# CONGENITAL ANOMALIES SURVEILLANCE

# 2011-2012

---

## REVIEW OF DATA RELATING TO CONGENITAL ANOMALIES DETECTED IN NHS GG&C BETWEEN 1ST APRIL 2011 AND 31ST MARCH 2012

Dr. James Robins

Source data provided by Hilary Jordan of Information Services

Final Draft

# Table of Contents

# Definitions

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.

**Connatal** may be a better term for 'lesions' present or acquired at birth.

Birth defect is a widely used term for congenital malformation which is recognizable at birth.

Congenital anomalies are of four clinically significant types.

- Malformations
- Deformations
- Disruptions
- Dysplasias

**Malformation**: In a malformation the development of a structure is arrested delayed or misdirected early in embryonic life and the effect is permanent.

**Deformations**: Are 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**: Describes a 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.

**Incidence**: Rate of occurrence of new cases of a disease or condition over a specified period of time expressed as a ratio or percentage.

$$\text{Incidence} = \frac{\text{number of new cases over specified period of time}}{\text{size of population under consideration}}$$

It is used rather than **prevalence** which describes how frequently a disease or condition occurs in a specified population at a particular point in time.

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 study it should be the number of maternities booked through antenatal services over the year 1st April 2011 and 31st March 2012, (n=15,098). This may not allow comparison with established anomaly rates which often use live-births as a denominator.

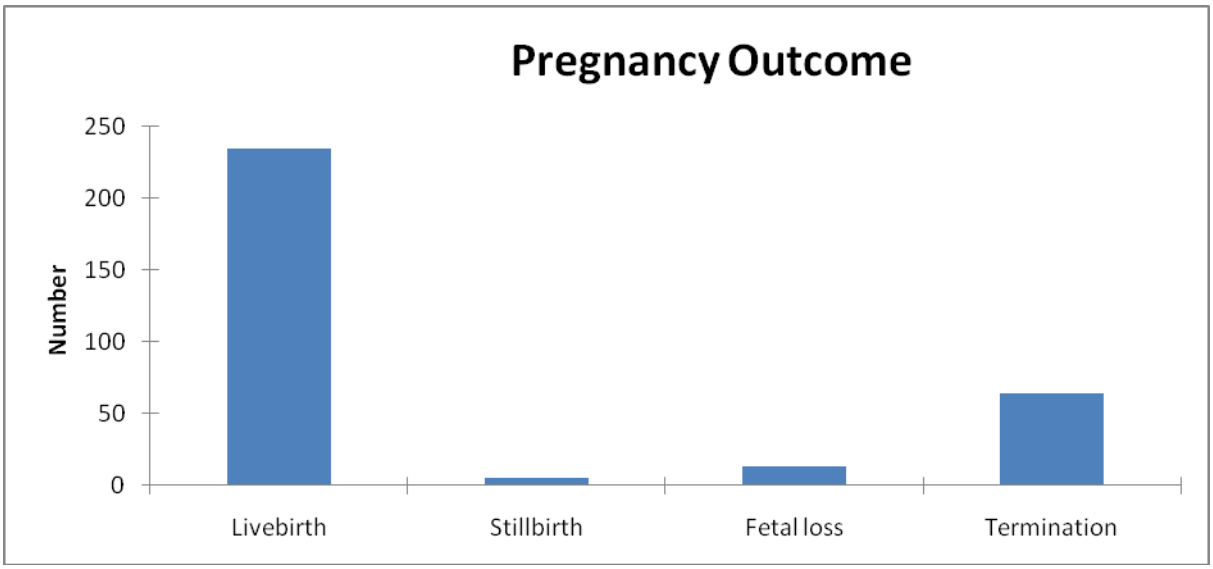
# 1. Core Data

**This report considers all live-births, stillbirths, fetal losses and terminations of pregnancy between 1st April 2011 and 31st March 2012 that were associated with one or more congenital abnormalities.**

## Case based review

A total of 316 cases were identified, this is a 27% increase over the 248 cases described in the 2010-2011 review. Case ascertainment would appear to have improved rather than any real increase in congenital anomaly.

**Figure 1.1: Pregnancy Outcome, (n=316).**




The majority of cases were live-births, (234; 74%). There were 5 stillbirths (2%) and 12 fetal losses (4%). Termination of pregnancy following pre-natal diagnosis of abnormality accounted for 64 cases, (20%), (Figure 1.1).

Overall a total of 573 abnormalities were classified using the ICD10 system in these 316 cases, the primary abnormality and a variable number of associated abnormalities. In 203 cases only the primary abnormality is listed. However in 113 cases, (36%), two or more abnormalities have been classified, (Figure 1.2). In six cases (2%) a total of 8 abnormalities were defined. These included Goldenhar Syndrome, Sirenomelia sequence, Trisomy 13, severe hydrocephalus and two cases with multiple abnormalities without defined syndrome or cause.

The data on the 316 cases is, however, provided listed and ranked on the basis of primary abnormality as defined under ICD10, (Figure 1.3). The classification is clearly not perfect. For example, one of the cases of multiple congenital abnormalities described above has 'Absent Left Arm' as the primary abnormality but also had absent lower limbs, renal agenesis, absent diaphragm, unicornuate uterus and tracheo-oesophageal fistula.

**Figure 1.2: Abnormalities per case, (n=316).**

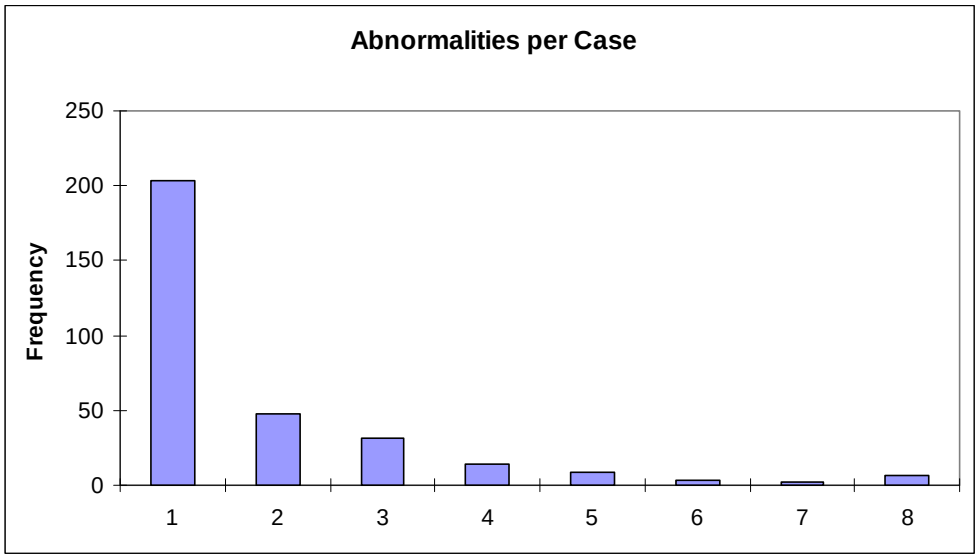
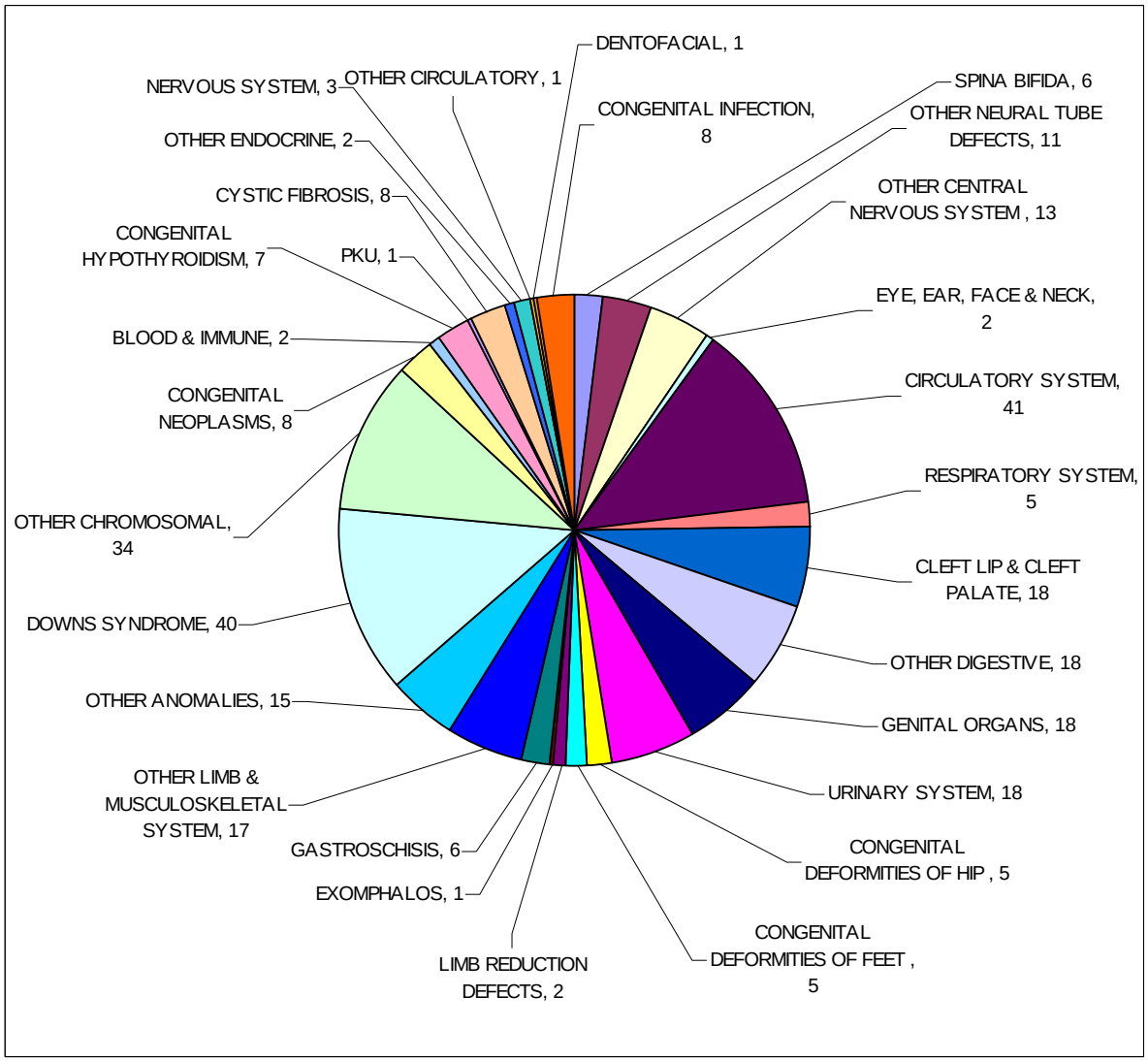


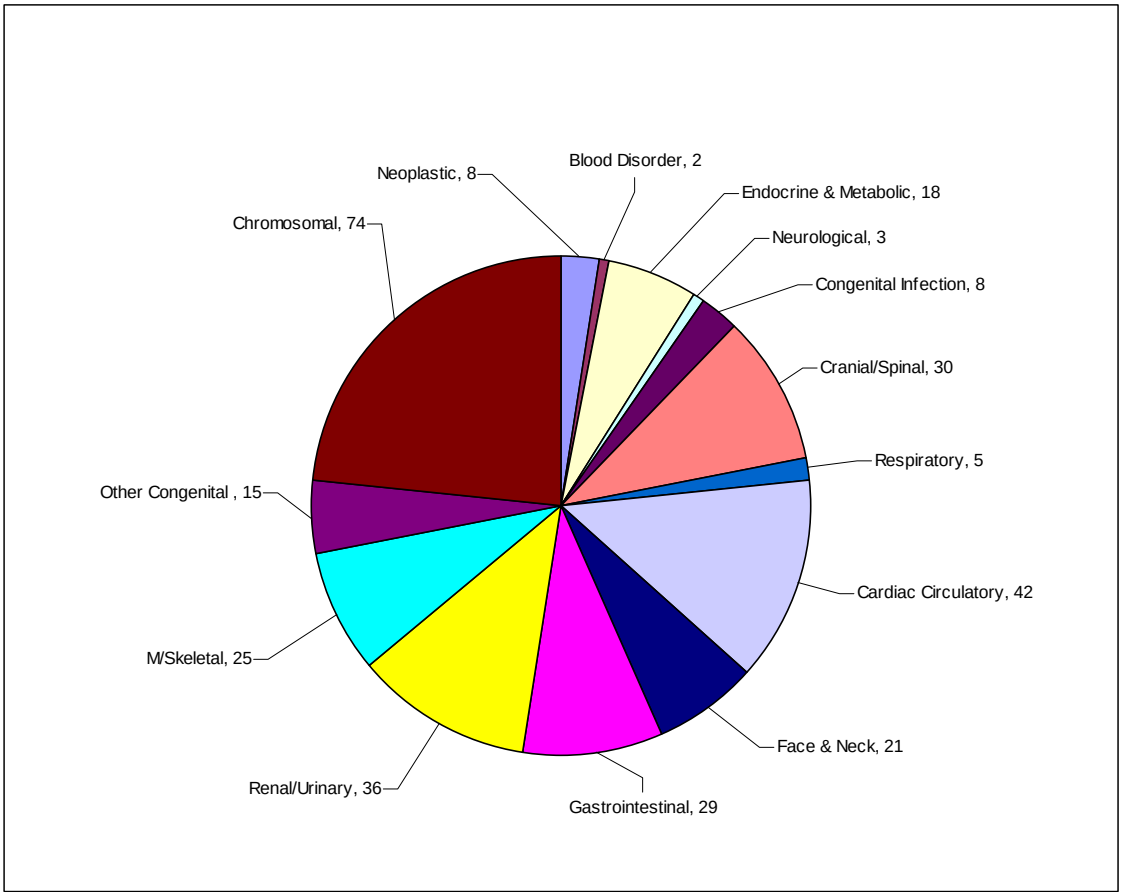

**Figure 1.3: Classification according to Primary Abnormality (ICD10), (n=316).**



Chromosomal abnormality, ('Down Syndrome' and 'Other Chromosomal Disorders'), is recorded as the primary abnormality in 74 cases, (23%). Disorders of the Heart and Circulatory System, ('Circulatory System' and 'Other Circulatory'), are the next most common group of primary abnormalities, (n=42; 13%). Cranial and spinal abnormality, ('Spina Bifida', 'Other Neural Tube Defects' and 'Other Central Nervous System'), is classified as the primary abnormality in 30 cases, (9%). An aggregated and simplified chart based on primary abnormality is presented in Figure 1.4.

