



Public Health
England

Protecting and improving the nation's health

National congenital anomaly and rare disease registration service

Congenital anomaly statistics 2019

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Executive summary

This is the fifth 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.

In 2018, NCARDRS achieved its goal of national data collection. This report, covering births between January and December 2019, represents the second year of national data coverage for England.

NCARDRS' first report, using data from 2015, reported on 21% of births in England. In both the 2016 and 2017 reports, data from 7 NCARDRS reporting regions, representing 49% coverage of births, were presented. We are pleased to report that, as in the 2018 report, this fifth report is based on data covering 100% of births in England.

NCARDRS currently collects data on over 1,400 different congenital anomalies and rare diseases across England. In 2019, there were a total of 13,306 babies¹ with one or more congenital anomalies notified to NCARDRS, covering 614,952 total births (live births and stillbirths). This gives an overall birth prevalence for these regions of 216.4 per 10,000 total births – one baby diagnosed with a congenital anomaly for every 46 births (**live births and stillbirths**).

Some congenital anomalies are detectable during pregnancy and others are not. In 2019, the timing of first diagnosis was known for 12,674 (95.0%) babies and of these, 68.0% were diagnosed antenatally. Where a congenital anomaly was diagnosed antenatally, 59.8% of these resulted in a live birth. Where a baby was diagnosed with a congenital anomaly postnatally, 98.2% of these were diagnosed following a live birth.

Of the 13,306 babies with a confirmed or probable congenital anomaly reported to NCARDRS, 633 died in their first year, giving an infant mortality rate of 10.3 per 10,000 live births. Of all the deaths associated with a congenital anomaly, congenital heart anomalies were most frequently identified in 51.8% of reported infant deaths, followed by chromosomal anomalies 22.7% and digestive system 18.3% anomalies

Data recorded in 2019 shows that the prevalence of genetic congenital anomalies increased with maternal age; the prevalence of these anomalies was around 9 times higher in older mothers (women aged 40 years and over) compared with younger mothers (women aged less than 20 years).

¹ Data downloaded August 2021

Data on Down's syndrome, Edwards' syndrome and Patau's syndrome (full trisomies) are presented for England for 2019. The prevalence per 10,000 total births for Down's syndrome was 25.4 (95% CI:24.1-26.6), or one in 394 total births, 6.9 (95% CI:6.2-7.6), or one in 1,449 for Edwards' syndrome and 2.5 (95% CI:2.1-2.9), or one in 4,000 total births for Patau's syndrome respectively.

Introduction

This report is the National Congenital Anomaly and Rare Disease Registration Service's (NCARDRS) fifth report on congenital anomalies and the second report describing national data for England. It describes the number of babies delivered between 1 January and 31 December 2019 in England with one or more congenital anomalies.

Readers who are interested in congenital anomalies prior to 2019 are directed to our [previous reports](#) on data from 2015 to 2018 which cite relevant sources of information for historical data collected before the inception of NCARDRS and give details of which regions were included in each report.

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 and they first reported in 2018.

National coverage of congenital anomaly reporting has only been possible since 2018. While the data in this report refers to babies born between January and December 2019, most of this data were registered and completed in 2020.

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 researchers and those seeking detailed information about congenital anomaly prevalence in England.

This annual report will also be of interest to healthcare professionals involved in the direct care of patients, patient groups and third-sector organisations.

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, ensures consistency and standardisation across the country and has been key to the delivery of national coverage.

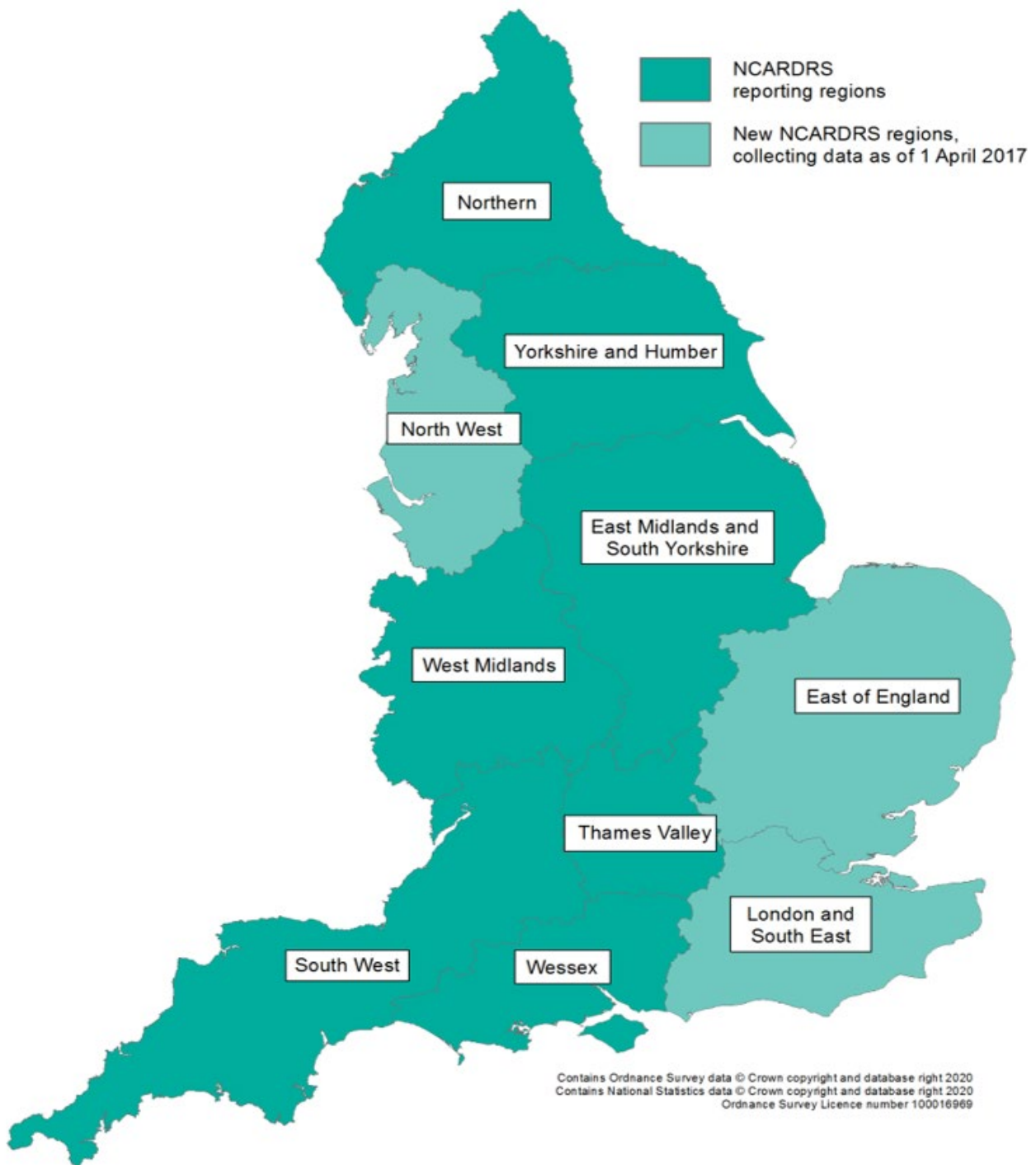
It is thanks to the dedication of these notifying healthcare professionals that this important and reliable information is available for clinicians, researchers, patients, and their families. More information about the data collection process can be found in the accompanying technical details document.

1.1 NCARDRS reporting regions in 2019

Figure 1 shows NCARDRS' 10 reporting regions. 7 regions have been collecting congenital anomaly data for some time, and 3 began congenital anomaly registration for births expected from 1 April 2017. The accompanying [technical details](#) document provides more information about geographical coverage of NCARDRS regions.

In 2015, congenital anomaly registration covered 21% births in England; the addition of 3 more regions for 2016 and 2017 took coverage to 49% of births. 2019 represents the second year of fully national congenital anomaly coverage for England.

