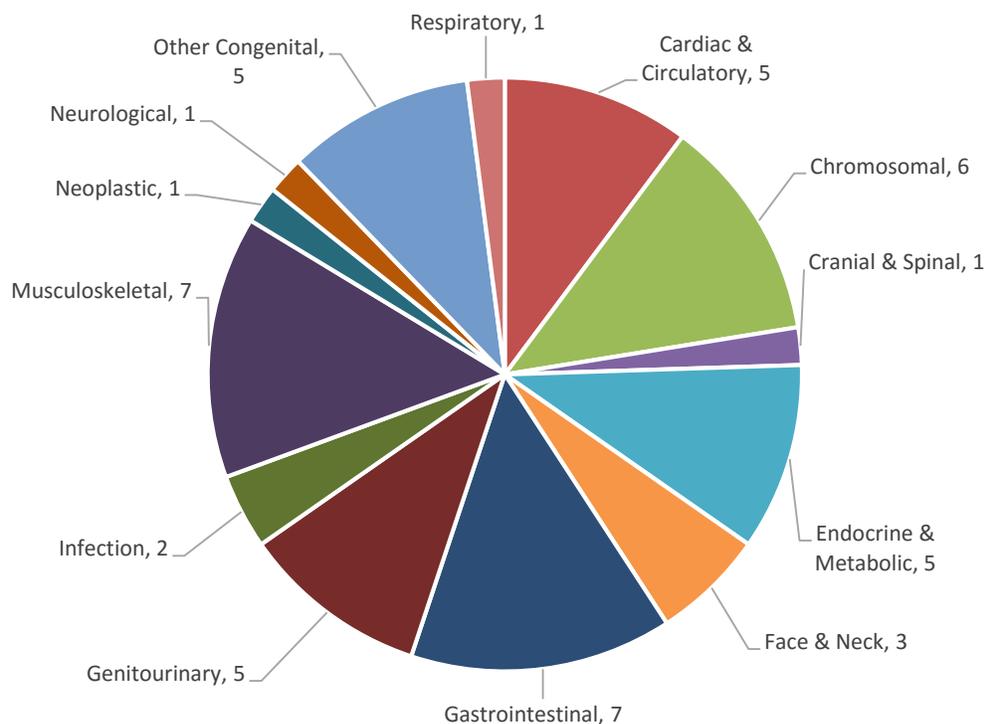
Q898 ACARDIAC TWIN SEQUENCE }Twin 1 Acardiac twin
 Q899 CONGENITAL ANOMS NOS }Twin 2 Pump-twin

Selective reduction of the acardiac twin was performed at 15 weeks gestation. The co-twin, (pump-twin), was subsequently terminated some 2 weeks later when a 'number of potentially significant abnormalities', (unfortunately not specified), were identified.

GESTATIONAL AGE

The frequency of some congenital anomalies varies according to gestational age at delivery. For example, preterm infants have a higher frequency of PDA and undescended testes than term infants, but these conditions are considered physiologically normal amongst preterm infants if they resolve within a short period of time, (and are therefore not routinely classified as abnormalities).

Figure 1.7: Preterm Live births by Primary Abnormality Category, (Simplified), (n=49)



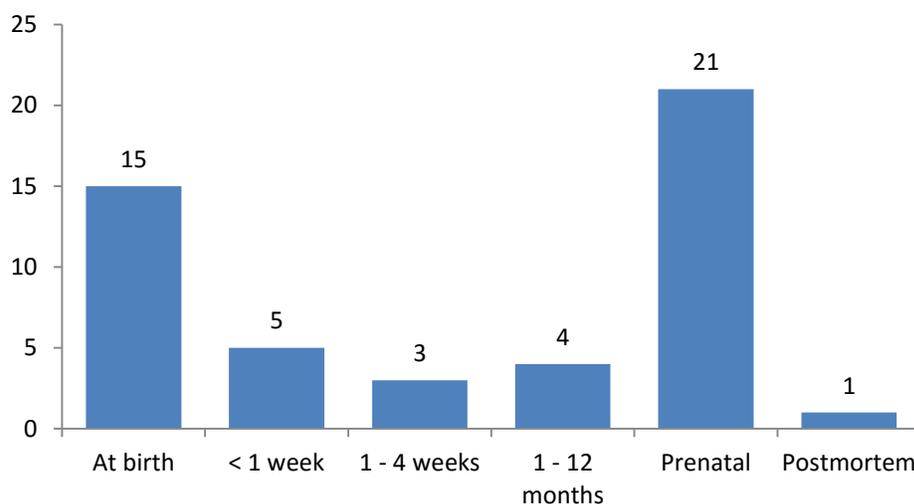
The mean gestation at delivery for live born infants with abnormality, (n=249), was 38 weeks, (range 23 to 43 weeks). Forty-nine of these infants were delivered prematurely, (< 37 weeks gestation), (Figure 1.7). There were two sets of twins. The mean maternal age at time of preterm live birth of an infant with abnormality was 29.1 years, (range 16 - 41 years).

CORE DATA

Forty percent of live born babies with a chromosomal abnormality are delivered prematurely and it is perhaps not surprising that an identical figure is seen for infants with a congenital infection. However, it is interesting that 25% of infants with a primary abnormality of the endocrine & metabolic system deliver before 37 weeks gestation.

Of those babies delivered prematurely a prenatal diagnosis of abnormality had been made in 21 cases, (43%), (Figure 1.8). A diagnosis of primary abnormality was made either at birth or within the first week of life in a further 41%, (n=20). A female infant live born at 35 weeks gestation was found to have polycystic kidneys on post-mortem, (see later).

Figure 1.8: Point of diagnosis of primary abnormality for infants delivered prior to 37 weeks gestation, (n=49)



Four babies with significant abnormality were delivered prior to 29 weeks gestation. All were singleton pregnancies.

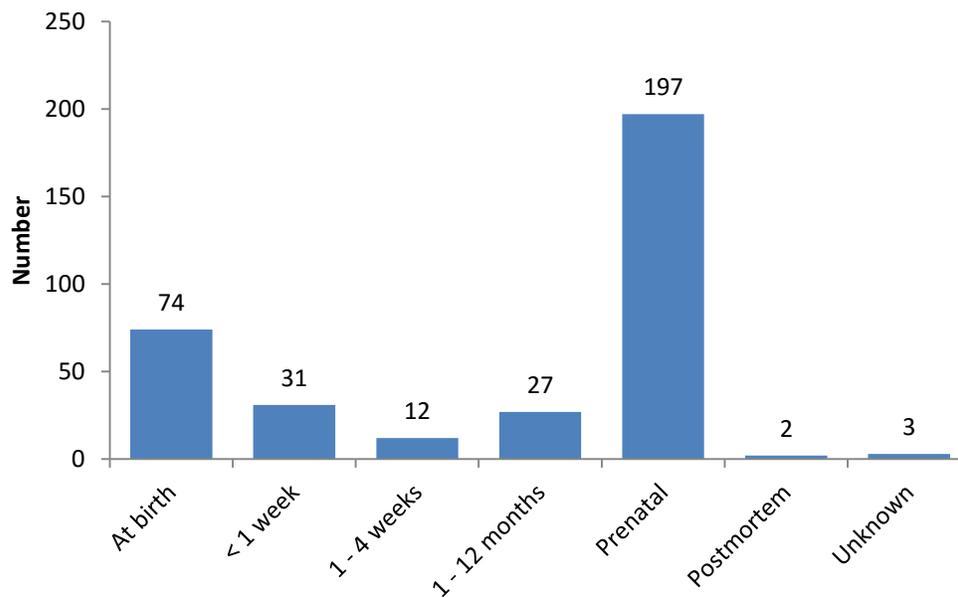
Q373	CLEFT LIP (L) INCOMPLETE & CLEFT PALATE (SOFT)	
Q900	TRISOMY 21	AVSD; Exomphalos
D180	MULTIPLE HAEMANGIOMA SCALP/NECK/TRUNK/LIMBS	
Q793	GASTROSCHISIS	

POINT OF DIAGNOSIS

Point of Diagnosis

Data are available for the 'point of diagnosis' or 'date of discovery' if it is preferred, (Figure 2.1). However it is important to recognize that this does not necessarily imply the point at which the primary abnormality was first detected or diagnosed and some care must be exercised when considering this data. Under EUROCAT definitions the 'point of diagnosis' is the date on which the fetus or infant is first suspected or recognized as being malformed even if a detailed diagnosis is not available.

Figure 2.1: Point of diagnosis for primary abnormality, (n=346)



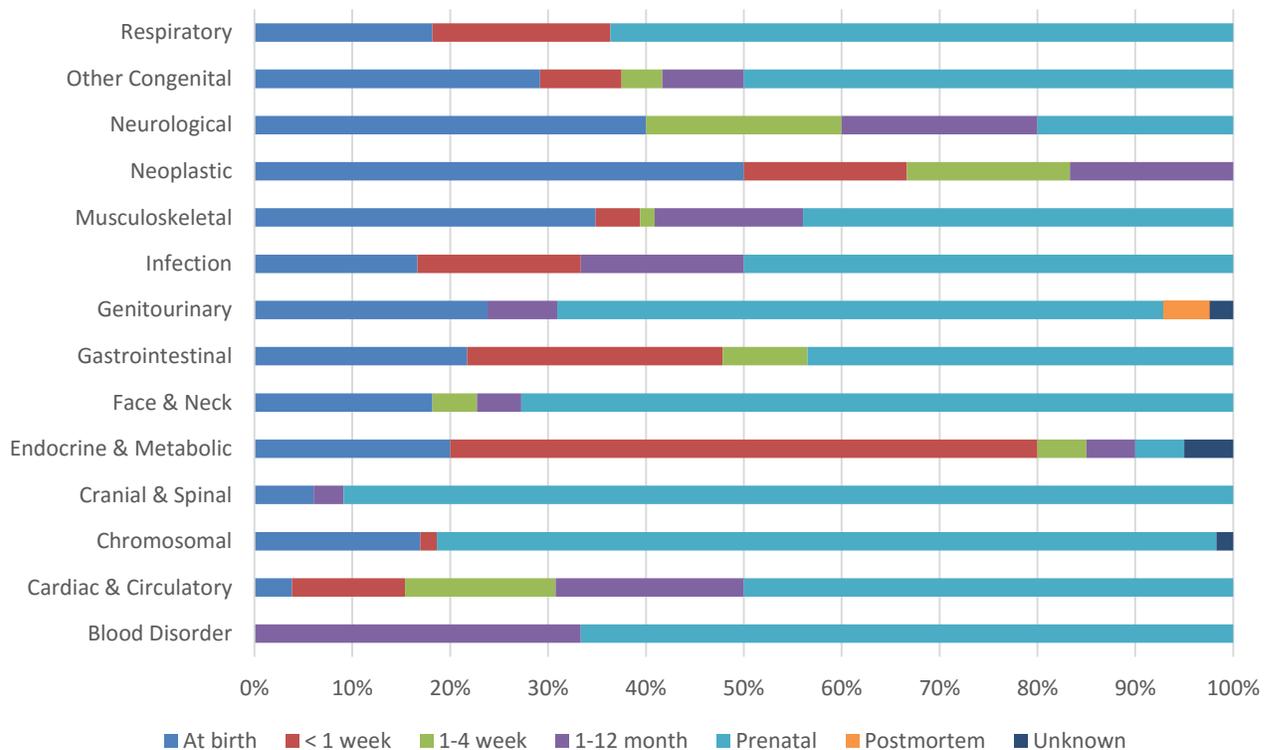
The majority of defined primary abnormalities were diagnosed prenatally, (n=197, 57%). The remaining cases were largely diagnosed within the first week of infant life, (n=105, 30%).

A chart demonstrating point of diagnosis of primary abnormality, as defined under the 'simplified' classification described above, is produced, (Figure 2.2).

Typically most diagnoses of primary abnormality are made either antenatally or within a few weeks of life. Some 90.9% of 'Cranial & Spinal' abnormalities and 79.7% of 'Chromosomal' abnormalities are diagnosed prenatally. Fifty percent of primary 'Cardiac & Circulatory' disorders are diagnosed on prenatal scan. All the lesions classified as 'neoplastic' were diagnosed after delivery.

POINT OF DIAGNOSIS

Figure 2.2: Point of diagnosis of primary abnormality by category, ('simplified'), (n=346)



AT BIRTH

A total of 74 primary abnormalities were diagnosed at birth. The majority were abnormalities of the musculoskeletal system, (n=23, 31.1%). Typically these were cases of talipes equinovarus, developmental dysplasia of the hip and limb defects. However two cases of diaphragmatic hernia were also diagnosed shortly after delivery. Chromosomal and genitourinary abnormalities were next most commonly diagnosed at birth with 10 cases in each category. Trisomy 21 accounted for all of the chromosomal abnormalities diagnosed at birth and hypospadias for all of the genitourinary abnormalities.

Skin disorders such as portwine stain, haemangioma, naevus flammeus and melanocytic naevi were also common. Melanocytic naevus was evident in two cases under two different ICD 10 codes and hence two different groupings.⁶

D224	MELANOCYTIC NAEVUS SCALP (L)	Neoplastic
Q825	MELANOCYTIC NAEVUS UPPER BACK SCAPULAR REGION	Other Congenital

⁶ Coders tend to use Q825 but the correct code should probably be D224.

POINT OF DIAGNOSIS

Beckwith-Wiedemann syndrome is a condition that affects many parts of the body. It is classified as an overgrowth syndrome, which means that affected infants are considerably larger than normal (macrosomia) and tend to be taller than their peers during childhood. However growth begins to slow by about age 8, and adults with this condition are not unusually tall. The signs and symptoms of Beckwith-Wiedemann syndrome vary among affected individuals. Some infants with Beckwith-Wiedemann syndrome have macroglossia which may interfere with breathing, swallowing, and speaking. Other major features of this condition include visceromegaly, creases or pits in the skin near the ears, episodes of hypoglycemia in infancy, and kidney abnormalities. The case described is of a female infant delivered at term. The only associated abnormality was a non-neoplastic naevus.

Q8730 BECKWITH-WIEDEMANN SYNDROME

Sotos syndrome is a disorder characterized by a distinctive facial appearance, overgrowth in childhood, and learning disabilities or delayed development of mental and movement abilities. Characteristic facial features include a long, narrow face; a high forehead; down-slanting palpebral fissures; flushed cheeks; and a small, pointed chin. Sotos syndrome is reported to occur in 1 in 10,000 to 15,000 newborns. However, many of the features of Sotos syndrome can be attributed to other conditions, and it is therefore possible that many cases are not properly diagnosed, and the true incidence may be higher. Most cases (95%) result from new mutations involving the NSD1 gene.

Q8731 SOTOS SYNDROME

This case was of a male infant delivered at term. He had a number of associated abnormalities including macrocephaly, persistent patent ductus arteriosus, accessory rib and malformation of the tricuspid valve.

WITHIN 1ST WEEK

Congenital abnormality was diagnosed in 31 cases during the first week of life. As might be expected the majority, (n=12, 38.7%), of these diagnoses were related to disorders of the endocrine and metabolic system. A diagnosis of congenital hypothyroidism was made on routine newborn blood spot testing in six infants. Testing in the first week also identified two cases of PKU and two cases of cystic fibrosis.

Two cases of coarctation of the aorta and one case of Tetralogy of Fallot were diagnosed within the first week of life.

There were four cases of Hirschprung's disease, a case of oesophageal atresia with trachea-oesophageal fistula and one ileal atresia. Developmental dysplasia of the hip was diagnosed in three infants.

A male infant was diagnosed with tuberous sclerosis within the first week of life. The features of this condition include developmental delay, a characteristic facial rash and epilepsy. This disorder is inherited in an autosomal dominant pattern.

Q851 TUBEROUS SCLEROSIS Male; Term delivery

POINT OF DIAGNOSIS

Prader-Willi syndrome is a complex genetic condition that affects many parts of the body. In infancy, this condition is characterized by weak muscle tone (hypotonia), feeding difficulties, poor growth, and delayed development. Beginning in childhood, affected individuals develop an insatiable appetite, which leads to chronic overeating (hyperphagia) and obesity. Some people with Prader-Willi syndrome, particularly those with obesity, also develop type 2 diabetes mellitus (the most common form of diabetes). People with Prader-Willi syndrome typically have mild to moderate intellectual impairment and learning disabilities. Behavioural problems are common, including temper outbursts, stubbornness, and compulsive behaviour such as picking at the skin. Sleep abnormalities can also occur.

Q8715 PRADER-WILLI SYNDROME Male; Preterm delivery at 33 weeks

BETWEEN 1-4 WEEKS

A total of 12 cases were diagnosed between 1 and 4 weeks of infant life. The majority, (n=4, 25%) were disorders of the cardiovascular system and included cases of Tetralogy of Fallot, VSD (Large) and Coarctation of the Aorta.

Congenital atypical teratoid/rhabdoid tumour of the brain was diagnosed in a male infant. He had been delivered at term.

C719 CONGENITAL ATYPICAL TERATOID RHABDOID TUMOUR BRAIN

Childhood atypical teratoid/rhabdoid tumour (AT/RT) of the central nervous system is a relatively recently described entity. Most AT/RT's demonstrate monosomy 22 or deletions of chromosome band 22q11.1 with alterations in the hSNF5/INI1 gene.

Duchenne muscular dystrophy is probably the commonest and most serious type of muscular dystrophy. Inheritance is as a sex-linked recessive but mutations are frequent and may be responsible for up to 30% of isolated cases.

G7106 DUCHENNE MUSCULAR DYSTROPHY Male; Preterm delivery

Finally a live born female infant was 'diagnosed' in early infant life as having a 'Syndrome of unknown origin'. There is little by way of explanatory information in the data other than the presence of a VSD.

DIAGNOSED AFTER 1 MONTH BUT WITHIN 1 YEAR

A primary congenital abnormality was diagnosed in a total of 27 cases after 1 month but within 1 year of infant life. Musculoskeletal abnormalities were once again common, (n=10, 37%) with developmental dysplasia of the hip the predominate diagnosis.

Cardiac abnormalities continue to be identified, (VSD, AVSD, aorto-pulmonary window, mitral regurgitation), as do abnormalities of the genitourinary system, (posterior urethral valves, renal cystic dysplasia and absent testis).

POINT OF DIAGNOSIS

Spinal muscular atrophy Type 1 was diagnosed in a female infant.⁷

G120 SPINAL MUSCULAR ATROPHY TYPE 1 Female; Term delivery

Bilateral hearing loss as a consequence of congenital CMV infection was identified in a female infant.

Epidermolysis bullosa is the term used to describe a group of hereditary diseases characterized by blistering of skin. The mode of inheritance is autosomal dominant or autosomal recessive depending on the form. The most severe form is Herlitz-type junctional epidermolysis bullosa which has an autosomal recessive inheritance and in which parental consanguinity is often present. There are reports that suggest ultrasound diagnosis is possible in a favourably positioned fetus. In such circumstances loosened epidermal areas can apparently be identified. The condition is more reliably diagnosed by prenatal skin biopsy.

This was a female infant delivered at term. There were no associated abnormalities.

Q810 EPIDERMOLYSIS BULLOSA SIMPLEX Male; Term delivery

Williams syndrome is a developmental disorder that affects many parts of the body. This condition is characterized by mild to moderate intellectual disability or learning problems, unique personality characteristics, distinctive facial features, and heart and blood vessel (cardiovascular) problems.

A form of cardiovascular disease called supra-valvular aortic stenosis (SVAS) occurs frequently in people with Williams syndrome. Young children with Williams syndrome have distinctive facial features including a broad forehead, a short nose with a broad tip, full cheeks, and a wide mouth with full lips. Williams syndrome is caused by the deletion of genetic material from a specific region of chromosome 7. The deleted region includes 26 to 28 genes.

Q8784 WILLIAMS SYNDROME Male; Term delivery

The case described in our data is of a male infant delivered at term to an older mother. Associated abnormalities included malformation of the aorta and a minor partial trisomy.