Overall these figures are similar to those from 2010-2011. However, chromosomal abnormality was defined as the primary abnormality in only 15% of the 248 cases recorded during that period. Again this is likely to be the result of better case ascertainment.

**Figure 1.4: Simplified Classification by Primary Abnormality, (n=316).**

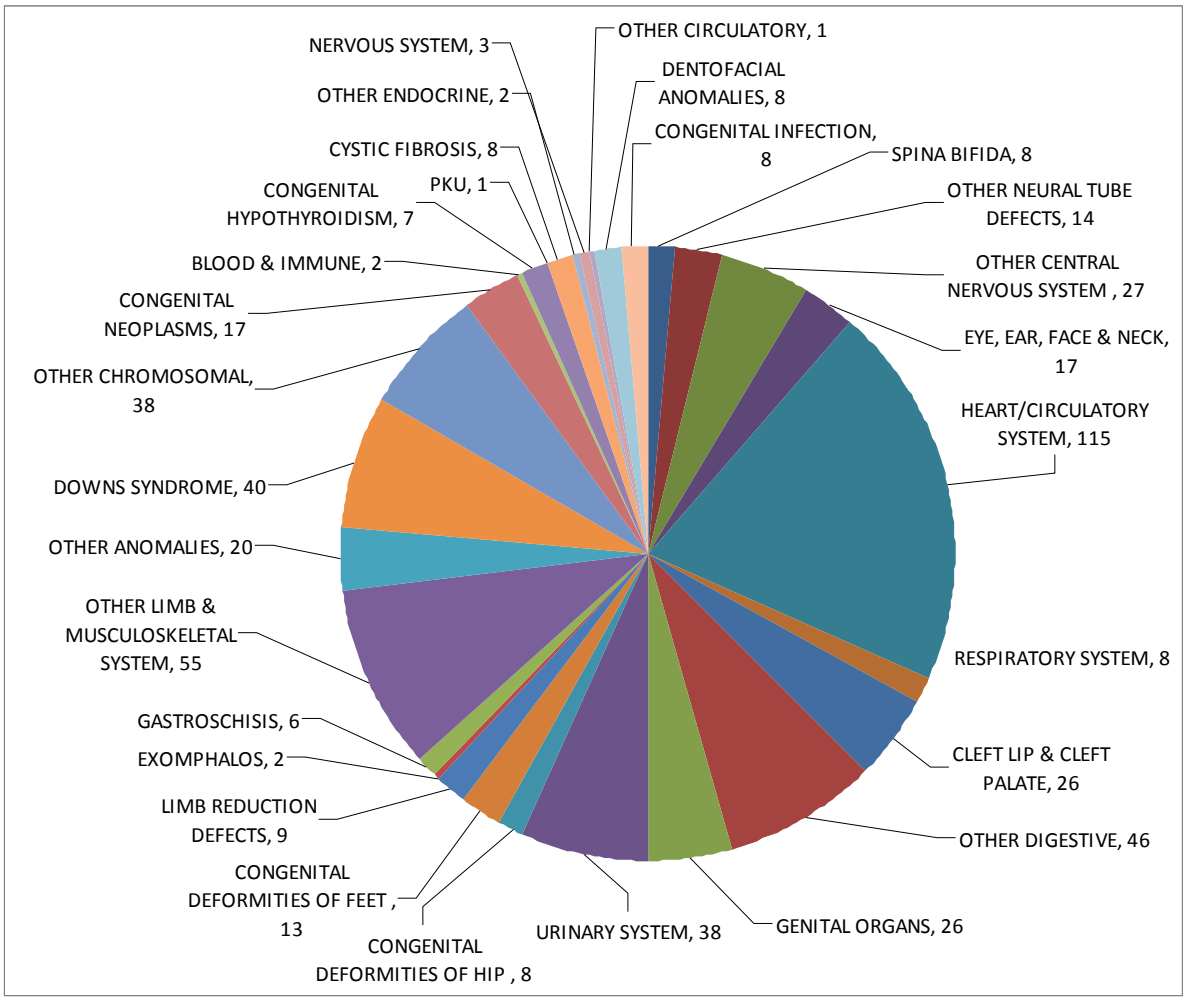



## Abnormality based review

The situation becomes a little more complex when all of the 573 defined abnormalities are considered, (Figure 1.5). Disorders of the 'Heart & Circulatory System' account for the majority of defined abnormalities, (n=115, 20%), and 35% of these abnormalities are in the primary diagnostic position, (41/115).

Abnormalities of the 'Limb & Musculoskeletal System' are also prevalent, accounting for 15% of all abnormalities classified. Once again 34% are in the primary position, (29/85).

**Figure 1.5 Anomalies in any diagnostic position (not mutually exclusive), (n=573)**

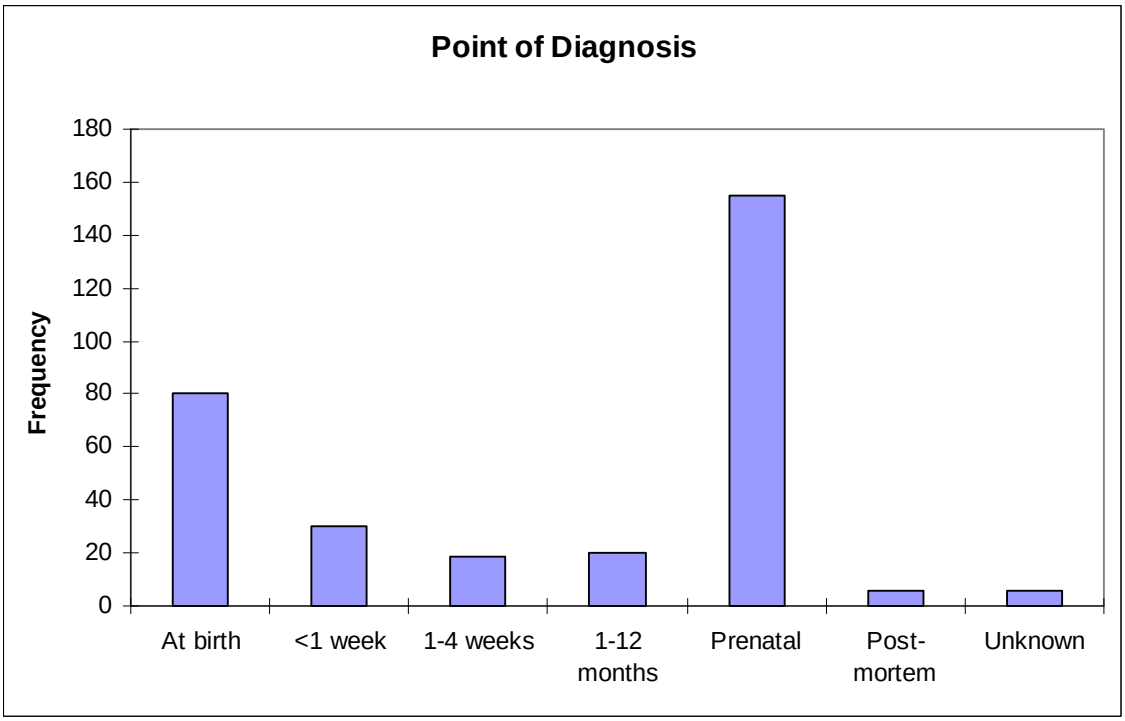



Chromosomal abnormalities were the predominate diagnosis on a case based review. They still account for 14% of all defined abnormalities yet were the most likely to be recorded in the primary diagnostic position, (95%). Likewise 62% of all disorders of the spine and central nervous system are in the primary diagnostic position.

## 2. Point of Diagnosis

Data are available for the point of diagnosis – when the primary abnormality was first recognized, (Figure 2.1).

**Figure 2.1: Point of Diagnosis, (n=316)**




Over 49%, (n=155), of abnormalities were diagnosed prenatally. In 110 cases, (34%), the diagnosis was made at birth or within the first week of life. Thirty-nine cases, (12%), were diagnosed after the first month but within 1 year. Six cases, (2%), were diagnosed at post-mortem. In a further 6 cases the point of diagnosis is recorded as 'unknown'.

A chart demonstrating Point of Diagnosis for primary abnormality in each of the main ICD10 Categories is produced, (Figure 2.2).

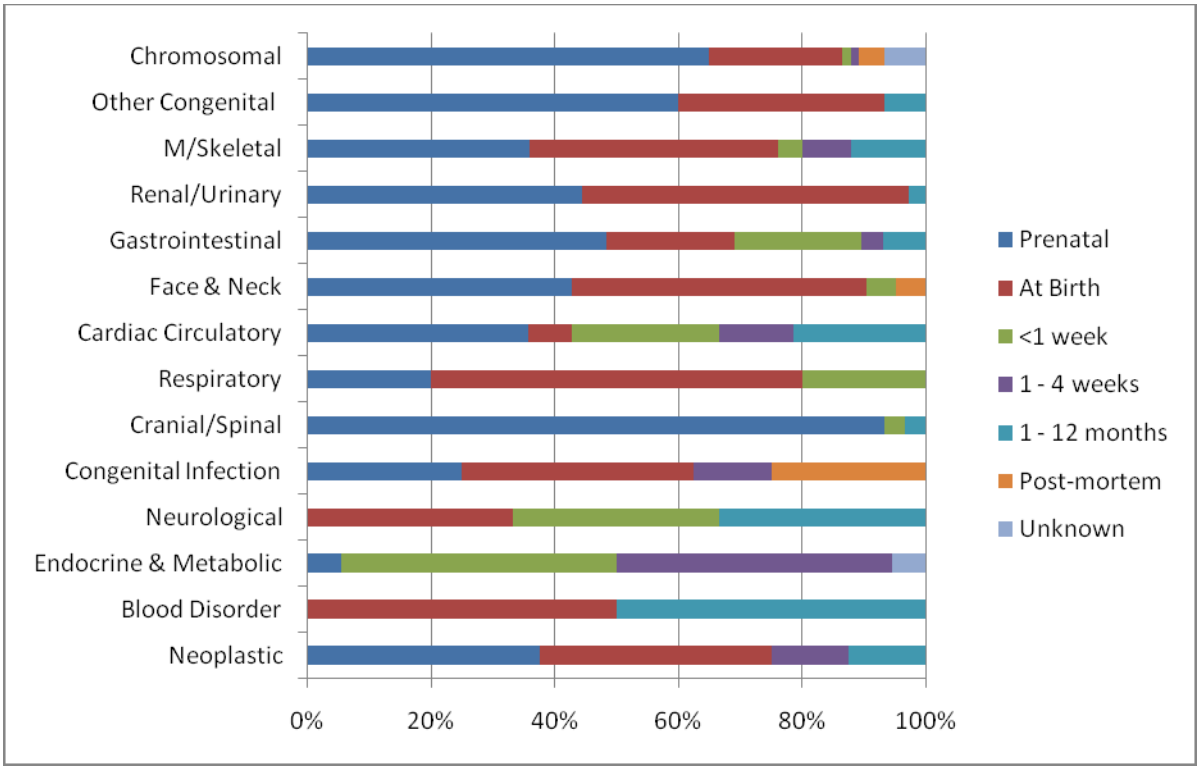
Ninety-three percent of all 'Cranial & Spinal' abnormalities are diagnosed prenatally.

The two cases of 'Blood Disorder' were both Di George Syndrome (22q11.2 deletion). Both were associated with cardiac abnormality. One was diagnosed at birth as a consequence of an aortic atresia. The other case was diagnosed between 1-12 months of life and is interesting in that it has also been labelled as having Angelman Syndrome. This is a neuro-genetic condition due to partial deletion of genes on Chromosome 15. Clearly these cases could easily have been classified in a number of the ICD10 categories.

Typically most diagnoses of primary abnormality are made either antenatally or within the first week of life. The results of routine blood spot analysis dictate that 'Endocrine & Metabolic' disorders will usually be diagnosed around 1- 4 weeks. Although the majority of 'Cardiac & Circulatory' disorders

are picked up either on antenatal scan or during the first week of life, a good proportion, (21%), are not diagnosed until 1 – 12 months of life.

**Figure 2.2: Point of Diagnosis for Main ICD10 Category, (n=316)**




## 2.1 At Birth

Eighty primary abnormalities are coded as being diagnosed at birth, (Figure 2.3).

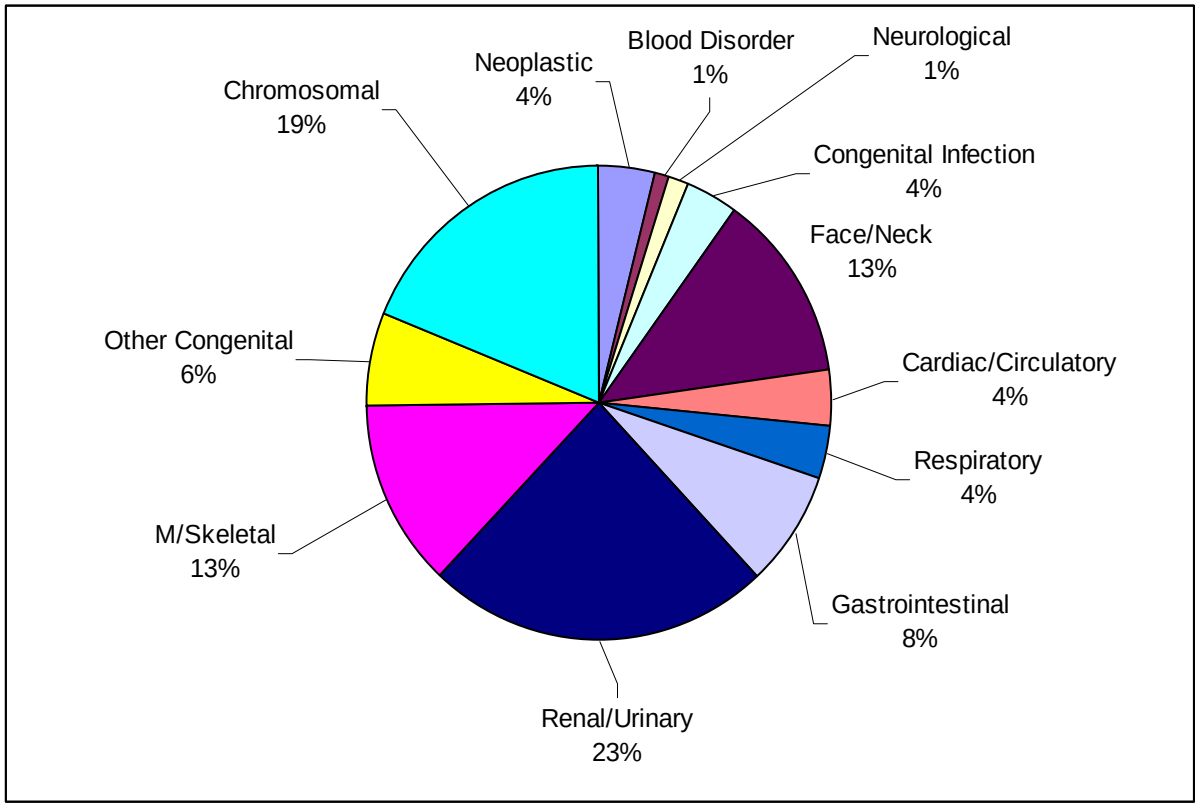
The greatest proportion are those of the Renal & Urinary Tract, (n=19; 23%). Hypospadias is the diagnosis in 17 of these cases. Micropenis and bladder exstrophy are the two further cases described.

