Public Health England

Protecting and improving the nation's health

National Congenital Anomaly and Rare Disease Registration Service

Congenital anomaly statistics 2017

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SUSTAINABLE
DEVELOPMENT GOALS

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Executive summary

This is the third National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) report on congenital anomaly data. Public Health England launched NCARDRS on 1 April 2015. Prior to this, registries existed in only some regions of England. In response to the UK Rare Disease Strategy and the Chief Medical Officer's recommendation to ensure national coverage, 3 new regions covering the East of England, London and the South East, and the North West were established. Data collection in the newly established regions started from 1 April 2017.

The first report, using data from 2015, reported on 21% of births in England. In both the 2016 report and this 2017 report, data from 7 NCARDRS reporting regions, representing 49% coverage of births, is presented.

NCARDRS currently collects data on 1,008 different congenital anomalies and rare diseases. In 2017, there were a total of 6,798 babies with 1 or more congenital anomalies notified to the 7 NCARDRS reporting regions, covering 320,013 total births (live births and stillbirths). This gives an overall birth prevalence for these regions of 212.4 per 10,000 total births – or 1 for every 47 births.

Some congenital anomalies are detectable during pregnancy and others are not. In 2017, the timing of first diagnosis was known for 6,211 (91.4%) babies and of these, 62.4% were diagnosed antenatally. Where a congenital anomaly was detected antenatally 51.1% of these resulted in a live birth. Where a baby was diagnosed with a congenital anomaly postnatally, 95.7% of these were diagnosed following a live birth.

Of the 6,798 babies with a congenital anomaly reported to NCARDRS, 310 resulted in an infant death, giving an infant mortality rate of 9.7 (95% CI 8.7 - 10.9) per 10,000 live births. Congenital heart anomalies were most frequently associated with 35.2% of reported infant deaths, followed by chromosomal anomalies (23.9%) and digestive system anomalies (15.8%).

Data recorded in 2017 shows that the prevalence of chromosomal congenital anomalies increased with maternal age; the prevalence of these anomalies was around 7 times higher in older mothers (women aged 40+ years) compared with younger mothers (women aged less than 20 years).

This report demonstrates further progress toward achieving national data collection, the data on Down's syndrome, Edwards' syndrome and Patau's syndrome is presented for England for 2015-2017. The prevalence per 10,000 total births for Down's syndrome was 28.3 (95% CI: 27.6-29.1), or 1 for 353 total births, 8.4 (95% CI: 8.0-8.8), or 1 for 1,190 for Edwards' syndrome and 3.5 (95% CI: 3.2-3.7), or 1 for 2,857 total births for

Patau's syndrome respectively. NCARDRS looks forward to presenting, for the first time in England, national coverage of further congenital anomalies and will be able to report on this data in our 2018 report, due out in 2020.

Chapter 1: Introduction

This report is the National Congenital Anomaly and Rare Disease Registration Service's (NCARDRS) third report on congenital anomalies. It describes the number of babies with 1 or more congenital anomalies delivered between 1 January and 31 December 2017. Readers who are interested in congenital anomalies prior to 2017 are directed to our previous reports on data from 2015 and 2016 which cite relevant sources of information for historical data collected before the inception of NCARDRS.

Public Health England (PHE) launched NCARDRS on 1 April 2015. Prior to this, registries existed in some regions of England, and they reported data for the benefit of clinicians, epidemiologists, researchers and patients. In response to the UK Rare Disease Strategy and the Chief Medical Officer's recommendation to ensure national coverage, 3 new reporting regions covering the East of England, London and the South East, and the North West were established. Data collection in new regions started from 1 April 2017. This means, for the first time, national coverage of congenital anomaly reporting on 2018 births will be possible next year. Information about the current level of coverage presented in this report is explained below.

This report is intended primarily as a useful resource for commissioners and providers of healthcare needed for the diagnosis and management of babies with congenital anomalies. It also provides high quality data for the use of researchers and those seeking detailed information about congenital anomaly prevalence in England. It is hoped that this annual public report will be of interest to healthcare professionals involved in the direct care of patients.

The ambition to provide a comprehensive national register relies on the commitment of healthcare professionals across the country to report babies diagnosed or suspected with congenital anomalies to NCARDRS. The multi source approach to data collection in NCARDRS is dependent on the dedication of healthcare staff in a range of settings including maternity units, neonatal units, diagnostic departments, genetic laboratories and many more. This collaborative approach enables high ascertainment and completeness of data and ensures consistency and standardisation across the country.
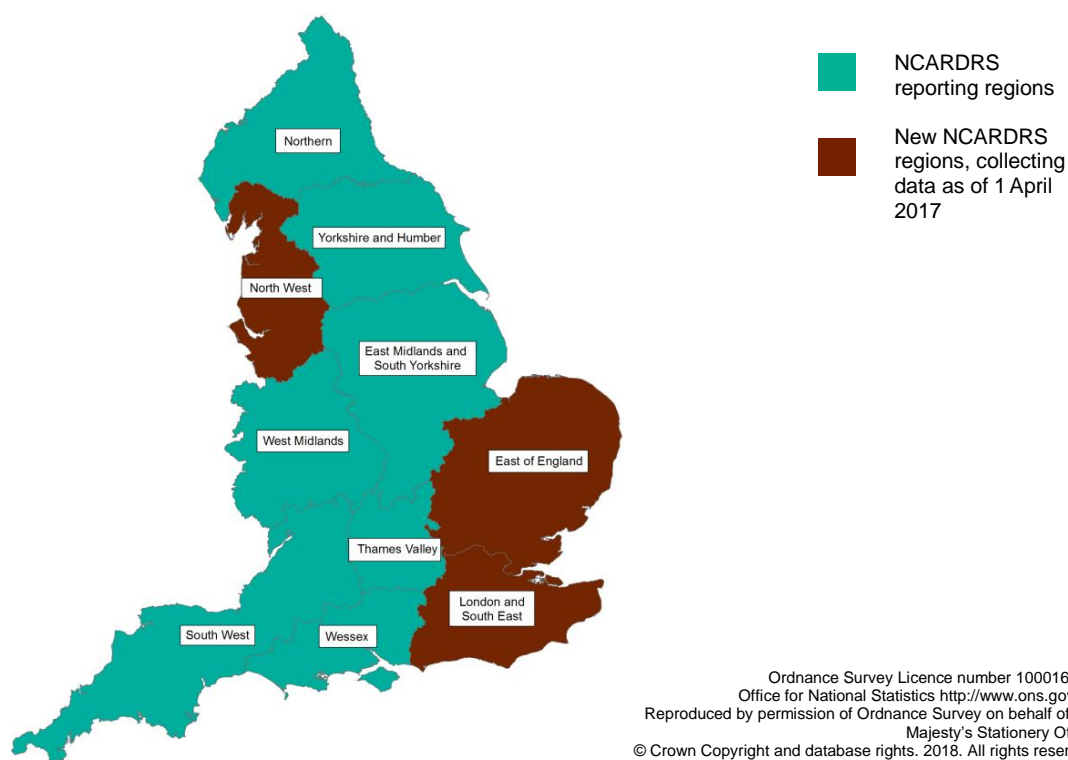
Thanks to the dedication of these notifying healthcare professionals, this important and reliable information is available for clinicians, researchers, patients and their families. More information about the data collection process can be found in the accompanying technical details document.

1.1 NCARDRS reporting regions in 2017

NCARDRS is made up of 10 reporting regions and the information presented in this document reports on data for 7 of those regions (Figure 1). The accompanying technical details document provides more information about geographical coverage of NCARDRS regions.

In 2015, 21% coverage of births was reported; the addition of 3 more regions for 2016 and this report for 2017 takes coverage to 49% of births.

Figure 1: Map of NCARDRS reporting regions England, 2017

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1.2 Data in this report

Congenital anomalies are defined as being present at delivery, probably originating before birth, and include structural, chromosomal, genetic and biochemical anomalies. Data are collected according to definitions and guidelines of the European Surveillance of Congenital Anomalies (EUROCAT) and the World Health Organization (WHO) Collaborating Centre for the Surveillance of Congenital Anomalies. Congenital anomalies are coded using the International Classification of Disease version 10 (ICD-10) with British Paediatric Association (BPA) extension, which gives supplementary 1 digit extensions to ICD-10 codes to allow greater specificity of coding. For more

information about data collection, definitions and coding see the technical document which accompanies this report.

In this report, comparisons were intentionally not made between previous years' data. This is because:

- as a minimum, 3 years' worth of comparable data are required to consider trend analysis
- data are not directly comparable as regional coverage and ascertainment is increasing annually
- comparing year on year data could lead to unreliable conclusions based on small numbers

This 2017 report is organised in 4 further chapters covering information about:

- prevalence of congenital anomalies (chapter 2)
- timing of diagnosis and outcome (chapter 3)
- key public health indicators (chapter 4)
- data on Down's syndrome, Edwards' syndrome and Patau's syndrome (chapter 5)

Information about the prevalence of congenital anomalies in chapter 2 outlines the types of anomaly most frequently reported to NCARDRS.

Chapter 3 describes the timing of diagnosis and the outcome of pregnancy. This relays important information about the number of babies born with congenital anomalies, some of whom will need ongoing health and social care service provision.

Currently available public health information is the focus of chapter 4. This includes estimates about the contribution made by congenital anomalies to perinatal and infant mortality rates, as well as information about how prevalence varies by maternal age.

Chapter 5 provides information on babies delivered between 2015 and 2017, diagnosed with Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13). This information is available for the whole of England.

A separate summary document, highlighting key messages about the prevalence of congenital anomalies, accompanies this report. A technical detail document and detailed data tables also accompany this report. A glossary for key terms is included within the report and these key terms are highlighted and hyperlinked in the text.

Chapter 2: Prevalence of congenital anomalies

Total birth prevalence was 212.4 per 10,000 births, reflecting 1 baby diagnosed with a congenital anomaly for every 47 births in 2017.

Regional variation in prevalence likely reflects differences in ascertainment. Severe congenital anomalies are well-ascertained.

The majority of babies (71.6%) in 2017 resulted in a live birth. 1 for every 66 live births had a congenital anomaly.

In 2017, there were a total of 6,798 babies with 1 or more congenital anomalies notified to the 7 NCARDRS reporting regions covering 320,013 total births (live births and stillbirths). This gives an overall birth prevalence for these regions of 212.4 per 10,000 total births (95% CI: 207.4-217.5). This reflects 1 for every 47 births (live births and stillbirths) (Table 1).