PRENATAL DIAGNOSIS

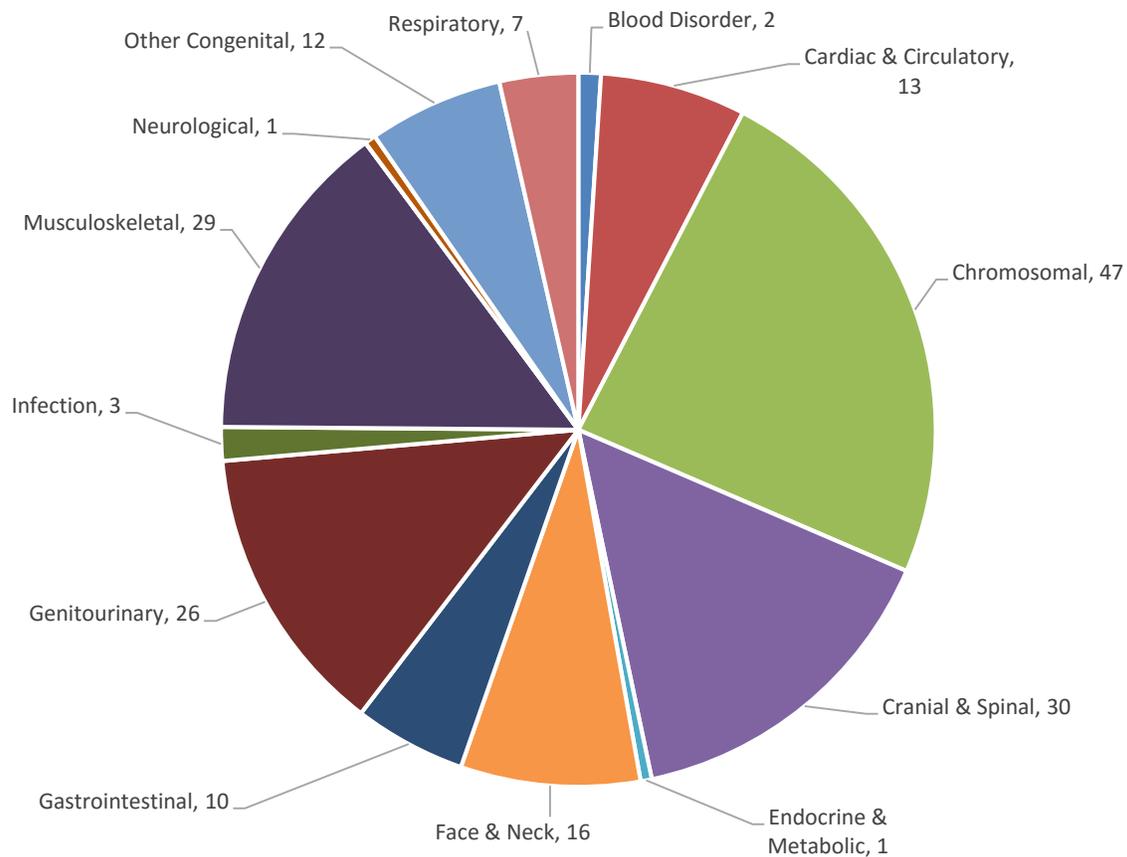
The majority of all diagnoses of congenital abnormality were made in the prenatal period, (n=197).

Chromosomal disorders and abnormalities of the cranio-spinal system were the predominate diagnostic groupings, closely followed by musculoskeletal and genitourinary disorders, (Figure 2.3).

⁷ A further case of SMA Type 1, (G120), was terminated at 13 weeks gestation following prenatal diagnosis.

POINT OF DIAGNOSIS

Figure 2.3: Prenatal diagnosis by primary abnormality (Simplified Classification), (n=197)



Of the 47 cases associated with chromosomal abnormality the majority were Down syndrome, (n=21, 44.7%).

Ninety-one percent of all cranial and spinal defects were diagnosed on prenatal ultrasound scan.

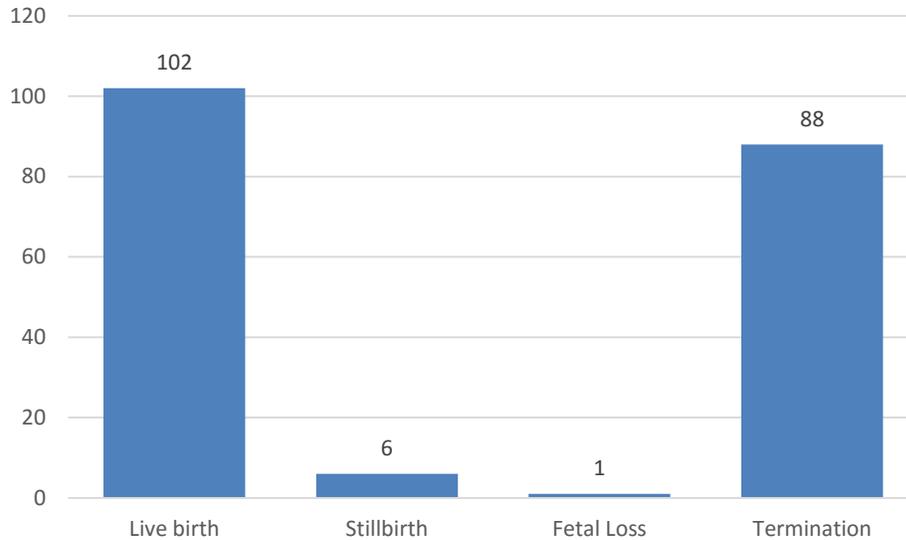
Cardiac and circulatory disorders diagnosed on antenatal scan included double outlet right ventricle, transposition of the great arteries, tetralogy of Fallot and coarctation of the aorta.

Primary disorders of the genitourinary system subject to prenatal diagnosis included hydronephrosis, multicystic dysplastic kidney, duplex kidney, ectopic kidney and posterior urethral valves.

When a prenatal diagnosis of abnormality was made 88 cases were terminated, (45%), but in the majority of cases, (n=102, 52%) the pregnancy continued to live birth, (Figure 2.4).

POINT OF DIAGNOSIS

Figure 2.4: Outcome of pregnancy following prenatal diagnosis of abnormality



Six cases, (3%), were stillborn and there was one fetal loss following prenatal diagnosis of congenital abnormality,

P351	CONGENITAL CMV INFECTION	Stillbirth at 29 weeks
Q000	ANENCEPHALY	Stillbirth at 32 weeks
Q204	UNIVENTRICULAR HEART	Stillbirth at 29 weeks
Q848	FIXED FLEXION DEFORMITIES	Stillbirth at term
Q914	TRISOMY 13	Cystic hygroma; Stillbirth at term
Q998	ISOCHROMOSOME TETRASOMY 9	Dandy-Walker anomaly; Stillbirth at 33 weeks
Q900	TRISOMY 21	Diagnosis at 12 weeks; Fetal loss at 20 weeks

POSTMORTEM DIAGNOSIS

There were two cases when the diagnosis has been recorded as having been made at post-mortem. One was a preterm live birth at 35 weeks gestation of a female infant with polycystic kidneys.

The other was a fetal loss at 20 weeks gestation with urethral atresia. Imperforate anus was also present. The gender is recorded as unknown which is unusual following post-mortem diagnosis.

Q613	POLYCYSTIC KIDNEYS	Unbooked; Live birth; NND
Q643	URETHRAL ATRESIA	Fetal loss at 20 weeks

POINT OF DIAGNOSIS

UNKNOWN

There were three cases listed where the point of diagnosis is recorded as unknown. Two of these were live births at term and it must be presumed that a diagnosis of abnormality was made in neonatal or early infant life.

E833	X-LINKED HYPOPHOSPHATAEMIC RICKETS	Live birth
Q642	POSTERIOR URETHRAL VALVES	Live birth
Q909	DOWNS SYNDROME (ABNORMAL QFPCR)	Stillbirth at 38 weeks

The case of Down syndrome was a stillborn female. Diagnosis was made by abnormal QFPCR and is probably best considered a post-mortem diagnosis.

PREGNANCY OUTCOME

Pregnancy Outcome

A pregnancy outcome is recorded for all 346 cases. The majority of cases, (n=249, 72%), were live-born, (Figures 3.1 and 3.2).

Figure 3.1: Pregnancy outcome, (n=346)

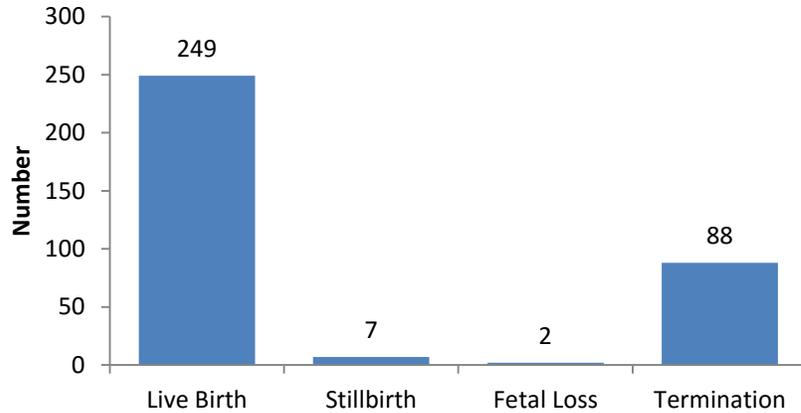
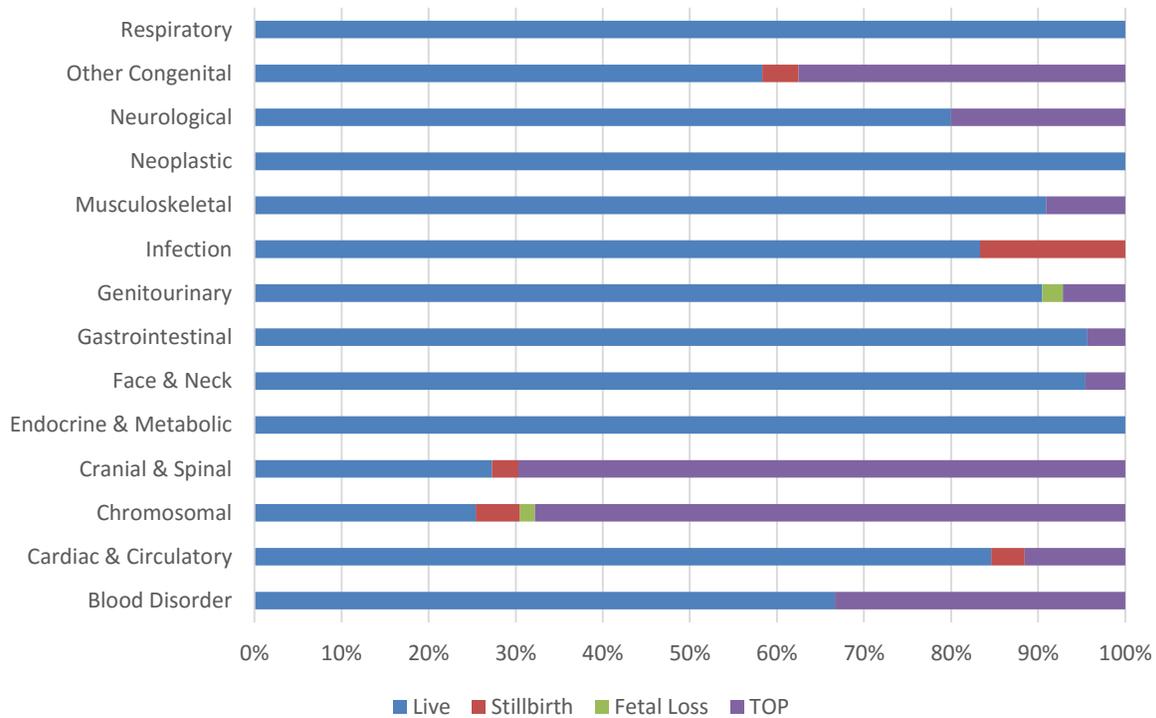


Figure 3.2: Pregnancy outcome by 'simplified' classification, (n=346)

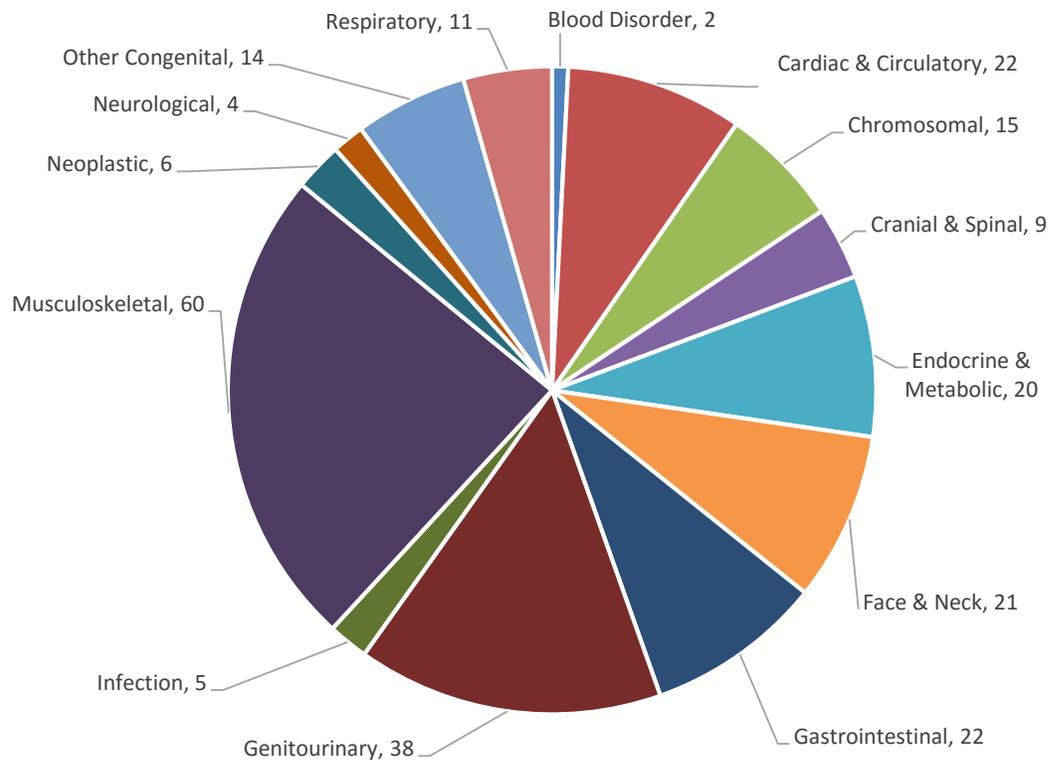


PREGNANCY OUTCOME

LIVE BIRTHS

Live birth was the documented outcome for 72% of the described cases, (n=249). The mean gestation at delivery was 38.1 weeks, (range 23 to 43 weeks).

Figure 3.3: Live birth by primary abnormality, ('simplified' classification), (n=249)



All infants with congenital neoplastic lesions or primary abnormalities of the respiratory, endocrine and metabolic systems were live born. Only 25% of diagnoses of primary chromosomal abnormality and 27% of cranial & spinal abnormalities resulted in live birth.

Five infants were born with a congenital infection. There were two cases of congenital pneumonia and three of congenital cytomegalovirus (CMV) infection. Two of the cases of congenital CMV had been diagnosed prenatally. Cytomegalovirus infection may present on ultrasound examination with non-immune hydrops, hydrocephalus, intracranial calcification, microcephaly and IUGR. However no associated abnormalities are listed in the current data.

PREGNANCY OUTCOME

STILLBIRTH

There were a total of 42 stillbirths in NHS Greater Glasgow & Clyde during 2014-2015. The data records that seven of these stillbirths had a defined congenital abnormality. In all but one case the diagnosis of congenital abnormality was made prenatally. The remaining case is likely to have been diagnosed at post-mortem.

P351	CONGENITAL CMV INFECTION	Stillbirth at 29 weeks
Q000	ANENCEPHALY	Stillbirth at 32 weeks
Q204	UNIVENTRICULAR HEART	Stillbirth at 29 weeks
Q848	FIXED FLEXION DEFORMITIES	Stillbirth at term
Q909	DOWNS SYNDROME (ABNORMAL QFPCR)	Point of diagnosis unknown; Stillbirth at 38 weeks
Q914	TRISOMY 13	Stillbirth at 37 weeks
Q998	ISOCHROMOSOME TETRASOMY 9	Stillbirth at 33 weeks

SPONTANEOUS FETAL LOSS

There were two cases classified as spontaneous fetal loss at 20 weeks gestation. Previous reports have documented a high proportion of chromosomal abnormalities in this group.

Q643	URETHRAL ATRESIA	Imperforate anus
Q900	TRISOMY 21	

TERMINATION OF PREGNANCY⁸

A total of 88 cases, (87 pregnancies), were terminated following prenatal diagnosis. The mean gestation for termination was 17.2 weeks, (range 10-31 weeks).

Chromosomal abnormality was the commonest indication for terminations, (n=40), followed by neural tube and other defects of the central nervous system, (n=23). Cranial and spinal indications for termination included anencephaly, spina bifida, Dandy-Walker malformation, holoprosencephaly and microcephaly, (Figure 3.4).

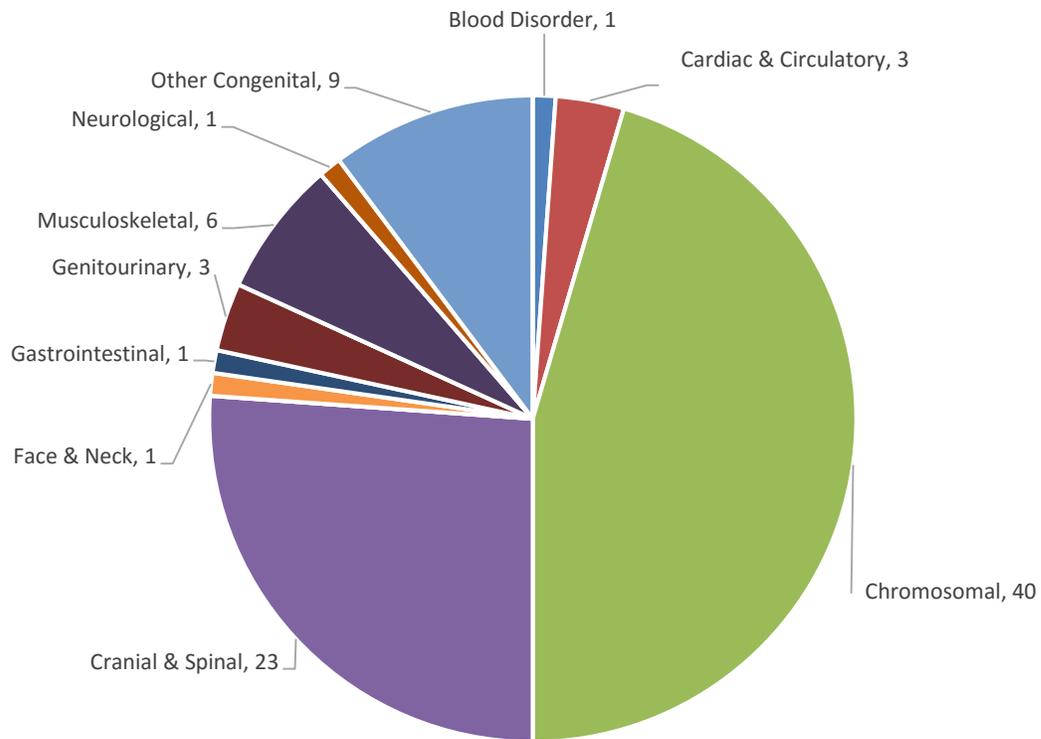
Termination of pregnancy was performed after 24 weeks gestation on two occasions.

Q039	VENTRICULOMEGALY - SEVERE	Prenatal diagnosis at 19 weeks gestation
Q971	PENTASOMY X	Prenatal diagnosis at 29 weeks gestation

⁸ With termination of pregnancy a prenatal diagnosis may not be verified for many reasons including the method of termination, the condition of the specimen or a lack of post-mortem examination.

PREGNANCY OUTCOME

Figure 3.4: Diagnostic Indication for Termination of Pregnancy, (n=87)

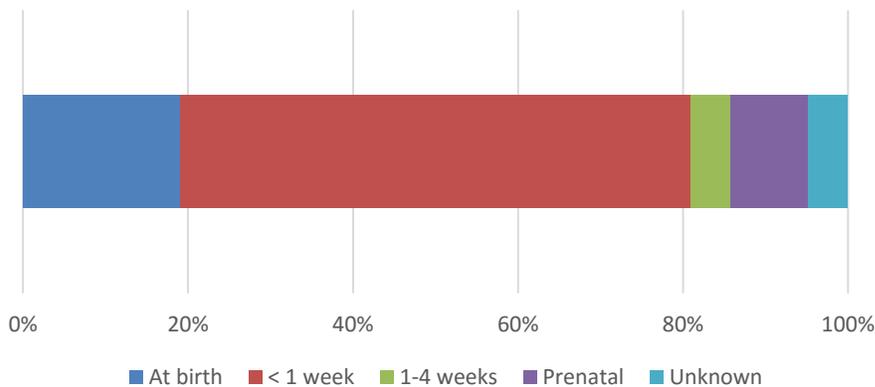


ENDOCRINE & METABOLIC DISORDERS

Endocrine & Metabolic Disorders

A total of 21 cases of endocrine and metabolic disorder are classified in the data. In all but one case the disorder is classified in the primary position. All infants with a defined endocrine or metabolic disorder were live born. These disorders are typically diagnosed as a consequence of new-born bloodspot screening within the first few weeks of life, (Figure 4.1).