Twelve cases of Trisomy 21 were diagnosed at birth, there is no record of whether or not the mother's had elected for prenatal screening in this data but this could be determined through linkage to the Pregnancy & Newborn Screening Programme, (PNBS). Other chromosomal disorders presenting at birth included Edward's Syndrome (Trisomy 18), Potocki-Lupiski Syndrome (duplication 17p11.2), Wolff-Hirschorn Syndrome (Deletion 4p), and a case with malposition of the heart where an abnormality of Chromosome 15 was found.

The gastrointestinal abnormalities were divided evenly between imperforate anus (n=3) and oesophageal atresia with tracheo-oesophageal fistula, (n=3).

Disorders of 'Face & Neck' accounted for 13%, (n=10), of abnormalities diagnosed at birth. These were typically isolated cleft palate. There was one case of isolated cleft lip and another of cleft lip and palate. The remaining case in this category was bilateral cataracts.

**Figure 2.3: Diagnosis at Birth by Primary Abnormality (ICD10), (n=80)**




Disorders of the musculoskeletal system diagnosed at birth included talipes equino varus, (n=2), congenital dislocation of hip, (n=2) and accessory digits, (n=3). A very rare diagnosis of metatropic dysplasia was made shortly after birth. Only 80 cases have ever been described in the literature. It is an autosomal dominant disorder arising from a mutation of the TRPV4 gene that controls calcium movement. Most cases of metatropic dysplasia are caused by new mutations in the gene and occur in people with no history of the disorder in their family. A diagnosis of slightly more common form of dwarfism, achondroplasia, was also made at birth.

The three congenital neoplasms identified at birth were a cystic hygroma (isolated), sacral haemangioma and hepatoblastoma.

## 2.2 Within 1st Week

Congenital abnormality was diagnosed in 30 cases during the first week of life. The majority were congenital abnormalities of the cardiac and circulatory system (n=10; 33%). These included two cases of Transposition of the Great Arteries (TGA), three ventricular septal defects (VSD's), two cases of Coarctation of the Aorta and a single case of Ebstein's Anomaly, (congenital displacement of the tricuspid valve towards the apex of the right ventricle which is often associated with other abnormalities – in this case Hirschprung's Disease).

Gastrointestinal disorders comprised the next largest group, (n=6). There was a further case of Hirschprung's Disease, four cases of mal-rotation of the duodenum and in one case a gastric duplication cyst, (associated with CDH and hemi-vertebrae).

As might be expected endocrine and metabolic problems are commonly diagnosed in the first week of life, typically from routine blood spot analysis. There were four cases of congenital hypothyroidism, two diagnoses of cystic fibrosis, and one case each of Phenylketonuria[1] and Medium Chain Acyl Dehydrogenase Deficiency, (MCADD)[2].

Other cases diagnosed in the first week of life included Trisomy 18 Mosaic, Muscular Dystrophy, Congenital Dislocation of the Left Hip, and Nasal Pyriform Aperture Stenosis, (unusual cause of upper respiratory obstruction in the neonate). Congenital Cataracts were diagnosed in two cases, one in association with microcephaly.

## 2.3 Between 1-4 Weeks

'Endocrine and metabolic' are still being diagnosed in the first four weeks of life. There were three cases of congenital hypothyroidism, one case of MCADD, and four cases of cystic fibrosis were diagnosed between 1 and 4 weeks of life.

Five further abnormalities of the 'Cardiac and Circulatory system are defined. These include two further VSD's, Pre-excitation syndrome, Coarctation of the Aorta and Aortic Stenosis.

Other abnormalities diagnosed include Klippel-Feil Syndrome, Biliary Atresia, Craniosynostosis, and Sacrococcygeal teratoma.

A single case of Congenital Toxoplasmosis is also recorded.

Overall 19 cases are recorded as being diagnosed with 1 and 4 weeks. However, a case of Trisomy for Chromosome 15 is included but this is almost certainly an error of classification. It was a fetal loss and the diagnosis was made at post-mortem, (see later).

## 2.4 Diagnosed after 1 month but within 1 year

There were a total of 20 cases in which the primary abnormality was diagnosed after 1 month but within 1 year. The majority of these were disorders of the heart and circulatory system, (n=9), and included Tetralogy of Fallot, Taussig-Bing Anomaly (double outlet right ventricle, pulmonary atresia, tricuspid atresia). There were 2 cases of persisting patent ductus arteriosus, (PDA), and 2 cases of isolated ventricular septal defect, (VSD). The single case of Tetralogy of Fallot was also associated with malformations of the face and lower limbs as well as an (as yet) unspecified chromosomal disorder.

Other 'late' diagnoses include Di George Syndrome (22q11.2 deletion), Emery-Dreyfus Muscular Dystrophy, Fetal Alcohol Syndrome, acetabular dysplasia, polymicrogyria and a rare case of anaplastic ependyoma grade 3.

Further 'late diagnoses' will undoubtedly be made as we are still only 8 months post-delivery of some of the 2011-2012 cohort.

[1] Phenylketonuria (PKU) is an inherited disorder that affects around one in 8,000 babies born in Scotland.

[2] About one in 10,000 babies born in Scotland has Medium chain acyl dehydrogenase deficiency (MCADD).

## 2.5 Prenatal Diagnosis

The majority of primary abnormalities were diagnosed during the antenatal period, (n=155), (Figure 2.4).

Forty-eight cases were associated with chromosomal abnormality of which the majority, (n=21) were Down syndrome (Trisomy 21). There were 12 cases of Trisomy 18, 5 cases of Trisomy 13, 2 cases of Triploidy and 4 cases of Turner's syndrome, (46, XO). Other chromosomal abnormalities diagnosed antenatally included Trisomy 8, Chromosome 15 abnormality (see later), Klinefelter's syndrome and Wolf-Hirschorn Syndrome. The latter is a contiguous gene deletion syndrome associated with a hemizygous deletion of chromosome 4p16.3. It is typically characterized by microcephaly, facial clefting, cardiac septal defect and a characteristic 'Greek Helmet' facies. This case, a live birth, was found to have an ASD.

Neural tube defects, (anencephaly, encephalocoele and spina bifida), and isolated hydrocephalus accounted for the majority of 'Cranial & Spinal' abnormalities diagnosed on antenatal ultrasound scan, (n=21).

'Cardiac & Circulatory' disorders diagnosed on antenatal scan included hypoplastic left heart disease, (n=4), transposition of the great vessels, (n=5), and truncus arteriosus, (n=2). Sixty percent of cases listed with a primary cardiac abnormality diagnosed on prenatal examination had an associated cardiac defect. One of the cases classified under 'Neoplastic' was a Cardiac Fibroma.

**Figure 2.4: Prenatal Diagnosis by Primary Abnormality (ICD10), (n=155)**

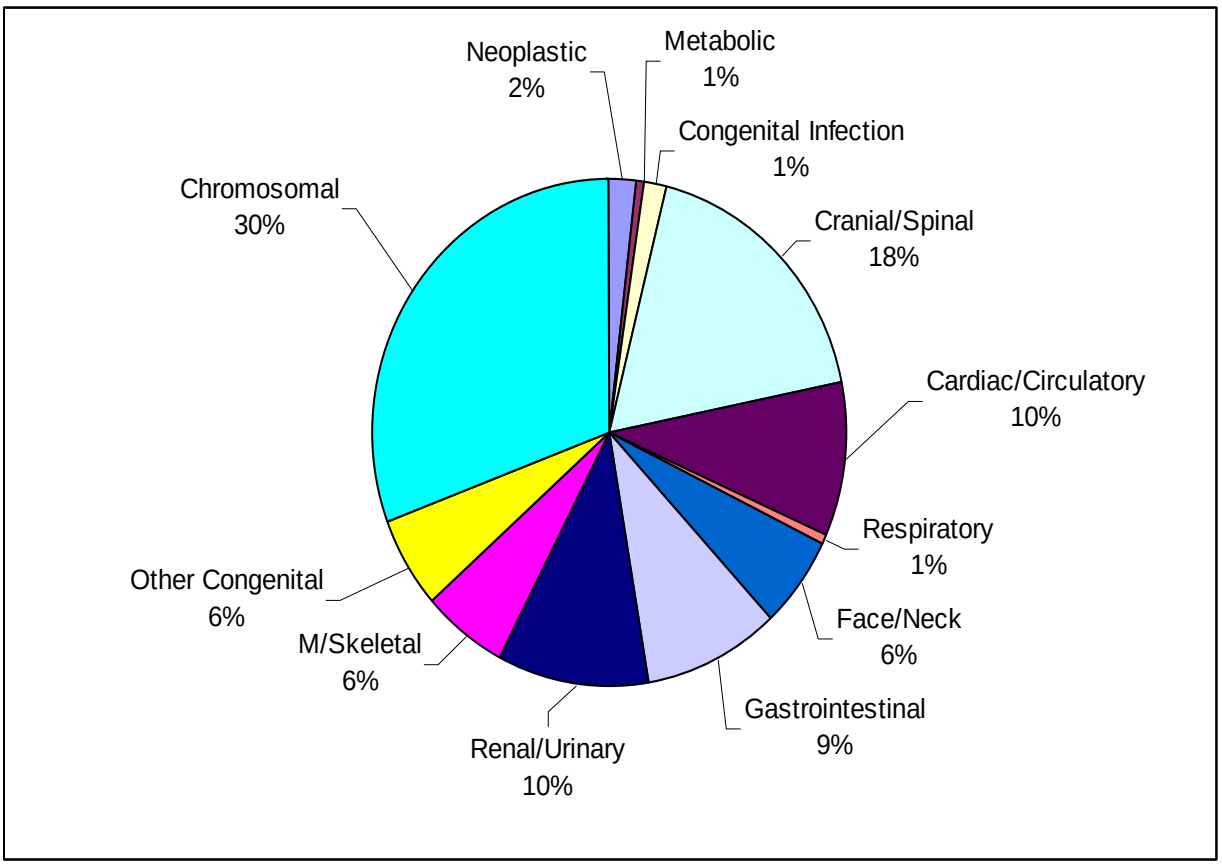
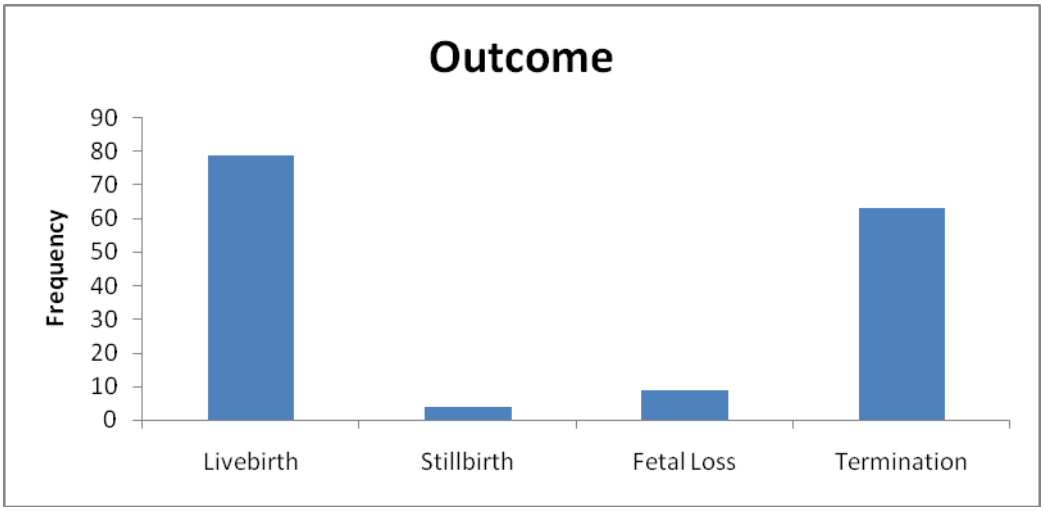


**Figure 2.5: Outcome of pregnancies in which there was prenatal diagnosis of abnormality, (n=155)**




Forty-one percent of pregnancies where a diagnosis of abnormality was made on scan or at amniocentesis/chorionic villus sampling, were terminated, (Figure 2.5). Chromosomal abnormality was the commonest underlying indication for termination of pregnancy.

## 2.6 Unknown

There were 6 cases in which the point of diagnosis is recorded as 'unknown'. All six were live births. The majority, (n=5), were cases of Down syndrome, (Trisomy 21). One of these was also associated with Atrio-ventricular Canal Defect and Double Outlet Left ventricle.

There was also a case of Cystic Fibrosis listed in this category. The diagnosis was likely to have been made in the early neonatal period.

## 2.7 Post-mortem

There were 6 cases where the diagnosis is recorded as being made at post-mortem, (Table 2.1). A further case was misclassified and has already been mentioned above bringing the total to 7 cases. The majority of these cases were fetal losses, (Figure 2.6).

**Table 2.1: Cases diagnosed at post mortem**

| | |
|---|---|
| K0700 | RETROMICROGNATHIA |
| P239 | CONGENITAL PNEUMONIA |
| P351 | CONGENITAL CMV INFECTION |
| Q900 | TRISOMY 21 (ON QF PCR) |
| Q909 | DOWNS SYNDROME |
| Q910 | TRISOMY 18 |
| Q928 | TRISOMY CHROMOSOME 15 |

There were 4 cases of chromosomal abnormality of which one was still born and the other three were fetal losses. There were 2 cases of Trisomy 21 and 1 case of Trisomy 18, (which was associated with multiple abnormalities).