Figure 1: Map of NCARDRS reporting regions England, 2019



1.1 Data in this report

Congenital anomalies are defined as being present at delivery, likely originating before birth, and include structural, chromosomal and genetic anomalies. Data are collected in accordance with definitions and guidelines of the European Surveillance of Congenital Anomalies (EUROCAT) and the World Health Organization’s Collaborating Centre for the Surveillance of Congenital Anomalies at the University of Ulster. Congenital anomalies are coded using the International Classification of Disease version 10 (ICD-10) with British Paediatric Association

(BPA) extension, which gives supplementary one-digit extensions to ICD-10 codes to allow greater specificity of coding. For more information about data collection, definitions and coding see the [technical details](#) 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 of comparable data are required to consider trend analysis, and this data are not available yet for England.
- data are not directly comparable as regional coverage increased in 2016 and in 2018, and ascertainment is increasing annually because of improved data collection
- comparing year on year data could lead to unreliable conclusions based on small numbers

This 2019 report is organised in 4 further chapters covering information about:

- prevalence of congenital anomalies (chapter 2)
- timing of diagnosis and outcome (chapter 3)
- important 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 shows 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 in 2019, diagnosed with Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13). This continues the longitudinal reporting that was conducted by [National Down Syndrome Cytogenetic Register \(NDSCR\)](#). These conditions are the only viable aneuploidies (wrong number of chromosomes) of the autosomes (non-sex chromosomes) and they are sufficiently common and serious to be included as part of routine antenatal screening in the [NHS Fetal Anomaly Screening Programme \(FASP\)](#).

A separate summary, highlighting key messages about the prevalence of congenital anomalies, accompanies this report. A [technical details](#) 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.

Data source update for 2019 births

Since publication of the report on 2018 births, there have been additions to the data sources for the registration of babies with congenital anomalies for the period covered in this report including the expansion of the anomalies ascertained using routine hospital activity datasets (Hospital Episode Statistics, HES) and validated according to a methodology developed by NCARDRS. In 2018, babies recorded in HES with polydactyly (ICD10 codes: Q69.0, Q69.9), congenital cataract (ICD10 code: Q12.0), hypospadias (ICD10 code: Q54*) and talipes equinovarus (ICD10 codes: Q66.0, Q66.8) alongside an appropriate procedure (OPCS) code were registered by NCARDRS in an automated process. For babies born in 2019, this list was extended to include choanal atresia (ICD10 code: Q30.0), atresia of oesophagus with tracheo-oesophageal fistula (ICD10 code: Q39.1), accessory kidney (ICD10 code: Q63.0) and congenital posterior urethral valves (ICD10 code: Q64.2) when occurring with a relevant and specific procedure code.

This development sits alongside national data extracts for neonatal data systems and cytogenetic and biochemical data extracts from every laboratory in the country along with local and regional sources of information.

Chapter 2: Prevalence of congenital anomalies



Total birth prevalence was 216.4 per 10,000 births, reflecting one baby diagnosed with a congenital anomaly for every 46 births in 2019.

Regional variation in prevalence likely reflects differences in ascertainment and the establishment of reporting in new regions.

Most babies with a congenital anomaly (73.4%) in 2019 were born alive. One in 63 live births had a congenital anomaly.

2.1 Total birth prevalence

Table 1 shows that a total of 13,306 babies with one or more congenital anomalies were notified to NCARDRS in 2019 out of 614,952 total births (live births and stillbirths) in England. This gives an overall **birth prevalence** of congenital anomalies of 216.4 per 10,000 total births (95% CI: 212.7-220.1). This reflects one baby diagnosed with a congenital anomaly for every 46 births (**live births** and **stillbirths**).

Figure 2a and Table 2 shows that the **birth prevalence** (the number of babies diagnosed with at least one congenital anomaly per 10,000 births) varied by NCARDRS region.

Prevalence was highest in regions with long-established registers (Northern and South West) and lowest in East of England (reporting its second year of data) and in East Midlands and South Yorkshire (EMSY).

Prevalence in the North West region – also reporting its second year of data collection – is significantly higher than the national prevalence and consistent with most existing regions. This reflects increasing ascertainment in a region that has been reporting only since 2018.

NCARDRS has worked with the **NHS Fetal Anomaly Screening Programme (FASP)** since 2015 in a partnership auditing detection rates for chromosomal, severe cardiac and abdominal wall conditions, along with spina bifida, lethal skeletal dysplasia, Cleft lip +/- palate anencephaly, bilateral renal agenesis and congenital diaphragmatic hernia. As part of this work, these conditions are subject to more intensive reporting, resulting in higher data quality and

ascertainment. While there is regional variation in the overall prevalence of congenital anomalies, Figure 2b shows that prevalence across NCARDRS regions was more consistent when regional prevalence is restricted to babies with one of the 11 FASP conditions. The prevalence in West Midlands and the North West was higher than the NCARDRS average.

Geographical variation in congenital anomaly prevalence is most likely due to differences in **case ascertainment** due to the infancy of the service and the regional variation in the length of time registration has been established. However there are other reasons which could influence the results presented such as disease clustering, exposure to **teratogens**, demographic variation including maternal age, deprivation profiles between regions and the composition of the local population.

As NCARDRS accumulates more data at a national level over time, and registration in newer regions matures, greater insights will be gained into underlying population characteristics contributing to regional variation, as well as the ability to analyse associations with lifestyle and environmental factors which may potentially be modifiable.

Figure 2a: The number of babies with at least one congenital anomaly per 10,000 total births (prevalence) and 95% confidence intervals for NCARDRS regions compared to England, 2019