Figure 4.1: Point of diagnosis for primary endocrine & metabolic disorders, (n=20)



CONGENITAL HYPOTHYROIDISM (E03)

Congenital hypothyroidism can be the result of a missing or 'misplaced' thyroid gland, hereditary condition, maternal iodine deficiency, maternal thyroid condition and medications. Six cases of congenital hypothyroidism are described in the data. All were live born with no associated abnormalities. In each case the diagnosis was made on bloodspot screening within the first week of life.

E031	CONGENITAL HYPOTHYROIDISM	Female
E031	CONGENITAL HYPOTHYROIDISM	Female
E031	CONGENITAL HYPOTHYROIDISM	Male
E031	CONGENITAL HYPOTHYROIDISM	Female
E0310	CONGENITAL HYPOTHYROIDISM (ABSENT THYROID GLAND)	Female
E0312	CONGENITAL HYPOTHYROIDISM - ECTOPIC THYROID GLAND	Female

Fifty percent of infants with congenital hypothyroidism delivered before 37 weeks gestation. The majority, (83.3%) were female.

ENDOCRINE & METABOLIC DISORDERS

CONGENITAL HYPERINSULINISM (E168)⁹

Congenital hyperinsulinism, (CHI), describes a variety of disorders in which hypoglycaemia results as a consequence of excessive insulin secretion. This may manifest in a variety of ways. For example, irritability, lethargy, cyanosis, hypothermia, and seizures are all associated with neonatal hypoglycaemia. Transient hyperinsulinaemia can also be seen in infants of diabetic mothers or as a consequence of IUGR.

One case of congenital hyperinsulinism was recorded.

E168 CONGENITAL HYPERINSULINISM Male; Live birth; Diagnosed at birth

Mutations in at least nine genes have been found to cause congenital hyperinsulinism. Mutations in the *ABCC8* gene are the most common known cause of the disorder. They account for this condition in approximately 40% of affected individuals.

PANHYPOPITUITARISM (E230)

Congenital panhypopituitarism is a rare condition, particularly in neonates, characterized by multiple pituitary hormone deficiencies. It is potentially fatal in the newborn but treatable if the diagnosis is made early. The clinical presentation is variable and may present as persistent neonatal hypoglycaemia. It can be mistaken for sepsis. Associated features can include cleft lip, single incisor or optic hypoplasia. Male infants typically have a micropenis.

E230 PANHYPOPITUITARISM Optic nerve hypoplasia

The data records a live born female infant delivered at term to a young mother. The diagnosis was made at birth. There was an associated optic nerve hypoplasia, (Q0781).

IN-BORN ERRORS OF METABOLISM

In-born errors of metabolism, (IEM), are a group of disorders in which a single gene defect causes a clinically significant block in a metabolic pathway leading either to an accumulation of the substrate or a deficiency of the product. They are individually rare but collectively common although some may be present in high frequency in certain ethnic groups. Many IEMs are associated with significant morbidity and mortality in affected individuals.

⁹ The ICD 10 classification is still a little vague. The ICD 10 code 'E161' simply means 'Other hypoglycaemia' and includes functional non-hyperinsulinaemic hypoglycaemia as well as hyperinsulinaemia and post hypoglycaemic coma encephalopathy. Likewise 'E169' encompasses any disorder of pancreatic cell secretion such as islet cell hyperplasia.

ENDOCRINE & METABOLIC DISORDERS

DISORDERS OF AROMATIC AMINO ACID METABOLISM (E70)

Phenylketonuria, ('Classical PKU') (E700)

Phenylketonuria (commonly known as PKU) is an inherited disorder that increases the levels of a substance called phenylalanine in the blood. Mutations in the *PAH* gene cause phenylketonuria. The *PAH* gene provides instructions for making an enzyme called phenylalanine hydroxylase. This enzyme converts the amino acid phenylalanine to other important compounds in the body. If gene mutations reduce the activity of phenylalanine hydroxylase, phenylalanine from the diet is not processed effectively. As a result, this amino acid can build up to toxic levels in the blood and other tissues. Because nerve cells in the brain are particularly sensitive to phenylalanine levels, excessive amounts of this substance can cause brain damage. Most cases of PKU are detected shortly after birth by newborn screening, and treatment is started promptly. As a result, the severe signs and symptoms of classic PKU are rarely seen.

E700	PKU	Male
E700	PKU	Female

In each case diagnosis was made on routine newborn blood spot screening in the first week of life.

Other hyperphenylalaninaemias (E701)

Severe 6-pyruvoyl-tetrahydrobiopterin synthase deficiency is a tetrahydrobiopterin deficiency disorder that presents in infancy with developmental delay, seizures, and abnormal movements associated with hyperphenylalaninemia usually detectable by neonatal phenylketonuria screening programmes.

E701	6-PYRUVOYL TETRAHYDROBIOPTERIN SYNTHASE DEFICIENCY
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This was a female infant delivered at 38 weeks gestation. Diagnosis was made at or shortly after birth. There were no associated abnormalities.

Albinism (E703)

Waardenburg syndrome, (E703)

Waardenburg syndrome is associated with disorder of skin and hair pigmentation and usually inherited in an autosomal dominant pattern. The four type of Waardenburg syndrome are typically distinguished by their physical characteristics rather their genetic cause which can be confusing, (types I and III Waardenburg syndrome are caused by mutations in the *PAX3* gene, mutations in the *MITF* and *SNAI2* genes are responsible for type II and type IV is associated with mutations in the *SOX10*, *EDN3*, or *EDNRB* genes).

Types I and II have very similar features, although people with type I almost always have eyes that appear widely spaced and people with type II do not. In addition, hearing loss occurs more often in people with type II than in those with type I. Type III is associated with limb defects and hearing loss. Type IV has signs and symptoms of Hirschsprung's disease.

E703	WAARDENBURG SYNDROME
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ENDOCRINE & METABOLIC DISORDERS

This was a female infant delivered at term. There were no associated abnormalities recorded in the data set. Diagnosis was made in the first week of life. No indication is given as to the diagnostic type.

Other Disorders of Aromatic Amino acid metabolism, E708

Typically this section is used to code for disorders of histidine and tryptophan metabolism. On this occasion the code is used to specify a secondary abnormality in a live born male infant with VACTERL association.¹⁰

Q8726 VACTERL ASSOCIATION Live birth; Pre-term delivery at 31 weeks;

DISORDERS OF BRANCHED CHAIN AMINO-ACID AND FATTY ACID METABOLISM, (E71)

Disorders of Fatty-Acid Metabolism, (E713)

This section of ICD 10 considers fatty acid oxidation defects and disorders such as Medium-chain-Acyl-Coa Dehydrogenase Deficiency, (MCADD), and Primary Carnitine Deficiency.

Primary carnitine deficiency is a condition that prevents the body from using certain fats for energy particularly during periods of fasting. Problems related to primary carnitine deficiency can also be triggered by viral illness. Signs and symptoms typically appear during infancy or early childhood and can include encephalopathy, confusion, vomiting, muscle weakness and hypoglycaemia. Mutations in the *SLC22A5* gene prevent the manufacture of OCTN2 a protein that transport carnitine into cells. Primary carnitine deficiency is inherited in an autosomal recessive pattern.

E713 PRIMARY CARNITINE DEFICIENCY No associated abnormalities.

The data describe a female infant delivered at term. This was a relatively late diagnosis made between 1 month and 1 year.

OTHER DISORDERS OF AMINO ACID METABOLISM (E72)

Disorders of Urea Cycle Metabolism: Citrullinaemia (E722)

Citrullinaemia is an inherited disorder of the urea cycle that causes ammonia and other toxic substances to accumulate in the blood. Two forms of citrullinaemia have been described; they have different signs and symptoms and are caused by mutations in different genes. Type I citrullinaemia is the most common form of the disorder, affecting about 1 in 57,000 people worldwide and is caused by mutations in the *ASS1* gene that

¹⁰ VATER/VACTERL is a non-random association of birth defects affecting multiple organ systems. The term VACTERL is an acronym where V=vertebral abnormality; A=anal atresia; C=cardiac defects; T=tracheal anomalies including tracheo-oesophageal fistula; E=oesophageal atresia; R=renal and /or radial abnormality and L= other limb abnormalities. In addition affected children may also exhibit growth deficiencies but mental functioning and intelligence are usually unaffected. The exact cause of VATER/VACTERL association is unknown with most cases being sporadic.

ENDOCRINE & METABOLIC DISORDERS

codes for the enzyme argininosuccinate synthase 1. Type II citrullinaemia is found primarily in the Japanese population and is typically of adult onset.

'Classic' citrullinaemia, (Type I) usually becomes evident in the first few days of life. Affected infants typically appear normal at birth, but as ammonia builds up in the body they experience a progressive lack of energy (lethargy), poor feeding, vomiting, seizures, and loss of consciousness.

E722 CITRULLINAEMIA Live birth

This case was in a male infant delivered at term. The diagnosis was made within the first week of life.

OTHER DISORDERS OF MINERAL METABOLISM (E83)

Disorders of phosphorous metabolism & phosphatases (E833)

This category includes all hypophosphataemias.

X-linked hypophosphataemic rickets

Hereditary hypophosphataemic rickets is a disorder related to low levels of phosphate in the blood (hypophosphatemia). The most common form of the disorder is known as X-linked hypophosphataemic rickets (XLH). In most cases, the signs and symptoms of hereditary hypophosphataemic rickets begin in early childhood. Mildly affected individuals may have hypophosphatemia without other signs and symptoms. More severely affected children experience slow growth and are shorter than their peers. Other signs and symptoms of hereditary hypophosphataemic rickets can include premature fusion of the skull bones, (craniosynostosis,) and dental abnormalities.

E833 X-LINKED HYPOPHOSPHATAEMIC RICKETS Live birth

This was a female infant delivered at term. She was also found to have a medial abnormality of the face and neck, (Q188). The point of diagnosis is recorded as 'unknown'.

ENDOCRINE & METABOLIC DISORDERS

CYSTIC FIBROSIS, (E84)

Cystic fibrosis is inherited as an autosomal recessive conditions and affects the lungs, pancreas, liver and intestine. It is caused by any one of a number of mutations in the gene responsible for the production of the protein cystic fibrosis transmembrane conductance regulator (CFTR). The most common mutation in the West of Scotland population is $\Delta F508$, a deletion of three nucleotides that results in the loss of the amino acid phenylalanine at the 508th position on the protein.

There were five cases of cystic fibrosis diagnosed in the 2014-2015 cohort. All were live births. In the majority the diagnosis was made on newborn blood spot testing. One case was a prenatal diagnosis.

E840	CYSTIC FIBROSIS	Female; Diagnosed at birth
E840	CYSTIC FIBROSIS	Male; Diagnosed < 1 week
E840	CYSTIC FIBROSIS	Female; Diagnosed < 1 week
E840	CYSTIC FIBROSIS	Female; Diagnosed 1-4 weeks
E840	CYSTIC FIBROSIS	Male; Prenatal diagnosis at 16 weeks

The ICD 10 code E840 implies 'cystic fibrosis with pulmonary manifestations'. A similar coding of E841 would suggest 'cystic fibrosis with intestinal manifestations' such as distal intestinal obstruction or meconium ileus in cystic fibrosis, (but not meconium ileus in cases where cystic fibrosis is not thought to be present). Given the multi-system nature of this disorder it is strange that such a distinction is made.

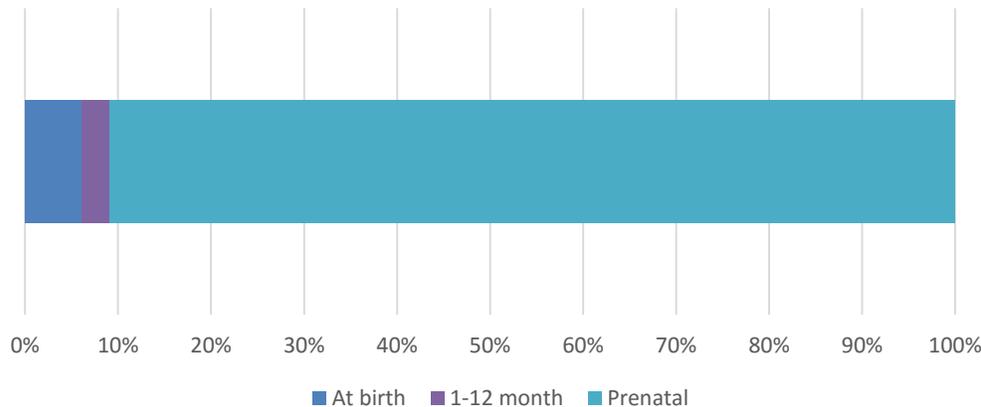
CRANIAL & SPINAL ABNORMALITIES

Cranial & Spinal Abnormalities

CONGENITAL MALFORMATIONS OF THE NERVOUS SYSTEM, (Q00-Q07)

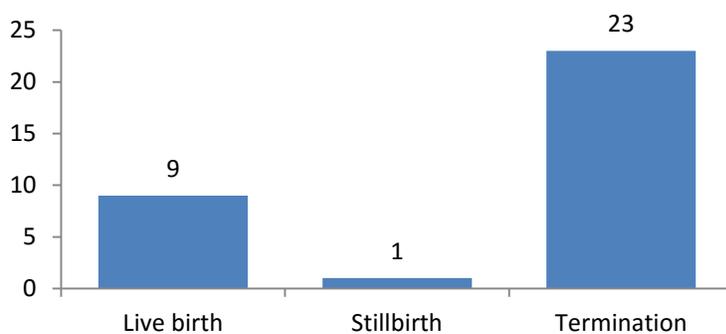
A total of 60 abnormalities of the central nervous system were recorded with 33 falling in the primary diagnostic position, (55%). Over 90% of diagnoses of primary cranial & spinal abnormality were made on prenatal ultrasound scan, (Figure 4.2).

Figure 4.2: Point of diagnosis bar chart, (n=33)



The majority of pregnancies in which a primary diagnosis of cranial spinal abnormality was made ended in termination following prenatal diagnosis, (n=23, 69.7%), (Figure 4.3)

Figure 4.3: Outcome of primary cranial & spinal abnormalities, (n=33)



NEURAL TUBE DEFECTS

Neural tube defects, (NTDs) are a heterogenous group of anomalies of the CNS resulting from defective closure of the neural tube during embryogenesis. NTDs can occur in association with chromosomal disorders, genetic syndromes and other patterns of multiple malformations or occasionally as the result of environmental teratogens. A common mechanism that explains all NTDs is yet to be defined.

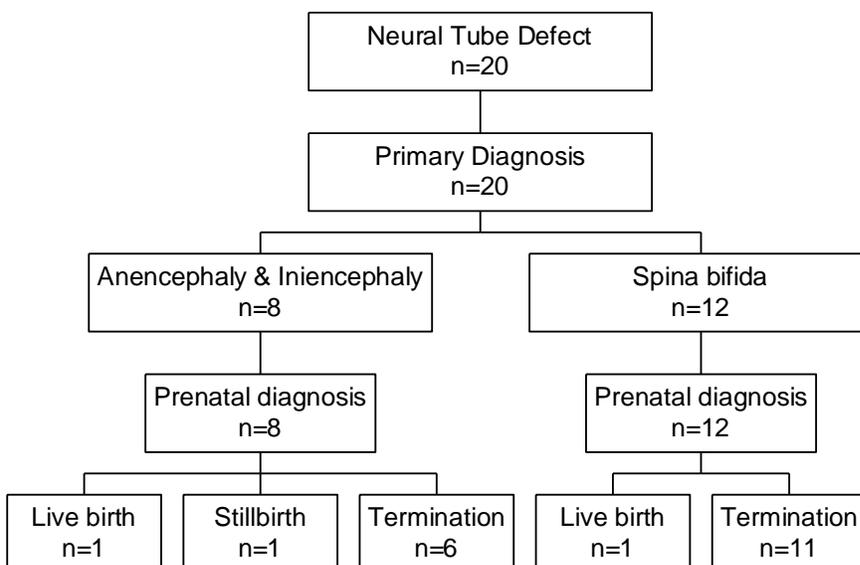
CRANIAL & SPINAL ABNORMALITIES

However most are isolated defects resulting from a presumed interaction between environmental and genetic risk factors. Folate deficiency is the most well established risk factor. Dietary folate supplementation has been shown to reduce the risk of recurrence and even provide some primary prevention

Whereas overall prevalence rates for NTDs are relatively stable, (although some reduction is anticipated through the introduction of folic acid supplementation), the birth prevalence has declined as a result of early prenatal diagnosis and elective termination of affected pregnancies.

Twenty NTDs were defined in the 2014-2015 data, (Figure 4.4). Neural tube defects were always coded in the primary position.

Figure 4.4: Overview of neural tube defects



Anencephaly, (Q000)

Anencephaly is defined as absence of the superior vault and cerebrum. It is the most common and severe anomaly of the central nervous system. The most striking feature at ultrasound is the presence of large bulging eyes marking the superior boundary of the fetus. Abrupt spasmodic body movements are not uncommon. The prognosis is grave and the severity of the condition justifies termination of the pregnancy.

Iniencephaly, (Q002)

A rare and complex neural tube defect involving the occiput and inion, resulting in extreme retroflexion the head variably combined with occipital encephalocoele or rachischisis of the cervical and thoracic spine. With iniencephaly, the cranium is always closed, which helps to differentiate iniencephaly from cases of anencephaly with spinal retroflexion.

CRANIAL & SPINAL ABNORMALITIES

Spina Bifida¹¹

Spina bifida is a general term used to describe a neural tube defect of the spine in which part of the meninges or spinal cord or both protrudes through an opening in the vertebral column. Posterior defects of neural tube closure are among the most common fetal abnormalities. Studies have shown that NTDs are ultimately based on the inadequate expression of certain pattern control genes. This may be caused by gene deletion, exogenous teratogenic agents, (e.g. valproic acid), or vitamin deficiency.

In closed spina bifida the bony defect of the posterior vertebral arches, the herniated meninges and neural tissue are covered by a layer of skin.

Q051	SPINA BIFIDA - LARGE + HYDROCEPH	Termination;
Q051	T/L MYELOMENINGOCELE (LARGE) + HYDROCEPH	Termination; Ectopic kidney
Q052	L/S SPINA BIFIDA (LARGE) w HYDROCEPH	Termination
Q052	L/S SPINA BIFIDA (LARGE) + HYDROCEPH	Termination
Q052	L/S SPINA BIFIDA + HYDROCEPH	Termination
Q052	L/S MYELOMENINGOCELE	Termination
Q052	L/S SPINA BIFIDA & HYDROCEPH	Termination
Q052	L/S MYELOMENINGOCELE (LARGE) + HYDROCEPH	Termination
Q0521	L/S MYELOMENINGOCELE (OPEN) + HYDROCEPH	Live birth; Agnesis Corp. Call.
Q0521	L/S MYELOMENINGOCELE (LARGE, OPEN) + HYDROCEPH	Termination
Q0571	L/S NTD - OPEN	Termination
Q0591	SPINA BIFIDA (LARGE OPEN)	Termination; Exomphalos

The commonest associated abnormality was Arnold-Chiari Malformation, (Q070), consisting of downward displacement of the cerebellar tonsils through the foramen magnum.

Although termination of pregnancy was the usual outcome, one female infant was delivered at term following prenatal diagnosis of abnormality at thirty-three weeks gestation. There was an open lumbo-sacral myelomeningocele with associated hydrocephalus, Arnold-Chiari malformation and agenesis of the corpus callosum.

MICROCEPHALY (Q02X)

Microcephaly is a relatively rare condition. Causes of microcephaly include CNS malformations, infections, (CMV, rubella and toxoplasmosis), chromosomal abnormalities, maternal PKU and certain teratogens, (including alcohol and cocaine). The ultrasound diagnosis is based on the detection of a small skull with the craniometric parameters seen to be reduced on serial scans.

¹¹ Coding of spina bifida should be based on one code only. The codes in the Q05 section describe both the site of the defect and if hydrocephalus is present or not. The highest position of the defect is coded e.g. 'thoracic' if both thoracic and lumbar. The RCPC (BPA) 4th digit codes record if the defect was 'open' (1), 'closed' (2) or 'unknown' (9). However the Q070 code is also used for any associated Arnold-Chiari malformation.

CRANIAL & SPINAL ABNORMALITIES

There were a total of eight cases of microcephaly described in the 2014-2015 data. In four cases microcephaly was the primary diagnosis.

Q02X	MICROCEPHALY	Live birth; Accessory auricle; Accessory rib
Q02X	MICROCEPHALY	Live birth
Q02X	MICROCEPHALY - SEVERE	Pre-term; Live birth; Micrognathia
Q02X	MICROCEPHALY	Termination at 12 weeks

Four further cases of microcephaly are listed with the abnormality as a secondary feature.