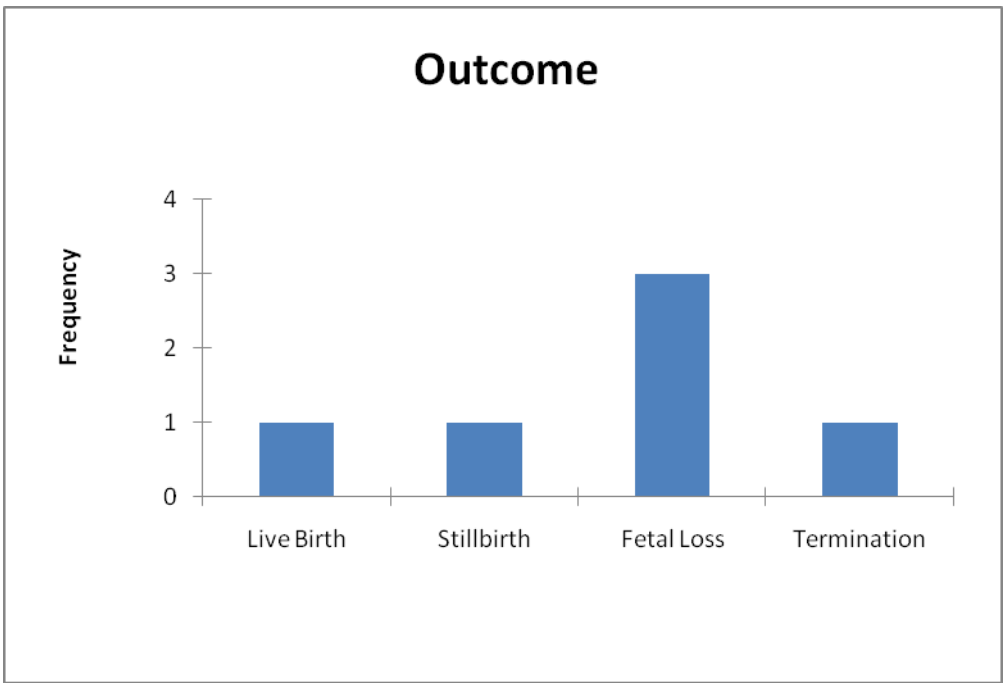
The case of Trisomy Chromosome 15 was misclassified as diagnosis at between 1- 4 weeks. This was actually a fetal loss at 7 weeks gestation, the diagnosis was confirmed on genetic analysis. An earlier

pregnancy to the same mother had been terminated following the antenatal diagnosis of a mosaic Chromosome 15 abnormality (Q998).

Two cases of congenital infection are recorded as being diagnosed at post-mortem. One was a live birth with congenital pneumonia the other a late fetal loss associated with Congenital CMV infection.

The final case was a termination of pregnancy for 'multiple abnormalities'. Post-mortem confirmed retromicrognathia, low-set ears and malrotation of the gut.

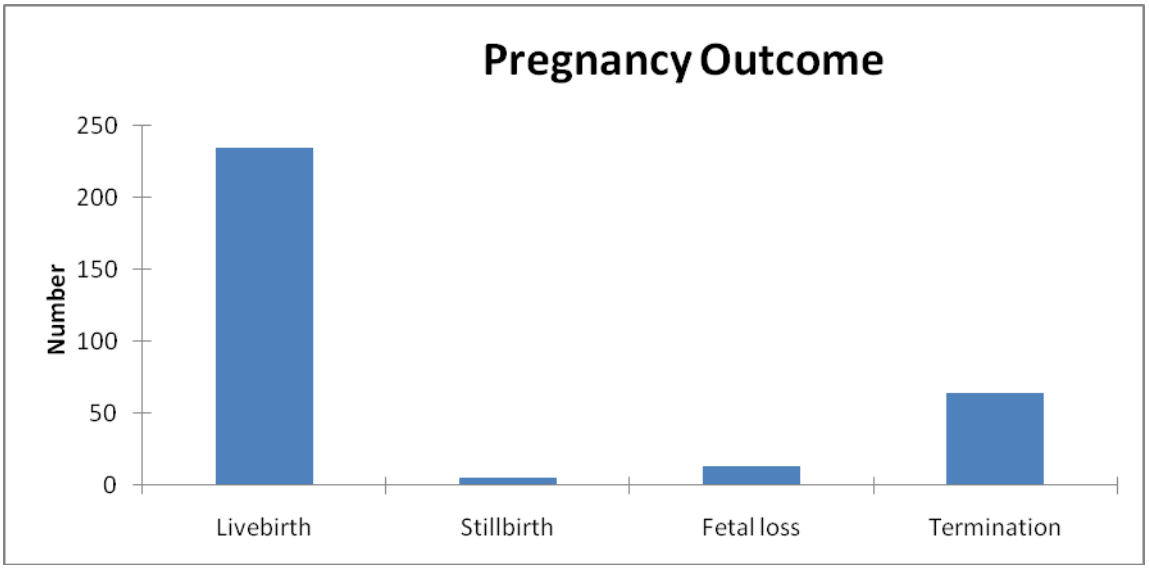
**Figure 2.6: Outcome of pregnancies in which diagnosis of abnormality was made at post-mortem, (n=6)**



# 3. Pregnancy Outcome

A pregnancy outcome is recorded for all 316 cases. The majority of cases were live-born, (Figure 3.1).

**Figure 3.1: Pregnancy Outcome, (n=316).**

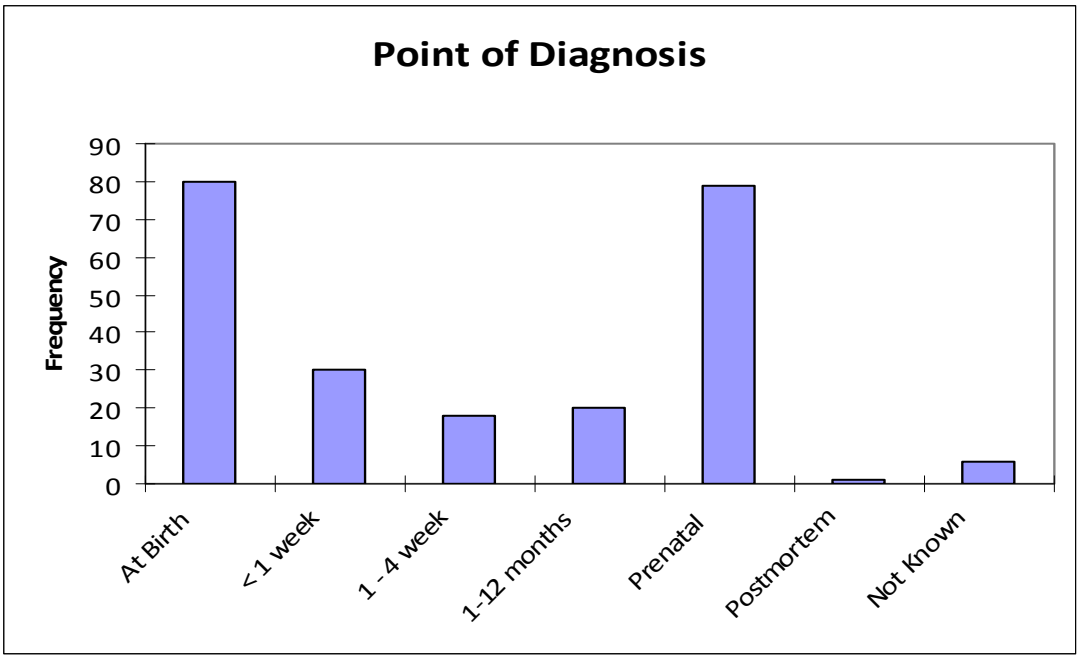



## 3.1 Live Birth

Live birth was the documented outcome for 74% of cases, (n=234).

Diagnosis of abnormality was made at birth for 34% of cases, (n=80), (Figure 3.2). Similarly prenatal diagnosis of abnormality was achieved for a further 34%, (n=79).

**Figure 3.2: Point of Diagnosis of Primary Abnormality for Live-births, (n=234)**



## 3.2 Still-Birth

The data records five stillbirths with a defined abnormality during the study period, (Table 3.1). In four cases the primary abnormality was diagnosed on antenatal ultrasound scan. These were cases of anencephaly, hydrocephalus, diaphragmatic hernia and truncus arteriosus. The remaining case was one of Trisomy 21 where the diagnosis was made at post-mortem.

**Table 3.1: Still-births**

| | | |
|---|---|---|
| Q000 | ANENCEPHALY | |
| Q039 | HYDROCEPHALUS | Lymphangioma |
| Q200 | TRUNCUS ARTERIOSUS | Multiple abnormalities |
| Q790 | DIAPHRAGMATIC HERNIA | |
| Q900 | TRISOMY 21 (ON QF PCR) | |

## 3.3 Spontaneous Fetal Loss

There were thirteen fetal losses, (Figure 3.3). Of these 'Chromosomal Disorders' accounted for 54%, and included Trisomy 21, (n=3), Trisomy 18, (n=3), and Trisomy 15,(n=1),

Congenital Cytomegalovirus infection was seen in two cases of fetal loss, (Table 3.2).

There were 3 cases associated with multiple fetal abnormalities which were very similar but classified variously as 'Absent Left Arm', 'Sirenomelia Sequence' and 'Caudal Regression'. Common features were renal agenesis and absence or reduction deformity of the lower limbs, (Table 3.2).

A case of isolated gastroschisis was also a fetal loss.

**Figure 3.3: Spontaneous Fetal Loss, (n=13)**

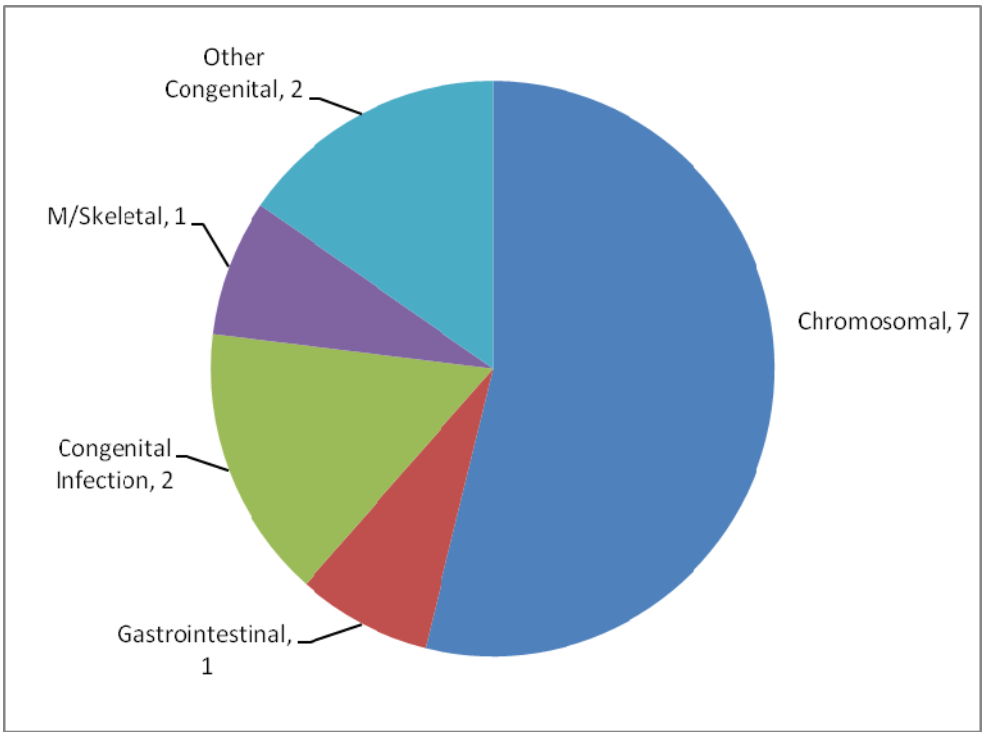


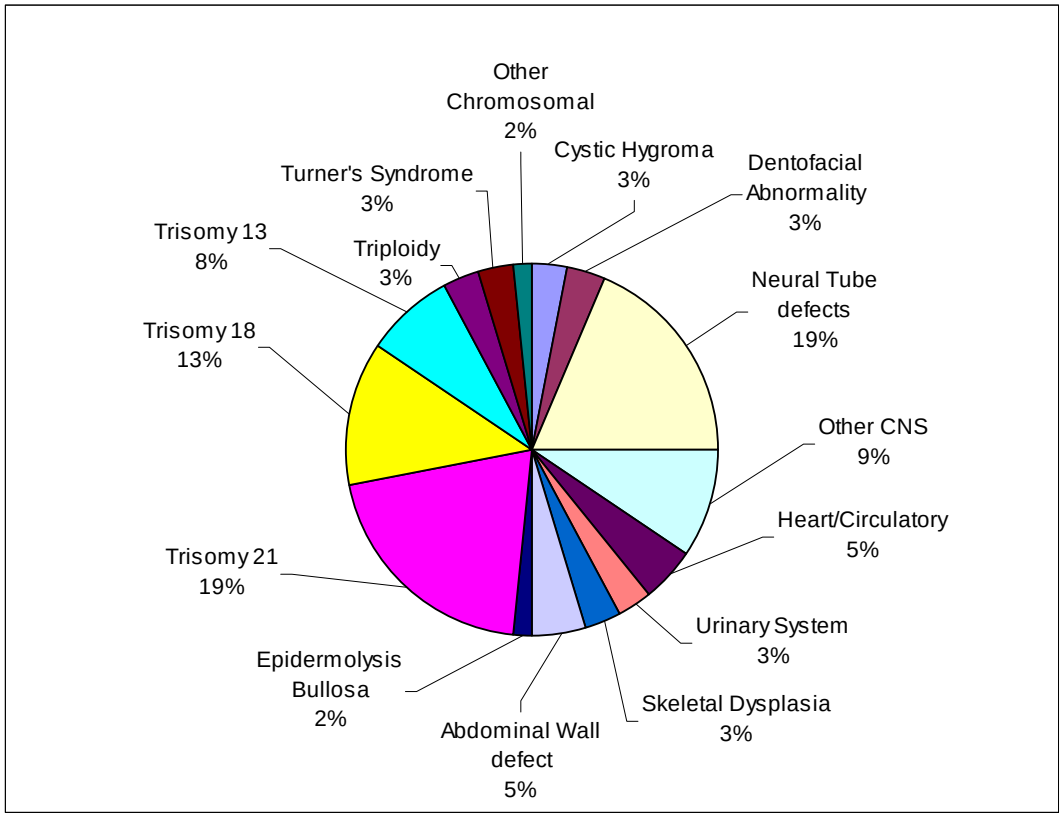
**Table 3.2: Fetal Loss**

| | | |
|---|---|---|
| P351 | CONGENITAL CMV INFECTION | Accessory finger & lymphangioma |
| P351 | CONGENITAL CMV INFECTION | |
| Q710 | ABSENT (L) ARM | Multiple abnormalities |
| Q793 | GASTROSCHISIS | |
| Q8724 | SIRENOMELIA SEQUENCE | Multiple abnormalities |
| Q8980 | CAUDAL REGRESSION | Multiple abnormalities |
| Q900 | TRISOMY 21 | AV Canal Defect |
| Q900 | TRISOMY 21 | VSD |
| Q909 | DOWNS SYNDROME | |
| Q910 | TRISOMY 18 | |
| Q910 | TRISOMY 18 | |
| Q910 | TRISOMY 18 | Lymphangioma |
| Q928 | TRISOMY FOR CHROMOSOME 15 | Holoprosencephaly |

## 3.4 Termination of Pregnancy

A total of 64 pregnancies were terminated following prenatal diagnosis of abnormality. Chromosomal abnormality was the commonest indication, (n=31), followed by Neural Tube Defects & CNS abnormality, (n=18), (Figure 3.3). The numbers of cases in each of the other categories are small. For example, the two cases terminated for abnormality of the urinary system were bilateral cystic dysplastic kidneys and bilateral renal agenesis: the two cases terminated for skeletal dysplasia were Thanatophoric Dysplasia Type 1 and Osteogenesis Imperfecta Type 2.