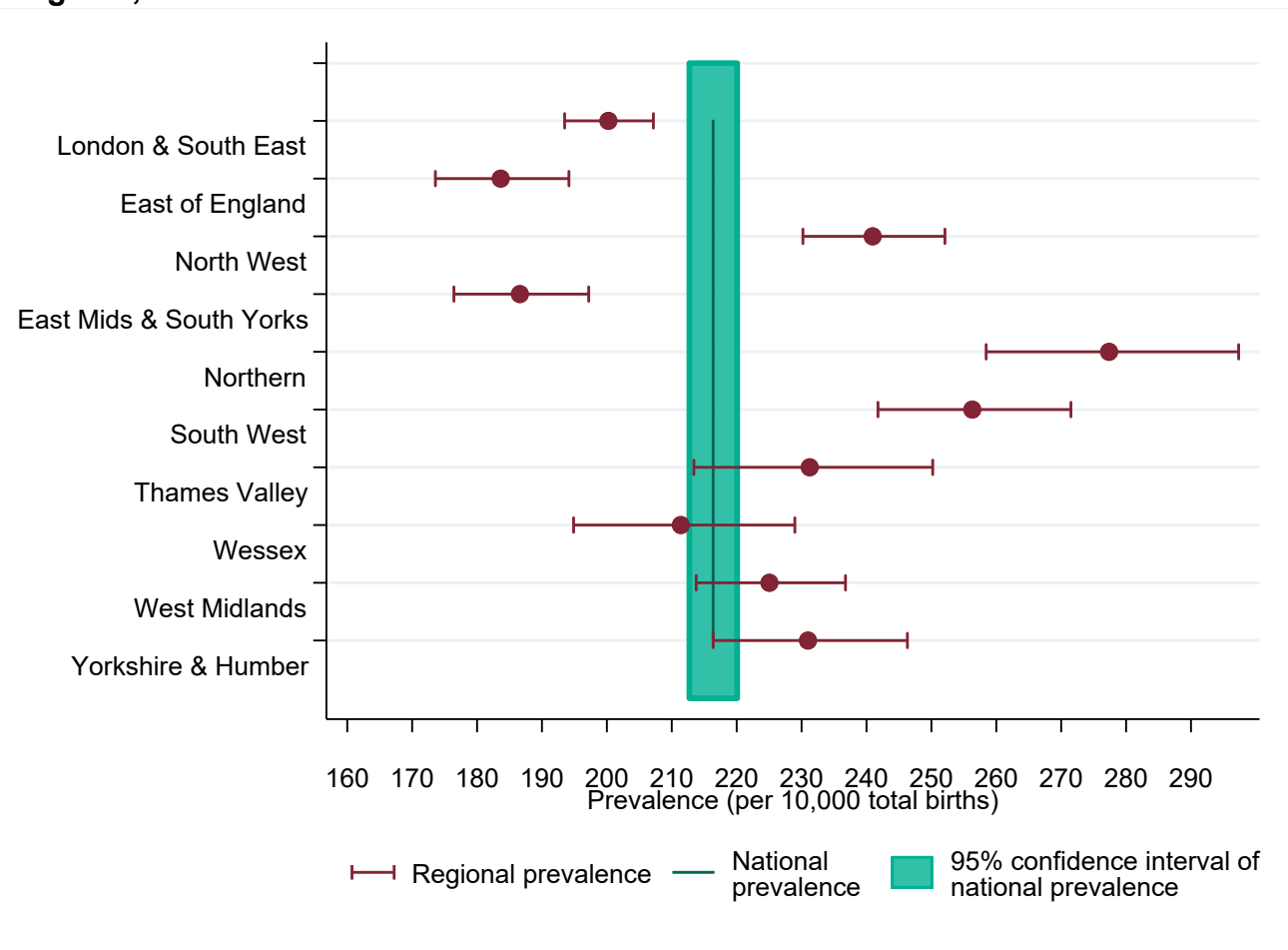
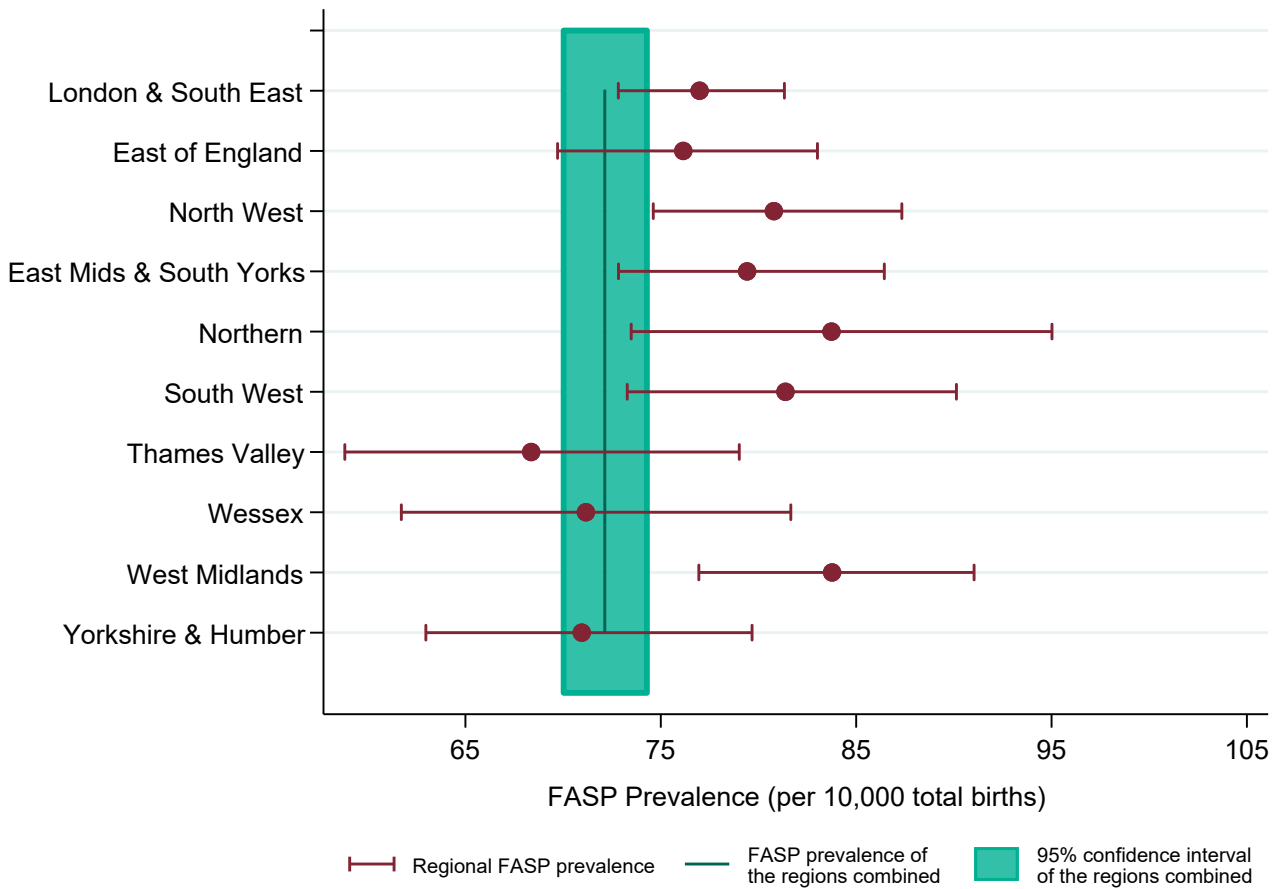


Figure 2b: The number of babies with at least one congenital anomaly that is a FASP condition per 10,000 total births (prevalence) and 95% confidence intervals, for NCARDRS regions compared to England, 2019



Figures 3a and 3b show the prevalence of the 12 major congenital anomaly subgroups for:

- a) all babies
- b) those that were live born

It is important to note that in Figures 3a, 3b and 3c, babies with multiple anomalies are counted in each applicable bar on the chart. A baby with a congenital heart, limb and chromosomal condition would be represented on 3 different bars. In these figures, conditions categorised as “Genetic” include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-genetic conditions include babies with one 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 “non-genetic” anomalies are of genetic origin.

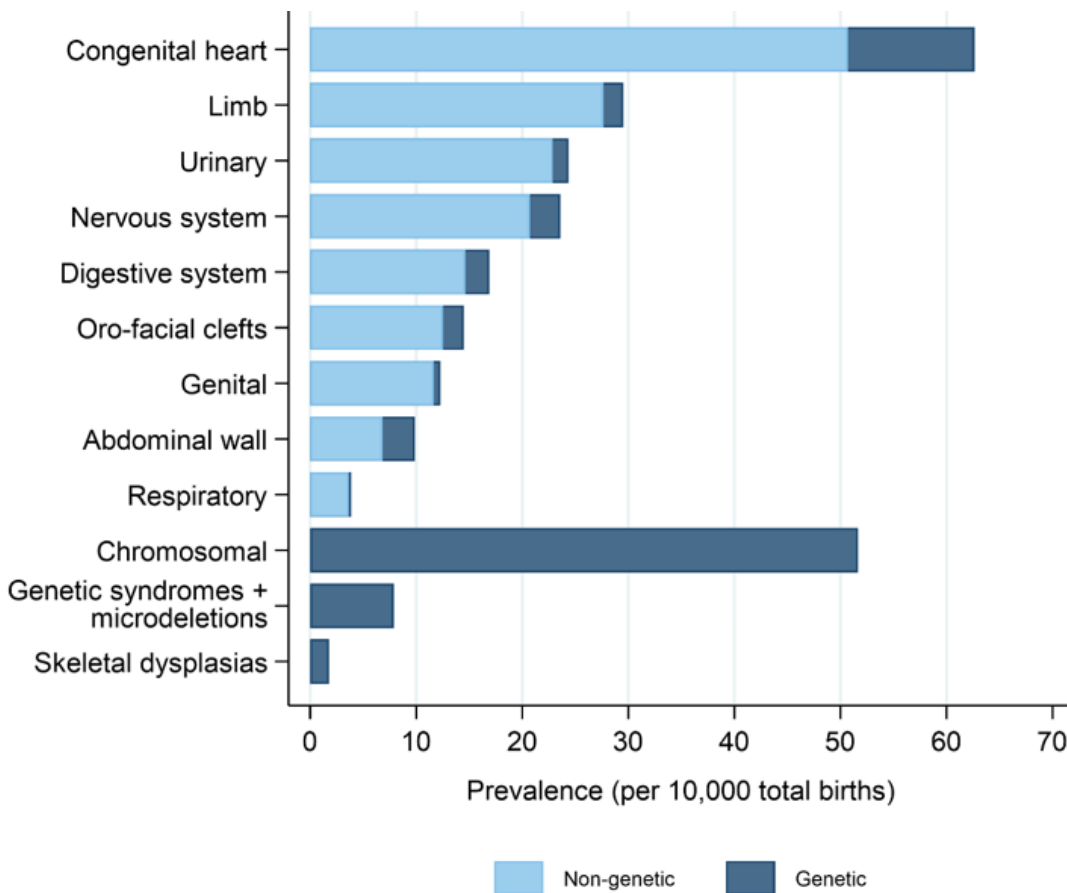
Figure 3a and Table 1 show that the prevalence for total births in 2019 was highest in the congenital heart anomalies subgroup (62.6 per 10,000, 95% Confidence Intervals (CI) 60.7-64.6), followed by those that are chromosomal in origin (51.7 per 10,000, 95% CI 49.9-53.5). Figure 3b and Table 3 show that the prevalence for those who are live born was also highest in