There was some variation in the birth prevalence (the number of babies diagnosed with at least 1 congenital anomaly per 10,000 births) by each reporting region (Figure 2, Table 2). The Northern region had significantly higher birth prevalence compared to the combined NCARDRS prevalence. Since the 2016 report, case ascertainment in the Yorkshire and Humber region has increased and it is now consistent with other reporting regions.

Possible reasons for geographical variations in congenital anomaly prevalence could include disease clustering, exposure to teratogens, demographic variation including age and deprivation profiles between regions and also the genetic composition of the local population. However, given the infancy of the service it is likely that much of the variation in prevalence between regions remains a result of different ascertainment sources. As NCARDRS moves to national coverage and the collection of longitudinal data, greater insights will be gained into underlying population characteristics contributing to regional variation, as well as the ability to analyse associations with environmental factors which may potentially be modifiable.

Figure 2: The number of congenital anomalies per 10,000 total births (prevalence) and 95% confidence intervals for NCARDRS reporting regions compared to regions combined, 2017
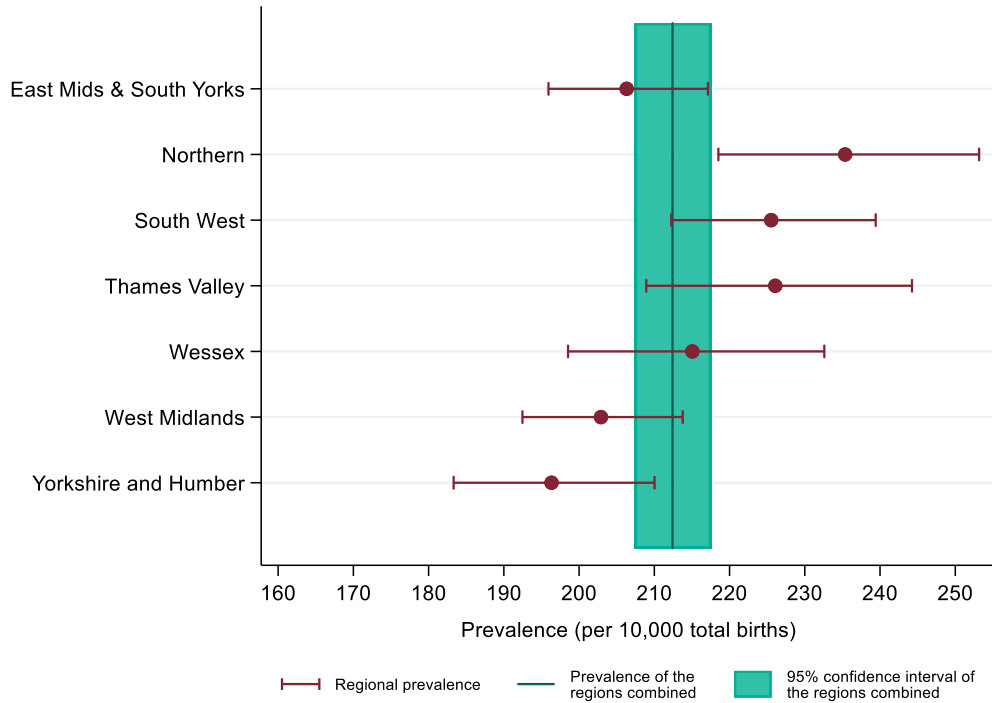

Figure 3 shows that of the 6,798 babies with 1 or more congenital anomalies, the majority (4,867, 71.6%) resulted in a live birth. Of the remaining 1,931 babies, 158 (2.3%) were stillbirths (24+ weeks' gestation), 59 (0.9%) were late miscarriages (20-23 weeks' gestation) and 1,714 (25.2%) were terminations of pregnancy. This includes terminations of pregnancy with fetal anomaly (TOPFA) as well as terminations of pregnancy for other reasons where a fetal anomaly was present. The outcome of pregnancy varies according to a range of factors including the severity of the anomaly, co-morbidities, accuracy of screening and choices around termination. The data presented relate to both antenatal and postnatal diagnoses. The timing of diagnosis is explored in more detail in chapter 3.

Figure 3: Percentage of babies with 1 or more reported congenital anomalies by outcome of pregnancy in 7 NCARDRS reporting regions, 2017
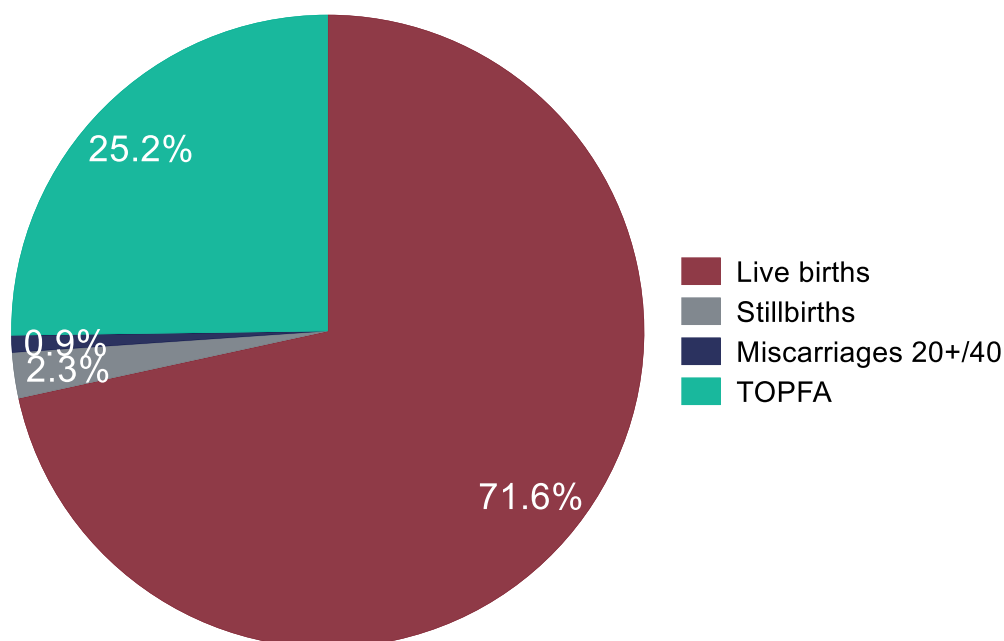
In the 2017 reporting year, congenital anomaly birth prevalence in England was statistically significantly lower than the pan-European overall rate reported by EUROCAT for European registries; 212.4 (95% CI 207.4-217.5) in England compared to 241.3 (95% CI 237.0-245.6) in Europe (Table 2). The breakdown by congenital anomaly subgroup shows that, as in 2016, prevalence in England was statistically significantly lower compared to European registries in 4 of these groups: congenital heart anomalies, urinary, genital and limb.

However, the data within these subgroups show that the pattern was reversed for more severe anomalies (Table 2). The prevalence of chromosomal, abdominal wall anomalies and severe congenital heart anomalies was significantly higher in the NCARDRS data compared to EUROCAT. This likely improvement in data quality is a result of NCARDRS work with the NHS Fetal Anomaly Screening Programme (FASP) and the establishment of data feeds from all the cytogenetics laboratories in England. This is a significant achievement in the progression of the service in the last year.

It is likely that the lower prevalence of congenital anomalies in England compared to European registries is a result of lower ascertainment in England of less severe anomalies. Less severe anomalies are often not detectable at screening, not obvious at birth or do not require surgery or treatment shortly after birth. This means that these anomalies are less likely to be recorded and notified to NCARDRS. NCARDRS continues to work with clinicians and with central data sources (such as HES and ONS) to improve notification of less severe anomalies.

Figures 4a and 4b show the prevalence of the 12 major congenital anomaly subgroups for (a) all babies and for (b) those live born. In 2017, the prevalence for total births (Figure 4a and Table 1) was highest in the congenital heart anomalies subgroup (68.4 per 10,000, 95% CI 65.5-71.3), followed by those that are chromosomal in origin (50.3 per 10,000, 95% CI 47.9-52.8) (Table 1). The prevalence for those who are live born (Figure 4b and Table 3) was also highest in congenital heart anomalies (58.0 per 100,000, 95% CI 55.4-60.7), followed by those that are chromosomal in origin (21.8 per 10,000, 95% CI 20.2-23.5). Not all babies undergo genetic testing, therefore "non-chromosomal" cases are those not known to be of genetic origin.

The pattern for all babies diagnosed with a congenital anomaly, and those that are live born, is similar for the majority of subgroups apart from chromosomal and nervous system anomalies, where prevalence is lower for those live born than for other pregnancy outcomes, reflecting the severity of these anomalies. Further detail stratified by specific congenital anomaly, including the number of cases reported, is available in Tables 1 and 3.

Many babies will have more than 1 anomaly. Babies with multiple anomalies are counted in each applicable bar in Figures 4a and b. The most frequently detected anomalies are congenital heart anomalies and chromosomal anomalies. Figure 5 demonstrates the overlap of selected anomalies by presenting the frequency with which severe cardiac and chromosomal anomalies occur in conjunction. Of the 900 severe cardiac anomalies (Box 1) in 2017 births, 599 (66.6%) occurred in isolation, 99 (11%) also had another structural anomaly, 139 (15.4%) also had a chromosomal anomaly, and 63 (7.0%) had both a chromosomal anomaly and another structural anomaly.