Q042	HOLOPROSENCEPHALY	Prenatal diagnosis; Live birth
Q8726	VATER ASSOCIATION	Dandy-Walker; TOF; Termination
Q897	MULTIPLE ANOMALIES	Double inlet ventricle; Termination
Q915	TRISOMY 13 MOSAIC	Holoprosencephaly; CTEV; Cleft lip & palate

ATRESIA OF FORAMINA OF MAGENDIE & LUSCHKA, (Q031)

Dandy Walker malformation is defined by hydrocephalus and partial or complete absence of the cerebellar vermis with a posterior fossa cyst that opens directly into the 4th ventricle. The aetiology is uncertain. The ICD 10 classification reflects the idea that atresia of the foramina of Magendie and Luschka is the underlying cause. However cases have been described in which atresia has not been present and it is considered that the anomaly is due to a more complex developmental error. Ultrasound scan reveals a cystic mass in the posterior fossa and an abnormally shaped cerebellum with some dilatation of the lateral ventricles.

One case is recorded with the abnormality as the primary diagnosis.

Q031	DANDY WALKER MALF	Prenatal diagnosis; Termination; No associated anomalies
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Dandy-Walker malformation is also described in a case of VATER association

Q8726	VATER ASSOCIATION	Prenatal diagnosis; Termination
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HOLOPROSENCEPHALY (Q042)

This is a condition in which only a single large ventricle is seen or with a small skull containing no midline echo, disorganized cerebral ventricles and prominent cerebral peduncles. The disorder is particularly associated with chromosomal defects, typically trisomy 13.

Three forms are distinguished: alobar, semi-lobar and lobar holoprosencephaly. Both the alobar and semilobar forms are characterized by a single cystic cavity between the two hemispheres in the anterior part of the skull.

CRANIAL & SPINAL ABNORMALITIES

Although holoprosencephaly is essentially a midline defect differentiation is required from pronounced hydrocephalus; in contrast to hydrocephalus ultrasound scan will show an absence of the midline echo and cavum septi pellucidi. Varying degrees of thalamic fusion are seen depending on the form. Prognosis depends on the form. The alobar form is fatal but the semi-lobar and lobar forms are compatible with life at least until childhood. Significant mental retardation is to be expected.

Holoprosencephaly was recorded as a primary abnormality in three cases.

Q042	HOLOPROSENCEPHALY - ALOBAR	Prenatal diagnosis; Live birth
Q042	HOLOPROSENCEPHALY	Prenatal diagnosis; Termination
Q042	HOLOPROSENCEPHALY	Prenatal diagnosis; Termination

The male infant alobar holoprosencephaly was a live birth at term. He had multiple associated abnormalities including microcephaly, microphthalmos, microcornea and choanal atresia but normal karyotype.

Holoprosencephaly is recorded in a further two cases associated with major chromosomal abnormality.

Q915	TRISOMY 13 MOSAIC	Prenatal diagnosis; Termination
Q927	TRIPLOIDY	Prenatal diagnosis; Termination

OTHER REDUCTION DEFORMITIES OF THE BRAIN, (Q043)

HYDRANENCEPHALY, (Q0435)

Hydranencephaly describes congenital absence of the cerebral hemispheres with preservation of midbrain and cerebellum. Occurrence is sporadic. It is generally considered to be an encepholoclastic lesion originating in the third trimester as a consequence of severe ischaemic insult(s) due to widespread vascular occlusion, infections or prolonged severe hydrocephalus.

On ultrasound examination an intracerebral fluid collection is seen. This differs from hydrocephalus in that the brain mantle is absent. The falx cerebri may be absent or only partially visualized. It can be difficult to differentiate from alobar holoprosencephaly. The prognosis is grave and with prenatal diagnosis pregnancy termination is an option.

Q0435	HYDRANENCEPHALY	Prenatal diagnosis; Termination
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The case described was perhaps unusually a second trimester prenatal diagnosis associated with porencephaly, micrognathia, TEV, congenital scoliosis and unspecified abnormalities of the limbs.

Cardiac & Circulatory Abnormalities

Congenital heart disease is a leading cause of infant mortality and structural cardiac anomalies are the most lesions most frequently missed by prenatal ultrasonography.

Congenital heart defects are those gross structural abnormalities of the heart or intra-thoracic vessels that are of actual or potential functional significance. They are one of the most important causes of infant morbidity and mortality and continue to constitute an important cause of disability and death in adult life. Birth prevalence is variously quoted between 50 and 150 per 10,000 total births.

There is a large body of evidence emerging on the genetic and non-genetic risk factors for congenital heart disease. The genetic cause include chromosomal syndromes, (e.g. trisomy 18) and single gene disorders, (e.g. 22q11 Di George syndrome). Other determinants, (some of which are potentially modifiable), include maternal diabetes, therapeutic and non-therapeutic drug exposure and lifestyle characteristics.

The most severe forms of congenital heart disease should be identifiable on prenatal ultrasound by 24 weeks gestation. The classic 'four-chamber view' will diagnose the majority but not all of these abnormalities. Additional views including visualization of both left and right outflow tracts are recommended to improve diagnostic ascertainment.

EUROCAT DEFINED SERIOUS CARDIAC ABNORMALITY

EUROCAT defines a list of severe congenital heart defects. These are cardiac malformations that require surgical resolution.

Overall 30 cases displayed 31 abnormalities that would fulfil the EUROCAT criteria for severe congenital heart disease, (Table 4.1). EUROCAT defined severe congenital heart defects are not always listed as the primary abnormality – they are secondary abnormalities in 39% of cases.

Twenty-three of these cases were live births, (76.7%). Six cases were terminated following prenatal diagnosis of abnormality, (20%). There was one stillbirth.

Twenty-one of these 31 EUROCAT defined cases had an abnormality diagnosed on prenatal scan giving an overall case detection rate for severe cardiac abnormality of 67.7%. This detection rate must be viewed with some caution because the cardiac lesions may not have been the defining feature for cases where they are classified in the secondary position. Yet looking only at the 18 cases where a primary diagnosis of severe cardiac anomaly was made, an almost identical prenatal detection rate of 66.7% is calculated, (n=12).

CARDIAC & CIRCULATORY ABNORMALITIES

Table 4.1: EUROCAT Severe Congenital Heart Disease

Common Arterial Truncus	1 case; 1 secondary; 1 live birth
Transposition of Great Arteries*	4 cases; 3 primary; 1 secondary; 4 live births
Single Ventricle	4 cases; 2 primary; 2 secondary; 1 stillbirth; 3 terminations
AVSD	6 cases; 1 primary; 5 secondary; 5 live births; 1 termination
Tetralogy of Fallot	3 cases; 3 primary; All live births
Tricuspid Atresia & Stenosis	2 cases; 1 primary; 1 secondary; 1 termination; 1 live birth
Ebstein's Anomaly	No cases
Pulmonary Valve Atresia	No cases
Aortic Valve Atresia/Stenosis	No cases
Hypoplastic Left Heart	3 cases; 3 primary; 2 live births; 1 termination
Hypoplastic Right Heart	No cases
Coarctation of Aorta*	8 cases; 6 primary; 2 secondary; 8 live births
Total Anomalous Pulmonary Venous Return	No cases

*One case had two EUROCAT defined abnormalities.

Common Truncus, (Q200)

Persistence of the single arterial trunk which arises from astride the intraventricular septum. Pulmonary, coronary and systemic arteries are established from this common trunk. In this condition the truncus arteriosus fails to properly divide into the pulmonary trunk and the aorta. There may be an associated ventricular septal defect. Usually the defect arises spontaneously. However, up to 50% of cases are associated with chromosome 22q11.2 deletions, (Di George syndrome). The four chamber view is generally normal in this condition.

Common truncus is listed as a secondary malformation in one case.

Q300 CHARGE SYNDROME Persistent truncus arteriosus;

The 'point of diagnosis' for this case would appear to have been the routine anomaly scan at 19 weeks gestation. Whether or not this was the cardiac abnormality or the bilateral cleft lip and palate that 'revealed' the abnormality is uncertain. The pregnancy resulted in the live birth of a male infant at 37 weeks gestation.

This case is also interesting in that it is an example of the considerable overlap in CHARGE & Di George syndrome. Di George is perhaps better considered as a 22q11.2 deletion syndrome. The signs and symptoms of this syndrome are varied. As a consequence similar groupings of anomalies have been labelled as separate conditions such as Di George syndrome, conotruncal anomaly face syndrome and velocardiofacial syndrome. ICD 10 still classifies Di George syndrome as a primary 'blood disorder'.

Transposition of the Great Arteries, (Q2013)

Complete transposition of the great vessels indicates that the aorta arises from the right ventricle and the pulmonary artery from the left ventricle. The four chamber view and the atrio-ventricular connections will appear normal, except in cases with an associated VSD. However the two great vessels will arise in parallel from the base of the heart.

CARDIAC & CIRCULATORY ABNORMALITIES

The three vessel view will be abnormal because the pulmonary artery lies below the aortic arch. Transposition is usually isolated but may be associated with a VSD and pulmonary stenosis either alone or in combination. Uncomplicated TGA is not associated with haemodynamic compromise in utero.

There were four cases where transposition of the great arteries is recorded. In three cases it is the primary abnormality.

Q203	TGA	Prenatal diagnosis; Live birth
Q203	TGA	Prenatal diagnosis; Live birth
Q203	TGA	Prenatal diagnosis; Live birth

In each case TGA was associated with other (multiple) abnormalities - never appearing as an isolated diagnosis. Associated anomalies included ASD, VSD, coarctation, micrognathia, endocardial fibroelastosis and congenital malformations of the limbs.

A further case is described with Di George syndrome as the primary coding.

D821	DI GEORGE	Prenatal diagnosis; Live birth
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Uncomplicated transposition of the great arteries requires surgical treatment in the first few weeks of life and long term outcome is generally good. However the outcome is less favourable if there is coexisting VSD or pulmonary stenosis.

Double Inlet Ventricle (Single Ventricle), Q204

In a double inlet connection both atrioventricular valves drain predominantly to one ventricle. In most cases there is one dominant ventricle and one rudimentary chamber. The four chamber view will be abnormal as no ventricular septum is seen to divide the ventricular mass equally between the two atrioventricular valves. The arterial connections may be concordant but are frequently discordant, (transposed). Staged surgery leading to one ventricle circulation, (Fontan), may be considered but quality of life and long-term outcome are poor.

The anomaly is classified on four occasions.

Q204	UNIVENTRICULAR HEART	Prenatal diagnosis; Stillbirth at 29 weeks
Q204	UNIVENTRICULAR HEART	Prenatal diagnosis; Termination
Q894	CONJOINED TWINS	Prenatal diagnosis; Termination
Q897	MULTIPLE ANOMALIES	Prenatal diagnosis; Termination

Multiple anomalies, (Q897), is another 'ICD 10 'bucket' coding. A male fetus was terminated at 20 weeks gestation following the diagnosis of multiple abnormalities on the routine fetal anomaly scan. Anomalies detected included microcephaly and univentricular heart. The parents declined post-mortem examination.

CARDIAC & CIRCULATORY ABNORMALITIES

ATRIOVENTRICULAR SEPTAL DEFECT, (AVSD), (Q212)

In this condition there is a defect in the lower part of the atrial septum and the inlet part of the ventricular septum. As a result the two atrioventricular valves do not form normally. Instead a common atrioventricular valves bridges the defect and there is loss of the normal differential insertion seen at the crux on the four chamber view. AVSDs are one of the most common forms of heart disease seen in prenatal life. The scan appearance is one of a single valve opening into both ventricular chambers. The sizes of both the atrial and ventricular components can be variable. This type of defect is often associated with extra cardiac defects and chromosomal disorders, in particular trisomy 21.

An AVSD is coded on six occasions, once as a primary abnormality.

Q212	AVSD	No associated abnormalities; Live birth; Diagnosed after 1 month
Q790	DIAPHRAGMATIC HERNIA	Prenatal diagnosis; Live birth; AVSD; ASD; Situs inversus
Q900	TRISOMY 21	Live birth; Diagnosed at birth; AVSD; ASD
Q900	TRISOMY 21	Prenatal diagnosis; Live birth; AVSD
Q900	TRISOMY 21	Prenatal diagnosis; Live birth; AVSD; Exomphalos
Q910	TRISOMY 18	Prenatal diagnosis; Termination; AVSD; Cong. Malf. Brain

Prognosis depends on the presence of other abnormalities but as an isolated lesion long-term prognosis following correctional surgery is generally good.

TETRALOGY OF FALLOT, (Q213)

Tetralogy of Fallot is characterized by ventricular septal defect, stenosis of the infundibulum of the pulmonary artery, aorta over-riding the intraventricular septum and right ventricular hypertrophy. However prenatally only three features are reliably seen: right ventricular hypertrophy may not be evident until the latter stages of pregnancy or indeed early neonatal life. The four chamber view alone cannot be relied upon to make the diagnosis. The diagnosis is usually made by demonstrating the aortic root. The aorta arises from the centre of the heart and sits astride the ventricular septum above the peri-membranous VSD. This is done by ensuring that there is continuity between the left ventricle and aortic outflow. The abnormality may also be suspected when there is difficulty identifying the right outflow tract owing to pulmonary stenosis or atresia.

Extra-cardiac defects, chromosomal anomalies and genetic conditions, (particularly 22q11.2 deletion), are seen in over 30% of cases. However no associated malformations were seen in the three cases described in the 2014-2015 data. Prenatal diagnosis was only achieved for one case.

Usually corrective surgery can be performed as a single procedure in the first year if life with good long-term outcome.

Q213	TETRALOGY OF FALLOT	Live birth; Diagnosed < 1 week
Q213	TETRALOGY OF FALLOT	Live birth; Diagnosed 1-4 weeks
Q213	TETRALOGY OF FALLOT	Live birth; Prenatal diagnosis

CARDIAC & CIRCULATORY ABNORMALITIES

HYPOPLASTIC LEFT HEART, (Q234)

This is a group of defects in which the left ventricle may be absent or extremely hypoplastic as a result of a combination of aortic atresia and mitral valve atresia or stenosis. Approximately 10% of cases are associated with a chromosomal abnormality, usually trisomy 13, trisomy 18 or Turner syndrome. Hypoplastic Left Heart syndrome is readily diagnosed on prenatal scan. In severe cases the four-chamber view is already abnormal in the second trimester. The lumen of the left ventricle may be extremely small or simply not visualized. The aorta is extremely hypoplastic and its origin and course are difficult to define. There may be reversed flow in the aortic arch. The mitral valve fails to open and there is no demonstrable flow from the left atrium to left ventricle on colour flow Doppler. Compensatory dilatation of the right ventricle and pulmonary trunk may be present.

Q234	HYPOPLASTIC (L) HEART	Prenatal diagnosis; Live birth
Q234	HYPOPLASTIC (L) HEART	Prenatal diagnosis; Live birth
Q234	HYPOPLASTIC LEFT HEART	Prenatal diagnosis; Termination at 22 weeks

Hypoplastic left heart syndrome can occasionally be associated with chromosomal anomalies, particularly Turner's syndrome but also trisomy 18 and trisomy 13. However, no associated abnormalities were seen in the three instances described above.

COARCTATION OF THE AORTA, (Q251)

Coarctation of the aorta is a narrowing of the aortic arch between the origin of the subclavian artery and the insertion of the arterial duct.

A simple coarctation of the aorta is difficult to diagnose on prenatal scan. The most reliable way to assess the aortic arch is in the transverse view in the upper thorax. However, visualization of the aortic arch in longitudinal section is not a usual component of the routine prenatal ultrasound scan. In this view the aortic arch is smaller than normal and smaller than the arterial duct. There may be disproportion between the left and right ventricles and between the aortic arch and pulmonary trunk. However, this is not a reliable diagnostic feature as a slight discrepancy in size between left and right ventricle will be seen in a healthy third trimester fetus.

Coarctation of the aorta is accompanied by extra-cardiac anomalies in 25% of cases. Typical anomalies include those whose embryonic development coincides with the timing and location of aortic arch development and include upper gastrointestinal tract anomalies such as oesophageal atresia and diaphragmatic defect. Monosomy X is also a recognized association.

A total of eight cases of coarctation of the aorta were diagnosed in 2014-2015, the majority, (n=6), had the abnormality coded in the primary position.

CARDIAC & CIRCULATORY ABNORMALITIES

Q251	COARCTATION AORTA	Live birth; Diagnosed < 1 week; VSD
Q251	COARCTATION AORTA	Live birth; Diagnosed < 1 week; Bicuspid aortic valve
Q251	COARCTATION AORTA	Live birth; Diagnosed 1-4 weeks
Q251	COARCTATION AORTA	Live birth; Diagnosed 1-4 weeks
Q251	COARCTATION AORTA	Live birth; Prenatal diagnosis; Bicuspid aortic valve
Q251	COARCTATION AORTA	Live birth; Prenatal diagnosis; Accessory rib
Q201	DOUBLE OUTLET ® VENTRICLE	Live birth; Prenatal diagnosis; ASD; VSD
Q203	TGA	Live birth; Prenatal diagnosis; VSD

OTHER CARDIAC ANOMALIES

Ventriculo-septal defect, (VSD)

The commonest recorded cardiac abnormality in the 2014-2015 data was ventriculo-septal defect, (n=16). These lesions can be located anywhere in the ventricular septum and vary in size. The majority are single but multiple defects can occur. Typically only the moderate or large defects are seen on prenatal scan. The defects are categorized according to position as peri-membranous, doubly commuted sub-arterial and muscular. Doubly commuted defects are rare and usually only delineated after birth. Ventriculo-septal defects may occur in isolation but are commonly associated with extra-cardiac and chromosomal abnormalities.

About 70% of prenatally diagnosed VSD's are either asymptomatic or close spontaneously within the first year of infant life.

Double Outlet Right Ventricle (Q201)

In double outlet right ventricle both great arteries arise from a morphological right ventricle. A VSD is commonly present. The abnormality is recognized in about 1:10,000 live births. It is known to be associated with chromosomal abnormalities particularly Edward's syndrome and Down syndrome.

Q201	DOUBLE OUTLET ® VENTRICLE	Coarctation of aorta (see above)
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If the ventricles are balanced surgical outcome is usually favourable but otherwise surgery will result in a one ventricle (Fontan) type circulation.

Aorto-pulmonary Window, (Q214)

This is a rare heart defect that results from a failure of fusion of the two conotruncal ridges that are responsible for separating the truncus arteriosus into the aorta and pulmonary artery. The 'window' occurs between the ascending aorta and the main pulmonary artery and is typically found just above the semilunar valves. Prenatal diagnosis has been described but the abnormality is typically diagnosed in early infant life. The presentation is similar to that of other causes of a left to right shunt and depends on the size of the defect. Failure to thrive is common with tachypnoea, diaphoresis and poor feeding. A systolic murmur is usually present.

Q214	AORTOPULMONARY WINDOW	Female infant delivered at term
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CARDIAC & CIRCULATORY ABNORMALITIES

The case described was diagnosed between one month and one year of birth. There were no associated abnormalities.

Aberrant Innominate Artery, (Q2780)

The brachiocephalic trunk, or innominate artery, is the first of three main branches of the aortic arch. It is a major vessel that supplies the head, neck and right arm. Soon after it arises from the upward convexity of the aortic arch it divides into the common carotid artery and right subclavian artery. There is no brachiocephalic artery for the left side of the body.

Q2780 ABERRANT INNOMINATE ARTERY Male infant delivered at term

The case described was diagnosed between one month and one year of birth. There were no associated abnormalities.

MALFORMATIONS OF THE RESPIRATORY SYSTEM

Malformations of the Respiratory System

A total of nine abnormalities of the respiratory system are classified under ICD 10 in the primary diagnostic position. All were live births.

CONGENITAL LOBAR EMPHYSEMA, (P2500)

Rather confusingly Congenital Lobar Emphysema, (CLE), is classified under ICD10 as a 'Congenital Infection' rather than a primary abnormality of respiratory tract development. This classification should perhaps be reserved for Swyer-James syndrome where pulmonary abnormality occurs secondary to infection.

Congenital lobar emphysema is a developmental abnormality of the lower respiratory tract that is characterized by hyperinflation of one or more of the pulmonary lobes. It is a rare condition with a quoted prevalence of 1:10,000. Males tend to be more affected than females. Progressive lobar hyperinflation results from a variety of disruptions of bronchopulmonary development. The most frequently identified cause is an obstruction of the developing airway but a definitive cause may not be identified in more than 50% of cases. It can be identified on prenatal scan as a fluid filled overinflated lobe, but the anomaly usually presents at birth.

P2500	CONGENITAL LOBAR EMPHYSEMA	Male; Live birth; Diagnosed in 1 st week
P2500	CONGENITAL LOBAR EMPHYSEMA	Prenatal diagnosis; Female; Live birth

CONGENITAL MALFORMATIONS OF THE NOSE, (Q30)

Choanal Atresia, (Q300)

This abnormality results from a failure of recanalization of the nasal fossae during fetal development and may be unilateral or bilateral, osseous or membranous, complete or partial. Newborn infants are obligate nose breathers and bilateral choanal atresia is noted at birth by the absence of nose-breathing in spite of inspiratory effort and variable cyanosis.