congenital heart anomalies (51.7 per 10,000, 95% CI 49.9-53.5), followed by the limb anomalies subgroup (26.0 per 10,000, 95% CI 24.8-27.3) and then those that are chromosomal in origin (23.1 per 10,000, 95% CI 22.0-24.4). Not all babies undergo genetic testing and not all babies have the same genetic tests, therefore ‘non-genetic’ 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 most subgroups apart from chromosomal and nervous system anomalies. The prevalence in these 2 groups is lower for those live born than for other pregnancy outcomes, reflecting the severity of these conditions. Further detail stratified by specific congenital anomaly, including the number of cases reported, is available in Tables 1 and 3.

More than a third (35.7%) of babies had more than one registered anomaly in 2019. Babies with more than one type of anomaly are counted in each applicable bar in Figures 3a and b. The most frequently detected conditions are congenital heart anomalies and chromosomal anomalies.

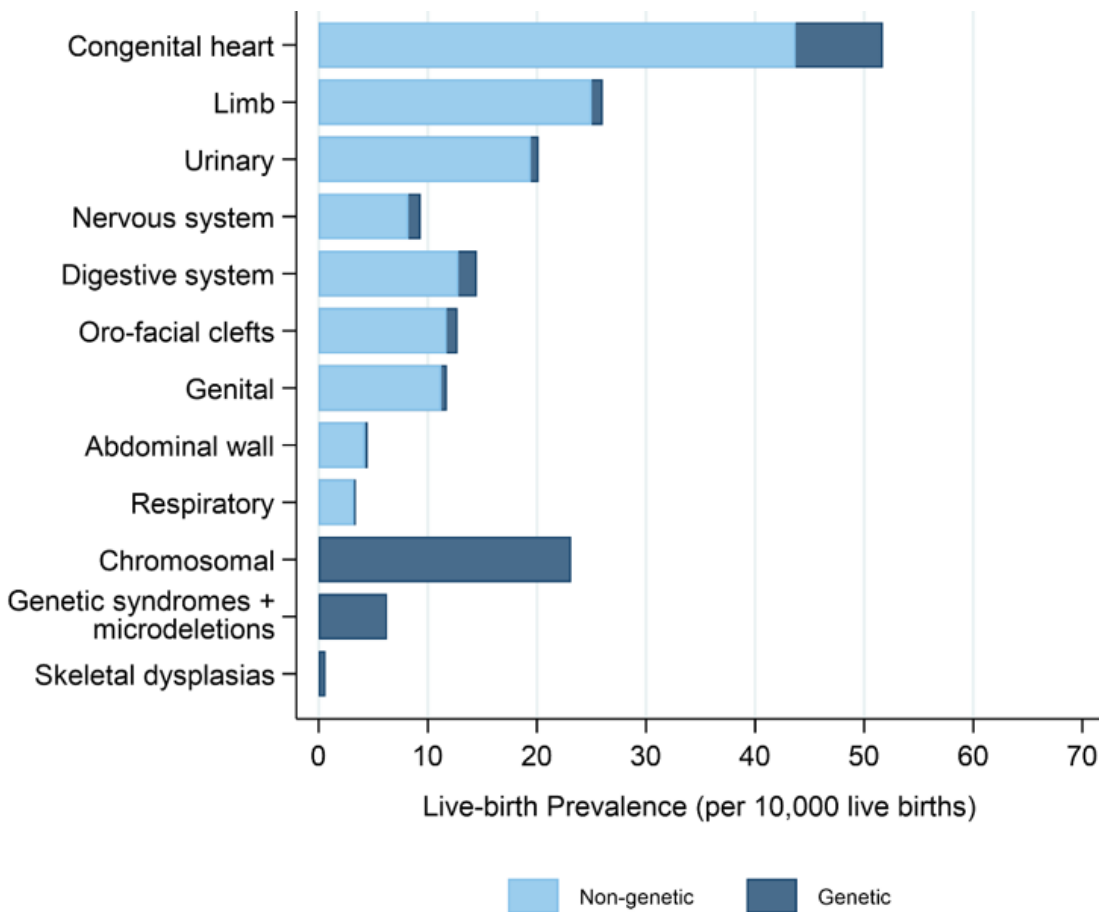
Figure 3a: Total birth prevalence: The number² of babies diagnosed with each congenital anomaly per 10,000 total births by congenital anomaly subgroup³ in England, 2019



² Babies with multiple anomalies will be counted in each applicable bar in figures 3a, b and c.

³ Conditions categorised as “Genetic” include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-genetic conditions include babies with one 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 3b: Live birth prevalence: The number of babies⁴ diagnosed with each congenital anomaly per 10,000 live births, by congenital anomaly subgroup⁵ in England, 2019



2.2 Impact of the addition of 3 new regions on congenital anomaly prevalence

NCARDRS achieved national coverage in 2018 when the 3 ‘new’ regions began reporting alongside the ‘existing’ regions that had been collecting data before the formation of NCARDRS. Figure 3c shows the variation in the prevalence of different anomaly groups according to the length of time registration has been established. The prevalence of congenital heart anomalies in existing regions (67.4 per 10,000, 95% CI 64.5-70.4) is still significantly higher than in new regions (58.0 per 10,000, 95% CI 55.4-60.7), reflecting developing ascertainment in these new regions.