Box 1: Severe cardiac anomalies

This includes the following congenital heart anomalies:
- common arterial trunk
- transposition of great vessels
- single ventricle
- atrioventricular septal defect
- tetralogy of Fallot
- tricuspid atresia and stenosis
- Ebstein's anomaly
- pulmonary valve atresia
- aortic valve atresia/stenosis
- hypoplastic left heart
- hypoplastic right heart
- coarctation of aorta
- total anomalous pulmonary venous return

Ref: EUROCAT

Figure 4a: Total birth prevalence (the number[1] of babies diagnosed with each anomaly per 10,000 total births) by congenital anomaly subgroup[2] in 7 NCARDRS reporting regions, 2017
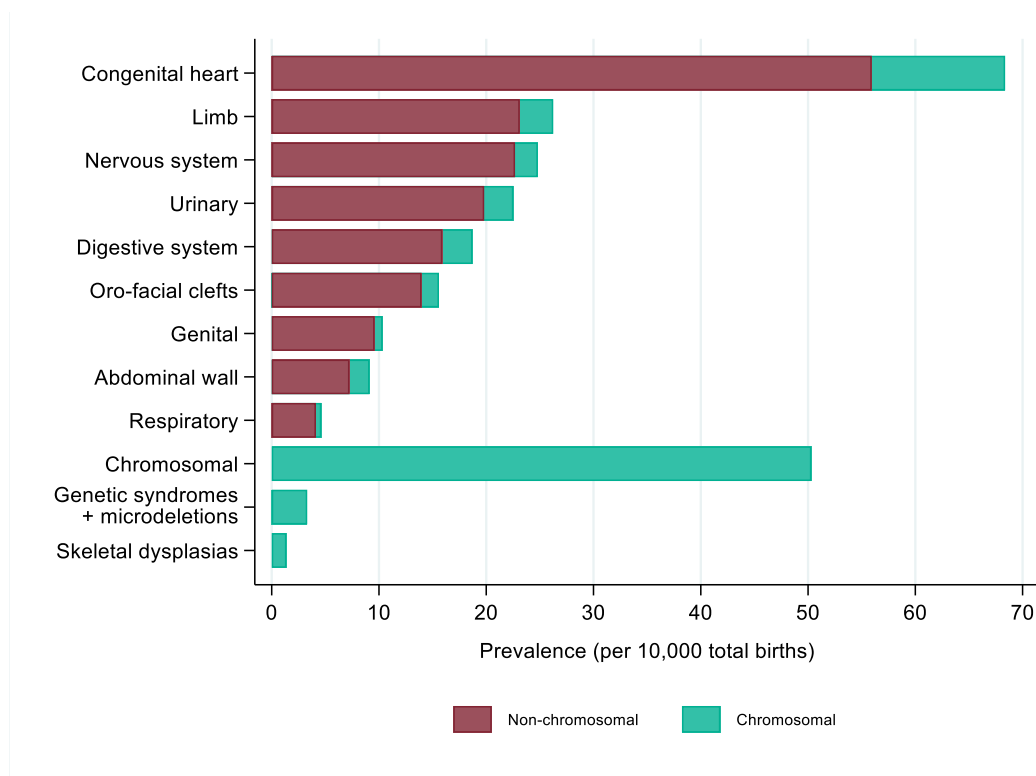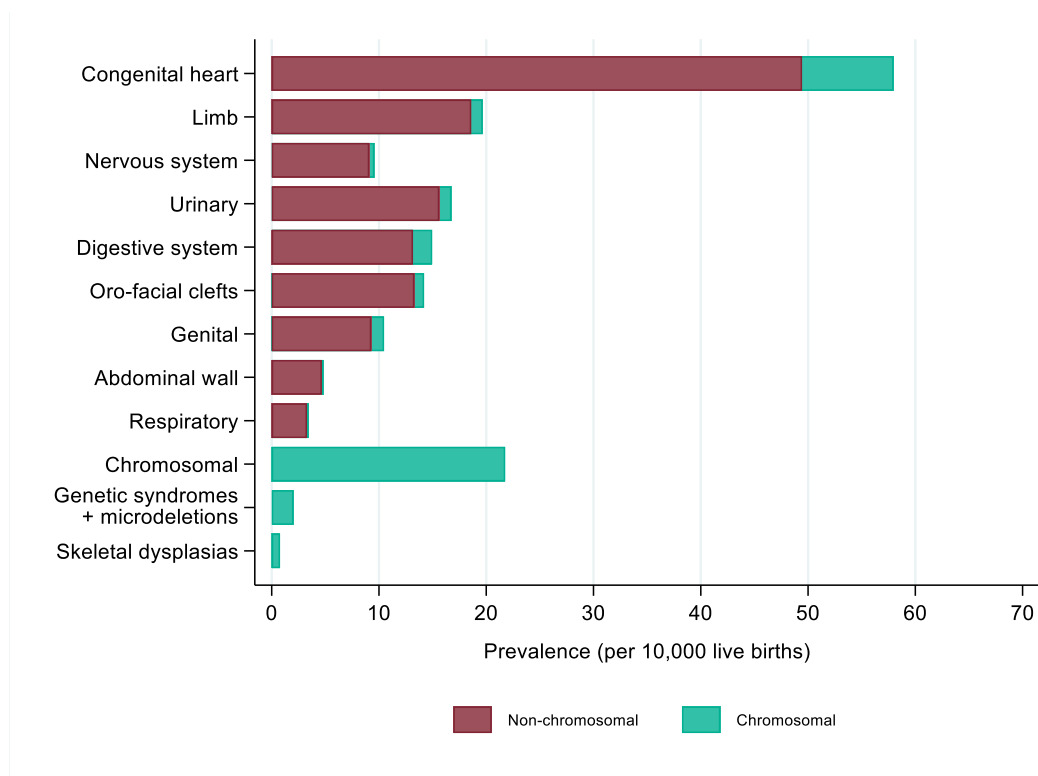

[1] Babies with multiple anomalies will be counted in each applicable bar in Figures 4a and b

[2] Some of the babies shown in these figures will have more than 1 anomaly and appear in more than 1 bar.
l Conditions categorised as "Chromosomal" include those babies with an identified chromosomal anomaly, but will also skeletal dysplasia, genetic syndrome and/or microdeletion.
Non-chromosomal conditions include babies with 1 or more congenital anomaly with no identified anomalies that are chromosomal, skeletal dysplasias, genetic syndromes or microdeletions. Not all babies undergo genetic testing and it is likely some of these are of genetic origin.

Figure 4b: Live birth prevalence (the number[3] of babies diagnosed with each anomaly per 10,000 live births) by congenital anomaly subgroup[4] in 7 NCARDRS reporting regions, 2017

[3] Babies with multiple anomalies will be counted in each applicable bar in Figures 4a and b

[4] Some of the babies shown in these figures will have more than 1 anomaly and appear in more than 1 bar.
Some of the babies shown in these figures will have more than 1 anomaly and appear in more than 1 bar.
l Conditions categorised as "Chromosomal" include those babies with an identified chromosomal anomaly, but will also skeletal dysplasia, genetic syndrome and/or microdeletion.
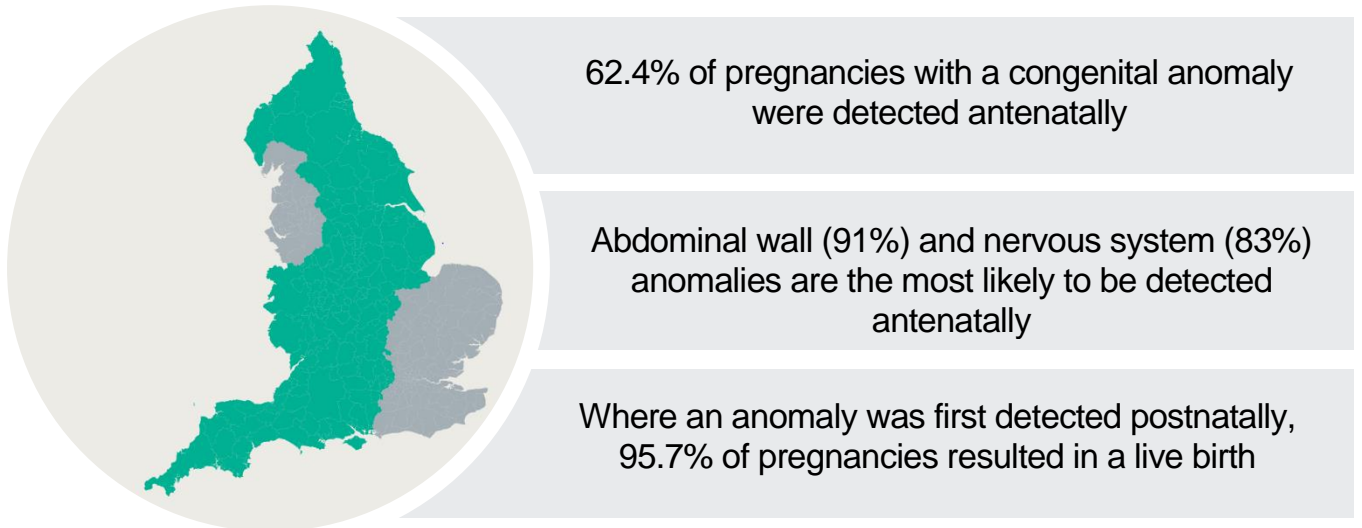Non-chromosomal conditions include babies with 1 or more congenital anomaly with no identified anomalies that are chromosomal, skeletal dysplasias, genetic syndromes or microdeletions. Not all babies undergo genetic testing and it is likely some of these are of genetic origin.

Figure 5: An example of the overlap of severe cardiac, chromosomal and other anomalies, in 7 NCARDRS reporting regions, 2017
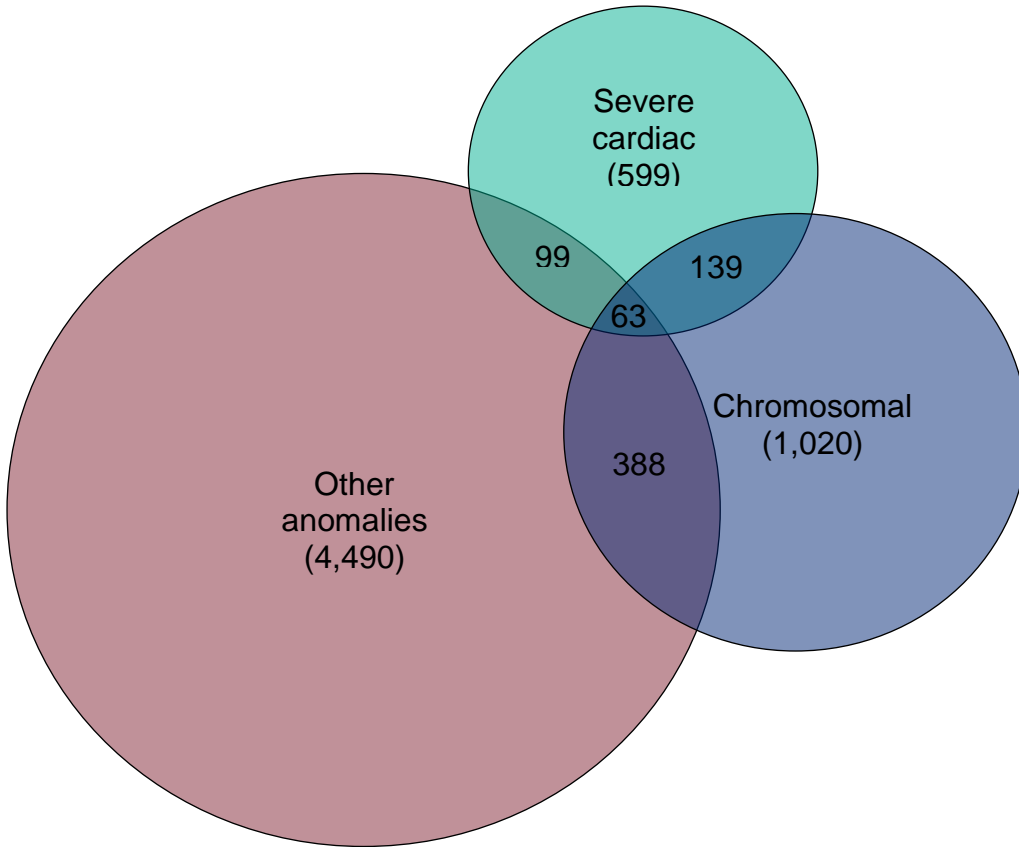
The approximate number of babies with at least 1 congenital anomaly delivered in 2017 in the whole of England can be estimated by applying the birth prevalence estimate for the 7 NCARDRS reporting regions in 2017 to the total number of births in England in 2017 (649,330). This extrapolation is an indication of prevalence and assumes that the birth prevalence was constant across England which is unlikely to be the case. Using this method it is estimated that there were between 13,467 and 14,123 babies with at least 1 reportable congenital anomaly in England in 2017 (Table 4). A breakdown by congenital anomaly subgroup is available in table 4. NCARDRS will report on national prevalence for further anomalies for 2018 data.