Choanal atresia is recorded as the primary coding for a case of CHARGE syndrome.¹²

Q300	CHARGE SYNDROME	Prenatal diagnosis; Live birth at term; Male
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CHARGE syndrome is a rare and complex condition affecting one in every 10-15,000 people. This syndrome is named as an acronym for the main features of the condition which are coloboma, heart defect, choanal atresia, retarded growth and development, genital abnormality, and ear abnormality.

The pattern of malformations varies among individuals. In the case described above the infant had bilateral cleft lip and soft palate, horseshoe kidney and persistent truncus arteriosus. CHARGE is caused by mutation on *CHD7* gene located on chromosome 8.

¹² Interesting use of the coding but follows the RCPCH classification – the paediatric adaptation of ICD 10.

MALFORMATIONS OF THE RESPIRATORY SYSTEM

Choanal atresia is recorded as a secondary malformation in three further cases.

Q541	HYPOSPADIAS - PENILE	
Q042	HOLOPROSENCEPHALY - ALOBAR	Microcephaly; Microphthalmis; Microcornea
Q308	PYRIFORM APERTURE STENOSIS	Atresia of auditory canal; Micrognathia; Webbing of neck

Congenital nasal pyriform aperture stenosis, (CNPAS), is a rare cause of nasal airway obstruction that mimics choanal atresia in terms of clinical presentation. The pyriform aperture is the narrowest part of the nasal airway. A female infant was delivered prematurely at 35 weeks gestation with multiple abnormalities evident at birth including webbing of the neck, micrognathia, atresia of the auditory canal and both choanal atresia and pyriform aperture stenosis.

CONGENITAL MALFORMATIONS OF THE LARYNX, (Q31)

Congenital Subglottic Stenosis, (Q311)

Congenital narrowing of the subglottic airway can present as a life threatening airway emergency or simply 'noisy breathing' in the neonate. It is the third most common cause of stridor in the neonate behind laryngomalacia and vocal cord paralysis. The proposed mechanism is incomplete recanalization during embryogenesis. There are two types of congenital subglottic stenosis: membranous and cartilaginous. The membranous type is usually circumferential, soft and dilatable. In contrast the cartilaginous can have a normal shape but narrowed lumen or an abnormal cricoid cartilage with prominent lateral shelves.

Q311	CONGENITAL SUBGLOTTIC STENOSIS	Male; Term delivery; Diagnosed at birth
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Typically symptoms of upper airway obstruction dominate with inspiratory stridor. It is said that glottic and subglottic stridor is usually biphasic in nature because the tissues are rigid and do not collapse during respiration.

CONGENITAL MALFORMATIONS OF THE TRACHEA & BRONCHUS, (Q32)

Bronchial Stenosis, (Q323)

Congenital bronchial atresia or stenosis (CBAS) is a benign bronchopulmonary anomaly characterized by a blindly terminating, or significantly stenosed, segmental or lobar bronchus. There is hyperinflation of the adjacent lung parenchyma and a mucous filled bronchocoele. A neonatal presentation is highly unusual.¹³

Q323	BRONCHIAL STENOSIS (L)	Female; Term delivery; Diagnosed < 1 week
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The data recorded a case in a female infant delivered at term. The diagnosis of bronchial stenosis was made within the first week of life. There were no associated abnormalities.

¹³ Poupalou A et al. (2011)

MALFORMATIONS OF THE RESPIRATORY SYSTEM

CONGENITAL MALFORMATIONS OF THE LUNG, (Q33)

Absent Lung, (Q333)

Pulmonary agenesis occurs in the developing embryo at about four weeks' gestation when the primitive lung is forming. The aetiology is uncertain but the abnormality is usually unilateral and there is no side or gender predominance. The majority of infants with pulmonary agenesis have associated congenital anomalies particularly of the cardiovascular, skeletal (limb and spine) and gastrointestinal systems. The contralateral lung is normal in structure but shows compensatory hypertrophy. The literature suggests that infants with right lung agenesis have a shorter life expectancy than those with left lung agenesis – perhaps as a consequence of mediastinal shift.

Q333 ABSENT LUNG (L) Prenatal diagnosis; Live birth at term; Male

In the above case prenatal diagnosis of abnormality was achieved on ultrasound at 22 weeks gestation. There were associated, but unspecified, abnormalities of the pulmonary artery and peripheral vascular system.

Congenital Cystic Adenomatoid Malformation, (CCAM), (Q3380)

The respiratory system starts to develop at around three weeks' gestation. Aberrations in the developmental process may give rise to a group of structural malformations collectively referred to as broncho-pulmonary foregut malformations, (BPFMs). The three commonest are Sequestration, Congenital Cystic Adenomatoid Malformation, (CCAM), and Congenital Lobar Emphysema.

Congenital cystic adenomatoid malformation (CCAM) is a rare unilateral hamartomatous dysplasia of the lung. Three pathological types are recognized: Type 1 with cysts >2cm diameter, Type II with cysts <1cm diameter and Type III a predominantly solid type with microcysts. The ultrasound features are consistent with the pathological changes. The affected lung is markedly enlarged in all three types and leads to a mediastinal shift to the opposite side and as a result normal lung tissues become compressed. The mediastinal displacement can also compromise venous return leading to fetal hydrops. Prognosis is dependent upon histological type, (in general Types II and III are associated with a poor prognosis), the development of hydrops, severity of pulmonary hypoplasia on the unaffected side, timing of diagnosis and early planned intervention.

Four cases described in the data were live births at term. The diagnosis of abnormality was made in each case on ultrasound examination at 20 weeks gestation.

Q3380	CCAM ®	Female
Q3380	CCAM	Male
Q3380	CCAM - HYBRID SEQUESTRATION LESION	Female
Q3380	CPAM (L) LUNG	Female; Sequestration of lung

MALFORMATIONS OF THE RESPIRATORY SYSTEM

In two cases a sequestration lesion was also present. Pulmonary Sequestration is a congenital developmental anomaly in which a portion of the lung is separated from the bronchial tree and rest of the lung. It may be intra or extra lobar. An extra-lobar sequestration appears as an isolated echogenic intrathoracic structure on prenatal ultrasound. It may be difficult to differentiate from CCAM. Associated abnormalities may involve organs that also develop from the foregut e.g. TOF and bronchogenic cyst.

ABNORMALITIES OF EAR, EYE, FACE & NECK

Abnormalities of Ear, Eye, Face & Neck

Congenital malformations of the head and neck are a wide and heterogeneous group that range in importance and severity from purely cosmetic defects to lethal anomalies. They can be isolated or occur as a component of a sequence, syndrome or chromosomal disorder.

Chapter XVII of the ICD 10 coding system has two sections directly related to face & neck abnormalities. These are 'Congenital Malformations of Eye, Ear, Face and Neck', (Q10-Q18) and 'Cleft Lip & Palate', (Q35-Q37). However facial abnormalities are also classified in a number of other locations under a variety of systems. This is simply because this region contains parts of almost all organ systems.

CYSTIC HYGROMA, (D1810)

Cystic hygroma is an anomaly of the lymphatic system that appears on ultrasound as a thin-walled multi-loculated cystic mass. The vast majority are located on the posterolateral aspect of the fetal neck although they may occur at other sites. Normally lymph is drained via the thoracic duct to the junction of the subclavian and internal jugular veins. When communication to the venous system is delayed or obstructed the lymph tissue undergoes cystic dilatation. If the connection with the venous system is 're-established' the cysts may regress and resolve. If the obstruction persists then the cysts may grow to huge proportions and non-immune hydrops develops resulting in intrauterine demise.

Cystic hygromas are associated with chromosomal abnormalities in 50-80% of cases. Coarctation of the aorta and conotruncal anomalies are also commonly seen with cystic hygroma. Ten cases are described in the current dataset. Eighty percent were associated with chromosomal abnormality.

D1810	CYSTIC LYMPHANGIOMA/CYSTIC HYGROMA NECK ®	Prenatal diagnosis; Live birth
D1810	CYSTIC HYGROMA	Prenatal diagnosis; Termination
Q900	TRISOMY 21	Prenatal diagnosis; Termination
Q900	TRISOMY 21	Prenatal diagnosis; Termination
Q910	TRISOMY 18	Prenatal diagnosis; Termination
Q910	TRISOMY 18	Prenatal diagnosis; Termination
Q910	TRISOMY 18	Prenatal diagnosis; Termination
Q910	TRISOMY 18	Prenatal diagnosis; Termination
Q914	TRISOMY 13	Prenatal diagnosis; Stillbirth
Q960	TURNER SYNDROME	Prenatal diagnosis; Termination

ANOPHTHALMOS, MICROPTHALMOS & MACROPTHALMOS, (Q11)

Congenital malformations of the eye can be dramatic reflecting early disruption of embryogenesis. When the anterior end of the notochord and surrounding mesoderm are not appropriately induced by the forebrain a spectrum of anomalies such as the absence of an eye (anophthalmia), partial or complete fusion (cyclopia) or small malformed globe associated with a cleft (microphthalmos with cysts and coloboma).

ABNORMALITIES OF EAR, EYE, FACE & NECK

Microphthalmos, (Q112)

Microphthalmos, an abnormally small globe, is a clinical spectrum of disease classified as either simple (without co-existent ocular defect) or complex (e.g., colobomatous, cataractous, with retinal detachment, syndromic). The prognosis of microphthalmic eyes depends upon the extent of coexisting ocular abnormality.

Q042 HOLOPROSENCEPHALY - ALOBAR

This case, a live born male infant, was also associated with choanal atresia, microcephaly and microcornea, (see below).

CONGENITAL LENS MALFORMATION, (Q12)

Congenital cataracts, (Q120)

Approximately one third of congenital cataracts are a component of a more extensive syndrome or disease. However the origin of a good 30% are unexplained. Metabolic disease tends to be associated with bilateral cataracts. Typical associations include Alports syndrome, Marfan syndrome, Down syndrome, myotonic dystrophy, galactosaemia, trisomy 13 and congenital infections such as rubella, toxoplasmosis, CMV and herpes simplex.

Q120 CONGENITAL CATARACTS - BILAT POSTERIOR POLAR

This was a male infant delivered at term. Cataracts were diagnosed between the 1st and 4th week of life. He also had an otherwise unspecified non-neoplastic naevus.

CONGENITAL MALFORMATION ANTERIOR SEGMENT OF EYE, (Q13)

Microcornea, (Q134)

Microcornea, reduced cornea size less than 11 mm horizontal diameter, is usually associated with other ocular and/or cranio-facial abnormalities. Isolated microcornea is a very rarely-described condition.

Q042 HOLOPROSENCEPHALY - ALOBAR

OTHER CONGENITAL MALFORMATIONS OF THE EYE, (Q15)

Childhood glaucoma is an unusual eye disease and significant cause of childhood blindness. It is caused by disease related abnormal increase in intraocular pressure. The multiple potential causes fall into one of two categories and may be primary or secondary to some other disease process. Primary congenital glaucoma results from abnormal development of the ocular drainage system. Ten percent of primary congenital glaucomas are present at birth, and 80 percent are diagnosed during the first year of life.

Q150 CONGENITAL GLAUCOMA - BILAT Male; Live birth

ABNORMALITIES OF EAR, EYE, FACE & NECK

CONGENITAL MALFORMATIONS OF EAR CAUSING IMPAIRMENT OF HEARING, (Q16)

Auricular Deformities, (Q160, Q161)

Auricular deformities are found in the setting of various syndromes and chromosomal abnormalities such as trisomy 18. They can assume a variety of forms. Auricular tags are most commonly located in front of the external auditory canal. The primordium of the external ear is located at the side of the neck in early development. If the lower jaw is underdeveloped the auricle does not undergo a normal ascension and retains its embryonic position at the level of the head and neck junction. It is very difficult to appreciate these lesions on ultrasound scan but if evident a diligent search should be made for additional abnormalities.

Q203	TGA	Absent auricle
Q308	PYRIFORM APERTURE STENOSIS	Atresia of auditory canal

OROFACIAL CLEFTS, (Q35 – Q37)

Cleft lip, with or without cleft palate, and cleft palate alone are collectively referred to as orofacial clefts, (OFC's). Cleft lip and palate are among the more common congenital malformations. The causes of orofacial clefting remain largely unknown. Some 70% of OFC's are considered to be multifactorial. The remaining cases may be associated with known teratogens, chromosomal abnormality or single gene defects. Smoking and obesity are modifiable risk factors that are consistently associated with OFC's.

Unilateral clefts arise when the maxillary process fails to reach and fuse with the medial nasal process. Bilateral clefts develop in the upper lip when the maxillary processes on both sides fail to fuse with the median nasal process. The degree of cleft formation may be equal or different on both sides. A median cleft lip is probably caused by a lack of mesenchymal tissue in the central portion of the lip. Cleft palate is characterized by incomplete fusion of the secondary palate and affect the soft and hard palate or only the soft palate. Most would deny cleft palate laterality as this defect is due to the failure of the palatal shelves to fuse in the midline.

Clefts are mainly isolated lesions but are also found in association with various syndromes and chromosomal abnormalities, particularly trisomy 13 and 18.

Cleft lip and palate can be diagnosed on prenatal ultrasound scan in a coronal or sagittal scan through the face or in a transverse scan at the level of the maxilla. Large clefts are fairly conspicuous but a small cleft may be easily overlooked: with a small lip cleft the coronal scan shows only a narrow defect in the upper lip.

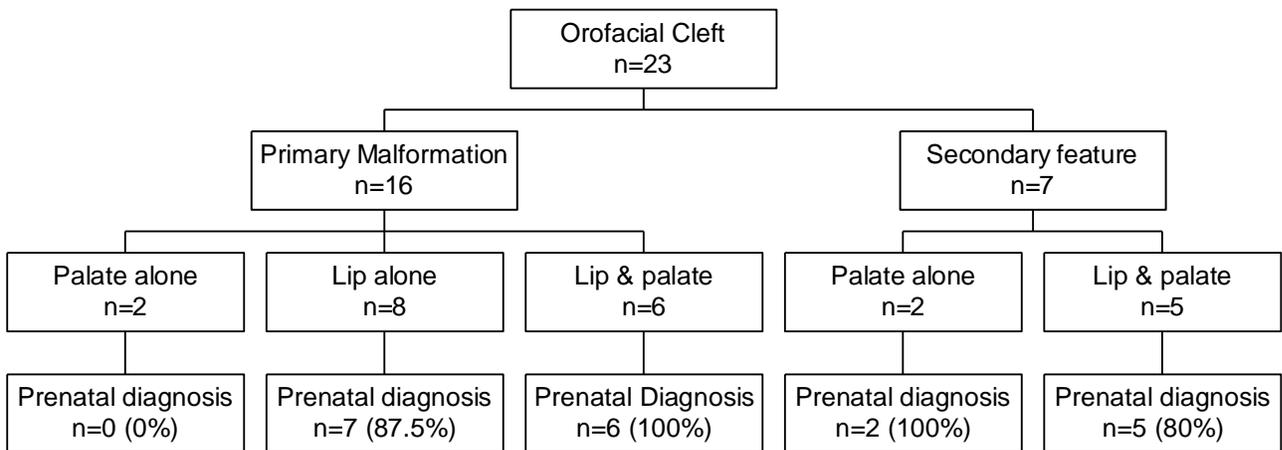
A total of 23 cases are recorded of cleft lip, cleft palate or both.

Overall 81.25% of cases of primary orofacial clefting were diagnosed prenatally, (Figure 4.5). It is difficult to comment on the accuracy of prenatal diagnosis when considering orofacial clefting as a secondary abnormality. The 'point of diagnosis' in these cases relates to the primary coded abnormality.

Prenatal detection rates are higher for OFC's associated with malformations in other systems than for isolated clefts. Termination of pregnancy is more common when the cleft is associated with other anomalies.

ABNORMALITIES OF EAR, EYE, FACE & NECK

Figure 4.5: Overview of Prenatal Diagnosis of Cleft Lip & Palate



PIERRE ROBIN SEQUENCE

A single case is recorded of Pierre Robin sequence. Pierre Robin sequence is characterized by micrognathia, glossoptosis, (posteriorly placed tongue), and clefting of the soft palate. Hypoplasia of the mandibular area prior to the 9th week of gestation causes the tongue to be posteriorly located, presumably preventing closure of the posterior palate

Q8708 PIERRE ROBIN SEQUENCE Live birth; Female infant; Micrognathia; Cleft hard & soft palate

OTHER FACIAL ABNORMALITIES

Dysmorphic Face, (Q189)

In a case where there are one or more malformations and there is also a dysmorphic face, (but no syndrome or karyotype anomaly), the code Q189 "malformation of face and neck unspecified" is used and the written text "dysmorphic face" applied.

Q189 DYSMORPHIC (NO DIAGNOSIS) Live birth; Male; Micrognathia; Imperforate anus

Hemihypertrophy, (Q748)

Craniofacial abnormalities such as hypertelorism, Crouzon's and oculomandibular dysostosis are classified under the musculoskeletal system.

Q7481 HEMIHYPERTROPHY: CHEEK/FACE/EAR/ARM/LEG/FOOT

This was a live born female infant delivered preterm at 34 weeks gestation. The diagnosis of facial abnormality was made between one and 12 months of life.

Gastrointestinal Abnormalities

The gastrointestinal tract is formed from anatomically and functionally distinct regions that may be subject to a variety of errors of embryological development. Patterns of malformation include abnormal lumenization, (e.g. stenosis and atresia), duplications, abnormal rotation and fixation and abdominal wall defects.

CONGENITAL MALFORMATIONS OF THE OESOPHAGUS, (Q39)

Oesophageal Atresia, (Q391, Q3911)

Oesophageal atresia, the anomalous closure of the oesophagus that is often associated with a trachea-oesophageal fistula, is a relatively common anomaly with an incidence of approximately 1:3000 live births. It arises following an error in the differentiation of the primitive foregut into the oesophagus, trachea and lung between four to six weeks gestation.

Diagnosis on prenatal ultrasound examination is difficult. The suspicion of an oesophageal atresia is raised by the presence of polyhydramnios and a small or absent gastric bubble. However, the detection of a fluid filled gastric bubble does not exclude the anomaly since fluid can enter the stomach through the low TOF that is usually present. Observation of fetal swallowing movements in these circumstances will demonstrate alternate filling and emptying of the proximal blind oesophageal pouch.

Associated abnormalities are fairly common and should be excluded. Oesophageal atresia also occurs as a feature of the VACTERL syndrome.

There were three instances where oesophageal atresia is the primary diagnosis– all live births.

Q3911	OESOPHAGEAL ATRESIA + TOF
Q3911	OESOPHAGEAL ATRESIA + TOF
Q3911	OESOPHAGEAL ATRESIA + TOF

Oesophageal atresia was also recorded as a secondary diagnosis in four further cases.

Q601	RENAL AGENESIS - BILAT	TOF
Q8726	VACTERL ASSOCIATION	TOF
Q8726	VATER ASSOCIATION	TOF
Q910	TRISOMY 18	TOF

CONGENITAL ABSENCE, ATRESIA & STENOSIS OF THE SMALL INTESTINE, (Q41)

Obstructions of the intestinal tract do not usually become evident until the late second trimester. They appear sonographically as unusual intra-abdominal cysts located at various sites depending on the level of the atresia. The development of polyhydramnios is also dependent on the level of closure. Duodenal atresia has a reported incidence of 1:10,000 live births.

GASTROINTESTINAL ABNORMALITIES

The condition results from a failure of recanalization of the duodenum during early embryonic life. The ultrasound hallmark is the 'double-bubble sign' of two adjacent fluid filled sacs in the upper abdomen. Duodenal atresia is frequently accompanied by polyhydramnios. Over 50% of fetuses with duodenal atresia have associated cardiac, renal, musculoskeletal or CNS anomalies.

Jejunal and ileal atresia can be a consequence of revacuolization/recanalization during intestinal development but may also be secondary to post-embolic or post-thrombotic ischaemia, volvulus or intussusception. Ileal and jejunal atresia usually appear as multiple cystic masses within the fetal abdomen. Polyhydramnios may occur but is less likely to be seen the more distal the atresia develops.

Q412 ILEAL ATRESIA Female; Live birth at term; Diagnosis made < 1 week

CONGENITAL ABSENCE, ATRESIA & STENOSIS OF THE LARGE INTESTINE, (Q42)

Imperforate Anus, Anal Stenosis & Anorectal Atresia, (Q423)

These abnormalities are associated with a variety of perineal appearances including complete absence of the anus or anterior stenosis and anal fistula. They are often seen in association with abnormalities of the renal tract. Anal atresia results from a failure of perforation of the embryonic anal membrane. Prenatal sonographic diagnosis has been achieved following the identification of abnormal large bowel dilatation. Tables are available of normal lumen diameters across gestation but are not commonly used.