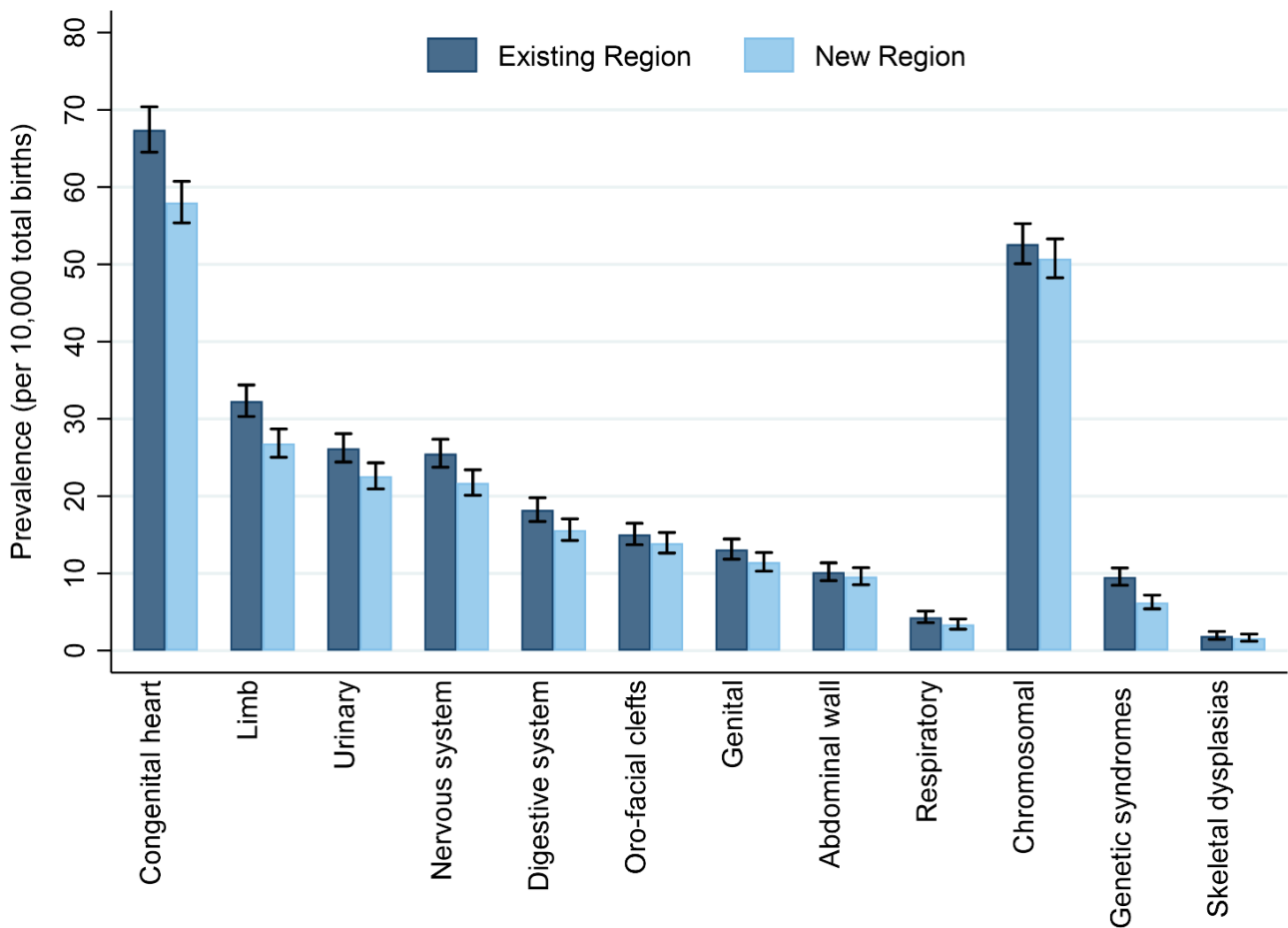
Figure 3c also shows that the prevalence of urinary, limb, and genetic syndromes are also significantly lower in new regions compared to those with long-standing registration. These conditions are more frequently identified postnatally, compared to nervous system, abdominal

⁴ Babies with multiple anomalies will be counted in each applicable bar in figures 3a, b and c.

⁵ Conditions categorised as “genetic” include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-genetic conditions include babies with one 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.

wall, digestive system, oro-facial cleft, genital, respiratory, chromosomal, and skeletal dysplasia conditions, where the prevalence in new areas was consistent with the prevalence in existing areas. This reflects work with the FASP programme and demonstrates the impact of clinical engagement on data quality. As registration becomes embedded and ascertainment increases, differences in prevalence because of data collection will dissipate, revealing true regional differences, if they exist.

Figure 3c: A comparison of total birth prevalence (the number⁶ of babies diagnosed with each anomaly per 10,000 total births) by congenital anomaly subgroup⁷ in the existing regions and new reporting regions in England, 2019



2.3 Pregnancy outcome

Figure 4 shows that of the 13,306 babies with one or more congenital anomalies, the majority (9,770, 73.4%) resulted in a live birth.

⁶ Babies with multiple anomalies will be counted in each applicable bar in figures 3a, b and c.

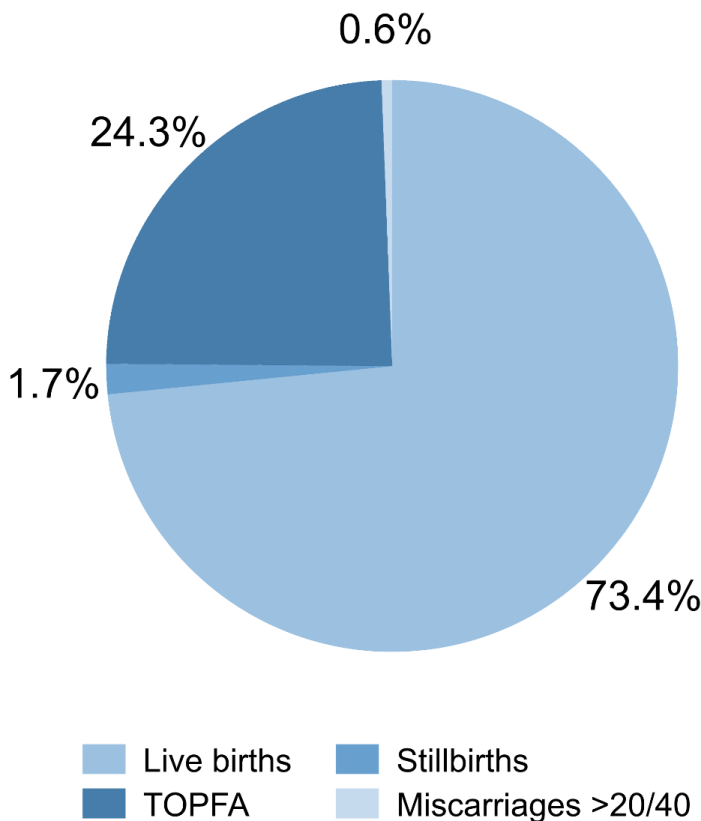
⁷ Conditions categorised as "genetic" include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-genetic conditions include babies with one or more congenital anomaly with no identified anomalies that are chromosomal, skeletal dysplasias, genetic syndromes or microdeletions. Not all babies undergo genetic testing and it is likely some of these are of genetic origin.

Of the remaining 3,536 babies, 226 (1.7%) were stillbirths (24+ weeks gestation), 80 (0.6%) were late miscarriages (20 to 23 weeks gestation) and 3,230 (24.3%) were terminations of pregnancy. This includes **terminations of pregnancy for fetal anomaly (TOPFA)** as well as terminations of pregnancy for other reasons, for example social reasons or maternal complications, 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 practices around termination. The data presented relate to both antenatal and postnatal diagnoses.

The timing of diagnosis is explored in more detail in chapter 3.

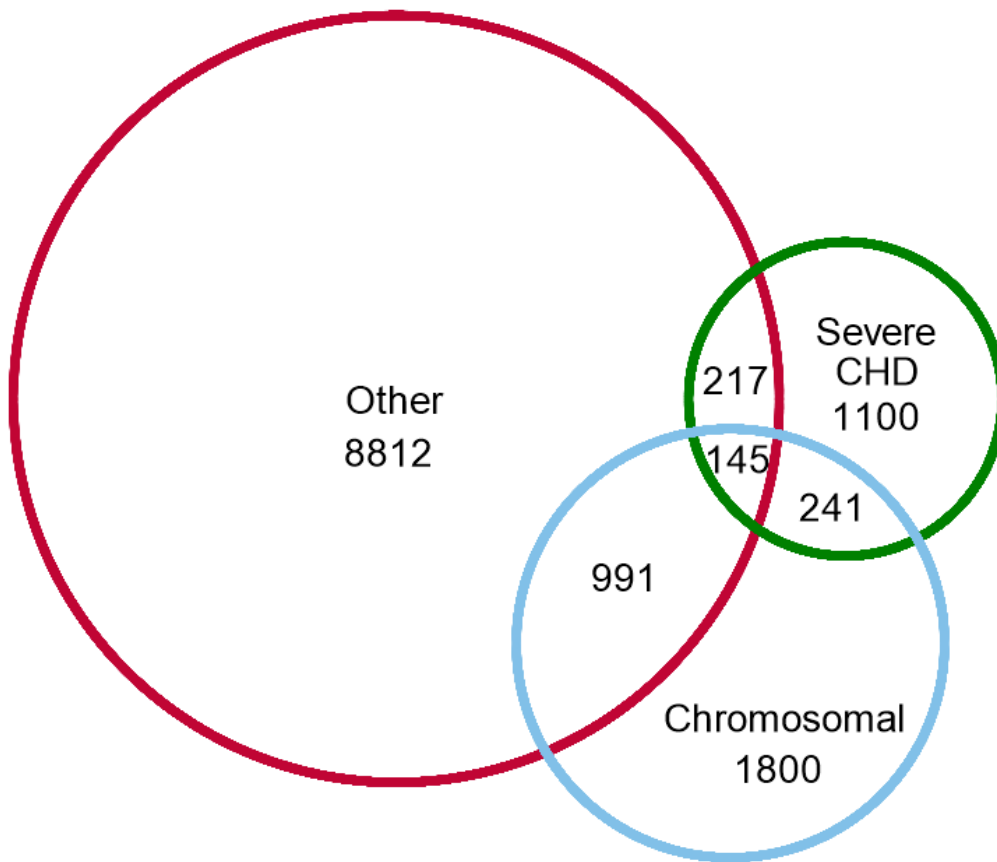
Figure 4: Percentage of babies with one or more reported congenital anomalies by outcome of pregnancy in England, 2019



2.4 Multiple anomalies

Figure 5 demonstrates the overlap of selected anomalies by presenting the frequency with which severe cardiac and chromosomal anomalies occur in conjunction with other conditions. Of the 1703 babies with **severe heart anomalies** in 2019 births; 1100 (65.0%) had no other type of anomaly, 362 (21.3%) also had another structural anomaly, which could have included a less severe cardiac anomaly, 363 (21.3%) had a chromosomal anomaly as well as their severe cardiac condition and 145 (8.5%) babies had both a chromosomal anomaly and another structural anomaly in addition to their severe cardiac anomaly.