Chapter 3: Timing of diagnosis and outcome

62.4% of pregnancies with a congenital anomaly were detected antenatally

Abdominal wall (91%) and nervous system (83%) anomalies are the most likely to be detected antenatally

Where an anomaly was first detected postnatally, 95.7% of pregnancies resulted in a live birth

Some congenital anomalies are detectable during pregnancy and others are not. Screening is offered by NHS maternity services to maximise antenatal detection of specified conditions where women choose, and present in time. NCARDRS provides a separate annual audit of the NHS Fetal Anomaly Screening Programme (FASP) to PHE and to individual NHS providers of maternity services to monitor the performance of this screening.

Early diagnosis of congenital anomaly (as early as possible in the pregnancy) gives women and their partners greater choice about their pregnancy, and enables better planning for the delivery of babies where specialist intervention or palliation may be required soon after birth.

The timing of first diagnosis of a congenital anomaly was known for 6,211 (91.4%) babies. 62.4% of babies were diagnosed antenatally in 2017. Of the 4,243 babies where a congenital anomaly was diagnosed antenatally, 2,487 (51.1%) resulted in a live birth and 1,610 (33.1%) resulted in termination of pregnancy with fetal anomaly (TOPFA) (Table 5). Where a congenital anomaly was first diagnosed postnatally, 95.7% were diagnosed following a live birth (Table 5).

Figure 6 shows that where a baby was liveborn with a congenital anomaly, an anomaly had been detected antenatally in 51.1% of cases (this may be an over-estimate as anomalies diagnosed postnatally are more difficult to ascertain). Where a baby was stillborn with a congenital anomaly, an anomaly had been detected antenatally in 73.4% of cases.

Figure 6: Timing of first diagnosis and pregnancy outcome in 7 NCARDRS reporting regions, 2017
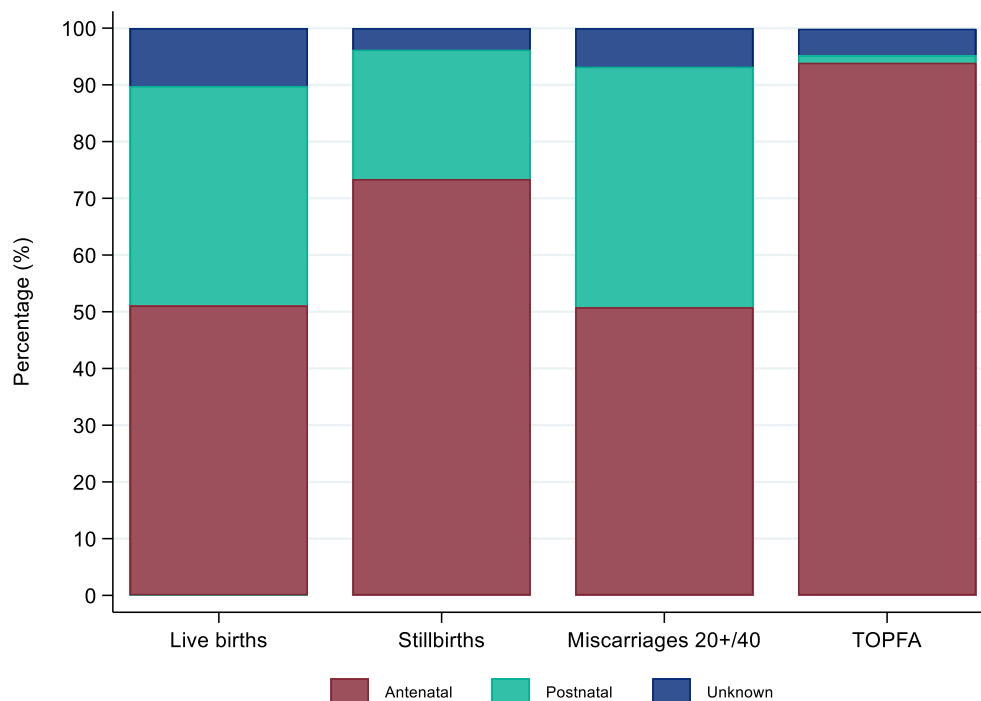
Some types of congenital anomalies are more likely to be diagnosed antenatally than others. Figure 7 shows that abdominal wall, nervous system, and urinary anomalies are the conditions most frequently diagnosed antenatally. Genital anomalies are unlikely to be diagnosed antenatally. It should be noted that individual anomalies within these subgroups may not follow these patterns. A more detailed breakdown by specific congenital anomaly, including the number of babies reported, is available in Table 6.

Figure 7: Timing of diagnosis by congenital anomaly subgroup – based on individual anomaly (percentage) in 7 NCARDRS reporting regions, 2017
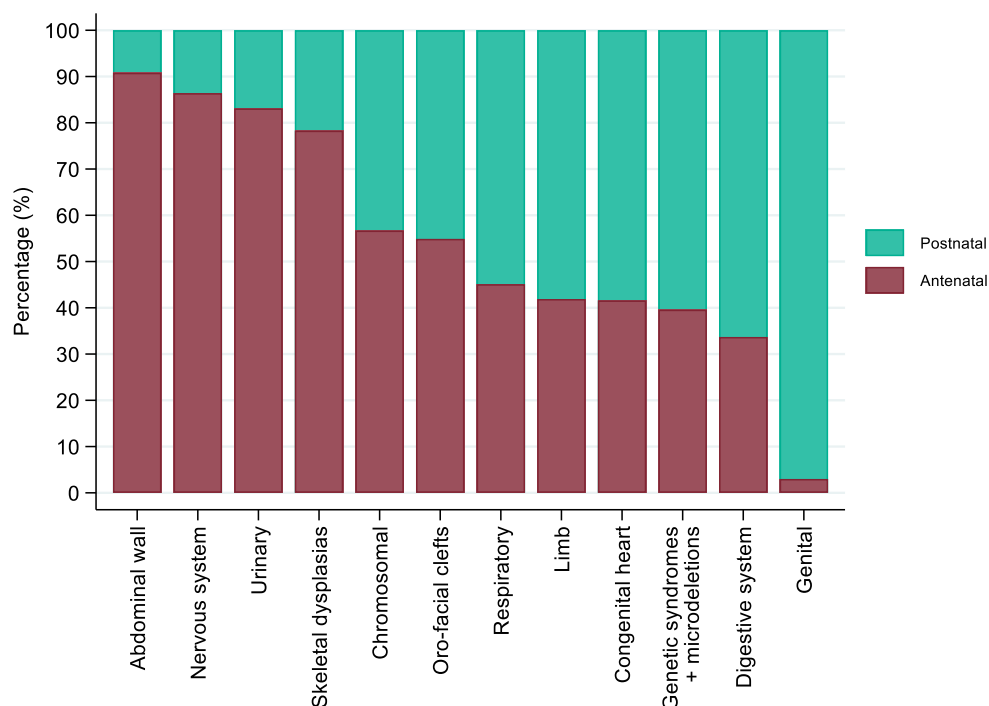
The overall rate of TOPFA for the 7 NCARDRS reporting regions was 53.6 per 10,000 total births. The rate of TOPFA at over 20 weeks' gestation was 17.2 per 10,000 total births (Table 7).

The data in Table 7 show the highest rate of TOPFA was associated with chromosomal anomalies (26.3 per 10,000 births). In the majority of babies with chromosomal, nervous system or abdominal wall anomalies that resulted in TOPFA, this was performed before 20 weeks' gestation. This outcome is likely to be associated with timing of diagnosis as these conditions are more likely to be diagnosed earlier in the pregnancy. In the case of congenital heart anomalies the TOPFA rate is higher after 20 weeks' gestation than before 20 weeks' gestation. Where congenital heart anomalies are diagnosed antenatally a heart anomaly is often first suspected at the routine fetal anomaly scan, which takes place at around 20 weeks gestation. Women are then offered referral to a tertiary service provider for specialist confirmation of the specific heart anomalies present.

Chapter 4: Key public health indicators

Congential anomalies are a leading cause of infant and perinatal mortality

Congenital heart, chromosomal and digestive anomalies are most frequently associated with infant and perinatal mortality

Higher and lower maternal age are linked with an increase in certain congenital anomalies

4.1 Perinatal and infant mortality

There were 310 infant deaths among babies with 1 or more congenital anomalies in the 318,729 live births in 2017, giving an infant mortaility rate of 9.7 per 10,000 live births. The rate of perinatal mortality was lower, at 7.9 per 10,000 births (Table 9).

Box 2: Mortality definitions

Infant mortality: Deaths under 1 year of age

Perinatal mortality: Stillbirths and deaths under 7 days of age

Figures 9a and 9b show that in cases of both perinatal and infant mortality the most frequently recorded anomalies were the same; with congenital heart anomalies (3.4, 3.8 per 10,000 births) followed by chromosomal (2.3, 1.8 per 10,000 births) and digestive (1.5, 1.7 per 10,000 births).