**Figure 3.4: Indication for termination of pregnancy (ICD10), (n=64)**



# 4. Review by Defined Abnormality

## 4.1 Chromosomal Abnormality

A chromosomal abnormality is recorded for 78 cases, (25%). They account for 14% of all abnormalities detected in the 2011-2012 cohort. The majority, (n=74), are recorded as the primary diagnosis.

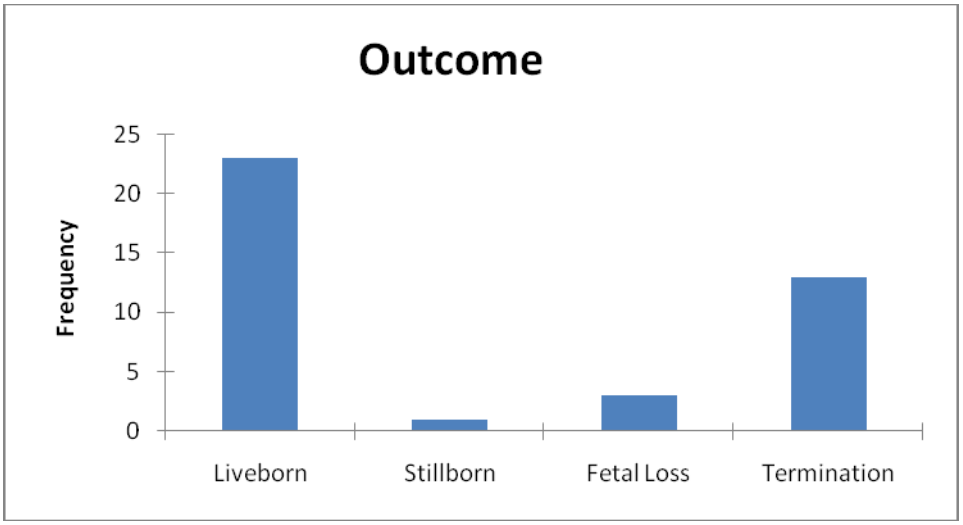
There were four cases where a defined chromosomal abnormality is not recorded as the primary diagnosis. In particular Di George Syndrome (22q11.2 deletion) is classified as a primary blood disorder under ICD10. All four cases were live births.

| | | |
|---|---|---|
| Q540 | GLANDULAR HYPOSPADIAS | Extra marker chromosome (Q926) |
| Q213 | TETRALOGY OF FALLOT | Unspecified chromosomal (Q999) |
| D821 | DI GEORGE SYNDROME | (22q11.2 deletion) |
| D821 | DI GEORGE SYNDROME | (22q11.2 deletion) |

### 4.1.1. Trisomy 21 (Down Syndrome), (Q900, Q909)

A total of 40 cases were associated with Trisomy 21, (incidence of 1:377 maternities).[3] Trisomy 21 was always recorded as a primary abnormality. Fifty-eight percent of cases, (n=23), were live born, (Figure 4.1).

**Figure 4.1: Outcome of pregnancies associated with Trisomy 21, (n=40)**



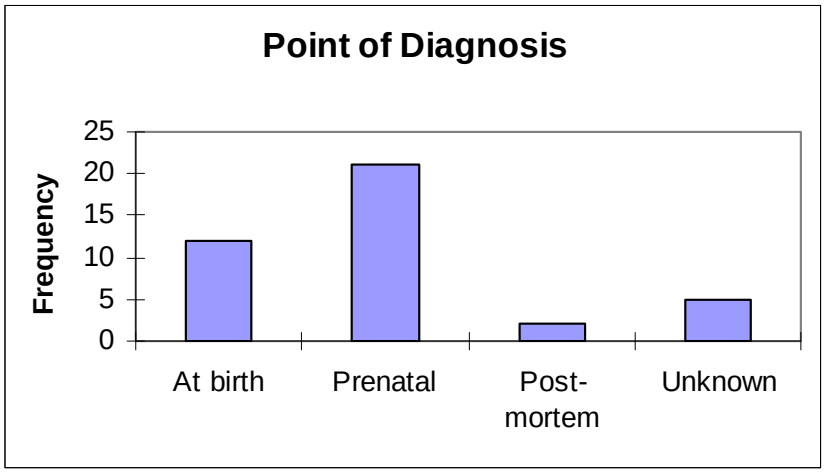

Twenty-one cases, (53%), of Trisomy 21 were diagnosed during the antenatal period, (Figure 4.2). The majority of these cases were terminated, (n=13, 62%).

Cardiac abnormalities are commonly associated with Trisomy 21. There were seven cases associated with Atrio-Ventricular Canal Defect.[4] Other cardiac abnormalities included ASD, VSD, Double outlet Left Ventricle, and Pulmonary Artery Stenosis.

[3] In comparision 17 cases of Trisomy 21 were defined in the 2010-2011 NHS GG&C Review

[4] Atrio-ventricular canal defect isn't actually a single defect, but rather a group or cluster of closely associated defects in various combinations and with varying degrees of severity.

**Figure 4.2: Point of diagnosis of Trisomy 21, (n=40)**




The finding of a Cystic Hygroma, (congenital lymphangioma), may have precipitated prenatal diagnosis in 6 cases. The classic 'double-bubble' of duodenal atresia was noted in one case.

The data does not provide any information on whether or not women were offered antenatal screening for Down Syndrome, if screening was performed but returned as low risk, or if a high risk on screening was not followed up by a diagnostic test. This more detailed information should be available through the GG&C PNBS programme and clearly this is an area for further review.

### 4.1.2. Trisomy 18, (Q910, Q911, Q913)

There were 15 cases of Trisomy 18 (Edward's Syndrome) listed in the data[5].

| | | |
|---|---|---|
| Q910 | TRISOMY 18 | Prenatal diagnosis |
| Q910 | TRISOMY 18 | Prenatal diagnosis |
| Q910 | TRISOMY 18 | Prenatal diagnosis |
| Q910 | TRISOMY 18 | Prenatal diagnosis; VSD; Malrotation gut |
| Q910 | TRISOMY 18 | Prenatal diagnosis; VSD, Double Aortic Arch |
| Q910 | TRISOMY 18 | Prenatal diagnosis |
| Q910 | TRISOMY 18 | Prenatal diagnosis |
| Q910 | TRISOMY 18 | Prenatal diagnosis; AV Canal Defect; Talipes; Cleft Palate |
| Q910 | TRISOMY 18 | Prenatal diagnosis; Malformation of Skull |
| Q910 | TRISOMY 18 | Prenatal diagnosis; Lymphangioma |
| Q910 | TRISOMY 18 | Diagnosed at post-mortem; Holoprosencephaly; Cleft Palate |
| Q910 | TRISOMY 18 | Prenatal diagnosis; Spina bifida; VSD; TGA |
| Q911 | TRISOMY 18 MOSAIC | Diagnosed in 1st week of life; VSD |
| Q913 | TRISOMY 18 | Prenatal diagnosis; VSD; Aortic atresia; Scoliosis |
| Q913 | EDWARDS SYNDROME | Diagnosed at birth |

Cardiac abnormalities are commonly associated with Trisomy 18, (40% in this series).

### 4.1.3. Trisomy 13, (Q914)

There were 5 diagnosed cases of Trisomy 13 (Patau's Syndrome). All were diagnosed antenatally and terminated. Holoprosencephaly was an associated feature in 60% of cases of Trisomy 13.

[5] In comparison 11 cases of Edward's Syndrome were defined in the 2010-2011 NHS GG&C Review

| | | |
|---|---|---|
| Q914 | TRISOMY 13 | |
| Q914 | TRISOMY 13 | Cleft palate |
| Q914 | TRISOMY 13 - ROBERTSONIAN | Holoprosencephaly |
| Q914 | TRISOMY 13 | Holoprosencephaly |
| Q914 | TRISOMY 13 | Holoprosencephaly, Absent nose, Cleft Palate |

### 4.1.4. Turner's Syndrome, (Q960, Q963, Q967)

An aneuploidy also known as 'Monosomy X', (45XO). Fifteen percent of cases demonstrate some mosaicism. Sometime a lymphangioma, (cystic hygroma), prompts investigation. Two cases were terminated following prenatal diagnosis. In only one case is a secondary abnormality declared.

| | | |
|---|---|---|
| Q960 | TURNER'S – 45X | Prenatal diagnosis; Termination |
| Q960 | TURNER'S SYNDROME | Prenatal diagnosis; Termination |
| Q963 | MOSAIC TURNERS SYNDROME | Prenatal diagnosis; Live birth |
| Q969 | TURNER'S SYNDROME | Prenatal diagnosis; Live birth; Coarctation aorta |

### 4.1.5. Other Chromosomal

**Wolff- Hirschorn Syndrome (Deletion 4p16.3), (Q933)**

This is a contiguous gene deletion syndrome that is classically associated with microcephaly, facial clefting, and cardiac septal defects. Two cases were seen, both live births.

| | | |
|---|---|---|
| Q933 | WOLFF-HIRSCHORN | Prenatal Diagnosis; ASD |
| Q933 | WOLFF-HIRSCHORN | Diagnosed at birth; Renal dysplasia; Pulmonary valve stenosis |

**Chromosome 15 Abnormality, (Q928, Q998)**

There were 3 cases where an abnormality of Chromosome 15 has been diagnosed, (although another possible abnormality of Chromosome 15 is described with one case of Di George Syndrome). Two of these relate to two pregnancies in the same mother.

| | | |
|---|---|---|
| Q928 | TRISOMY FOR CHROMOSOME 15 | Fetal Loss |
| Q998 | CHROMOSOME 15 ABNORMALITY (MOSAIC) | Prenatal diagnosis; Termination |

The remaining, (unrelated), case was a live birth associated with malposition of the heart chromosome analysis was to reveal additional material on the short arm of chromosome 15.

| | | |
|---|---|---|
| Q998 | ADDITIONAL MATERIAL CHROMOSOME 15 | Live birth |

**Potocki-Lupski Syndrome (Duplication 17p11.2)**

Well described but rare (1:20,000 births), microduplication syndrome featuring cognitive and language deficits, developmental delay, autistic behaviour, structural cardiovascular anomalies and dysmorphism. The single case described had renal dysplasia but no cardiovascular anomalies.

**Di George Syndrome (22q11.2 deletion), (D821)**

There were two cases of Di George Syndrome described in the data.

| | | |
|---|---|---|
| D821 | DI GEORGE SYNDROME | Live birth; Aortic atresia; VSD |
| D821 | DI GEORGE SYNDROME | Live birth; VSD; Pulmonary valve stenosis; Aortic septal defect; Angelman Syndrome, (Q935). |

This interesting condition is confusing classified under 'Blood Disorders' by ICD10. The underlying problem is a deletion of a small piece of Chromosome 22, (del22q11.2). There is certainly an issue of defective immunity due to aplasia of the thymus however other features include birth defects congenital cardiac abnormality, defects in the palate, learning disabilities, hypothyroidism, hypoparathyroidism and thrombocytopenia. Interestingly microdeletions in the 22q11.2 region are associated with a 20-30 time greater risk of schizophrenia, a commonly occurring late feature of this disorder. Classically cardiac lesions are in the region of the truncus arteriosus e.g. Transpositions and Fallot's Tetralogy. The two cases seen in NHS GG&C both had cardiac defects.

Interestingly one of the cases is also classified as 'Angelman Syndrome', (Q935), although this is a 'bucket' classification of ICD10 for 'Other deletions of part of a chromosome'. Angelman Syndrome is a neurodevelopmental disorder which may arise from a small deletion of the 15q11.13 region. This level of detail is, however, not available from the current data set.

## 4.2 Cranial & Spinal Abnormalities

Sixty-two percent of diagnoses of cranial & spinal abnormality appear in the primary position. Ninety-three percent of all 'Cranial & Spinal' abnormalities are diagnosed prenatally.

### 4.2.1. Neural Tube Defect, (NTD)

A group of malformations of the brain and spinal cord. The clinical spectrum includes anencephaly, encephalocoele, craniorachischsis, hydranencephaly, iniencephaly, spina bifida cystica and spina bifida occulta. In all nineteen cases of NTD the diagnosis was made antenatally.

**Anencephaly, Acrania & Exencephaly, (Q000)**

There were seven cases of anencephaly/exencephaly. They are all listed in the primary position, (there are no cases listed in the secondary position), and were all evident on prenatal scan.

| | | |
|---|---|---|
| Q000 | EXENCEPHALY | Termination; Spina bifida |
| Q000 | ANENCEPHALY | Stillbirth |
| Q000 | ANENCEPHALY | Termination; Scoliosis & Horseshoe kidney |
| Q000 | ANENCEPHALY | Termination; Craniorachisis & exomphalos |
| Q000 | ANENCEPHALY | Termination |
| Q000 | ANENCEPHALY | Termination; Craniorachisis |
| Q000 | ANENCEPHALY | Termination |

**Encephalocoele, (Q010, Q012, Q019)**

All cases of encephalocoele were diagnosed on prenatal scan and listed in the primary diagnostic position.

| | | |
|---|---|---|
| Q010 | ENCEPHALOCELE- LARGE ANTERIOR | Termination |
| Q012 | OCCIPITAL ENCEPHALOCELE | Live birth; VSD |
| Q012 | OCCIPITAL ENCEPHALOCELE | Termination; Renal agenesis & Talipes |
| Q019 | OCCIPITAL MENINGOCELE (SMALL) | Live birth |

**Spina Bifida, (Q0511, Q0521, Q0531, Q055, Q0572, Q0582, Q059)**

There were 6 cases where spina bífida is recorded as the primary abnormality.

| | | |
|---|---|---|
| Q0511 | L/S SPINA BIFIDA – SEVERE | Termination; Arnold-Chiari Malformation |
| Q0531 | SACRAL SPINA BIFIDA (OPEN) | Termination |
| Q0572 | L/S SPINA BIFIDA – CLOSED | Termination |
| Q0572 | MENINGOCOELE – LUMBAR | Live birth |
| Q0582 | SACRAL MENINGOCOELE | Live birth |
| Q059 | SPINA BIFIDA | Termination |

Spina Bifida is also recorded as a secondary diagnosis in two further cases.

| | | |
|---|---|---|
| Q000 | EXENCEPHALY | Termination; |
| Q910 | TRISOMY 18 | Termination; TGA, VSD & Polydactyly |

All diagnoses of spina bífida were made on prenatal ultrasound scan.