Figure 5: Multiple anomalies: babies with severe congenital heart disease (CHD), chromosomal and/or other anomalies, in England, 2019



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 or stenosis
- hypoplastic left heart
- hypoplastic right heart
- coarctation of aorta
- total anomalous pulmonary venous return

(Ref: EUROCAT (2013))

Chapter 3: Timing of diagnosis and outcome



68.0% of pregnancies with a congenital anomaly were detected antenatally, where timing of diagnosis was known.

Abdominal wall (95.7%) and skeletal dysplasia (93.6%) anomalies are most likely to be detected antenatally.

Where a baby was diagnosed with a congenital anomaly postnatally, 98.2% of these were diagnosed following a live birth.

3.1 Timing of diagnosis and outcome

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.

NCARDRS recognises that women make a personal informed decision whether to have fetal anomaly screening or not. Early diagnosis of a 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 **palliative care** may be required soon after birth.

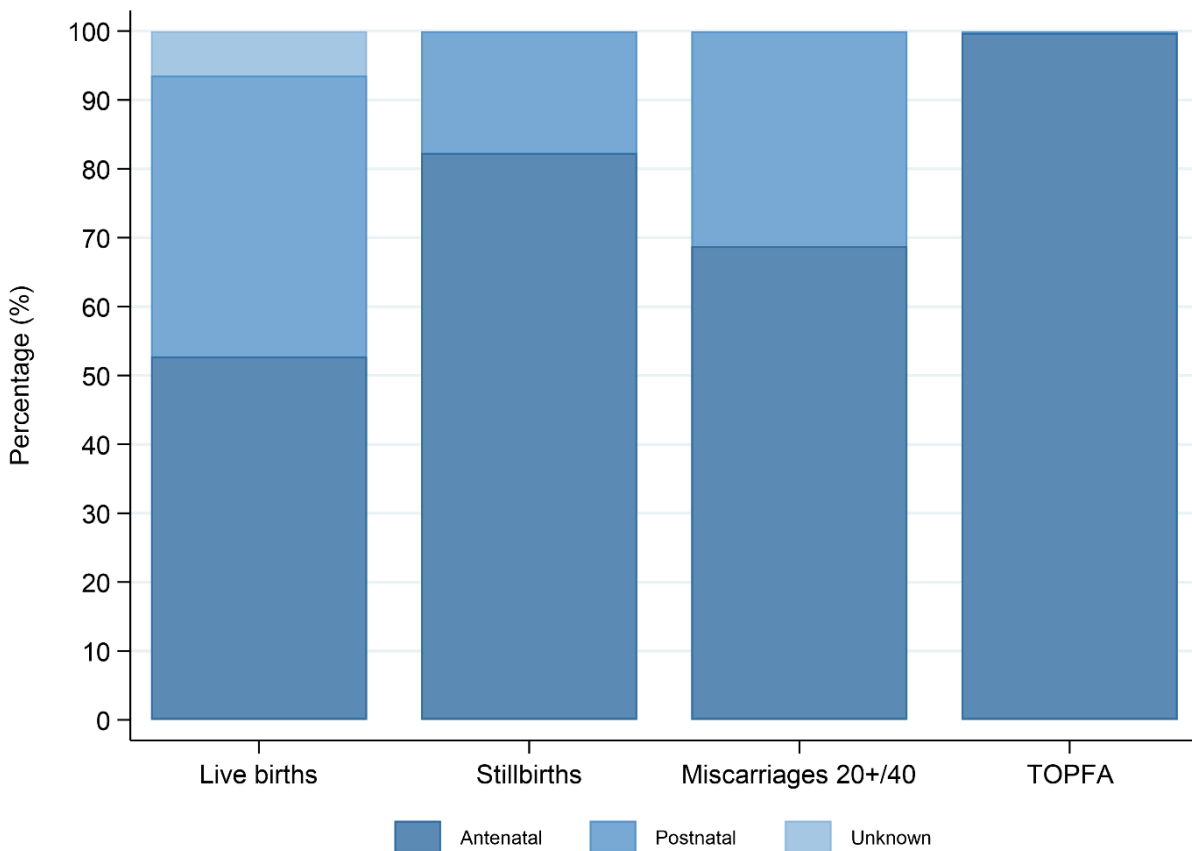
In this chapter, the timing of diagnosis relates to the first anomaly diagnosed in a baby and so is designated at a case-level. Other anomalies in a baby may be identified at a later stage, and where there are multiple anomalies, the timing of diagnosis of all these subsequently diagnosed anomalies will be when the baby was first suspected as having a congenital anomaly. For example, in a baby with a congenital heart anomaly that was detected antenatally and a digestive anomaly detected postnatally, the timing of diagnosis for the baby (and for both conditions) would be antenatal.

The timing of first diagnosis of a congenital anomaly was known for 12,674 (95.0%) babies. Where the timing of diagnosis was known, 68.0% of babies were diagnosed antenatally in 2019. Table 4 shows that of the 8,616 babies where a congenital anomaly was diagnosed antenatally,

5,154 (59.8%) were born alive and 3,221 (37.4%) resulted in termination of pregnancy for fetal anomaly (TOPFA). It also shows that where a congenital anomaly was first diagnosed in a baby postnatally, 98.2% were diagnosed following a live birth.

Figure 6 shows that where a baby was live born with a congenital anomaly, an anomaly was detected antenatally in 52.8% 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 82.3% of cases.

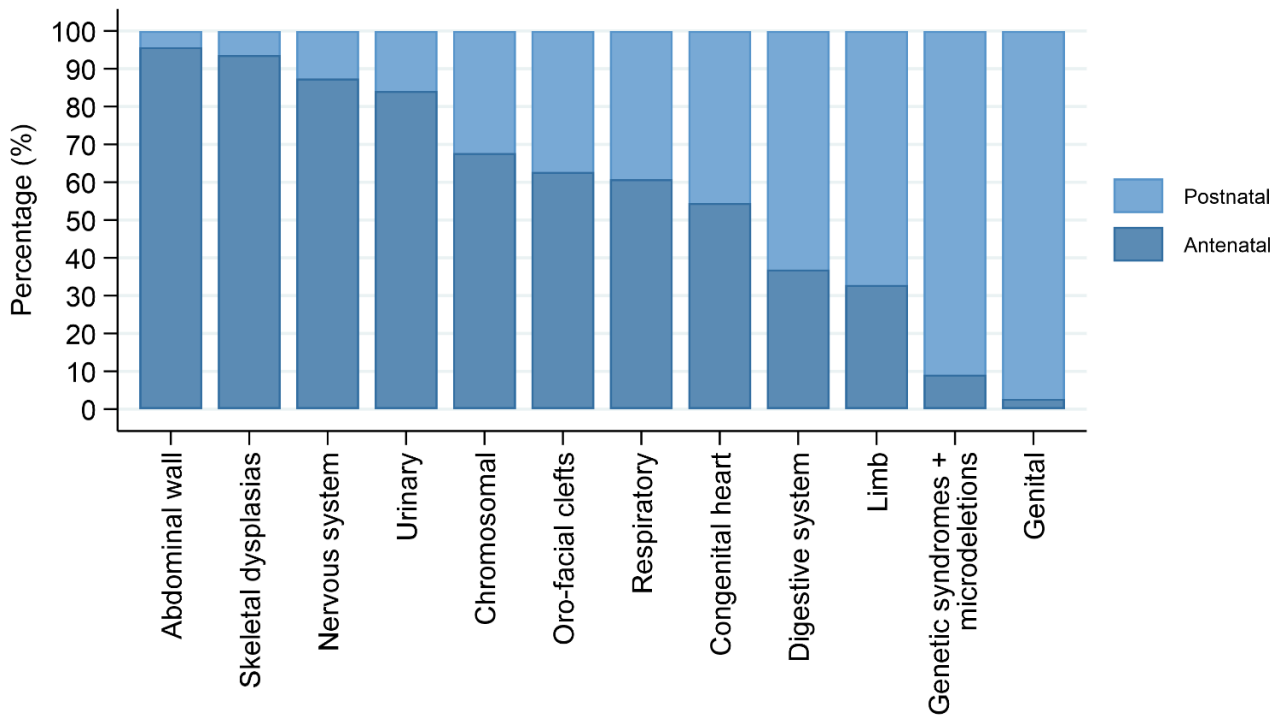
Figure 6: Timing of first diagnosis⁸ and pregnancy outcome (percentage) in England, 2019