The data presented here should be viewed with some caution, as babies with more than 1 anomaly will appear in each anomaly subgroup. Additionally, a link between the presence of a congenital anomaly and the cause of death has not been established, therefore it is possible that the identified congenital anomaly had no bearing on mortality. These figures also do not include conditions with a high level of antenatal

mortality, pregnancy loss or rate of TOPFA, where few pregnancies result in either a live birth or stillbirth, for example, anencephaly.

Despite the caveats referenced above, infant and child mortality data from the Office for National Statistics for 2017 shows that congenital anomalies were the most common cause of death in the post neonatal period. Congenital anomalies were also listed as the cause of 31.1% of infant deaths and 22.1% of perinatal deaths, the second highest cause in both categories. While the data within this report should be viewed in a wider context of perinatal and infant mortality, congenital anomalies, particularly heart, chromosomal and digestive system anomalies, are a common factor in infant and perinatal deaths.

Figure 9a: Perinatal mortality (stillbirths and deaths under 7 days of age) by congenital anomaly subgroup in 7 NCARDRS reporting regions, 2017
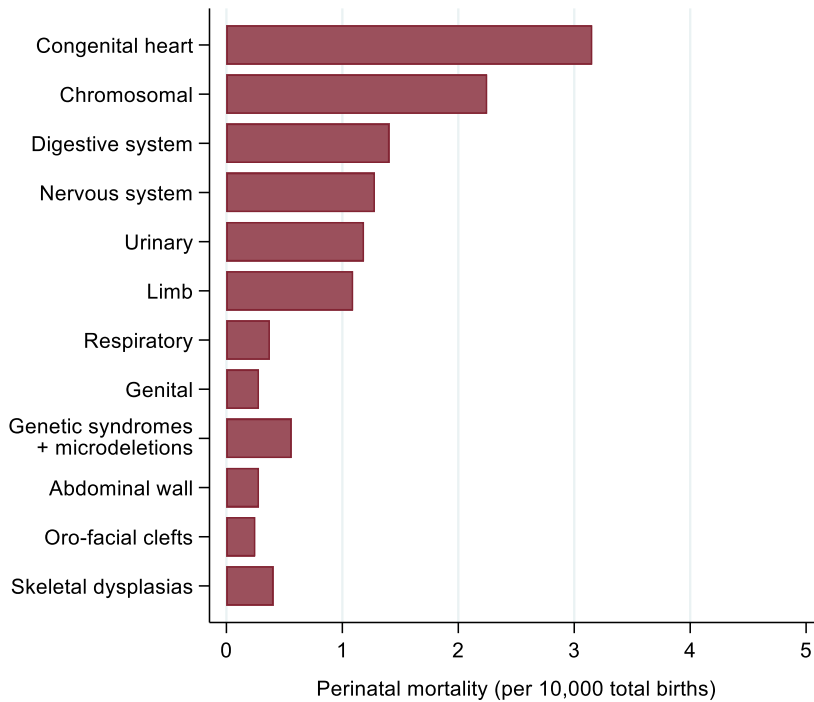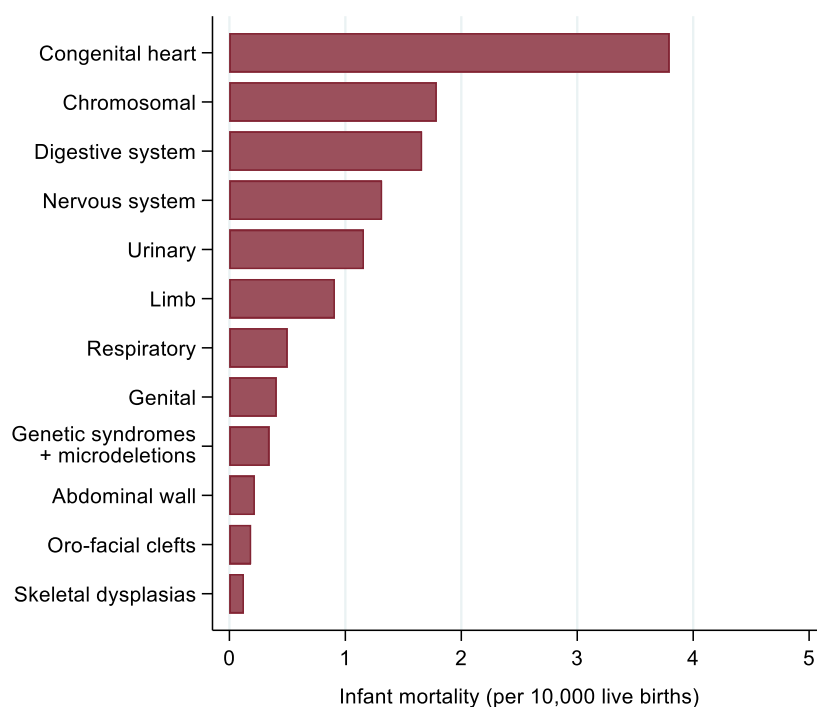

Perinatal mortality (per 10,000 total births)

Figure 9b: Infant mortality (deaths under 1 year of age) by congenital anomaly subgroup in 7 NCARDRS reporting regions, 2017

4.2 Maternal age

The birth prevalence of all anomalies was very similar in mothers aged between 30 and 34 years at delivery to the prevalence in those aged between 25 and 29 years (192.4 and 192.5 per 10,000 total births respectively). Compared to these groups, the birth prevalence was significantly higher in mothers aged 35 to 39 years (245.6 per 10,000 total births) and those 40 years and over (401.6 per 10,000 total births). For mothers in the under 20 years and 20-24 years age groups the rates were broadly similar to those aged between 30 and 34 years (Table 10).

The association beween higher maternal age and certain chromosomal disorders, including Down's syndrome, is well established. Mothers aged 40 and over had a significantly higher prevalence of chromosomal anomalies compared to all other age groups (Figure 10). The rate of chromosomal congenital anomalies in women over 40 years (n=287) was 7 times higher (6.6; 95% CI 4.7-9.2) compared to women under 20 years (n=39). Down's syndrome is the most common chromosomal anomaly (23.8 per 10,000 births) and is likely a primary factor in the higher rate in older age groups.

The rate of non-chromosomal anomalies in women aged under 20 years is significantly higher than the rate in women in the 30-34 years age group (Figure 10, Table 10). The increased rate in women aged under 20 years is primarily driven by the significantly

higher prevalence of abdominal wall anomalies in women within this age group (26.7 per 10,000 births) compared to 3.9 per 10,000 births in women aged 30-34 years.

Gastroschisis, an abdominal wall anomaly, is known to be associated with lower maternal age, and this relationship is demonstrated within this data as the prevalence among those under 20 is 19.9 per 10,000 births compared to 0.4 per 10,000 births in women aged over 40 (Figure 11).

Figure 10: Prevalence (per 10,000 total births) and 95% confidence intervals of chromosomal and non-chromosomal[5] congenital anomalies by maternal age in 7 NCARDRS reporting regions, 2017

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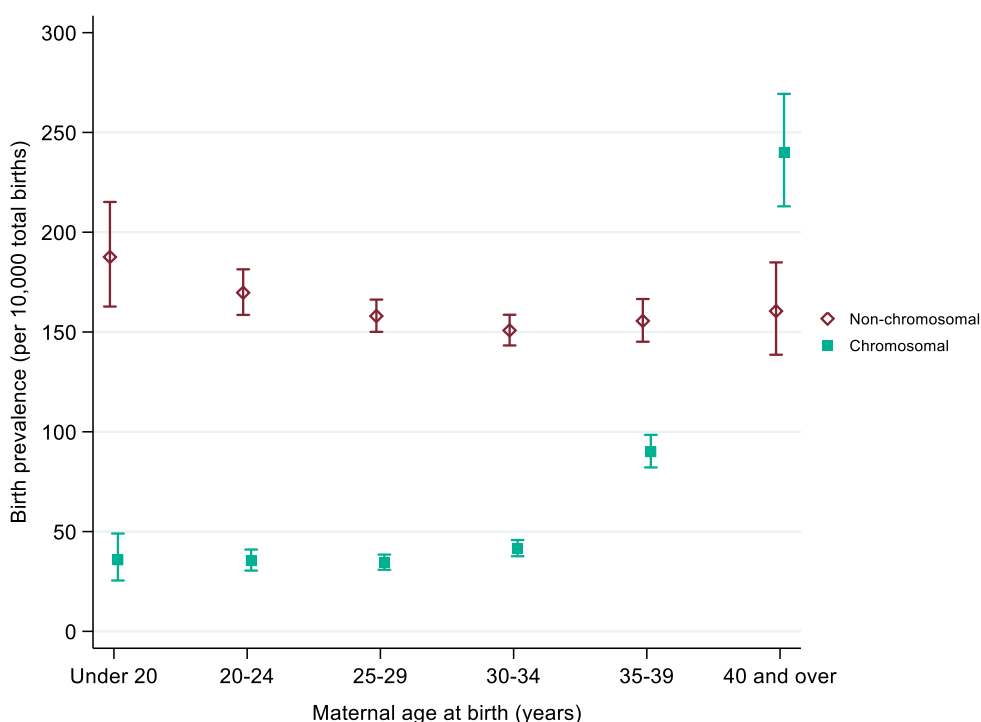
[5] Chromosomal conditions include babies with an identified chromosomal anomaly and also include skeletal dysplasia, genetic syndrome and/or microdeletion.
Non-chromosomal conditions include babies with 1 or more congenital anomaly none of which are chromosomal, skeletal dysplasias, genetic syndromes or microdeletions. Not all babies undergo genetic testing and it is likely some of these are of genetic origin