Q423 IMPERFORATE ANUS Female; Live birth; Diagnosis made at birth

In the above case the finding of a number of associated abnormalities including a persistent cloaca, malformation of the spinal cord, hemivertebrae, bicornuate uterus and absent ovary raise the possibility of a VATER/VACTERL type syndrome.

Imperforate anus was also seen in a further four cases.

Q643	URETHRAL ATRESIA	Imperforate anus
Q8726	VATER ASSOCIATION	Imperforate anus
Q8980	CAUDAL DYSPLASIA SEQUENCE	Imperforate anus
Q189	DYSMORPHIC (NO DIAGNOSIS)	Imperforate anus

OTHER CONGENITAL MALFORMATIONS OF THE INTESTINE, (Q43)

Hirschsprung's Disease, (Q431)

Hirschsprung's disease is due to an absence of parasympathetic ganglion cells in the myenteric submucosal plexus of the rectum: parasympathetic neuroblasts normally migrate into the bowel during the 9th to 12th weeks of embryonic development. This disorder sometimes extends to the colon. It occurs predominantly males with an incidence of 1:5000 births.

GASTROINTESTINAL ABNORMALITIES

Q431	HIRSCHSPRUNG'S DISEASE	Male; Diagnosed at birth
Q431	HIRSCHSPRUNG'S DISEASE	Male; Diagnosed <1 week
Q431	HIRSCHSPRUNG'S DISEASE	Male; Diagnosed <1 week
Q431	HIRSCHSPRUNG'S DISEASE	Female; Diagnosed <1 week
Q431	HIRSCHSPRUNG'S DISEASE	Male; Diagnosed <1 week
Q431	HIRSCHSPRUNG'S DISEASE	Female; Diagnosed after 1 week
Q030	AQUEDUCT STENOSIS - VENTRICULOMEGALY	Male;

Hirschsprung's disease typically presents with abdominal distension and failure of passage of meconium within the first 48hrs. Recognized associations include multiple endocrine neoplasia, Waardenburg's syndrome, (see earlier), & Down syndrome.

Marked dilatation of the large bowel may be seen on prenatal ultrasound examination but dilated fluid filled bowel segments are often seen in healthy fetuses in the third trimester. In the last case listed above the point of diagnosis is given as 'prenatal' but this relates only to the primary coding of aqueduct stenosis.

Congenital Malformations of Intestinal Fixation, (Q433)

This grouping includes a variety of conditions of the small and large bowel.

During normal development the foregut, midgut and hindgut herniate out of the abdominal cavity where they undergo a 270 degree counter clockwise rotation around the superior mesenteric vessels. Following this the bowel returns to the abdominal cavity with fixation of the duodenal-jejunal loop to the left of the midline and the caecum to the right lower quadrant. Intestinal malrotation refers to any variation in this process of rotation and fixation. The most common presentation of incomplete rotation is midgut volvulus.

Q433	MALROTATION	Live birth; Male; Diagnosis after 1 week
Q433	INTRA-ABDOMINAL BANDS	Live birth; Male; Diagnosis at birth
Q501	OVARIAN CYST ®	Prenatal diagnosis; Female; Live birth

Duplication

Gastrointestinal duplication cysts may be of foregut, small bowel and large bowel. Foregut duplication cysts are categorized on the basis of their embryonic origin as oesophageal, bronchogenic and neurogenic. Gastrointestinal tract duplication cysts most commonly occur in the ileum and colon. They may be contained within the gastrointestinal tract wall or exterior to it.

Q434	DUPLICATION CYST	Prenatal diagnosis; Female; Live birth
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GENITOURINARY SYSTEM

Genitourinary System

Renal tract abnormalities may be isolated or components of a recognizable syndromes. The ICD10 classification divides the abnormalities into renal agenesis and reduction defects, cystic kidney disease and congenital obstruction defects. Fetal renal tract anomalies will usually be detected at routine 20 week scan.

OVARIAN CYST, (Q501)

An ovarian cyst will typically appear on prenatal scan as a sharply circumscribed cystic mass in the lower to mid-abdomen. An ovarian cyst cannot confidently be distinguished from a mesenteric cyst on prenatal scan.

Q501	OVARIAN CYST ®	Prenatal diagnosis; Live birth; Malrotation of bowel
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HYPOSPADIAS, (Q540)

Displacement of the urethral meatus ventrally and proximally from the tip of the penis. It is classified according to the position of the meatus on the penis. The shortening of the ventral side of the penis found in hypospadias can result in penile curvature known as chordee. The diagnosis was made at birth for all primary malformation cases.

Q540	HYPOSPADIAS - CORONAL	
Q540	HYPOSPADIAS - SUBCORONAL	
Q540	HYPOSPADIAS - CORONAL	
Q540	HYPOSPADIAS - CORONAL	
Q540	HYPOSPADIAS	
Q540	HYPOSPADIAS - SUBCORONAL	
Q540	HYPOSPADIAS - SUBCORONAL	
Q541	HYPOSPADIAS - PROXIMAL PENILE	
Q541	HYPOSPADIAS - PENILE	Choanal atresia
Q549	HYPOSPADIAS	

Hypospadias is also classified in the secondary position in five further cases.

Q6580	DDH ®	Diagnosis < 1 week
Q790	DIAPHRAGMATIC HERNIA (L)	Diagnosis at birth
Q8680	FETAL VALPROATE SYNDROME (LIKELY)	Preterm live birth; Diagnosis at birth
Q378	CLEFT LIP (BILAT) & CLEFT PALATE (UNILAT)	
Q3690	CLEFT LIP ®	

RENAL AGENESIS & OTHER REDUCTION DEFECTS

These are typically the result of failure of the ureteric bud to develop so that the ureter and kidney are absent. If unilateral the child will live a full and healthy life provided the other kidney is normal. Bilateral agenesis is lethal and is usually diagnosed when profound oligohydramnios is seen on antenatal scan.

GENITOURINARY SYSTEM

Unilateral Renal Agenesis

Unilateral renal agenesis has an incidence of 1:1000 births and can be sporadic or inherited as an autosomal dominant trait. The left kidney is more commonly absent. There is an association with anomalies of the reproductive tract. Compensatory hypertrophy of the contralateral side may not be seen in utero.

Q600 ABSENT (L) KIDNEY Prenatal diagnosis; Live birth at term; Female

Unilateral renal agenesis is not usually of any major health consequence provided that the other kidney is healthy. However it is associated with an increased incidence of abnormality of the development of the female reproductive tract which may present as infertility.

Unilateral renal agenesis was also seen as part of the VATER association.

Q8726 VATER ASSOCIATION Prenatal diagnosis; Termination at 20 weeks; MALE

Bilateral Renal Agenesis

There were two cases of bilateral renal agenesis. In one it is classified as the primary abnormality.

Q601 RENAL AGENESIS - BILAT Prenatal diagnosis; Termination

This case, a termination of pregnancy at 21 weeks gestation following prenatal ultrasound imaging, was also associated with agenesis of the ureter, tracheo-oesophageal fistula, hemi-vertebrae and abnormalities of the female genital tract including absent uterus.

The other case was also associated with multiple similar abnormalities but the primary diagnosis is given as Caudal Dysplasia Sequence. This pregnancy was also terminated following prenatal diagnosis. Anomalies included imperforate anus, hemivertebrae, ambiguous genitalia and congenital absence of the bladder and urethra.

Q8980 CAUDAL DYSPLASIA SEQUENCE Prenatal diagnosis; Termination

CYSTIC KIDNEY DISEASE

Multicystic Dysplastic Kidney, (Q614, Q6140, Q6141)

This sporadic condition is thought to be caused by atresia of the ureter or uretero-pelvic junction during the meta-nephric stage of development. It is characterized by multiple cysts of varying sizes that do not interconnect with each other or the renal collecting system. The cysts are seen within a framework of echogenic dysplastic renal tissue. Generally one kidney is affected and bilateral involvement is rare. The changes may affect the entire kidney or just segments. Cystic dysplastic renal disease is usually sporadic but it may be a feature of several syndromes including trisomy 13, trisomy 18 and Meckel.

GENITOURINARY SYSTEM

Q614	DYSPLASTIC KIDNEY(L)	Prenatal diagnosis; Live birth; Male
Q6140	MULTICYSTIC KIDNEY (L)	Prenatal diagnosis; Live birth; Female
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Prenatal diagnosis; Live birth; Male
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Prenatal diagnosis; Live birth; Male
Q6140	MULTICYSTIC KIDNEY ®	Prenatal diagnosis; Live birth; Female
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Prenatal diagnosis; Live birth; Female
Q6140	MULTICYSTIC DYSPLASTIC KIDNEY ®	Prenatal diagnosis; Live birth; Female
Q6141	RENAL CYSTIC DYSPLASIA - BILAT	Live birth; Diagnosis after 1 month; Female
Q6141	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Prenatal diagnosis; Live birth; Male
Q6141	MULTICYSTIC DYSPLASTIC KIDNEYS	Prenatal diagnosis; Live birth; Male
Q6141	MULTICYSTIC RENAL DYSPLASIA - BILAT	Prenatal diagnosis; Termination

With unilateral renal dysplasia the contralateral side appears normal with bladder filling and normal amniotic fluid volumes. If bilateral the bladder may not be visualized and oligohydramnios develops such as in the case of Potters sequence below.

D821	DI GEORGE	Prenatal diagnosis; Live birth
Q606	POTTERS SEQUENCE	Prenatal diagnosis; Termination

Potter's Sequence is the result of oligohydramnios leading to pulmonary hypoplasia, low set ears, broad flattened nose and limb abnormalities. This deformation sequence can result from a number of pathological processes including pre-term rupture of membranes, polycystic or multicystic renal disease, and agenesis or obstruction of the ureter, but was initially intended to only refer to cases resulting from Bilateral Renal Agenesis, (the 'Classic' form).

CONGENITAL OBSTRUCTIVE DEFECTS OF RENAL PELVIS & MALFORMATION OF URETER, (Q62)

This ICD10 category includes a variety of abnormalities of the renal and urinary system including, congenital hydronephrosis, atresia and stenosis of the ureter, agenesis of ureter and congenital PUJ obstruction.

Congenital hydronephrosis (Q620)

Renal pelvis dilatation (pyelectasis) is a commonly recognized problem at antenatal scan. It is defined as pelvic dilatation that does not involve the renal calices. While there can be many conditions that lead to hydronephrosis, the most common causes are obstructions that reduce the ability of urine to flow out of the kidney and into the bladder. Many children who are diagnosed with hydronephrosis before they are born will have the condition resolve on its own without medical intervention. Various 'cut-off' measurements have been suggested but these have little clinical significance and in general only an AP measurement of greater than 10mm warrants further postnatal follow-up.

If enlargement of the renal pelvis exceeds 15mm then it is considered to be hydronephrosis. In these circumstances there is calyceal dilatation. Attempts must be made to define the underlying cause. Infants

GENITOURINARY SYSTEM

with a continuing abnormality on post-natal assessment may go on to have functional nuclear medicine studies.

Q620	HYDRONEPHROSIS (L)	Male; Prenatal diagnosis; Live birth
Q620	HYDRONEPHROSIS @ KIDNEY	Male; Prenatal diagnosis; Live birth
Q642	POSTERIOR URETHRAL VALVES	Male; Live birth; Point of diagnosis unknown

Congenital PUJ Obstruction, (Q6210)

The most common cause of obstruction (blockage) in the urinary tract in children is a congenital obstruction at the point where the ureter joins the renal pelvis – the ureteropelvic junction, (UPJ or PUJ). Most PUJ obstructions are identified long before birth by prenatal scan. Urine is produced by the fetus at a rate that exceeds the amount able to drain out of the renal pelvis into the ureter. This causes accumulation of urine within the kidney and dilatation of the renal pelvis which is clearly visible on scan.

Although ‘renal pyelectasis’ a very common prenatal observation, congenital PUJ obstruction was only formally diagnosed on one occasion.

Q6210	PUJ OBSTRUCTION (L)	Male; Prenatal diagnosis; Live birth
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OTHER CONGENITAL MALFORMATIONS OF THE KIDNEY, (Q63)

Duplex Kidney & Collecting System, (Q630)

These terms cover a wide range of duplication variants. The classic complete duplex kidney follows the ‘Weigert-Meyer’ rule of “the upper moiety ureter inserts more inferiorly and medially than the lower moiety ureter”. The upper moiety ureter is often associated with an ureterocele. The lower moiety ureter has a shorter more vertical course and is therefore more prone to vesico-ureteric reflux and uretero-pelvic junction obstruction.

Q6300	DUPLEX KIDNEY (L)	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY BILAT	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY (L)	Male; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEY (L)	Female; Prenatal diagnosis; Live birth
Q6300	DUPLEX KIDNEYS - BILAT	Female; Prenatal diagnosis; Live birth

Abnormally Sited Kidney, (Q631, Q632)

These are fairly common abnormalities that are often discovered incidentally.

Horseshoe Kidney, (Q6310)

This is the most common renal anomaly with an overall incidence of 1:600. The inferior mesenteric artery prevents the connecting isthmus between the two kidneys from ascending. The connecting isthmus may be functioning renal tissue or a simple fibrous band, (which may not be apparent on ultrasound scan). The lower poles of a horseshoe kidney will have a more medial orientation than expected and may be difficult to clearly delineate. There is an association with both Turners syndrome and trisomy 18.

GENITOURINARY SYSTEM

Q8726	VACTERL ASSOCIATION	Horseshoe kidney
Q300	CHARGE SYNDROME	Horseshoe kidney

Ectopic Kidney, (Q632)

The incidence of renal ectopia is 0.2%. The urethral bladder insertion may be on the same or opposite side of the ectopic kidney. Where there is fusion of the two kidneys with the urethral bladder insertion on the opposite side to the ectopic kidney it is referred to as 'crossed fused ectopia'. Most ectopic kidneys demonstrate a degree of malrotation. The incidence of associated anomalies is generally considered to be low.

Q632	ECTOPIC (PELVIC) KIDNEY (L)	Male; Prenatal diagnosis
Q632	ECTOPIC KIDNEY (L) - IN (L) FLANK	Female; Prenatal diagnosis
Q6141	MULTICYSTIC DYSPLASTIC KIDNEY (L)	Male; Ectopic kidney
Q051	T/L MYELOMENINGOCELE (LARGE) + HYDROCEPH	Male; Ectopic kidney; Termination

OTHER CONGENITAL ABNORMALITIES Q64

Posterior Urethral Valves, (Q642, Q6420)

Posterior urethral valves are the most common cause of lower urinary tract obstruction in the male neonate. The disorder is of variable severity. The condition arises around the fourth week of gestation as the Wolffian ducts fuse with the developing cloaca.

A pair of sail-shaped valves develops adjacent to the verumontanum with appearances not unlike valves in a vein. Consequences are bilateral hydronephrosis and hydroureter, hypertrophy of the bladder detrusor and a dilated prostatic urethra.

Q642	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth
Q642	POSTERIOR URETHRAL VALVES	Male; Live birth; Point of diagnosis unknown
Q6420	POSTERIOR URETHRAL VALVES	Male; Live birth; Diagnosis 1-12 months
Q6420	POSTERIOR URETHRAL VALVES	Male; Prenatal diagnosis; Live birth

Urethral Atresia, (Q643)

Urethral atresia is uncommon but leads to anuria and intrauterine death in the second trimester.

Q643	URETHRAL ATRESIA	Diagnosis made on post-mortem examination
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This was a fetal loss at 20 weeks gestation. Fetal gender is recorded as 'unknown'.

MUSCULOSKELETAL ABNORMALITIES

Musculoskeletal Abnormalities

Skeletal abnormalities are either malformations or dysplasia. Malformations include amelia, polydactyly, syndactyly and ectrodactyly. Dysplasias are less common and are characterized by generalized defective development of bone and cartilage. Ultrasonically it is not possible to give a precise pathological diagnosis of dysplasias but in general two main groups are recognized. Firstly short limbs with severely defective ossification with or without fractures will be seen in severe osteogenesis imperfecta or hypophosphatasia. Secondly short limbs with or without spinal deformity are features of thanatophoric dysplasia, achondrogenesis, Jeune syndrome, (asphyxiating thoracic dystrophy) and Jarco-Levin syndrome amongst others.

CONGENITAL DEFORMITIES OF THE HIP, (Q65)

Developmental Dysplasia of the Hip, (Q658)

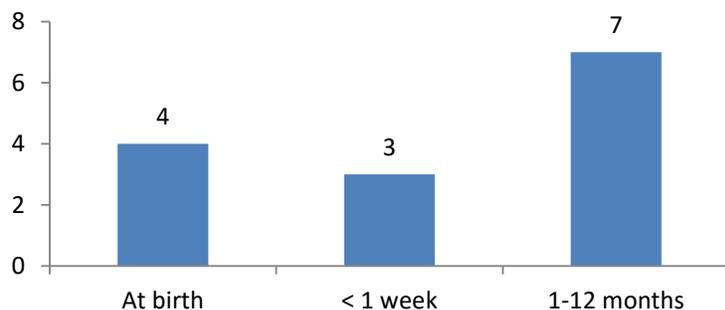
Dislocated hips are associated with joint laxity and acetabular dysplasia. Postural features often play a role in their causation. They are commonest in female infants, term deliveries, breech presentation and the left hip. Diagnosis is made at birth by specifically testing the hips

Q6580	DDH (L)	Female
Q6580	DDH (L)	Female
Q6580	DDH ®	Female
Q6580	DDH (L)	Female
Q6580	DYSPLASTIC (L) HIP	Male
Q6580	DDH ®	Male; Hypospadias
Q6580	DDH (L)	Female
Q6580	DDH (L)	Female
Q6580	DDH (L)	Male
Q6580	DDH ®	Female
Q6580	DDH ®	Female
Q6581	DYSPLASIA HIP - BILAT	Female; Congenital dislocation of knee
Q6581	DDH BILAT	Female
Q6581	DDH - BILAT	Female

A total of 14 cases are listed in the 2014-2015 data. Developmental dysplasia of the hip was always recorded as a primary diagnosis. The observed female:male ratio in this series was almost 4:1. Fifty percent were diagnosed within the first week of life but diagnosis was not made until after one month in the remaining 50%, (Figure 4.6).

MUSCULOSKELETAL ABNORMALITIES

Figure 4.6: Point of diagnosis for developmental dysplasia of the hip



TALIPES EQUINOVARUS, (Q660)¹⁴

This condition, which has a wide spectrum of severity, is characterized by adduction of the forefoot and midfoot, adduction of the heel or hind foot and a fixed plantar flexion (equinus) of the ankle. The foot therefore points downwards and inward but is rotated outward axially. The male:female predisposition is about 2:1. The anomaly is not a single entity and may be considered as extrinsic, (deformation), or intrinsic, (true malformation). Talipes may also be unilateral or bilateral, isolated or complex. There were 20 cases where talipes equinovarus is classified as a primary abnormality.

Q660	CTEV (L)	Female; Diagnosed at birth
Q660	TALIPES - BILAT	Male; Diagnosed at birth
Q660	TEV (L)	Female; Diagnosed at birth
Q660	TALIPES ®	Male; Diagnosed at birth
Q660	CTEV ®	Male; Diagnosed at birth
Q660	CTEV (L)	Male; Diagnosed at birth
Q660	TEV ®	Male; Prenatal diagnosis
Q660	TEV(L)	Male; Prenatal diagnosis
Q660	TEV - BILAT	Male; Prenatal diagnosis
Q660	CTEV - BILAT	Female; Prenatal diagnosis
Q660	CTEV - BILAT	Female; Prenatal diagnosis
Q660	CTEV - BILAT	Male; Prenatal diagnosis
Q660	CTEV (L)	Female; Prenatal diagnosis
Q660	TEV - BILAT	Male; Prenatal diagnosis
Q660	TEV ®	Female; Prenatal diagnosis
Q660	TEV (L)	Female; Prenatal diagnosis
Q660	CTEV (L)	Female; Prenatal diagnosis
Q660	TALIPES - BILAT	Male; Prenatal diagnosis
Q660	CTEV - BILAT	Male; Prenatal diagnosis
Q660	CTEV ®	Male; Prenatal diagnosis

¹⁴ Talipes associated with neuromuscular diagnosis or a syndrome such as arthrogryposis multiplex congenital, myotonic dystrophy or diastrophic dysplasia are excluded from this coding.

MUSCULOSKELETAL ABNORMALITIES

Complex talipes is considered to be chromosomal, neurological, musculoskeletal or syndromic. The most commonly associated chromosomal anomaly is trisomy 18. The majority of cases with complex aetiologies will be bilateral.

Talipes is recorded as an associated abnormality in a further four cases

Q748	SHORT LIMBS	Termination at 21 weeks
Q8680	FETAL VALPROATE SYNDROME (LIKELY)	Live birth
Q915	TRISOMY 13 MOSAIC	Termination at 14 weeks
Q0435	HYDRANENCEPHALY	Termination at 20 weeks

POLYDACTYL, (Q69) AND SYNDACTYL, (Q70)

The hands are fully differentiated in the human embryo by the end of the eighth week. When the finger buds have completed growth in length they are still joined by webs which break down by progressive cell death until the normal proximal web configuration is reached. Failure of cell death results in syndactyly, the commonest congenital hand abnormality. The appearance of abnormality depends on the time of interference with the developing part.