### 4.2.2. Holoprosencephaly, (Q042)

Holoprosencephaly was recorded as a secondary abnormality in four cases.

| | | |
|---|---|---|
| Q910 | TRISOMY 18 | Late fetal loss |
| Q914 | TRISOMY 13 | Termination of pregnancy |
| Q914 | TRISOMY 13 | Termination of pregnancy |
| Q914 | TRISOMY 13 – ROBERTSONIAN TRANS | Termination of pregnancy |

### 4.2.3. Microcephaly, (Q02X)

Microcephaly is associated with many causes and usually results in severe mental retardation. Diagnosis does not usually become apparent until the end of the second trimester when there is a reduction in brain growth leading to corresponding decrease in head size. Therefore diagnosis at the time of the routine anomaly scan is unlikely. Causes include CNS malformations, infections (CMV, rubella, and toxoplasmosis), chromosomal abnormalities, maternal PKU and certain teratogens.

There were two cases of microcephaly, both associated with other abnormalities. One case, a live birth associated with congenital cataract, was diagnosed in the first week of life. No cause is given but congenital infection should be suspected. The other case, with single palmar creases and abnormal male genitalia, was terminated following prenatal diagnosis and chromosomal cause suspected.

### 4.2.4. Hydrocephalus, (Q030, Q039)

Eight cases of hydrocephalus are listed. All cases were diagnosed on antenatal ultrasound scan and all but one case were associated with other abnormalities.

| | | |
|---|---|---|
| Q039 | HYDROCEPHALUS-SEVERE | Live birth; Multiple abnormalities |
| Q039 | HYDROCEPHALUS | Stillbirth; Lymphangioma |
| Q039 | HYDROCEPHALUS | Live birth; Cleft palate |
| Q039 | HYDROCEPHALUS | Live birth; Renal agenesis (unilateral) |
| Q039 | HYDROCEPHALUS | Termination; Intestinal atresia |
| Q039 | HYDROCEPHALUS | Termination; Single umbilical artery |
| Q039 | HYDROCEPHALUS – MASSIVE BILAT | Termination; Isolated |

Congenital Hydrocephalus is also listed as a secondary diagnosis in a case of Trisomy 21.

| | | |
|---|---|---|
| Q900 | TRISOMY 21 | Termination; Prenatal diagnosis |

### 4.2.5. Other Cranial & Spinal

Four other ‘Cranial & Spinal’ abnormalities are recorded in the primary diagnostic position.

| | | |
|---|---|---|
| Q031 | DANDY-WALKER MALFORMATION | Prenatal Diagnosis; Termination |
| Q0400 | AGENESIS OF CORPUS CALLOSUM | Prenatal Diagnosis; Termination |
| Q0434 | POLYMICROGYRIA | Diagnosis after 1 month; Live birth |
| Q046 | ARACHNOID CYST | Prenatal Diagnosis; Live birth |

The above case of Agenesis of the Corpus Callosum was associated with other abnormalities including malformation of the skull and porencephalic cysts. There was a further case where Agenesis of the Corpus Callosum is recorded as an associated anomaly with a primary diagnosis of ‘Chonal Atresia – Bilateral Mid-nasal Stenosis’.

## 4.3 Abdominal Wall Defect

ICD10 Codes Q790-Q799 are 'Congenital malformations of the musculoskeletal system, NEC'.

### 4.3.1. Congenital Diaphragmatic Hernia, (Q790)

This is a defect of the hemi-diaphragm, usually on the left side. All cases are associated with an abnormality of gut rotation.

A total of four cases of congenital diaphragmatic hernia are described by the data. The overall incidence of 1:3774 maternities is less than expected, (typically around 1:2200maternities).

| | | |
|---|---|---|
| Q790 | DIAPHRAGMATIC HERNIA (L) | Prenatal diagnosis; Live birth |
| Q790 | DIAPHRAGMATIC HERNIA | Prenatal diagnosis; Live birth |
| Q790 | DIAPHRAGMATIC HERNIA | Prenatal diagnosis; Stillbirth |
| Q710 | ABSENT (L) ARM | Prenatal diagnosis; Multiple anomalies; Fetal loss |

In three cases this was the primary diagnosis. All were diagnosed antenatally on ultrasound scan. There were no associated abnormalities. One case was stillborn the other two were live births.

Congenital diaphragmatic hernia is coded as a secondary abnormality in case diagnosed on antenatal scan with multiple abnormalities including absent left arm, absent lower limbs, renal agenesis, unicornuate uterus and tracheo-oesophageal fistula.

### 4.3.2. Gastroschisis, (Q793)

Six cases of gastroschisis were diagnosed on antenatal scan. There were no associated abnormalities; gastroschisis was an isolated lesion in all cases. Overall incidence for this lesion was 1:2516 maternities. There were four live births, one late fetal loss and one termination of pregnancy following antenatal diagnosis.

### 4.3.3. Exomphalos, (Q792)

Exomphalos is the result of the physiological herniation of the gut into the umbilical cord and the failure of the intestinal loops to return to the fetal abdomen. Typically membrane covered, it is often seen with associated malformations.

Two cases of exomphalos are coded in the data, an incidence of 1:7549 maternities which is lower than maybe expected. Both were diagnosed on antenatal scan. One case was associated with anencephaly, (which was considered the primary diagnosis). Termination of pregnancy was performed following antenatal diagnosis for both cases.

### 4.3.4 Other Abdominal Wall Defect

A further abdominal wall defect is coded as 'unspecified'. There were no secondary abnormalities listed. This ICD10 code specifically excludes Umbilical hernia.

| | | |
|---|---|---|
| Q795 | ANTERIOR ABDOMINAL WALL DEFECT | Prenatal diagnosis; Termination |

Interestingly **NO** cases of Prune Belly Syndrome, (Q794) were recorded in the NHS GG&C data for 2011-2012 although there were two cases in 2010-2011.

## 4.4 Renal & Urinary System

Renal tract abnormalities are seen in about 10% of live born babies. They may be isolated or components of a recognizable syndromes. They are simply divided into malformations of the kidneys (i.e. renal agenesis & renal dysplasia) and abnormalities of the collecting system (i.e. posterior uretheral valves).

### 4.4.1. Hypospadias, (Q540, Q549)

Hypospadias occurs in 1:350 male children. It is the commonest abnormality of male genitalia. The urethra opens on the ventral aspect of the penis at a point proximal to the normal site.

There were seventeen cases where hypospadias was recorded as the primary diagnosis. It is also recorded as a secondary diagnosis in two further cases, (Trisomy 8 and Cleft Palate). The overall incidence of this abnormality is 1:795 maternities - no gender specific data is available from this audit. All were diagnosed at live birth, (including the case of Trisomy 8).

### 4.4.2. Renal Agenesis, (Q600, Q601)

This is the result of the ureteric bud failing 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. Oligohydramnios is usually noted on antenatal scan.

**Bilateral Renal Agenesis, (Q601)**

There were three cases recorded of bilateral renal agenesis; two cases as the primary diagnosis and another in association with Sirenomelia sequence.

| | | |
|---|---|---|
| Q601 | RENAL AGENESIS- BILATERAL | Live birth and early NND |
| Q601 | ABSENT KIDNEYS (ON A/N USS) | Absent bladder; VSD; Malformation tricuspid valve |
| Q8724 | SIRENOMELIA SEQUENCE | Multiple abnormalities incld. renal agenesis |

All cases of bilateral renal agenesis were diagnosed on prenatal ultrasound scan. The Sirenomelia sequence was a spontaneous fetal loss. The case with absent kidneys, absent bladder, and cardiac anomalies was terminated. One case was live born but survived for less than 1hour.

**Unilateral Renal Agenesis, (Q600)**

There were a total of 4 cases of unilateral renal agenesis but only one where this was the primary diagnosis.

| | | |
|---|---|---|
| Q600 | ABSENT KIDNEY (RIGHT) | Prenatal diagnosis; Live birth |
| Q710 | ABSENT (L) ARM[6] | Fetal loss; Multiple abnormalities |
| Q8726 | VACTERL ASSOCIATION[8] | Live birth; |
| Q012 | OCCIPITAL ENCEPHALOCELE | Livebirth; Talipes; Malformation of spine |

[6] This case makes a frequent appearance in this report. However, no formal diagnosis seems to have been made. The abnormalities listed include - absent Left arm, absent lower limbs, absent diaphragm, renal agenesis, single umbilical artery, unicornuate uterus, and TOF. It could easily have been included with the 'VACTERL Association' cases.

### 4.4.3. Dysplastic Kidneys, (Q6140, Q6141)

Dysplastic kidneys contain abnormally differentiated parenchyma. They are commonly associated with obstruction and other abnormalities of the urinary tract. Six diagnoses of Multicystic dysplastic kidney were made on prenatal scan. In all cases this was the sole abnormality detected. One severe bilateral case was terminated following prenatal diagnosis. The remainder were live births.

| | | |
|---|---|---|
| Q6140 | MULTICYSTIC DYSPLASTIC KIDNEY (L) | Prenatal diagnosis; Live birth |
| Q6140 | MULTICYSTIC DYSPLASTIC KIDNEY ® | Prenatal diagnosis; Live birth |
| Q6140 | MULTICYSTIC RENAL DYSPLASIA ® | Prenatal diagnosis; Live birth |
| Q6140 | MULTICYSTIC DYSPLASTIC KIDNEY (L) | Prenatal diagnosis; Live birth |
| Q6140 | MULTICYSTIC DYSPLASTIC KIDNEY ® | Prenatal diagnosis; Live birth |
| Q6141 | CYSTIC RENAL DYSPLASIA - BILAT | Prenatal diagnosis; Termination |

Dysplastic kidneys are recorded as a secondary abnormality in a further four cases.

| | | |
|---|---|---|
| Q039 | HYDROCEPHALUS - SEVERE | Prenatal diagnosis; Live birth |
| Q423 | ANORECTAL ATRESIA | Prenatal diagnosis; Live birth |
| Q928 | POTOCKI-LUPSKI SYNDROME | Live birth; Diagnosed at Birth |
| Q933 | WOLFF-HIRSCHORN SYNDROME | Prenatal diagnosis; Live birth |

### 4.4.4. Congenital Hydronephrosis, (Q620)

Three cases of congenital hydronephrosis.

| | | |
|---|---|---|
| Q620 | CONGENITAL HYDRONEPHROSIS | Prenatal diagnosis; Live birth |
| Q620 | CONGENITAL HYDRONEPHROSIS | Prenatal diagnosis; Live birth |
| Q620 | HYDRONEPHROSIS (L) | Prenatal diagnosis; Live birth |

In a further case congenital hydronephrosis is recorded as a secondary abnormality.

| | | |
|---|---|---|
| Q929 | TRISOMY 8 | Prenatal diagnosis; Live birth |

### 4.4.5. Other Renal & Urinary

A variety of other renal and urinary abnormalities are defined.

| | | |
|---|---|---|
| Q630 | DUPLEX COLLECTING SYSTEM | Live birth; Diagnosed after 1 month |
| Q630 | DUPLEX KIDNEY (L) | Prenatal diagnosis; Live birth |
| Q6300 | DUPLEX KIDNEY ® | Prenatal diagnosis; Live birth |
| Q632 | ECTOPIC (PELVIC) KIDNEY | Prenatal diagnosis; Live birth |
| Q641 | EXTROPHY BLADDER | Diagnosed at birth; Imperforate anus |
| Q642 | POSTERIOR URETHERAL VALVES | Prenatal diagnosis; Live birth |

Abnormalities of accessory and horseshoe kidneys are also recorded as secondary features.

| | | |
|---|---|---|
| Q423 | IMPERFORATE ANUS | Accessory kidney; Double uterus; Persistent cloaca |
| Q000 | ANENCEPHALY | Horseshoe kidney |

Malformation of the male genital organs (unspecified) is seen in association with the following cases.

| | |
|---|---|
| Q02X | MICROCEPHALY |
| Q210 | VSD |

## 4.5. Face & Neck

### 4.5.1. Cleft Lip & Palate, (Q3539, Q359, Q3599 , Q3690, Q3699, Q372, Q374, Q378, Q3799)

Cleft lip and palate are common abnormalities seen in approximately 1:600 births. The majority are isolated lesions but may be part of a chromosomal or other malformation syndrome, (Table 4.1).

**Table 4.1: Abnormalities associated with cleft lip and palate.**

| | |
|---|---|
| Q039 | HYDROCEPHALUS |
| Q549 | HYPOSPADIAS |
| Q750 | CRANIOSYNOSTOSIS |
| Q7581 | MALFORMATION OF SKULL |
| Q870 | PIERRE ROBIN SEQUENCE |
| Q897 | MULTIPLE CONGENITAL ANOMALIES |
| Q914 | TRISOMY 13 |
| Q914 | TRISOMY 13 |
| Q929 | TRISOMY 8 |

A total of 24 cases are recorded with cleft lip, cleft palate or both.

There were four cases of isolated cleft lip. All were live born. The majority, (n=3, 75%) were diagnosed on prenatal scan. The remaining case was diagnosed at birth.

Cleft palate, (with or without cleft lip), was seen in 20 cases. Cleft palate was recorded as a secondary diagnosis in six cases. Sixty percent, (n=12), of cases of cleft palate were diagnosed prenatally. Where prenatal diagnosis was achieved it was usually in association with another anomaly such as cleft lip or a chromosomal syndrome. Of the 7 cases of isolated cleft palate only one was diagnosed on antenatal scan, the rest were diagnosed at birth.