Figure 11: Prevalence (per 10,000 total births) and 95% confidence intervals of gastroschisis by maternal age in 7 NCARDRS reporting regions, 2017
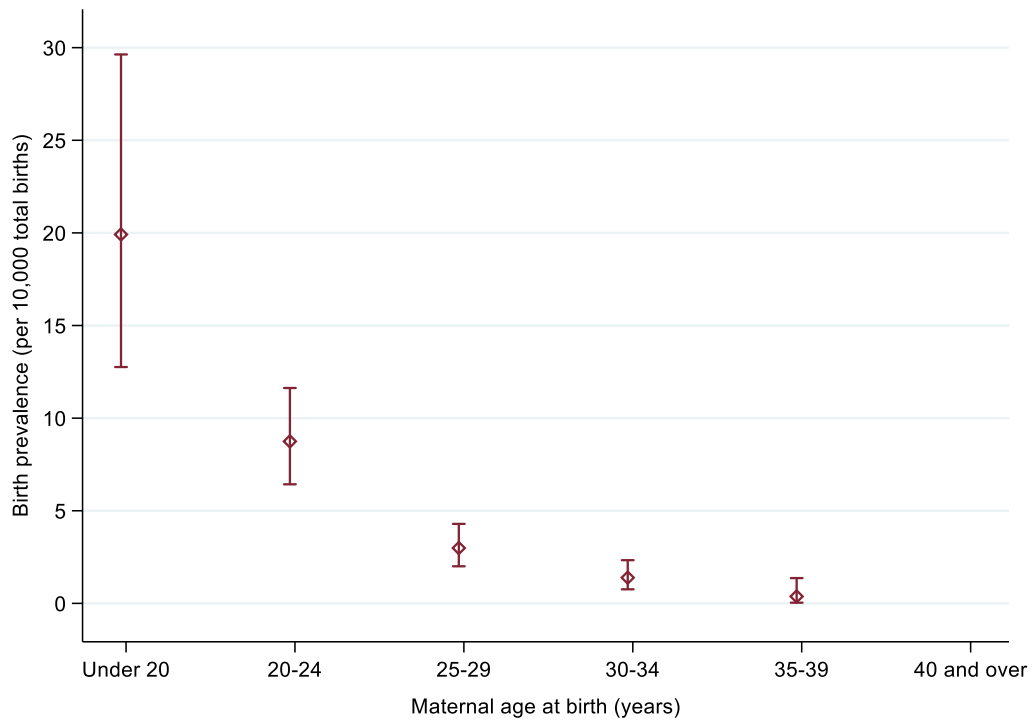
Chapter 5: Down's syndrome, Edwards' syndrome and Patau's syndrome

National coverage of babies delivered in 2015-2017 and diagnosed with Down's, Edwards' or Patau's syndrome

Overall birth prevalence (2015-2017): Down's syndrome 1 for 353 births; Edwards' syndrome 1 for 1,190 births; Patau's syndrome 1 for 2,857 births.

43.0% of babies with Down's syndrome, 10.8% of babies with Edwards' syndrome and 8.7% of babies with Patau's syndrome diagnoses resulted in a live birth

5.1 Background

From 1989 to 2013, detailed data on trisomies of chromosomes 21, 18 and 13, Down's syndrome, Edwards' syndrome and Patau's syndrome respectively, were collated and published by the National Down Syndrome Cytogenetic Register (NDSCR). When NCARDRS was established in 2015, it incorporated the work of the NDSCR, and national trisomy data for 2014 were published in the 2015 NCARDRS report. Subsequently, data collection methods were modernised, and a broad range of data are now collected electronically. This chapter contains data on all babies and fetuses delivered between 2015 to 2017, diagnosed with Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13).

Box 3: Trisomy definitions

Trisomy: Babies normally inherit 2 copies of each chromosome, 1 from their mother and 1 from their father. A baby with a trisomy has 3 copies of a particular chromosome. The imbalance in the genetic material causes the baby to have developmental difficulties and physical differences or anomalies.

Meiotic non-disjunction: This is the most common way in which a trisomy arises. During the formation of the egg or sperm, a chromosome pair does not separate properly, so the egg or sperm contains a complete extra copy of 1 chromosome. This occurs randomly, but is more common in older mothers.

Translocation trisomy: This is much rarer, and occurs when 2 different chromosomes are physically joined together, so are inherited as a single unit. Often, 1 of the parents carries this translocation in a balanced form, meaning that there is the right amount of genetic material, but it is arranged in the wrong order. However, they can pass on the translocation in an unbalanced form, meaning that the baby has too much (or too little) genetic material. Importantly, translocation trisomy indicates a significant recurrence risk in subsequent pregnancies, so families in this situation are offered genetic counselling.

Mosaic trisomy: Only some cells in the body have an extra copy of the chromosome. The rest of the body cells usually have a normal set of chromosomes. Mosaic trisomies occur due to random errors in cell division after conception. Mosaic trisomies can have milder effects, but this can vary depending on the proportion of cells with the additional chromosome, and where in the body these cells are located.

Partial trisomy: Extra genetic material is present, but only from part of the chromosome, not the entire chromosome. Partial trisomies are not counted in this report.

5.2 Diagnoses and Prevalence of Down's syndrome, Edwards' syndrome and Patau's syndrome

Between 1 January 2015 to 31 December 2017 inclusive, there were 5,619 babies with Down's syndrome, 1,668 babies with Edwards' syndrome and 690 babies with Patau's syndrome delivered in England. Based on the 1,982,731 births during the period, this gives a prevalence per 10,000 total births of 28.3 (95% CI: 27.6-29.1), or 1 for every 353 total births for Down's syndrome, 8.4 (95% CI: 8.0-8.8), or 1 for 1,190 for Edwards' syndrome and 3.5 (95% CI: 3.2-3.7), or 1 for 2,857 total births for Patau's syndrome respectively. Live birth prevalence, per 10,000 live births, was 11 (95% CI: 10.5-11.4), or 1 for 909 total births for Down's syndrome, 0.8 (95% CI: 0.7-0.9), or 1 for 12,500 for Edwards' syndrome and 0.2 (95% CI: 0.2-0.3), or 1 for 50,000 for Patau's syndrome respectively. Historical data from NDSCR presented in the NCARDRS 2015 report[6]

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[6] NCARDRS congenital anomaly statistics, 2015

indicates that the live birth prevalence of Down's syndrome has remained largely stable since 2005.

The prevalence for Down's syndrome, Edwards' syndrome and Patau's syndrome based on national data for 2015-2017 (Table 17) is higher than that reported for EUROCAT reporting regions (Table 1). The prevalence based on national data is likely overestimated, as there is a higher proportion of babies where we do not know the gestation and outcome of the pregnancy in new NCARDRS regions compared to the 7 established regions. This means that some miscarriages that occurred before 20 weeks gestation are included, inflating the national prevalence estimate.

5.3 Diagnostic specimens

Antenatal diagnoses were primarily made from chorionic villus sampling (CVS) (59.6%) or amniocentesis (39.5%), with occasional fetal blood sampling. Postnatal diagnoses include blood or saliva taken after a live birth, and postmortem tissue specimens tested following a late miscarriage, termination of pregnancy with fetal anomaly (TOPFA), or a stillbirth. Miscarriages known to have occurred before 20 weeks' gestation are excluded, where gestation and outcome are known, as it is not possible to get complete ascertainment before this gestation.

5.4 Diagnosis - Timing and outcomes

National data are presented in Tables 11, 12 and 13. As the gestation and outcome data are incomplete for newer reporting regions, the data discussed in Section 5.4 are calculated only for regions of the country with well-established congenital anomaly registers, where the data are complete (Tables 14, 15, 16).

Out of all diagnoses in babies delivered between January 2015 and December 2017, those resulting in live birth comprise 43.0% of Down's syndrome, 10.8% of Edwards' syndrome and 8.7% of Patau's syndrome.

Most babies with a trisomy were diagnosed antenatally (Figure 12, Table 14, 15, 16), usually by rapid aneuploidy testing followed by a full karyotype (Figure 13). 57.6% of Down's syndrome (Table 14), 72.2% of Edwards' syndrome (Table 15) and 64.3% of Patau's syndrome cases (Table 16) were antenatally diagnosed. For pregnancies with a trisomy that was diagnosed antenatally, the TOPFA rate between 2015 and 2017 was quite similar across all 3 conditions, at 85.1% (95% CI: 83.1-86.8%) for Down's syndrome, 86.9% (95% CI: 83.6-89.6%) (Table 14) for Edwards' syndrome (Table 15) and 90.4% (95% CI: 85.2-94%) for Patau's syndrome (Table 16).

Postnatal diagnoses represent cases where women made a choice not to accept the offer of antenatal screening, declined invasive testing following a higher chance

screening result or detection of indicative structural anomaly, for example atrioventricular septal defect (AVSD), or whose screening test gives a false negative result. Some of these babies were clinically detected at the 20-week fetal anomaly scan, then were cytogenetically diagnosed following either termination of pregnancy, miscarriage, stillbirth or livebirth. Of those babies that were diagnosed postnatally, 86.8% (95% CI: 84.7-88.7%) of those with Down's syndrome, 28.9% (95% CI: 22.9-35.6%) of those with Edwards' syndrome and 20.2% (95% CI: 13.5-29.2%) of those with Patau's syndrome were live born. The difference in livebirth rates between these 3 trisomies was largely due to different rates of TOPFA: only 6.3% (95% CI: 5-7.9%) of non-antenatally detected Down's syndrome pregnancies were terminated, compared to 55.7% (95% CI: 48.6-62.5%) for Edwards' syndrome and 58.6% (95% CI: 48.7-67.8%) for Patau's syndrome. Natural attrition rates in pregnancy played a smaller role; post-20 week fetal losses were higher for Edwards' syndrome and Patau's syndrome than for Down's syndrome.

Taking into account both antenatal and postnatal diagnoses, the overall rate of TOPFA for the 3 conditions was therefore 51.6% (95% CI: 49.6-53.5%) for Down's syndrome and approximately 80% for both Edwards' syndrome (95% CI: 78.2%, 75.0-81.1%) and Patau's syndrome (79.1%, 95% CI: 73.9-83.4%).