Some types of congenital anomalies are more likely to be diagnosed antenatally than others. Figure 7 shows that babies with abdominal wall, skeletal dysplasia, and nervous system anomalies are most frequently identified antenatally. Babies with genital anomalies are unlikely to be identified antenatally. It should be noted that individual anomalies within these subgroups may not follow these patterns, and also that diagnosis refers to the first suspicion of any anomaly in a baby, and babies with more than one anomaly will be represented in each applicable bar. A more detailed breakdown by specific congenital anomaly, including the number of babies reported, is available in Table 5.

⁸ Identification of any congenital anomaly-if there are multiple anomalies than this will be the first anomaly detected.

Figure 7: Timing of diagnosis⁹ by congenital anomaly subgroup – based on individual anomaly (percentage) in England, 2019



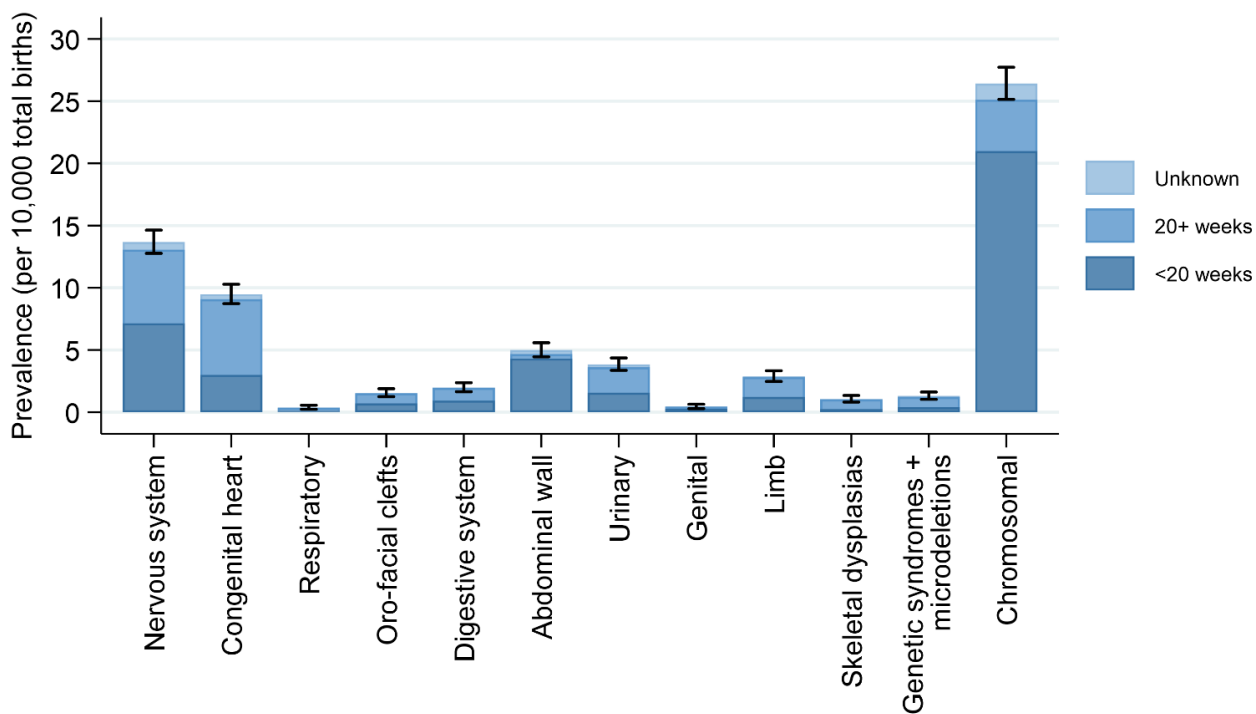
The overall rate of TOPFA for England was 52.5 per 10,000 total births. Table 6 shows that the rate of TOPFA at over 20 weeks gestation was 17.3 per 10,000 total births.

Figure 8 shows that the highest rate of TOPFA was associated with chromosomal anomalies (26.4 per 10,000 births) followed by nervous system conditions (13.7 per 10,000 births). In most 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. For 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 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.

It is important to note that in Figure 8 babies with multiple anomalies will be represented in each applicable bar. For example, a baby with an oro-facial cleft or limb condition may also have had an associated chromosomal or cardiac condition. More information about the anomalies included in these sub-groups is available in the **technical details** document.

⁹ Identification of any congenital anomaly-if there are multiple anomalies than this will be the first anomaly detected.

Figure 8: Prevalence (per 10,000 total births) and 95% confidence intervals of termination of pregnancy with fetal anomaly (TOPFA) in England, 2019



Chapter 4: Important public health indicators



Congenital anomalies are a leading cause of infant and perinatal mortality.

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

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

4.1 Perinatal and infant mortality

There were 633 infant deaths among babies with one or more congenital anomalies in the 612,606 live births in 2019, giving an infant mortality rate of 10.3 per 10,000 live births. Table 8 shows that the rate of perinatal mortality was 7.7 per 10,000 births.

Mortality definitions

Infant mortality refers to deaths under one year of age.

Perinatal mortality refers to 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; congenital heart anomalies (2.6-perinatal, 5.4-infant per 10,000 births respectively) followed by chromosomal (2.2-perinatal, 2.4-infant per 10,000 births respectively).

The data presented here should be viewed with some caution, as babies with more than one 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.

Figure 9a: Perinatal mortality (stillbirths and deaths under 7 days of age) by congenital anomaly subgroup in England, 2019