Four terminations of pregnancy were performed following prenatal diagnosis. The presence of a cleft palate was a secondary consideration in each case.

| | | |
|---|---|---|
| Q039 | HYDROCEPHALUS | |
| Q374 | CLEFT LIP & PALATE – VERY SEVERE | Malformation of Skull (Q7581) |
| Q914 | TRISOMY 13 | |
| Q914 | TRISOMY 13 | Holoproscencephaly, VSD, ASD |

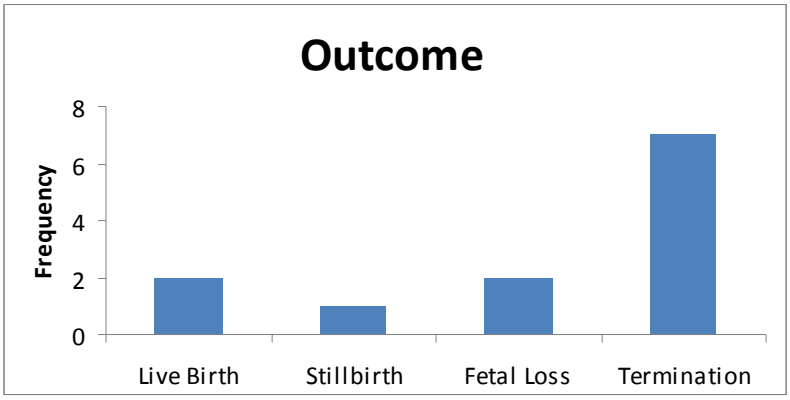
### 4.5.2. Cystic Hygroma, (D1800, D1810).

The presence of a cystic hygroma, (congenital cavernous lymphangioma), is recorded for 12 cases. It was a primary isolated finding in 3 cases and a secondary abnormality in the remaining 9 cases.

Overall cystic hygroma was associated with chromosomal abnormality in 7 cases, (58%). The majority of cases, (n=11), were identified prenatally. One case of isolated cystic hygroma was diagnosed at birth.

Seven cases were terminated following prenatal diagnosis including 2 cases of isolated abnormality. There were 2 live births, one where cystic hygroma was an isolated finding and the other in association with Trisomy 21. The latter case had been diagnosed antenatally and the decision made to continue the pregnancy. There was one stillbirth, (associated with hydrocephalus), and 2 fetal losses, (associated with congenital CMV and Trisomy 18), (Figure 4.3).

**Figure 4.3: Outcome of pregnancies associated with cystic hygroma**




The data only records a congenital lymphangioma it does not record location. The presumption is often made that cystic hygroma is seen at the neck but they may, of course, present at other locations such as the limbs.

### 4.5.3. Pierre-Robin Sequence, (Q870)

Already mentioned above, there was one case recorded of Pierre Robin Sequence, (severe micrognathia with a secondary cleft palate).[7]

| | | |
|---|---|---|
| Q870 | PIERRE ROBIN SEQUENCE | Prenatal diagnosis; Live-birth; Cleft palate |

### 4.5.4. Other Face & Neck

**Goldenhar Syndrome, (Q8704)**

| | | |
|---|---|---|
| Q8704 | GOLDENHAR SYNDROME | Live birth; Diagnosed at Birth |

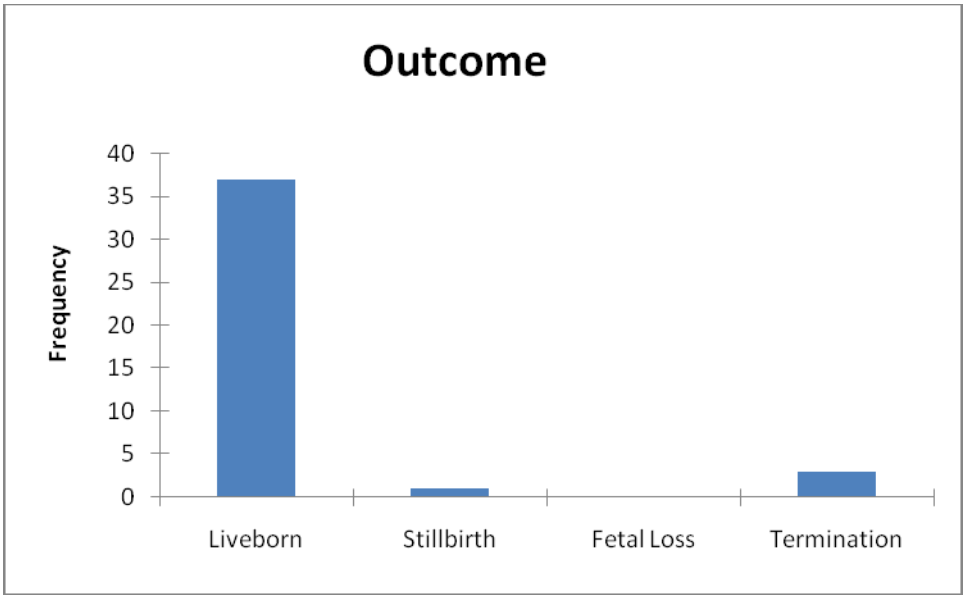
Also known as Oculo-Auriculo-Vertebral Syndrome and presents as incomplete development of the ear, nose, soft palate, lips and mandible. It is believed to be due to anomalous development of the first and second branchial arches late in the first trimester.

[7] In comparison 3 cases of Pierre Robin Sequence were diagnosed in 2010-2011.

## 4.6 Cardiac & Circulatory

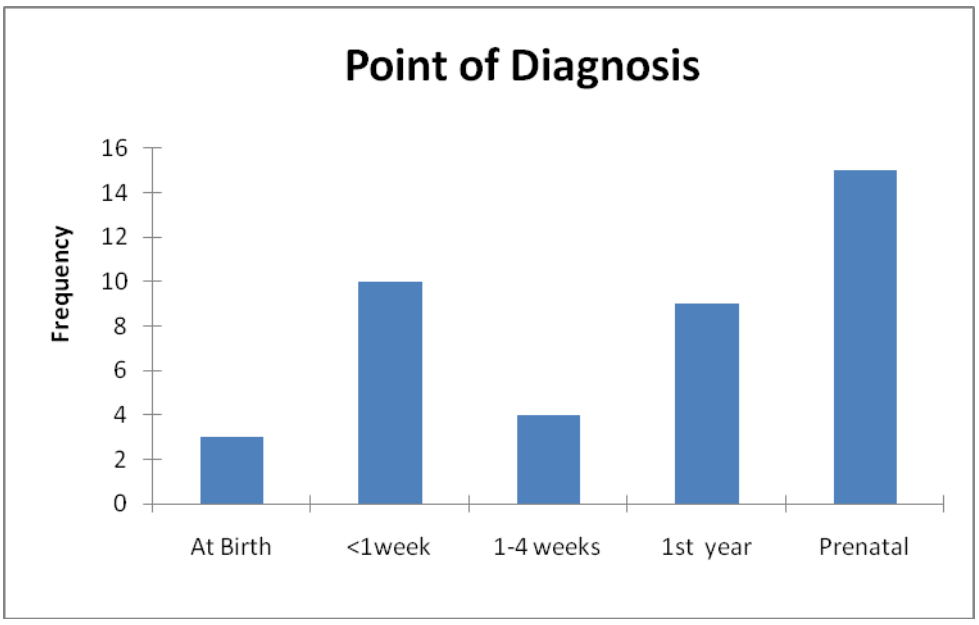
Disorders of the 'Heart & Circulatory System' account for the majority of defined abnormalities, (n=115, 20%), and 35% of these abnormalities are in the primary diagnostic position, (41/115).

**Figure 4.4: Outcome of pregnancy associated with primary cardiac abnormality, (n=41).**




The majority of cases were live born, (Figure 4.4). There were 3 terminations of pregnancy following prenatal diagnosis of significant abnormality, (hypoplastic left heart (2) and uni-ventricular heart). There was one stillbirth associated with uni-ventricular heart, asplenia , pancreatic malformation and truncus arteriosus. The majority of primary cardiac abnormalities were diagnosed in the first 4 weeks of life, (n=17, 41%). However 37%, (n=15), were diagnosed on prenatal scan, (Figure 4.4).

**Figure 4.5: Point of diagnosis of primary cardiac abnormalities, (n-41)**



### 4.6.1. Hypoplastic Left Heart Syndrome, (Q234, Q248)

In these cases the left ventricle is under-developed. The abnormality is frequently associated with hypoplasia or atresia of the mitral valve, aortic valve and arch of the aorta. Typically quoted at an incidence of 0.2/1000 live-births, (0.02%). Hypoplastic left heart accounts for 7-9% of all cases of congenital heart disease diagnosed during the first year of life.

Four cases of hypoplastic left heart syndrome were diagnosed.

| | | |
|---|---|---|
| Q234 | HYPOPLASTIC (L) HEART | Prenatal diagnosis; Live birth |
| Q234 | HYPOPLASTIC (L) HEART | Prenatal diagnosis; Live birth |
| Q234 | HYPOPLASTIC (L) HEART | Prenatal diagnosis; Termination |
| Q248 | SEVERELY HYPOPLASTIC (L) VENTRICLE | Prenatal diagnosis; Termination |

The two cases of univentricular heart should also be mentioned.

| | | |
|---|---|---|
| Q204 | UNIVENTRICULAR HEART | Prenatal diagnosis; Live birth |
| Q204 | UNIVENTRICULAR HEART | Prenatal diagnosis; Termination |

### 4.6.2. Transposition of the Great Vessels, (Q203)

This abnormality results from an abnormal division of the truncus arteriosus. In transposition the septum dividing the truncus has failed to rotate so that the aorta arises from the right ventricle and the pulmonary artery from the left. This leads to two independent circulations and would be incompatible with ex-utero life if it wasn't for the fact that there is nearly always a communication in the form of ASD, VSD or PDA.

There were seven cases, all live born, where Transposition of the Great Vessels is recorded as the primary abnormality. Five were diagnosed on prenatal scan the other two within the first week of life.

| | | |
|---|---|---|
| Q203 | TGA | VSD |
| Q203 | TGA | |
| Q203 | TGA | Coarctation; VSD; Facial malformation (unspecified) |
| Q203 | TGV | |
| Q203 | TGA | Double outlet right ventricle; VSD; Atrial isomerism; Pulmonary stenosis |
| Q203 | TGV | VSD; ASD |
| Q203 | TGA | |

One further case is described where Transposition is classified as a secondary abnormality with a main diagnosis of Trisomy 18.

| | | |
|---|---|---|
| Q910 | TRISOMY 18 | Prenatal diagnosis; Termination; Spina bifida; VSD; Accessory digit |

### 4.6.3. Fallot's Tetralogy, (Q213)

Fallot's Tetralogy is a single error of development with four consequences. The septum dividing the truncus instead of joining up with the inter-ventricular septum deviates to the right. The right ventricular outflow is therefore restricted, (pulmonary stenosis or atresia), the aorta extends to the right of the septum, (over-riding aorta), and receives blood from both ventricles and there is a deficiency in the upper part of the membranous septum, (VSD). The right ventricle hypertrophies to pump blood through both a narrowed pulmonary orifice and the aorta.

One case of Fallot's Tetralogy is listed. This case was a late diagnosis between 1 and 12 months of life.

| | | |
|---|---|---|
| Q213 | FALLOT'S TETRALOGY | Malformation lower limbs; Facial abnormality; Unspecified Chromosomal abnormality |

In comparison there were 2 cases of Fallot's Tetralogy identified in the 2010-2011 review.

### 4.6.4. Coarctation of the Aorta, (Q251)

A total of nine cases of coarctation of the aorta were seen during 2011-2012. In 4 cases coarctation is the primary diagnosis and in a further 5 cases it is listed as a secondary abnormality. All were live births.

| | | |
|---|---|---|
| Q201 | TAUSSIG-BING ANOMALY | Diagnosed 1 -12 months; |
| Q203 | TGA | Prenatal diagnosis; VSD; Malformation of face |
| Q204 | UNIVENTRICULAR HEART | Prenatal diagnosis; VSD; Mitral Stenosis |
| Q251 | COARCTATION AORTA | Diagnosed in 1st week |
| Q251 | COARCTATION AORTA | Diagnosed in 1st week; VSD |
| Q251 | COARCTATION AORTA | Diagnosed 1 – 4 weeks |
| Q251 | COARCTATION AORTA | Prenatal diagnosis; PDA |
| Q4228 | IMPERFORATE ANUS | Diagnosed at birth |
| Q969 | TURNER'S SYNDROME | Prenatal diagnosis; |

## 4.7. Musculo-Skeletal Abnormalities

### 4.7.1. Congenital dislocation of the hip, (Q6580, Q6581)

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.

A total of 8 cases of Congenital Dislocation of the Hip are listed. In five cases CDH is the main diagnosis and in the remaining three is noted as a secondary abnormality.

| | | |
|---|---|---|
| Q402 | GASTRIC DUPLICATION CYST | Live birth; Diagnosed <1week |
| Q6580 | DDH (L) | Live birth; Diagnosed at birth |
| Q6580 | DDH (L) | Live birth; Diagnosed <1week |
| Q6580 | ACETABULAR DYSPLASIA ® | Live birth; Diagnosed 1-12 months |
| Q6580 | DEVELOPMENTAL DYSPLASIA HIP (L) | Live birth; Diagnosed 1-12 months |
| Q6581 | DDH - BILAT | Live birth; Diagnosed at birth |
| Q8726 | VACTERL ASSOCIATION[8] | Prenatal diagnosis; Live birth |
| Q8726 | VACTERL ASSOCIATION[8] | Prenatal diagnosis; Live birth |

### 4.7.2. Achondroplasia, (Q774)

There were 3 cases of Achondroplasia in the 2011-2012 data. All were live born with no associated abnormalities. Prenatal diagnosis was achieved in 2 cases.

### 4.7.3. Thanatophoric Dysplasia Type 1, (Q771)

This is a lethal skeletal dysplasia seen to occur in about 1:60,000 births. Most cases are stillborn or die shortly after birth from respiratory failure. There was a single case observed in 2011-2012. Of the two main subtypes, Type 1 is the most severe with extreme rhizomelia, bowed bones, narrow thorax, and a large (non-Cloverleaf) head with hypertelorism. The pregnancy was terminated following prenatal diagnosis. There were no associated abnormalities.

### 4.7.4. Talipes Equino Varus, (Q660)

Minor degrees of talipes are common at birth, resulting from mechanical pressure in utero. Congenital defects of the spinal cord such as spina bifida are commonly associated with severe talipes. The commonest deviation is one in which there is plantar flexion (equinus) and foot adduction (varus) at the mid-tarsal joint. Incidence stated as 1:1000. In primary diagnostic position recorded on five occasions.

| | | |
|---|---|---|
| Q660 | TEV - BILAT | Isolated; Live birth; Diagnosed at birth |
| Q660 | CTEV (RIGHT) | Isolated; Live birth; Diagnosed at birth |
| Q660 | TEV (RIGHT) | Isolated; Prenatal diagnosis; Live birth |
| Q660 | CTEV (RIGHT) | Isolated; Prenatal diagnosis; Live birth |
| Q660 | CTEV - BILAT | Isolated; Prenatal diagnosis; Live birth |

Talipes is recorded as a secondary diagnosis in the following cases.