Figure 12: The number of babies with Down's Sydrome, Edwards's Syndrome and Patau's syndrome diagnosed in England from 2015-2017 inclusive, and categorised by the timing of diagnosis[7]

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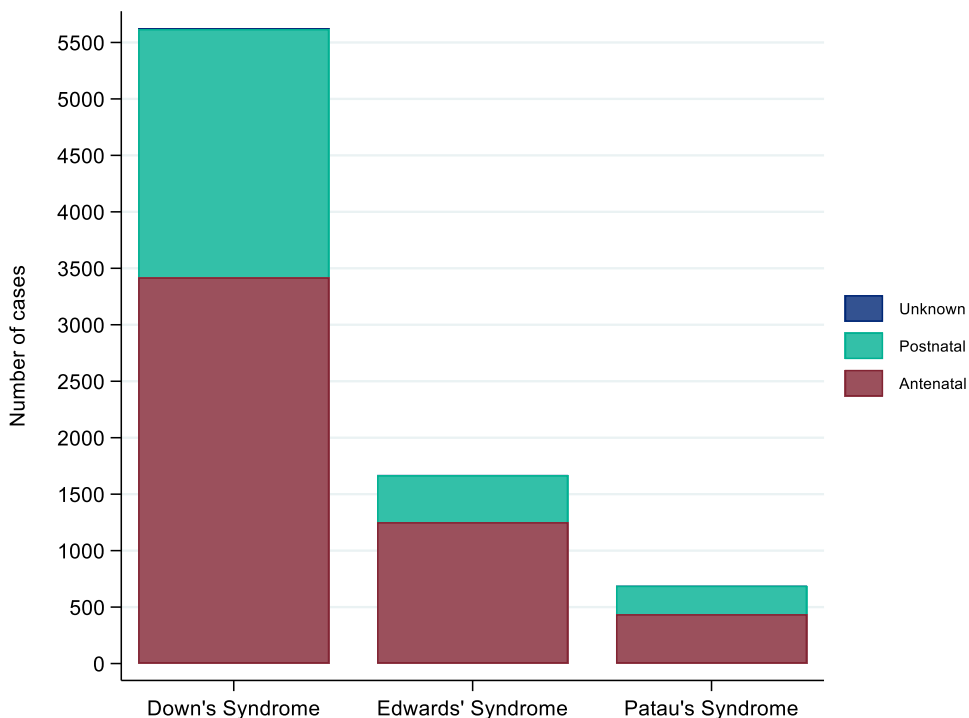
[7] Postnatal diagnoses include fetal losses (all stillbirths and terminations with fetal anomaly, and miscarriages between 20-23 weeks gestation). Miscarriages known to have occurred before 20 weeks' gestation are excluded, as it is not possible to get complete ascertainment before this gestation. Where a miscarriage has occurred, but the gestation is unknown, this is included in the data, so there is likely to be a degree of over-ascertainment (i.e. some pre-20-week fetal losses) in this category. Where a baby has had both a prenatal and a postnatal diagnostic test, the earlier diagnosis is taken as the point of ascertainment.

Underlying numbers are shown in Tables 11, 12, 13.

Figure 13: Timing of diagnosis and laboratory test method for Down's Sydrome, Edwards's Syndrome and Patau's syndrome combined in England 2015-2017[8]
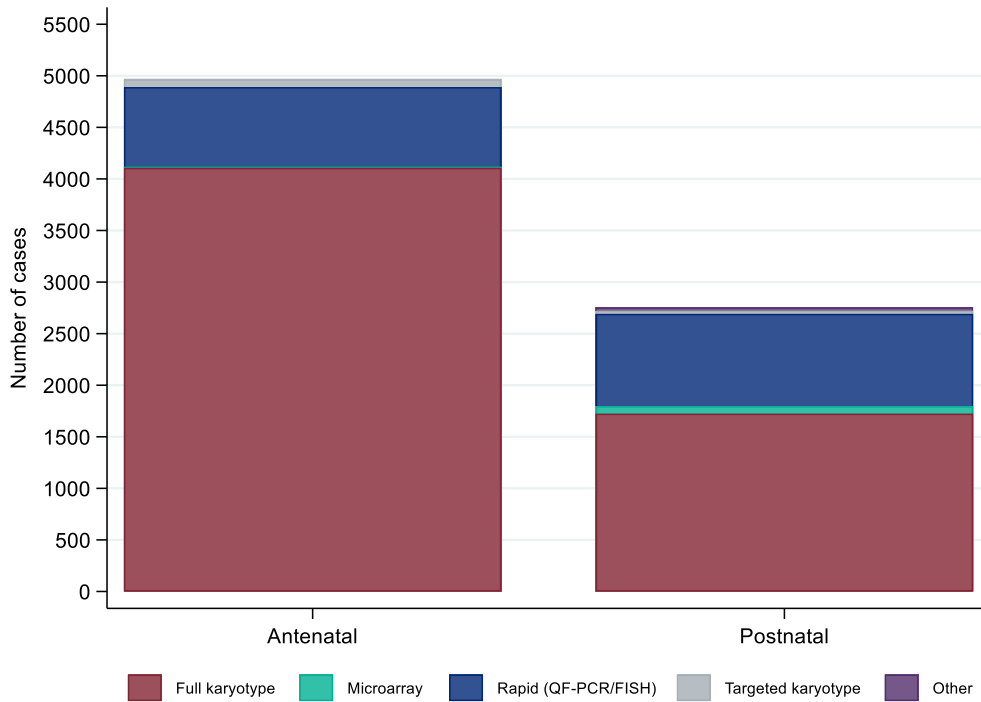

5.5 Origin of Trisomies

Down's Sydrome, Edwards's Syndrome and Patau's syndrome can arise by several different mechanisms, outlined in Box 3. As expected, meiotic non-disjunction (which is strongly associated with maternal age) accounted for the majority of babies diagnosed with Down's Sydrome, Edwards's Syndrome or Patau's syndrome, with fewer translocation and mosaic cases being observed (Figure 14). Note that mosaic trisomies are likely to be underascertained: low-level mosaicism (especially of trisomy 21) may result only in sub-clinical features, so may remain undiagnosed, particularly if the trisomic cell line is absent in the lymphocyte lineage.

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[8] Where multiple cytogenetic tests are performed, only the single most informative / definitive test is counted for each case. Thus a full karyotype would be counted in preference to a microarray or a rapid aneuploidy test, and a prenatal test in preference to a postnatal 1. Note also the same caveats regarding post-mortem diagnosis on fetal losses as described for Figure 12.

Figure 14: The number of babies diagnosed with Down's Sydrome, Edwards's Syndrome and Patau's syndrome combined all delivered in England in 2015-2017 categorised by chromosome and underlying genetic mechanism[9].
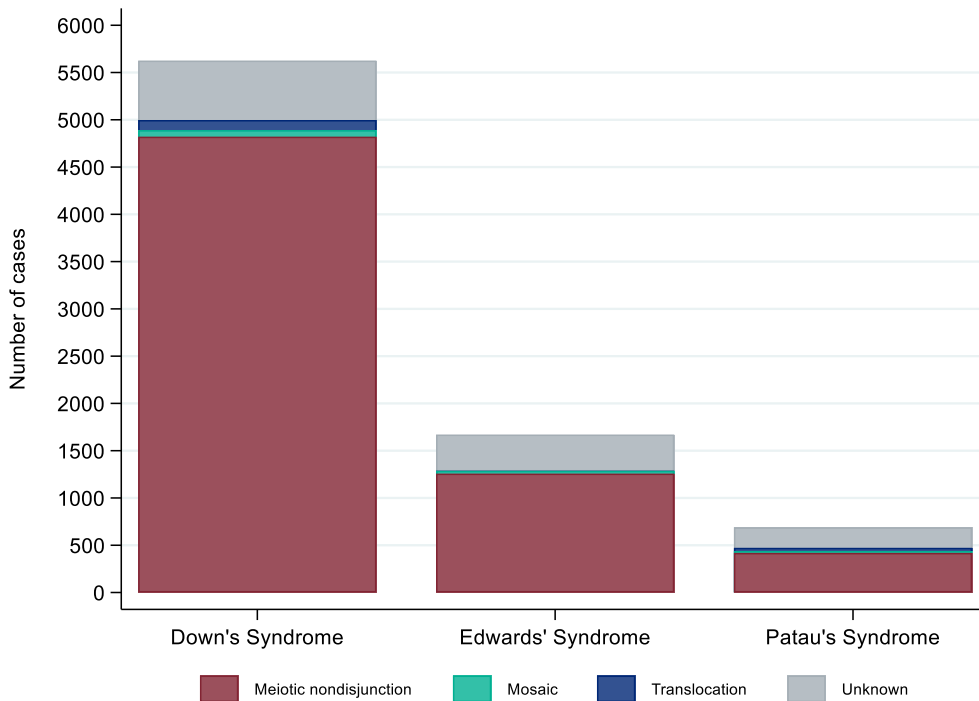

5.6 Regional differences in outcomes

Figures 15 and 16 show timing of diagnosis and differences in outcome split by geographical region. The outcome data (Figure 16) is incomplete for regions where congenital anomaly registration is new (East of England, London & South East, and North West). As congenital anomaly registration becomes embedded in these regions, it will be possible to build up a more complete picture of regional variations. Nevertheless, some general patterns are apparent.
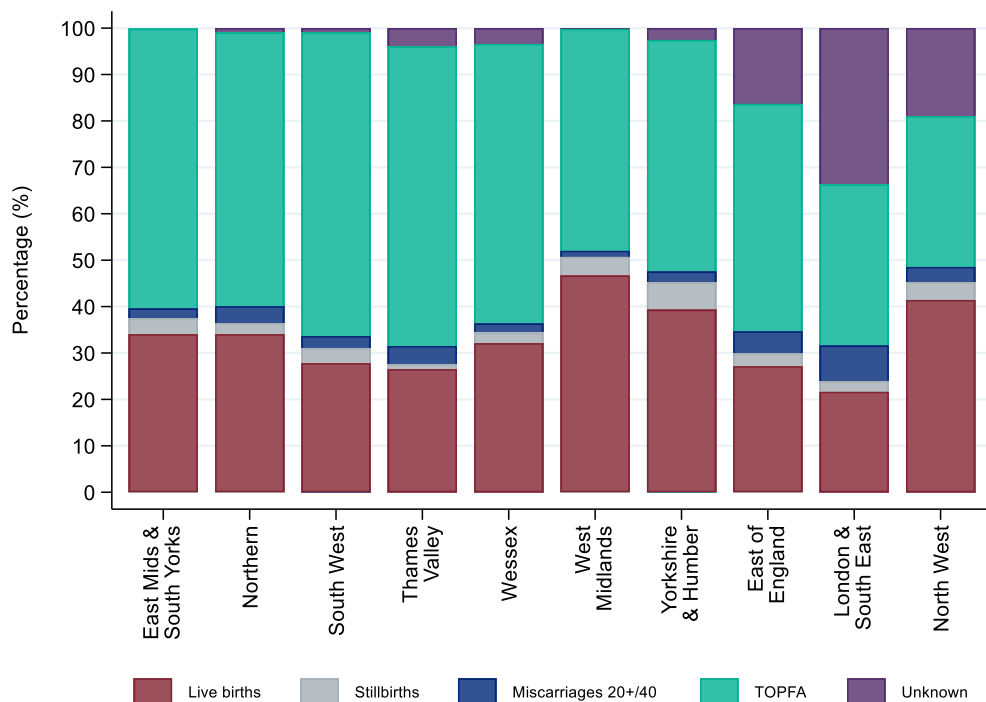
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[9] See Box 3 for explanatory notes. Babies where the genetic type of trisomy is unspecified are those where conventional karyotyping failed or was not performed, i.e. they were diagnosed only by a rapid aneuploidy test or microarray; these latter tests cannot distinguish between standard and translocation trisomies. Note that complete trisomy of chromosome 18 arising from an unbalanced translocation is an extremely rare entity (only 2 cases diagnosed over this three-year period); this is because of the different architecture of chromosome 18 (submetacentric) compared to 13 and 21 (acrocentric). Robertsonian translocations (fusion of 2 acrocentric chromosomes at the centromere, with loss of the heterochromatic satellite p-arms) are relatively common, with around 1 in 1000 people thought to carry a balanced Robertsonian translocation. Where such a translocation involves chromosome 13 or 21, there is an increased chance that any child of the carrier will be affected with Patau's syndrome or Down's syndrome respectively.