Q700	SYNDACTYL (COMPLETE COMPLEX) (L) HAND/3RD WEB SPACE ® HAND	
Q702	FUSION (COMPLETE) GREAT TOE & 1ST & 2ND TOES BILAT	Syndactyly

Other deformities such as reduplications (partial as in bifid thumb or complete with extra digits) and inversions ('mirror hand') are likely to be related to specific gene defects.

Q691	DUPLICATE THUMB ®	Live birth; Diagnosis at birth
Q691	DUPLICATION OF THUMB (L)	Live birth; Diagnosis at birth
Q691	DUPLICATION OF THUMB ®	Live birth; Diagnosis at birth
Q691	BIFID THUMB (L)	Live birth; Diagnosis at birth
Q692	ACCESSORY TOE (L): BONE PRESENT	Live birth; Diagnosis at birth

REDUCTION DEFECTS OF THE UPPER (Q71) AND LOWER, (Q72) LIMBS

Major limb defects are usually diagnosed at routine second trimester ultrasound imaging. Risk factors include pre-gestational diabetes, drug exposures, (e.g. valproic acid, methotrexate, misoprostal), ethnicity, smoking, early chorionic villus sampling, single gene defects, and chromosomal abnormalities, (particularly when bilateral). Infants born after IVF show an increased risk for limb reduction defects.

Limb deficiencies are characterized by either the total or partial absence of the skeletal structure of the limbs or different degrees of limb hypoplasia. Limb deficiencies may be longitudinal, transverse or intercalary. Interference with the development of blood supply is the most likely mechanism in the appearance of many congenital limb deformities.

MUSCULOSKELETAL ABNORMALITIES

Longitudinal limb deficiencies, (Q714-Q716, Q724-Q727), refer to the partial absence of a limb extending parallel to the long axis of the limb. They typically involve specific components of the limbs: pre-axial (first ray: thumb or radius in the arms or first toe or tibia in the leg); postaxial (fifth ray: fifth finger or ulna in the arm, fifth toe or fibula in the leg); or central components (typically third or fourth rays in the hand or foot such as lobster-claw hand).

There were six cases associated with a longitudinal reduction defect of the radius, (Q714) – radial aplasia or ‘the club-hand’.

Q7131	HYPOPLASTIC ® THUMB	Live birth; Diagnosed at birth
Q8680	FETAL VALPROATE SYNDROME (LIKELY)	Live birth; Diagnosed at birth
Q8709	ROBERTS SYNDROME	Prenatal diagnosis; Termination
D610	FANCONI PANCYTOPENIA	Prenatal diagnosis; Termination
Q000	ANENCEPHALY	Prenatal diagnosis; Termination
Q606	POTTERS SEQUENCE	Prenatal diagnosis; Termination

In transverse limb defects, (Q710, Q712, Q713, Q720, Q722, Q723), there is complete or partial absence of distal structures of a limb in a transverse plane at the point where the deficiency begins. The proximal structures remain intact. They may be described as ‘congenital amputations’.

Q710	ABSENT UPPER LIMBS	Amelia or complete absence of a limb
Q712	ABSENT FOREARM - BILAT	Congenital absence of both forearm and hand
Q7130	FINGER BUDS ® HAND	Prenatal diagnosis; Live birth
Q7131	HYPOPLASTIC ® THUMB	Diagnosis at birth

Intercalary cases, (Q711 & Q721), are where there is complete or partial absence of the proximal or mid segments of a limb but preservation of distal limb structures. There were no cases of intercalary limb deficiency recorded in the current cohort.

OTHER CONGENITAL MALFORMATIONS OF THE LIMBS, (Q74)

This grouping and its subcategories includes a variety of abnormalities: everything from accessory carpal bones, macrodactylia and triphalangeal thumb to cleidocranial dysostosis and arthrogryposis multiplex congenital. The coding Q748 has been used in the current data set to specify ‘Short Limbs’.

Q748	SHORT LIMBS	Arthrogryposis; Prenatal diagnosis; Termination; Male
Q910	TRISOMY 18	Congenital abnormality of limbs; Termination
G118	ATAXIA - EPISODIC TYPE 1	Congenital malformation of upper limb; Live birth; Male
Q0435	HYDRANENCEPHALY	Unspecified abnormality of limbs; Termination
Q204	UNIVENTRICULAR HEART	Unspecified malformation of limbs; Stillbirth; Male

MUSCULOSKELETAL ABNORMALITIES

ARTHROGRYPOSIS, (Q688 & Q743)¹⁵

Arthrogyrosis is not really a diagnosis but a description that refers to a number of pathological processes resulting in limb immobilization and multiple congenital joint contractures. It is therefore a rather heterogenous grouping of conditions both syndromic, (e.g. Larsen syndrome, Freeman-Shelden syndrome and Multiple Pterigium syndrome) and non-syndromic. Therefore it may not be surprising to find that two different codes have been used to classify arthrogyrosis in the current data, 'Q688' and 'Q743'. Sometimes these codes are used to differentiate between a presentation with primary involvement of the limbs and more complex abnormality where limb deformity is combined with other congenital anomalies.

There were a total of four cases in the 2014-2015 data where arthrogyrosis is recorded.

Q688	ARTHROGRYPOSIS-SEVERE	Prenatal diagnosis; Live birth; Male
Q743	ARTHROGRYPOSIS	Prenatal diagnosis; Termination; Male
Q748	SHORT LIMBS	Prenatal diagnosis; Termination; Male
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth; Female

The live born male infant had a number of associated abnormalities. In this case the severe limb deformities were most likely a consequence of an hereditary myopathy.

CRANIOSYNOSTOSIS, (Q750)

Craniosynostosis results from premature closure of one or more of the skull sutures. It affects about 1:2500 children. Craniosynostosis causes distortion of the shape of the skull owing both to failure of bone growth at the prematurely closed suture site and to compensatory overgrowth at the sutures that remain open. The different types of craniosynostosis are classified by which sutures have closed prematurely.

Q750	METOPIC SYNOSTOSIS/CRANIOSYNOSTOSIS	Live birth; Female; Diagnosis at birth
Q750	SAGITTAL SYNOSTOSIS	Live birth; Male; Diagnosis after 1 month
Q7501	SAGITTAL SYNOSTOSIS	Live birth; Male; Diagnosis at birth

OTHER CONGENITAL MALFORMATIONS OF SPINE AND BONY THORAX, (Q76)

This is a broad classification under ICD10 and includes fusion of the spine, absence of vertebrae, hemi-vertebrae, malformation of the lumbo-sacral joint and supernumerary vertebrae. The use of the RCPCH (BPA) adaptation of ICD 10 allows the malformations to be accurately specified. In the case below, a female infant delivered at term, congenital scoliosis is specifically defined as being due to a vertebral abnormality at T11 & T12.

Q7638	SCOLIOSIS: SEGMENTATION ANOMS w BUTTERFLY V'BRA T11 & L2
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¹⁵ Q688 'Other specified congenital musculoskeletal deformities': Q743 'Arthrogyrosis multiplex congenita'.

MUSCULOSKELETAL ABNORMALITIES

Sacral Dysgenesis, (Q7641)

Even with the paediatric adaptation some anomalies remain unspecified. In this case a female infant was delivered at term with sacral dysgenesis, clearly specified by the RCPCH code 'Q7641', but an unclassified malformation of the spinal cord, (Q068).

Q7641 SACRAL DYSGENESIS (SEE REMARKS) Female; Prenatal diagnosis; Live birth

However, sacral dygenesis may also be seen as part of the caudal regression sequence or syndrome.¹⁶

Caudal regression sequence is a disorder that impairs the development of the lower, (caudal), half of the body. Areas affected include the lower back and limbs, the genitourinary system and the gastrointestinal tract. The bones vertebrae of the lower spine, particularly the sacrum, are frequently misshapen or missing. Scoliosis is common and the lower limbs are typically underdeveloped. Abnormalities in the genitourinary tract are extremely varied. Defects include unilateral renal agenesis, horseshoe kidney, bladder exstrophy, ureteral duplication, hypospadias, cryptorchidism in the male and rectovaginal fistula in the female. Individuals with caudal regression syndrome may have malrotation of the large bowel and imperforate anus.

Caudal regression sequence occurs sporadically. The condition is likely to be caused by the interaction of multiple genetic and environmental factors resulting in a combination of abnormal mesoderm development and decreased blood flow to the caudal areas of the fetus. Caudal regression sequence is estimated to occur in 1 to 2.5 per 100,000 newborns but is much more common in infants born to diabetic mothers, (up to 1:350 newborns), particularly if the diabetes is poorly controlled.

Q8980 ¹⁷	CAUDAL REGRESSION SEQUENCE	Prenatal diagnosis; Termination
Q8980	CAUDAL DYSPLASIA SEQUENCE	Prenatal diagnosis; Termination
Q8726	VACTERL ASSOCIATION	Prenatal diagnosis; Live birth at 31 weeks; Male

OSTEOCHONDRODYSPLASIA WITH DEFECTS OF GROWTH OF THE TUBULAR BONES & SPINE, (Q77)

Thanatophoric dysplasia, (Q771)

This is the most common lethal skeletal dysplasia and is associated with a large skull, narrow and short thorax and pronounced rhizomelic dwarfism. Type 1 accounts for 85% of all cases and is classically associated with a 'clover-leaf' skull, which is a consequence of craniosynostosis.

¹⁶ Caudal Regression Sequence or Syndrome? Congenital disorders may consist of more than one abnormality. When multiple effects occur in a specified order the disorder is known as a sequence. When the order is not known it is called a syndrome.

¹⁷ Q898 is a very general ICD 10 coding for 'Other Congenital Abnormality' and has been used already for Acardiac Twin Sequence, (see earlier). However the RCPCH (BPA) extension further defines the code as caudal dysplasia sequence.

MUSCULOSKELETAL ABNORMALITIES

Prenatal diagnosis is based on very short bowed long tubular bones, a very narrow thorax that tapers superiorly to a conical shape, macrocephaly with frontal bossing and depressed nasal bridge. Polyhydramnios is present in most cases. Affected infants are either stillborn or die shortly after birth from cardiorespiratory failure secondary to pulmonary hypoplasia.

Q771 THANATOPHORIC DYSPLASIA Male; Prenatal diagnosis; Termination at 23 weeks

Hypochondroplasia, (Q774)

This is a form of short limbed dwarfism. A rare inherited dysplasia causing short stature not unlike a mild form of achondroplasia. It can be difficult to diagnose. Features other than short stature include macrocephaly, lordosis, disproportionate arms and legs with short but broad hands and feet, limitation of elbow movement but hypermobility of other joints. Due to a mutation of FGFR3 gene on chromosome 4p16.3.

Q774 HYPOCHONDROPLASIA Prenatal diagnosis; Live birth at term; Male

OTHER OSTEOCHONDRODYSPLASIAS, (Q78)

Osteogenesis Imperfecta, (Q780)

Osteogenesis imperfecta is a heterogenous condition characterized by disproportionate dwarfism and multiple fractures of the long bones of the extremities. Four types are distinguished, (Sillence et al.). Type II is the most severe and not compatible with life. The main features on scan are shortened and deformed limbs with multiple fractures. The head is typically large and shows defective ossification of the calvaria.

Q780 OSTEOGENESIS IMPERFECTA Live birth; Female; Diagnosis after 1 week

Q780 OSTEOGENESIS IMPERFECTA Prenatal diagnosis; Live birth at term; Male

ABDOMINAL WALL DEFECTS

Abdominal Wall Defects

ICD 10 codes Q790-Q799 are 'Congenital Malformations of the Musculoskeletal System, NEC' and include congenital diaphragmatic hernia, exomphalos, gastroschisis and amniotic rupture sequence which are collectively considered here as 'Abdominal Wall Defects'.

CONGENITAL DIAPHRAGMATIC HERNIA, (CDH), (Q790)

The diaphragm is formed from the septum transversum, pleuroperitoneal membranes and the oesophageal mesentery. It forms between the eighth and tenth week and fusion is normally complete before the intestines return to the abdominal cavity. The pleuroperitoneal canal in the fetus closes as the diaphragm is formed. Persistence of this 'canal' may be the main cause of CDH. Typically there is a posterolateral 'Bochdalek' hernia through the pleuroperitoneal canal. Approximately 80% of CDH occur through the left diaphragm and approximately 30% of patient have an intact peritoneal sac partially confining the content of the hernia in the chest. The time of herniation into the chest is likely to be the most important factor influencing the degree of pulmonary hypoplasia.

Ultrasound enables the diagnosis of CDH to be made prenatally on routine second trimester fetal anomaly scan. Suspicions regarding the diagnosis are often raised when a cystic structure is visualized at the level of the four-chamber view. However it is well recognized that the ultrasound diagnosis may not occur until the third trimester. Some cases are not recognized until after delivery.

Although the prenatal diagnosis of congenital diaphragmatic hernia is well established the outcome continues to be poor. Polyhydramnios is a predictor of poor outcome as is left heart underdevelopment, the presence of intrathoracic liver and early gestation at diagnosis. In the presence of a karyotype abnormality or lesions associated with genetic syndromes the prognosis obviously depends on the underlying aetiology. The principal cause of death with CDH is the associated pulmonary hypoplasia and pulmonary hypertension. All cases are associated with an abnormality of gut rotation although this may not necessarily be classified in our data.

Q790	DIAPHRAGMATIC HERNIA (L)	Live birth; Diagnosed at birth
Q790	DIAPHRAGMATIC HERNIA (L)	Live birth; Diagnosed at birth
Q790	DIAPHRAGMATIC HERNIA	Live birth; Prenatal diagnosis:
Q790	DIAPHRAGMATIC HERNIA	Live birth; Prenatal diagnosis:
Q790	DIAPHRAGMATIC HERNIA	Live birth; Prenatal diagnosis:
Q8680	FETAL VALPROATE SYNDROME (LIKELY)	Live birth; Diagnosed at birth

It is essential that babies identified to have a CDH are delivered in a tertiary referral centre for paediatric surgery.

ABDOMINAL WALL DEFECTS

GASTROSCHISIS, (Q793)

Gastroschisis results from the herniation of small bowel into the amniotic cavity through a small defect in the right para-umbilical region. Attachment of the umbilical cord is normal. The small bowel is always herniated but large bowel, pancreas and stomach can occasionally be found in the eviscerated organs. It is usually an isolated abnormality and the prognosis is generally good but depends on the condition of the bowel at birth and a small proportion will experience significant morbidity.

The antenatal detection of gastroschisis is uniformly good. The features are easily recognized on prenatal ultrasound scan.

Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth
Q793	GASTROSCHISIS	Prenatal diagnosis; Live birth; Arthrogryposis

There appears to have been a worldwide rise in gastroschisis over the last few decades. The pathogenesis is poorly understood. Young maternal age and smoking are the only factors that are consistently associated with this condition. In this small sample the mean maternal age was 21.1 years, (range 16 – 25 years).

EXOMPHALOS (OMPHALOCOELE), (Q792)

The gut normally returns to the abdominal cavity by the 10th week of gestation undergoing rotation at this time. Omphalocele results when this process fails. It has an incidence of 1:5000 live births. The defect comprises a herniation of intra-abdominal contents within the umbilical stalk covered by a layer of peritoneum and amnion. The severest consequences are associated with failure of the closure of the lateral fold at four weeks gestation resulting in a very large abdominal wall defect which may include bladder exstrophy. After post-natal repair of the omphalocele a defective anterior abdominal wall remains as normal apposition of the rectus muscles does not occur.

The primary abnormality is an anterior abdominal wall defect involving the umbilical cord. The contents may include peritoneal fluid, bowel liver and spleen. Associated anomalies are observed in 30% of cases and are predominantly cardiac in nature. Karyotypic abnormalities, particularly trisomy 18, are said to be present in 10-20% of cases.

Q792	EXOMPHALOS (LARGE)	Prenatal diagnosis; Termination; Other malformations
Q0591	SPINA BIFIDA (LARGE OPEN)	Prenatal diagnosis; Termination
Q900	TRISOMY 21	Prenatal diagnosis; Live birth at 24 weeks; AVSD
Q910	TRISOMY 18	Prenatal diagnosis; Termination; VSD
Q980	KLINFELTER SYNDROME	Prenatal diagnosis; Live birth at 38 weeks

ABDOMINAL WALL DEFECTS

PRUNE BELLY SEQUENCE, (Q794)

Prune-belly syndrome describes the association of hypotonic abdominal wall, large hypotonic bladder with dilated ureters, renal dysplasia and genital abnormalities. It may be considered a malformation sequence due to intrauterine abdominal wall distention. Such distention is usually due to an obstructive uropathy, (e.g. obstruction of the urethra leads to megacystis and bilateral megaureters), but other causes could lead to the morphological features of the syndrome in the absence of urinary involvement.

The incidence varies from 1:35,000 to 1:50,000 live births. The overwhelming majority of affected infants are male, (97%). There is a wide spectrum of severity. Congenital heart anomalies are reported in 10% of cases. Absence of prostate and cryptorchidism in males.

Prognosis is uncertain. There is a 20% risk of stillbirth and only 50% of children survive the first 2 years of infant life. Pregnancy termination may be considered.

Q794 PRUNE BELLY SEQUENCE Prenatal diagnosis: Termination: Female

Affected females typically have associated genital abnormalities including vaginal atresia, rectovaginal or rectovesical fistulas and bicornuate uterus. Unfortunately no further information is available on this particular case.

ABDOMINAL WALL DEFECTS

LIMB BODY WALL COMPLEX ANOMALY, (Q798)¹⁸

Limb body wall complex is a rare fetal malformation that is characterized by body wall, limb and neural tube defects. The association between body wall structural defects with limb reduction anomalies was first recognized in the 17th century. Similar anomalies were described as cyllosomes or pleurosomas¹⁹ in the 19th century.

Sonographic features include craniofacial defects, transverse limb defects, short umbilical cord and evisceration of abdominal content, urogenital abnormalities, spinal anomalies in the form of scoliosis or sacral agenesis and lumbosacral meningocele. However not all defects need to be present and in general two main groups can be identified those with and those without craniofacial abnormalities.

One case is recorded in the data. It is a 'presumed' diagnosis based on scan findings without the confirmation of a post-mortem examination. A termination of pregnancy was performed at 12 weeks gestation. As a consequence there is no record of associated abnormalities.

Q798 LIMB BODY WALL COMPLEX (PRESUMED)²⁰ Prenatal diagnosis; Termination

¹⁸ Q795 is usually the appropriate coding for Limb Body Wall Complex. All major anomalies, (encephalocele, craniofacial defects, limb defects, internal organ defects etc.), should also be coded.

¹⁹ Pleurosoma/Pleurosomatoschisis: The defective development of the body wall in the thoracic and/or abdominal regions permitting variable eventeration of viscera through an open abdominal wall. Typically associated with meromelia (congenital absence of part of an arm or leg) on the same side of the body as the defect.

²⁰ When the diagnosis is uncertain, (e.g. suggested by ultrasound but where no postnatal confirmation is undertaken), it is beneficial to distinguish possible diagnoses from confirmed diagnoses in the text.

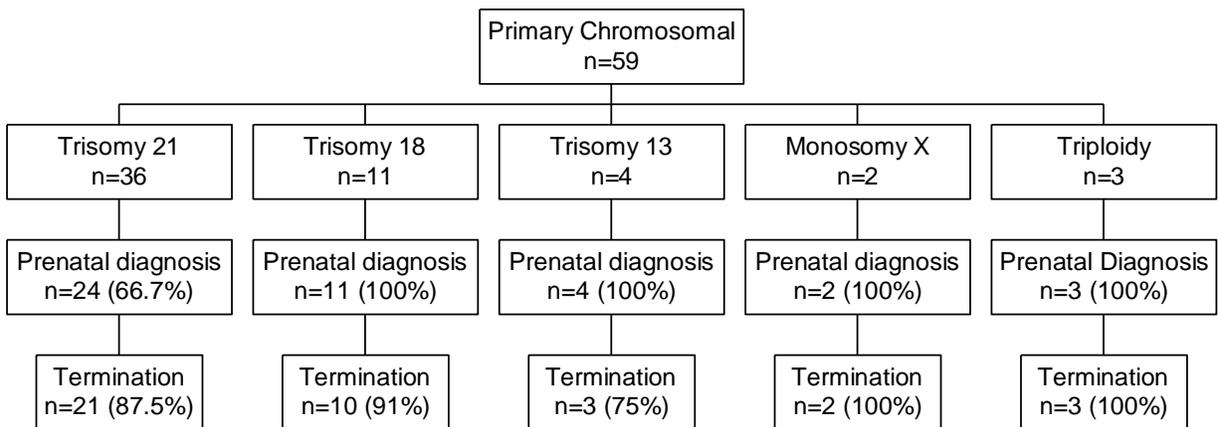
CHROMOSOMAL ABNORMALITY

Chromosomal Abnormality

A chromosomal abnormality is recorded for 63 cases. The majority, (n=59, 93.7%) are listed in the primary diagnostic position. In the four cases where chromosomal abnormality is listed as a secondary malformation there has been a partial deletion.