[8] VACTERL Association: **V**ertebral/vascular; **A**nal atresia; **C**ardiac; **T**racheo - **E**osphageal fistula; **R**enal/radial; **L**imbs. The severity of the defects may vary considerably from one case to another. The association exists if three or more of these major anomalies is present.

| | | |
|---|---|---|
| Q012 | OCCIPITAL ENCEPHALOCELE | Prenatal diagnosis; Termination |
| Q391 | OESOPHAGEAL ATRESIA | Live birth; Diagnosed at birth |
| Q763 | SCOLIOSIS - T/L | Live birth; Prenatal diagnosis |
| Q8726 | VACTERL ASSOCIATION[8] | Live birth; Prenatal diagnosis |
| Q8726 | VACTERL ASSOCIATION | Live birth; Prenatal diagnosis |
| Q875 | SHORT ARMS & LEGS | Live birth; Prenatal diagnosis |
| Q928 | POTOCKI-LUPSKI | Live birth; Diagnosed at birth |

### 4.7.5. Osteogenesis Imperfecta Type 2, (Q780)

There was a single case of Osteogenesis Imperfecta. Termination of pregnancy followed prenatal diagnosis. There were no associated abnormalities.

### 4.7.6. Other Musculo-Skeletal Abnormalities

Klippel-Feil Syndrome is a congenital fusion of cervical vertebrae that occurs in 1:40,000 births. Associated abnormalities typically include scoliosis, spina bifida, abnormalities of the kidneys and congenital heart malformations. One case was observed associated with malrotation of the gut.

| | | |
|---|---|---|
| Q761 | KLIPPEL-FEIL SYNDROME | Live birth; Malrotation of gut; Diagnosed 1-4 weeks |
| Q7780 | METATROPIC DYSPLASIA | Live birth; Diagnosed at birth |

Metatropic Dysplasia is a severe skeletal dysplasia. It is caused by a mutation in the TRPV4 gene.

## 4.8. Endocrine & Metabolic Disorders

### 4.8.1. In-born Errors of Metabolism

In the majority of cases in-born errors of metabolism are genetically determined. Typically they demonstrate an autosomal recessive inheritance pattern.

**Phenylketonuria, (E700)**

In this disorder, which affects about 1:8,000 live births, deficiency of phenylalanine hydroxylase interferes with the conversion of phenylalanine to tyrosine. Phenylalanine levels in the blood and tissues rise, and abnormal metabolites, (phenylketones), are excreted in the urine. Only one case of PKU was diagnosed during 2011-2012.

| | | |
|---|---|---|
| E700 | PKU | Live birth; Diagnosed < 1 week |

**Medium Chain Acyl Dehydrogenase Deficiency, (MCADD), (E713)**

This is another autosomal recessive disorder. Approximately 1:80 of the population are carriers of the mutation which restricts the ability to breakdown medium-chain fatty acids into acetyl CoA. The Newborn Screening Programme in England detects about 60 cases per year. There are no current figures for Scotland. The incidence of MCADD in this 2011-2012 cohort is 1:7500.

| | | |
|---|---|---|
| E713 | MCADD | Diagnosed < 1 week |
| E713 | DISORDER OF FATTY ACID METAB | Diagnosed 1 - 4 week |

### 4.8.2. Congenital Hypothyroidism, (E0310; E0312; E039)

Congenital hypothyroidism can be the result of a missing or misplaced thyroid gland, hereditary, maternal iodine deficiency and maternal thyroid conditions and medication. Seven cases of congenital hypothyroidism are described.[9] All were live births.

| | | |
|---|---|---|
| E0310 | CONGENITAL HYPOTHYROIDISM | Diagnosed 1 - 4 weeks; No normal thyroid tissue |
| E0312 | CONGENITAL HYPOTHYROIDISM | Diagnosed < 1 week; Ectopic thyroid |
| E0312 | CONGENITAL HYPOTHYROIDISM | Diagnosed < 1 week; Ectopic thyroid tissue |
| E0312 | CONGENITAL HYPOTHYROIDISM | Diagnosed < 1 week; Sublingual/ectopic thyroid |
| E0312 | CONGENITAL HYPOTHYROIDISM | Diagnosed 1 - 4 weeks; Subhyoid Ectopia |
| E0312 | CONGENITAL HYPOTHYROIDISM | Diagnosed 1 - 4 weeks; Ectopic thyroid |
| E039 | CONGENITAL HYPOTHYROIDISM | Diagnosed < 1 week |

### 4.8.3. Cystic Fibrosis, (E840; E841; E849)

Approximately 1:2,500 babies born in the UK have cystic fibrosis. There were eight cases of cystic fibrosis diagnosed in 2011-2012 giving an NHS GG&C incidence of 1:1887 maternities. All were live births. There were no associated abnormalities.

[9] In comparison only 2 cases of Congenital Hypothyroidism were diagnosed in 2010-2011.

| | | |
|---|---|---|
| E840 | CYSTIC FIBROSIS | Diagnosed < 1 week |
| E840 | CYSTIC FIBROSIS | Diagnosed < 1 week |
| E840 | CYSTIC FIBROSIS | Diagnosed 1 - 4 weeks |
| E840 | CYSTIC FIBROSIS | Diagnosed 1 - 4 weeks |
| E840 | CYSTIC FIBROSIS | Diagnosed 1 - 4 weeks |
| E840 | CYSTIC FIBROSIS | Point of diagnosis unknown |
| E841 | CYSTIC FIBROSIS | Prenatal diagnosis |
| E849 | CYSTIC FIBROSIS | Diagnosed 1 - 4 weeks |

### 4.8.4. Other Metabolic

**Zellweger, Alport or Similar, (Q878)**

| | | |
|---|---|---|
| Q878 | UNDIAGNOSED DYSMORPHIC HYPOTONIC GENETIC SYNDROME | Live birth |

No formal diagnosis seems to have been made for this case. The ICD10 code of Q878 basically means 'Other specified congenital malformation syndrome(s), not elsewhere classified'. There are no structural abnormalities listed in association with this case.

## 4.9. Gastrointestinal Abnormalities

Abnormalities of the abdominal wall such as gastroschisis, exomphalos and congenital diaphragmatic hernia have already been considered, (above). Although most textbooks would consider them as Gastrointestinal Tract Malformations ICD10 codes them as Musculoskeletal Abnormalities.

### 4.9.1. Oesophageal Atresia, (Q391)

Oesophageal atresia affects 1:3000 pregnancies and tracheo-oesophageal fistula (TOF) co-exists in over 90%. A total of 5 cases are described in the data giving an NHS GG&C incidence of 1:3000.

Oesophageal atresia with TOF was the primary diagnosis in 3 cases. All were live births and the abnormality was diagnosed at birth.

| | | |
|---|---|---|
| Q391 | OESOPHAGEAL ATRESIA + TOF | |
| Q391 | OESOPHAGEAL ATRESIA + TOF | Meckel's Diverticulum |
| Q391 | OESOPHAGEAL ATRESIA + TOF | Talipes |

Oesophageal atresia with TOF was a secondary diagnosis in two further cases confirming previously established associations with Cranial/Spinal abnormalities and the VATER/VACTERL Association.

| | | |
|---|---|---|
| Q8726 | VACTERL ASSOCIATION | Prenatal diagnosis; Live birth |
| Q039 | HYDROCEPHALUS – SEVERE | Prenatal diagnosis; Live birth |

### 4.9.2. Imperforate Anus/Anal Stenosis/Anorectal Atresia, (Q4228, Q423)

Anorectal atresia affects approximately 1:5000 pregnancies. It is the primary diagnosis in 5 cases.

| | |
|---|---|
| Q4228 | IMPERFORATE ANUS WITH RECOVAGINAL FISTULA |
| Q4228 | IMPERFORATE ANUS WITH PERINEAL FISTULA |
| Q423 | ANAL STENOSIS |
| Q423 | ANORECTAL ATRESIA |
| Q423 | IMPERFORATE ANUS |

Anorectal atresia is also described in association with a number of other abnormalities e.g. as a component of VACTERL association. It is recorded as a secondary diagnosis in 7 further cases.

| | |
|---|---|
| Q039 | HYDROCEPHALUS - SEVERE |
| Q321 | MALFORMATION TRACHEA |
| Q641 | EXTROPHY BLADDER |
| Q8724 | SIRENOMELIA SEQUENCE |
| Q8726 | VACTERL ASSOCIATION |
| Q897 | MULTIPLE CONGENITAL ANOMALIES |
| Q8980 | CAUDAL REGRESSION |

The overall incidence of anorectal atresia in the NHS GG&C 2011-2012 cohort is 1:1258, much higher than might be typically expected. There was also a case classified of 'Ano-rectal Malformation – Tight Anus', (Q438)

### 4.9.3. Malrotation of Bowel, (Q433)

In ICD10 this is technically 'Congenital Malformations of Intestinal fixation' and includes a variety of conditions of small and large bowel. There were four cases where this is the primary diagnosis. All

were live births. With no associated abnormalities. The diagnosis of gastrointestinal abnormality was made within the first week of life.

| | | |
|---|---|---|
| Q433 | MALROTATION DUODENUM | Live birth |
| Q433 | MALROTATION DUODENUM | Live birth |
| Q433 | MALROTATION DUODENUM | Live birth |
| Q433 | MALROTATION BOWEL | Live birth |

There were 6 further cases where a 'Congenital malformation of intestinal fixation' is recorded as a secondary diagnosis.

| | | |
|---|---|---|
| K0700 | RETROMICROGNATHIA | Termination |
| Q761 | KLIPPEL-FEIL SYNDROME | Live birth |
| Q792 | EXOMPHALOS | Termination |
| Q8704 | GOLDENHAR SYNDROME | Live birth |
| Q893 | ABDOMINAL SITUS INVERSUS | Prenatal diagnosis; Live birth |
| Q910 | TRISOMY 18 | Termination |

### 4.9.4. Other Gastrointestinal Abnormalities

**Congenital Bilary Atresia, (Q442)**

| | | |
|---|---|---|
| Q442 | ATRESIA BILE DUCTS | Live birth; Diagnosed in first month |
| Q442 | BILARY ATRESIA (TYPE 3) | Live birth; Diagnosed after first month |

**Hirschsprung's Disease, (Q431)**

A single case is listed as a primary diagnosis with no associated abnormalities. This was a diagnosis made within the first week of neonatal life. There was a further case associated with Ebstein's Anomaly, (Q225).

**Small Bowel Atresias, (Q419)**

Three cases, one as a primary diagnosis and two as secondary abnormalities.

| | | |
|---|---|---|
| Q039 | HYDROCEPHALUS | Prenatal diagnosis; Live birth |
| Q419 | BOWEL ATRESIAS – MULTIPLE | Prenatal diagnosis; Live birth |
| Q900 | TRISOMY 21 | Duodenal atresia; Prenatal diagnosis; Live birth |

**Gastric Duplication Cyst, (Q402)**

| | | |
|---|---|---|
| Q402 | GASTRIC DUPLICATION CYST | Live birth; Diagnosed in first week |

## 4.10. Congenital Neoplastic Disorders

Excluding the cases of congenital lymphangioma (cystic hygroma)

| | | |
|---|---|---|
| C220 | HEPATOBLASTOMA (L) LOBE LIVER | Live birth; Diagnosed at birth |
| C719 | ANAPLASTIC EPENDYMOMA (GRADE 3) | Live birth; Diagnosed after 1 month |
| D180 | HAEMANGIOMA-SACRAL | Live birth; Diagnosed at birth |
| D125 | SACROCOCCYGEAL TERATOMA | Live birth; Diagnosed after 1 week |
| D487 | CARDIAC TUMOUR - FIBROMA | Prenatal diagnosis; Live birth |

An Ependymoma is a tumour that arises from the ependyma, a tissue of the Central Nervous System. The tumour is typically located in the 4$^{th}$ Ventricle. No location is given for this case.

Sacrococcygeal Teratoma (SCT) is seen in 1:35,000 live births. Prenatal diagnosis is increasingly common but this case was not diagnosed until after 1 week of life. A small SCT, if it is entirely inside the body, may not present for years.

# Appendix 1

## Table 1: Incidence: Comparison with 'established' data

| Abnormality | Incidence Primary Position | Incidence Any Position | Quoted |
|---|---|---|---|
| PKU (E700) | 0.007% | 0.007% | 0.007% |
| Cystic Fibrosis | 0.05% | 0.05% | 0.04% |
| Cleft Lip/Palate | 0.119% | 0.159% | 0.125% |
| NTD | 0.11% | 0.126% | 0.3% |
| Hypoplastic Left Heart (Q234) | 0.04% | 0.04% | 0.026% |
| Fallot's Tetralogy | 0.007% | 0.007% | 0.045% |
| Congenital Diaphragmatic Hernia (Q790) | 0.019% | 0.026% | 0.045% |
| Thanatophoric Dysplasia | 0.007% | 0.007% | 0.05% |
| Congenital Dislocation Hip (Q658) | 0.03% | 0.05% | 0.07% |
| Hypospadias (Q549) | 0.113% | 0.126% | 0.27% |

## Table 2: Prenatal Detection Rates: Comparison with 'established' data

| Abnormality | Observed Prenatal Detection Rate | Expected Detection Rate* |
|---|---|---|
| Anencephaly | 100% | 98% |
| Open Spina Bifida | 100% | 90% |
| Diaphragmatic Hernia (Q790) | 100% | 60% |
| Cleft Lip ◊ | 83% | 75% |
| Gastroschisis | 100% | 98% |
| Exomphalos | 100% | 80% |
| **Serious Cardiac Abnormalities** | | 50% |
| Hypoplastic Left Heart (Q234, Q248) | 100% | |
| Univentricular Heart (Q204) | 100% | |
| Transposition of Great Vessels (Q203) | 60% | |
| Fallot's Tetralogy (Q213) | 0% | |
| Bilateral Renal Agenesis | 100% | 84% |
| **Lethal Skeletal Dysplasia** | | 60% |
| Thanatophoric Dysplasia | 100% | |
| Trisomy 21 | 53% | 95% |
| Trisomy 18 | 80% | 95% |
| Trisomy 13 | 100% | 95% |

◊ Figures vary depending on whether or not looking at cleft lip alone, in combination with palate defect, or as part of a complex or syndrome. Figure given is for any cleft lip, (primary or secondary abnormality, isolated or in association with cleft palate).

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