Figure 15: Timing of diagnosis for Down's Sydrome, Edwards's Syndrome and Patau's syndrome delivered in 2015-2017, stratified by region[10].

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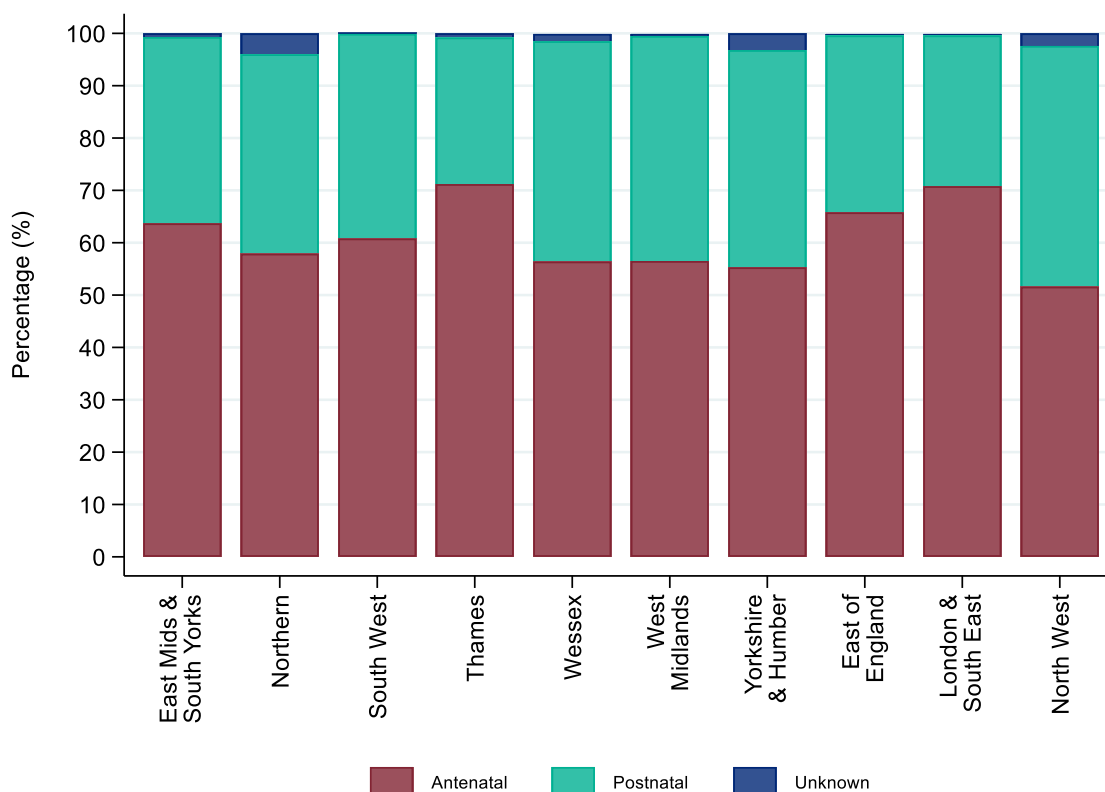
[10] Note that postnatal diagnoses include fetal losses (all stillbirths and terminations for anomaly, and miscarriages between 20-23 weeks gestation). Miscarriages known to have occurred before 20 weeks gestation are excluded. Where a miscarriage has occurred, but the gestation is unknown, this is included in the data, so there is likely to be a degree of over-ascertainment (i.e. some pre-20-week fetal losses) in this category. Where a baby has had both a prenatal and a postnatal diagnostic test, the earlier diagnosis is taken as the point of ascertainment. Underlying numbers are shown in Tables 11, 12 & 13.

Figure 16 – Outcome of pregnancy for Down's Sydrome, Edwards's Syndrome and Patau's syndrome delivered in 2015-2017, stratified by region[11].

Appendix 1: Glossary of terms

Term	Definition
Amniocentesis	Antenatal procedure involving the removal of a sample of amniotic fluid for the purposes of chromosomal or genetic testing
Antenatal	The period from conception to birth.
Antenatal diagnosis	A diagnosis made in a live fetus at any gestation.
Birth prevalence	The total number of babies diagnosed with a congenital anomaly (live births, stillbirths, late miscarriages and terminations of pregnancy with fetal anomaly) compared to the total number of births (live births and stillbirths).[i]
Births/total births	Live births and stillbirths.[ii]
Case ascertainment	Proportion of notifications of congenital anomalies reported to NCARDRS out of all cases of congenital anomaly in the population.
Chorionic villus sampling (CVS)	Antenatal procedure involiving the removal of a sample of placental tissue for the purposes of chromosomal or genetic testing
Chromosmal anomalies	Includes chromosomal abnormalities and this group also includes skeletal dysplasias, genetic syndromes and microdeletions[i]
Confidence interval (see Technical Guidance document for more information)	The range (confidence interval) about the sample proportion/mean will actually contain the true - but unknown - proportion/mean value in the population. It is usual practice to create confidence intervals at the 95% level which means 95% of the time our confidence intervals should contain the true value found in the population.
Congenital anomaly	Present at delivery, probably originating before birth, and includes structural, chromosomal, genetic and biochemical anomalies.

Congenital hydronephrosis	An obstruction of the urinary flow from kidney to bladder. Cases are registered where the renal pelvis measurement is ≥10 mm after birth.[i]
Estimated date of delivery (EDD)	The estimated delivery date of a pregnancy, calculated as 40 weeks gestation
EUROCAT	European network of population-based registries for the epidemiological surveillance of congenital anomalies
NHS Fetal Anomaly Screening Programme (FASP)	NHS screening for specified structural and chromosomal anomalies during pregnancy using laboratory and/or ultrasound tests
Fetal medicine	Sub-speciality of antenatal care focused on high-risk pregnancies including those affected by a congenital anomaly
Feticide	A procedure to stop the fetal heart and cause the demise of the fetus in the uterus.[iii]
Full karyotype	Visual inspection of all chromosomes down the microscope, enabling assessment of chromosome number and integrity.
Hospital episode statistics (HES)	Database of all admissions, A&E attendances and outpatient appointments at NHS hospitals in England
Infant deaths	Deaths under 1 year of age.[ii]
Infant mortality	The number of infant deaths per 10,000 live births.
Invasive testing	Antenatal tests including amniocentesis and chorionic villus sampling used to diagnose chromosomal and genetic anomalies
Late miscarriage	Late fetal deaths from 20-23 completed weeks of gestation.
Live birth	A baby showing signs of life at birth.[ii]
Live birth prevalence	The total number of babies diagnosed with a congenital anomaly that are live born compared to the total number of live births
Major congenital anomaly subgroup (see Technical Guidance document for more information on these subgroups)	The high level body system and anomaly type groupings of congenital anomalies. [i]
Non-chromosomal anomalies	Includes anomalies with no known chromosomal or genetic cause though as not all babies undergo genetic testing, it is likely that some of these are of chromosomal or genetic origin

Non-invasive prenatal testing (NIPT)	Screening test for specific chromosomal disorders by testing fragments of fetal DNA found in the maternal blood stream
Office for National Statistics (ONS)	Body responsible for collection and production of statistics related to the economy, population and society of the UK.
Palliation	Medical care for a condition focusing on relief of symptoms rather than treating the underlying condition
Perinatal deaths	Stillbirths and deaths under 7 days of age.[ii]
Perinatal mortality	The number of perinatal deaths per 10,000 total births.
Postneonatal period	From 28 days to 1 year of age
Rapid aneuploidy testing	A genetic test with a short turnaround time; it counts the copy number of specific regions on chromosomes 13, 18, 21, X and Y.
Severe congenital heart disease (CHD)	This includes the following congenital heart anomalies: • common arterial truncus • transposition of great vessels • single ventricle • atrioventricular septal defect • tetralogy of Fallot • tricuspid atresia and stenosis • Ebstein's anomaly • pulmonary valve atresia • aortic valve atresia/stenosis • hypoplastic left heart • hypoplastic right heart • coarctation of aorta • total anomalous pulmonary venous return
Severe microcephaly	Where the head circumference is less than -3 standard deviations for sex and gestational age.[i]
Stillbirths	A baby born after 24 or more weeks completed gestation and which did not, at any time, breathe or show signs of life.[ii]

Statistical significance (see Technical Guidance document for more information)	Statistical testing is undertaken by comparing the confidence intervals to see if they overlap - with non-overlapping confidence intervals being considered as statistically significantly different.
Teratogen	Substance or other factor that can cause congenital anomaly by affecting fetal development
Termination of pregnancy with fetal anomaly (TOPFA)	Term used to describe the deliberate ending of a pregnancy with the intention that the fetus will not survive and which is carried out when the fetus is diagnosed prenatally as having a major congenital anomaly. This includes terminations of pregnancy for fetal anomaly as well as terminations of pregnancy for other medical reasons where a fetal anomaly was present. Where a pregnancy ends in a TOPFA, the baby may be born dead, or if parents have not opted for prior feticide the baby may be born alive but die shortly after. Depending on the gestation at which a TOPFA takes place (before or after 24 weeks) it may also be registered as a stillbirth.
Tertiary service	A hospital whihch provides specialist care following referral from a local provider, this may include antenatal or postnatal specialities

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i www.eurocat-network.eu

ii www.ons.gov.uk

iii Royal College of Obstetricians and Gynaecologists. The Future Workforce in Obstetrics and Gynaecology in England and Wales. Working Party Report. London: RCOG; 2009.