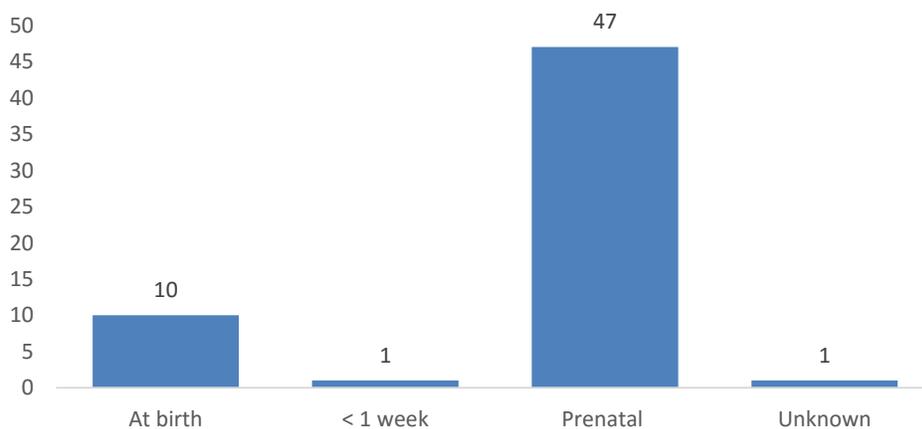
Figure 4.7: Overview of Prenatal Diagnosis of Primary Chromosomal Abnormality, (n=59).

**Excludes individual cases of Klinefelter syndrome, Pentasomy X and isochromosome tetrasomy 9*



Almost 80% of all primary chromosomal abnormalities were diagnosed prenatally, (Figures 4.7 & 4.8). Eleven cases, all trisomy 21, were diagnosed within the first week of infant life.

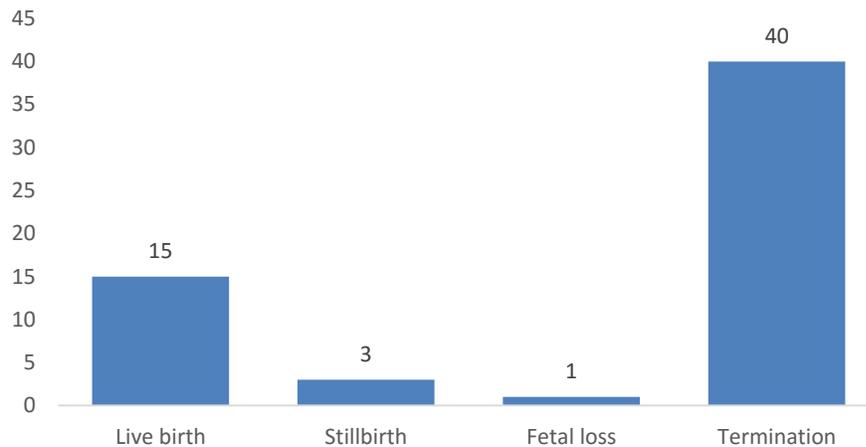
Figure 4.8: Point of diagnosis of Primary Chromosomal Abnormality, (n=59)



CHROMOSOMAL ABNORMALITY

Termination of pregnancy is the predominate outcome, (n=40, 68%). When a prenatal diagnosis of chromosomal abnormality is made termination of pregnancy is performed in 85% of cases.

Figure 4.9: Outcome of pregnancy for Primary Chromosomal Abnormality, (n=59)



TRISOMY 21 (DOWN SYNDROME), (Q900, Q909)

Trisomy 21 is one of the most common congenital anomalies. There is a well-defined phenotype, intellectual delay and major and minor structural anomalies – most commonly cardiac and gastrointestinal. Infants tend to be small and have a low birthweight. Advanced maternal age is the most significant established risk factor.

A total of 36 cases were associated with trisomy 21. It was always recorded as the primary abnormality. Thirteen cases, (36.1%), were live born. There was one stillbirth and one fetal loss. The remaining twenty-one cases were all terminated following prenatal diagnosis, (Figure 4.10). Prenatal screening has had a significant impact on live birth prevalence across all maternal ages.

Associated anomalies included cystic hygroma, VSD, ASD, AVSD, bicuspid aortic valve, situs inversus and exomphalos. Recognizable abnormalities, (including AVSD and situs inversus), were present in five of the thirteen cases where the diagnosis was made at birth.

There were 12 cases of trisomy 21 where prenatal diagnosis was not achieved. One pregnancy resulted in stillbirth the other eleven in live birth with diagnosis of trisomy 21 being made within the first week of life. All women in NHS GG&C are offered screening for trisomy 21. Information is available through the PNBS system regarding this screening process including those mothers who were offered yet declined prenatal screening and where screening was performed but a diagnostic test was declined. This additional data is reported separately through the annual NHS GG&C Public Health Screening Programmes Annual Report 2014/15 and is therefore not included here.

CHROMOSOMAL ABNORMALITY

Figure 4.10: Outcome of pregnancies associated with Trisomy 21, (n=36)

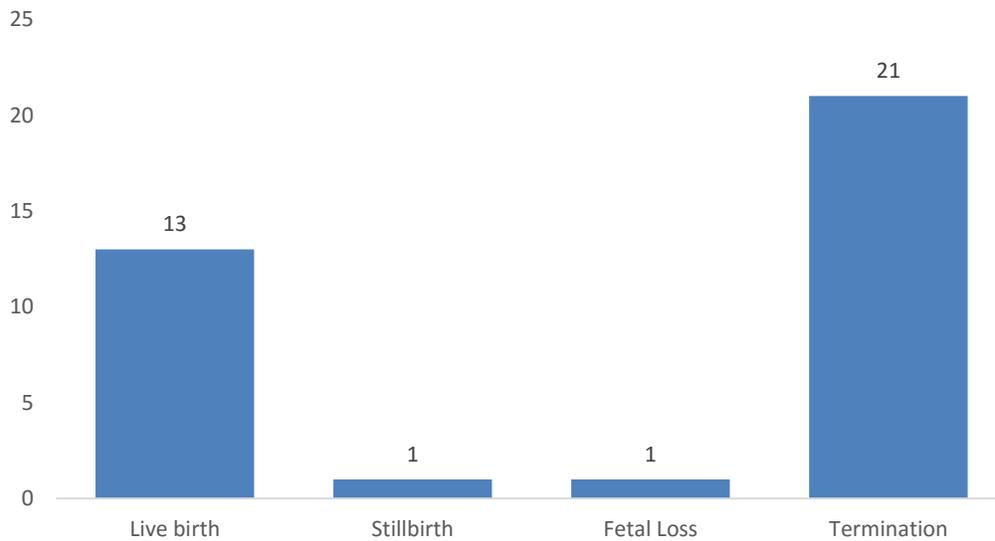
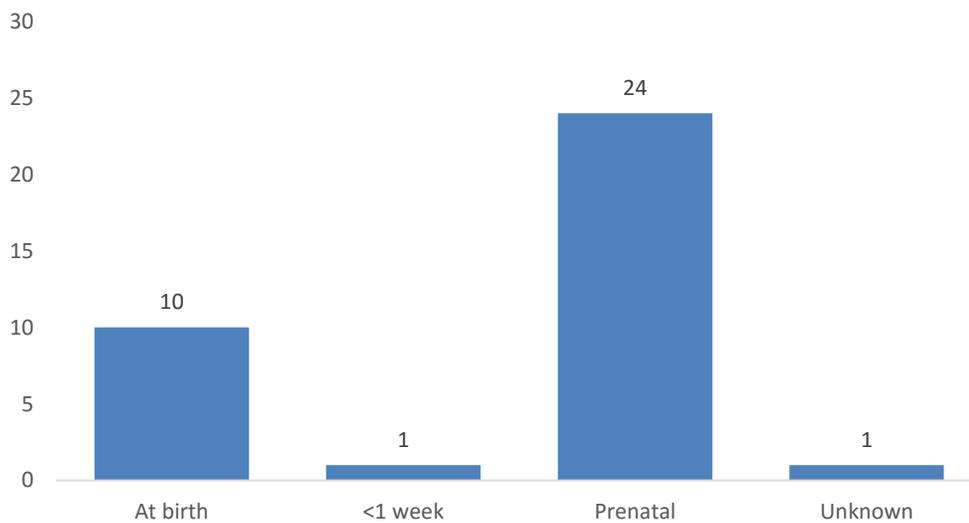


Figure 4.11: Point of diagnosis for Down syndrome, (n=36)



CHROMOSOMAL ABNORMALITY

TRISOMY 18, (Q910)

Trisomy 18, also called Edward's syndrome, is a chromosomal condition associated with abnormalities affecting a number of body systems. The condition is increasingly diagnosed in prenatal life. Typically ultrasound examination will reveal signs of intrauterine growth retardation associated with features such as neural tube defect, exomphalos, congenital heart defects and polyhydramnios.

There were 11 cases of trisomy 18, (Edward's syndrome) listed in the data. They were all diagnosed antenatally. The majority were terminated with only one live birth recorded. Cardiac abnormalities are commonly associated with Edward's syndrome and were seen in 36.4% of cases.

Q910	TRISOMY 18	TOF; Reduction deformity of brain; Live birth
Q910	TRISOMY 18	
Q910	TRISOMY 18	Cystic hygroma
Q910	TRISOMY 18	Cystic hygroma
Q910	TRISOMY 18	Cystic hygroma
Q910	TRISOMY 18	Cystic hygroma
Q910	TRISOMY 18	VSD
Q910	TRISOMY 18	Congenital malformation of limbs
Q910	TRISOMY 18	Exomphalos; VSD
Q910	TRISOMY 18	AVSD; Congenital malformation of brain
Q910	TRISOMY 18	Aortic stenosis; VSD; Malposition of heart

TRISOMY 13, (Q914, Q915)

Trisomy 13, also called Patau syndrome, is a chromosomal condition associated with severe intellectual disability and physical abnormalities in many parts of the body. Like trisomy 18 this condition is often diagnosed through a recognizable pattern of dysmorphism and malformation. Individuals with trisomy 13 often have heart defects, brain or spinal cord abnormalities, very small or poorly developed eyes (microphthalmia), extra fingers or toes, an opening in the lip (a cleft lip) with or without an opening in the roof of the mouth (a cleft palate), and weak muscle tone (hypotonia).

Q914	TRISOMY 13	Prenatal diagnosis; Stillbirth; Cystic hygroma
Q914	TRISOMY 13	Prenatal diagnosis; Termination
Q914	TRISOMY 13	Prenatal diagnosis; Termination; Dandy-Walker; Orofacial clefting
Q915	TRISOMY 13 MOSAIC	Prenatal diagnosis; Termination; Holoprosencephaly; Orofacial clefting

TRIPLOIDY, (Q927)

Triploidy, a complete extra set of chromosomes, is a common chromosomal anomaly in human gestation occurring in 1-2% of all conceptions. Most triploidies abort spontaneously in the first trimester. Triploidy accounts for 10% of spontaneous miscarriage. Triploidy may result from either diandric or digynic fertilizations.

CHROMOSOMAL ABNORMALITY

In diandry the extra set of chromosomes is of paternal origin either from a meiotic error leading to a diploid sperm or more typically dispermic fertilization, Diandry predominates in cases of triploidy without embryos after nine weeks or in the second trimester with fetuses of relatively normal size and placental features of a partial hydatidiform mole. Digyny, (fertilization of a diploid oocyte) predominates in early miscarriages with embryos before nine weeks or in second trimester loss of a fetus with marked asymmetrical growth retardation.

Q927	TRIPLOIDY	Prenatal diagnosis; Termination; Female
Q927	TRIPLOIDY	Prenatal diagnosis; Termination; Female
Q927	TRIPLOIDY	Holoprosencephaly; Prenatal diagnosis; Termination; Female

TURNER SYNDROME, (Q960)

Turner syndrome is an aneuploidy, and is also known as 'monosomy X', (45X0). The incidence is roughly 1:2500 live-born girls. Fifteen percent of cases demonstrate some mosaicism. Sometimes a lymphangioma, (cystic hygroma), prompts diagnostic investigation.

Q960	TURNER SYNDROME - 45X	Prenatal diagnosis; Termination
Q960	TURNER SYNDROME	Cystic hygroma; Prenatal diagnosis; Termination

Most girls and women with Turner syndrome have normal intelligence. Developmental delays, nonverbal learning disabilities, and behavioural problems are possible, although these characteristics vary among affected individuals.

PENTASOMY X, (Q971)

Pentasomy X, (or 49, XXXXX syndrome), is an aneuploidy associated with three additional X chromosomes. The condition was first described in 1963 in a two year-old girl. Very few cases have been reported in the literature. It is characterized by severe mental impairment, delayed speech development, congenital heart defects, short stature, osseous and articular abnormalities and abnormalities to the head and face presumably resulting from failure or disruption of X chromosome inactivation.

Q971	PENTASOMY X	Prenatal diagnosis; Termination
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This was a prenatal diagnosis made at 29 weeks gestation. Late, (third trimester) termination of pregnancy was performed. Apparently there were no associated abnormalities. It is uncertain what might have prompted prenatal diagnosis.

CHROMOSOMAL ABNORMALITY

KLINFELTER SYNDROME, (Q980)

Klinefelter syndrome, (47, XXY), affects 1:1000 males and is typically diagnosed in early adulthood during investigations of infertility. A single case of Klinefelter syndrome is listed. Prenatal diagnosis was made on amniocentesis following the identification of exomphalos. A male infant was live born at 38 weeks gestation.

Q980	KLINFELTER SYNDROME	Exomphalos; Prenatal diagnosis; Live birth;
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DELETIONS, (Q935), (Q936)

The varied presentations of Di George syndrome have already been considered. It is perhaps better considered a 22q11.2 deletion syndrome. This was a male infant delivered at term. Associated features included renal dysplasia, transposition of the great arteries and VSD.

D821	DI GEORGE	Prenatal diagnosis; Live birth; Male
Q8784	WILLIAMS SYNDROME	Live birth; Male; Minor partial trisomy

The case of Williams syndrome, a sporadic congenital syndrome that is a consequence of a micro-deletion of chromosome 7, (7q11, 23) at the elastin gene focus, was also considered earlier.

OTHER SPECIFIED CHROMOSOMAL ABNORMALITIES, (Q998)

As discussed in previous reports the ICD 10 code 'Q998' is used for a collection of chromosomal abnormalities that are not easily categorized elsewhere. The code is used on three occasions in the current data set.

Q6141	RENAL CYSTIC DYSPLASIA - BILAT	Live birth; Diagnosed between 1 – 12 months
Q688	ARTHROGRYPOSIS-SEVERE	Prenatal diagnosis; Live birth at term
Q998	ISOCHROMOSOME TETRASOMY 9	Prenatal diagnosis; Stillbirth at 33 weeks

An isochromosome is chromosome that has lost one of its arms and replaced it with an exact copy of the other arm. Tetrasomy 9p is a rare chromosomal disorder in which the short arm of the 9th chromosome (9p) appears 4 times in all or some of the cells. It is associated with craniofacial abnormalities, hand and limb abnormalities, skeletal malformations and cardiac defects. Only 30 cases have been reported in the literature and they are mostly male.

Unusually this was a female infant that was stillborn at 33 weeks. There was an associated Dandy-Walker malformation. Prenatal diagnosis had been made at 13 weeks and it is likely that it was recognition of the cranial abnormality that gave the 'point of diagnosis'.

APPENDIX 1: GENERAL STATISTICS

Appendix 1: General Statistics

NHS GREATER GLASGOW & CLYDE MATERNITIES 1ST APRIL 2014 TO 31ST MARCH 2015

Maternity Unit	Appointed Referrals Not NHSGGC Residents	Appointed Referrals NHSGGC Residents	Appointed Referrals Total	Bookers Not NHSGGC Residents	Bookers NHSGGC Residents	Bookers Total
Not assigned to a unit	136	320	456	143	333	476
Princess Royal Maternity Hospital (PRM)	2061	4619	6680	1862	4156	6018
Royal Alexandra Hospital (RAH)	442	3383	3825	398	3121	3519
Southern General Hospital (SGH)	535	6515	7050	476	5908	6384
Total	3174	14837	18011	2879	13518	16397

Source: NHS GG&C Pregnancy & Newborn Screening System: NHS Greater Glasgow & Clyde Hospitals & Residents

NHS GREATER GLASGOW & CLYDE BIRTHS 1ST APRIL 2014 TO 31ST MARCH 2015

Area	Live Births	Stillbirths	Overall Total
Clyde	3,160		
Greater Glasgow	10,093		
Total	13,253	42	13,295

Source : Child Health Universe Extract run 28th August 2015

APPENDIX 2: CASE PREVALENCE

Appendix 2: Case Prevalence

CASE PREVALENCE COMPARISON, (PER 10,000 BIRTHS) ‡

Abnormality	Prevalence in Primary Position	Prevalence in any Position	EUROCAT Prevalence Data
Amniotic Band Sequence	N/A	N/A	0.51
CCAM (Q338)	3.01	3.01	0.95
Bilateral Renal Agenesis (Q602)	1.50	1.50	1.18
Congenital Cataract, (Q120)	0.75	0.75	1.23
Hirschprung's Disease, (Q431)	4.51	5.27	1.24
Turner syndrome, (Q914-917),(Q960-969)	1.50	1.50	2.24
Craniosynostosis, (Q750)	2.26	3.76	2.39
Hypoplastic Left Heart, (Q234)	2.26	2.26	2.66
Congenital Diaphragmatic Hernia, (Q790)	3.76	4.51	2.76
Gastroschisis, (Q793)	5.27	5.27	2.85
Exomphalos, (Q792)	0.75	3.76	3.00
Fallot's Tetralogy, (Q213)	2.26	2.26	3.45
Transposition of Great Arteries, (Q203)	2.26	3.01	3.52
Coarctation of Aorta, (Q251)	4.51	6.02	3.85
Atrioventricular Septal Defect, (Q212)	0.75	4.51	4.09
Edwards syndrome, (Q910-913)	8.27	8.27	5.13
Hydrocephalus, (Q030-Q039)	2.26	3.01	5.77
Developmental Dysplasia of the Hip, (Q65)	10.53	10.53	8.07
Cleft Lip/Palate, (Q352-Q279)	12.03	17.30	8.77
NTD's , (Q000, Q010-Q019, Q051-Q059)	15.04	15.04	9.66
Hypospadias, (Q549)	7.52	11.28	18.01
Down syndrome, (Q900-Q909)	27.08	27.08	22.10

‡Denominators: The congenital anomaly surveillance tool that has been used to compile the data within this report is restricted to mothers' resident within the geographically defined area of NHS GG&C at the time of birth. In order to allow comparison with the EUROCAT prevalence data the appropriate denominator for the prevalence data is therefore the total live births and stillbirths for that area between 1st April 2014 and 31st March 2015 which is 13,295. Data was extracted on 28th August 2015.

*Source for comparison data: EUROCAT Website Database. The EUROCAT prevalence data quoted is for 2007-2011.

APPENDIX 3: PRENATAL DETECTION RATES

Appendix 3: Prenatal Detection Rates

PRENATAL DETECTION RATES: COMPARISON WITH 'ESTABLISHED' DATA

Abnormality	Observed Prenatal Detection Rate	Expected Detection Rate*	EUROCAT Observed
Anencephaly	100%	98.0%	96.7%
Spina Bifida	100%	90.0%	82.9%
Congenital Diaphragmatic Hernia, (Q790)	50%	60.0%	58.0%
Cleft Lip	81.3%	75.0%	50.7%
Gastroschisis	100%	98.0%	91.6%
Exomphalos	100%	80.0%	83.0%
Serious Cardiac Abnormalities (EUROCAT defined)	67.7%	50.0%	
Transposition of Great Vessels, (Q203)	100%		41.4%
Atrioventricular Septal Defect, (Q212)	66.7%		
Fallot's Tetralogy	33.3%		
Ebstein's Anomaly	N/A		
Hypoplastic Left Heart, (Q234)	100%		71.9%
Hypoplastic Right Heart, (Q226)	N/A		
Coarctation of the Aorta, (Q251)	50%		
Bilateral Renal Agenesis	100%	84.0%	88.1%
Talipes Equino-varus	70%		39.8%
Trisomy 21	67%	95.0%	63.8%
Trisomy 18	100%	95.0%	90.9%
Trisomy 13	100%	95.0%	90.9%

*Ward P & Soothill P. Fetal Anomaly ultrasound scanning: the development of a national programme for England. TOG 2011; 13: 211-217.