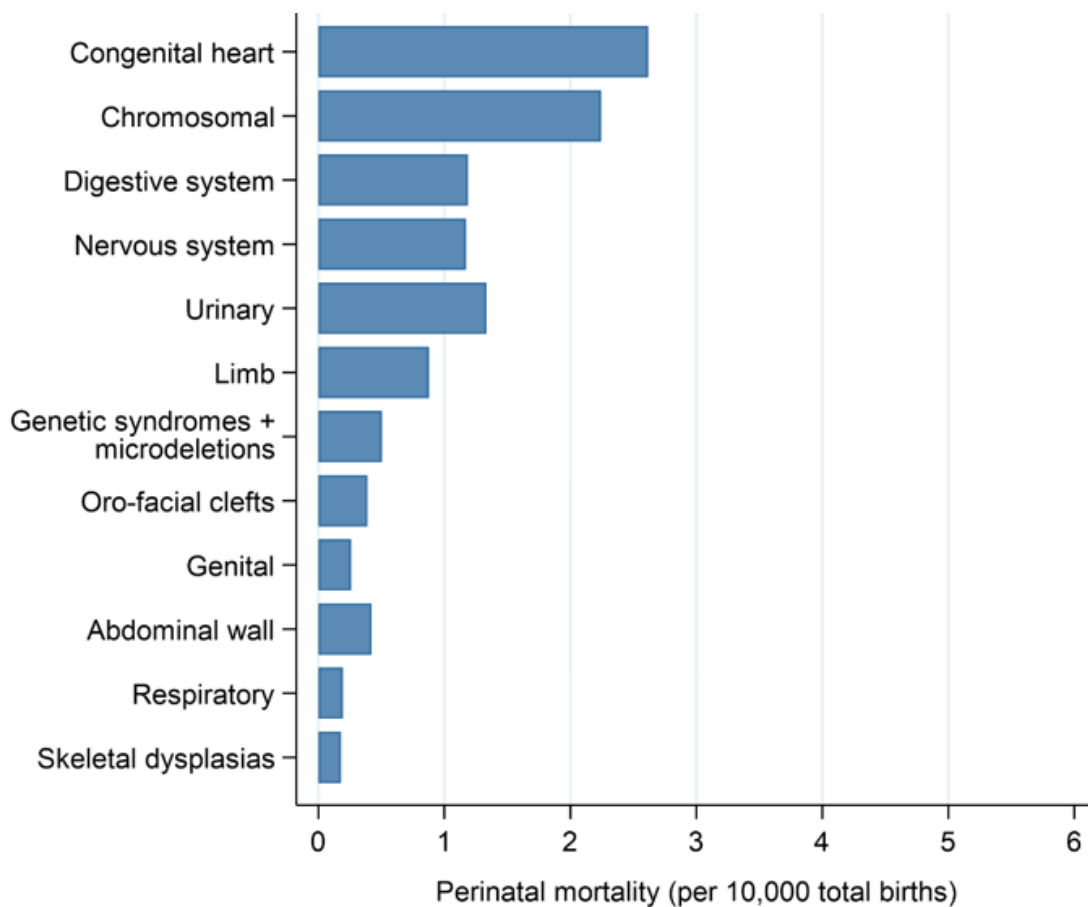
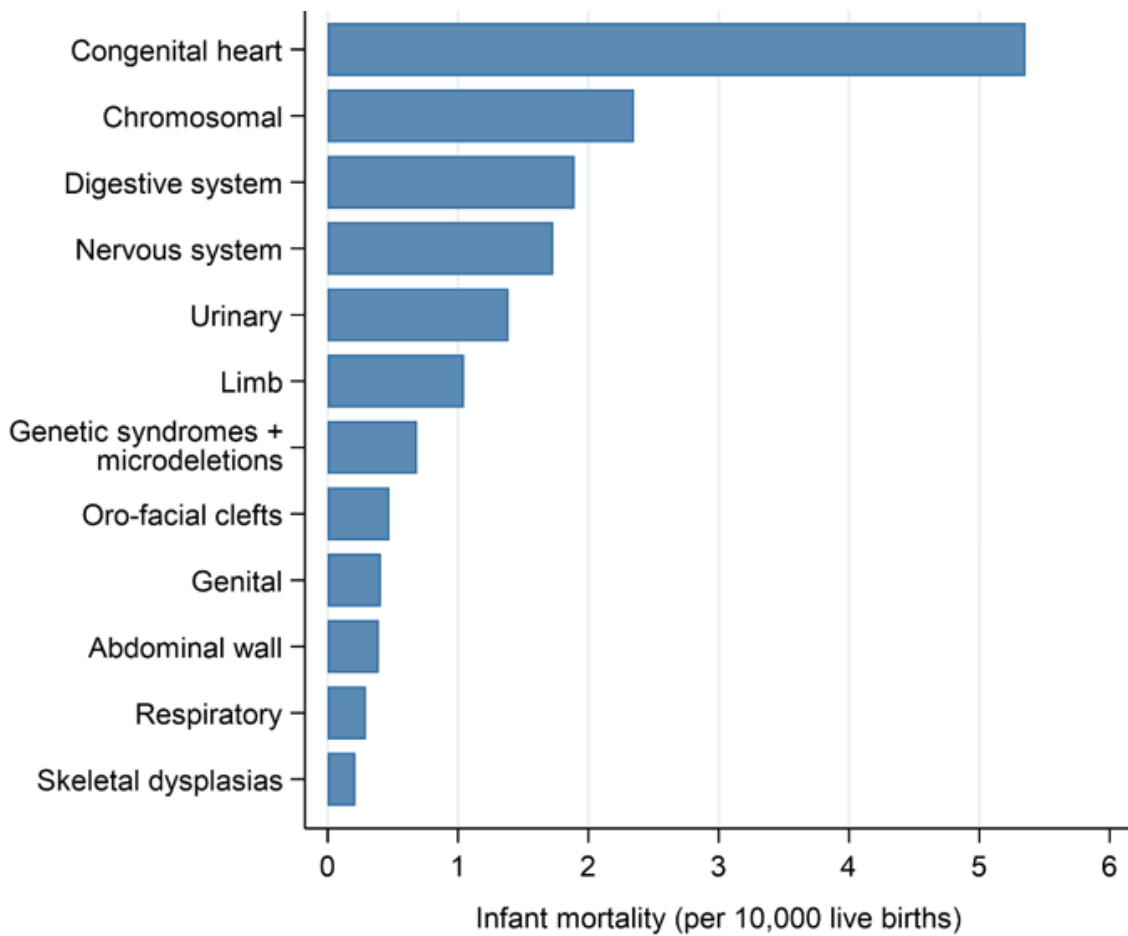


Figure 9b: Infant mortality (deaths under one year of age) by congenital anomaly subgroup in England, 2019



Child and infant mortality data from the ONS for 2019 shows that congenital anomalies were the most common cause of death in the **post neonatal period**, accounting for 39.3% of deaths. Congenital anomalies were also listed as the cause of 32.3% of **infant deaths** and 24.0% of **perinatal deaths**, the second highest cause in both categories after prematurity. While the data within this report should be viewed in a wider context of perinatal and infant mortality, congenital anomalies, particularly congenital heart, chromosomal and digestive system anomalies, are a common factor in infant and perinatal deaths.

4.2 Maternal age

There was a U-shaped relationship with maternal age. Table 9 shows that mothers under 20 years had a significantly higher rate of congenital anomalies compared to those aged between 30 and 34 years. The birth prevalence of all anomalies was similar in mothers aged between 30 and 34 years at delivery compared to the prevalence in those aged between 25 and 29 years (195.9 and 195.3 per 10,000 total births respectively). Compared to these groups, the birth prevalence was significantly higher in mothers aged 35 to 39 years (243.7 per 10,000 total births) and those 40 years and over (399.3 per 10,000 total births).

The association between higher maternal age and certain genetic disorders, including Down's syndrome, is well established. Figure 10 shows that mothers aged 40 and over had a significantly higher prevalence of **genetic anomalies** compared to all other age groups. The rate of genetic congenital anomalies in women over 40 years (n=622) was almost 9 times higher (8.5 95% CI 6.3-11.6) relative to women under 20 years (n=41). Down's syndrome is the most common genetic anomaly (25.4 per 10,000 births) and is likely a primary factor in the higher rate in older age groups.

Figure 10 and Table 9 show that the rate of **non-genetic anomalies** in women aged under 20 years is significantly higher than the rate in women between 25 to 39 years. The increased rate in mothers under 20 years is primarily driven by the significantly higher prevalence of abdominal wall anomalies in women within this age group (24.0 per 10,000 births) compared to 5.4 per 10,000 births in women aged 30 to 34 years.

Gastroschisis, an abdominal wall anomaly, is known to be associated with lower maternal age (Baldacci and others 2020; Fillingham and Rankin 2008), and this relationship is demonstrated within Figure 11 as the prevalence among those under 20 is 20.4 per 10,000 births compared to 0.8 per 10,000 births in women aged between 35 and 39. There were no babies with gastroschisis recorded in women aged over 40 in England in 2019.

Figure 10: Prevalence (per 10,000 total births) and 95% confidence intervals of genetic and non-genetic congenital anomalies by maternal age in England, 2019

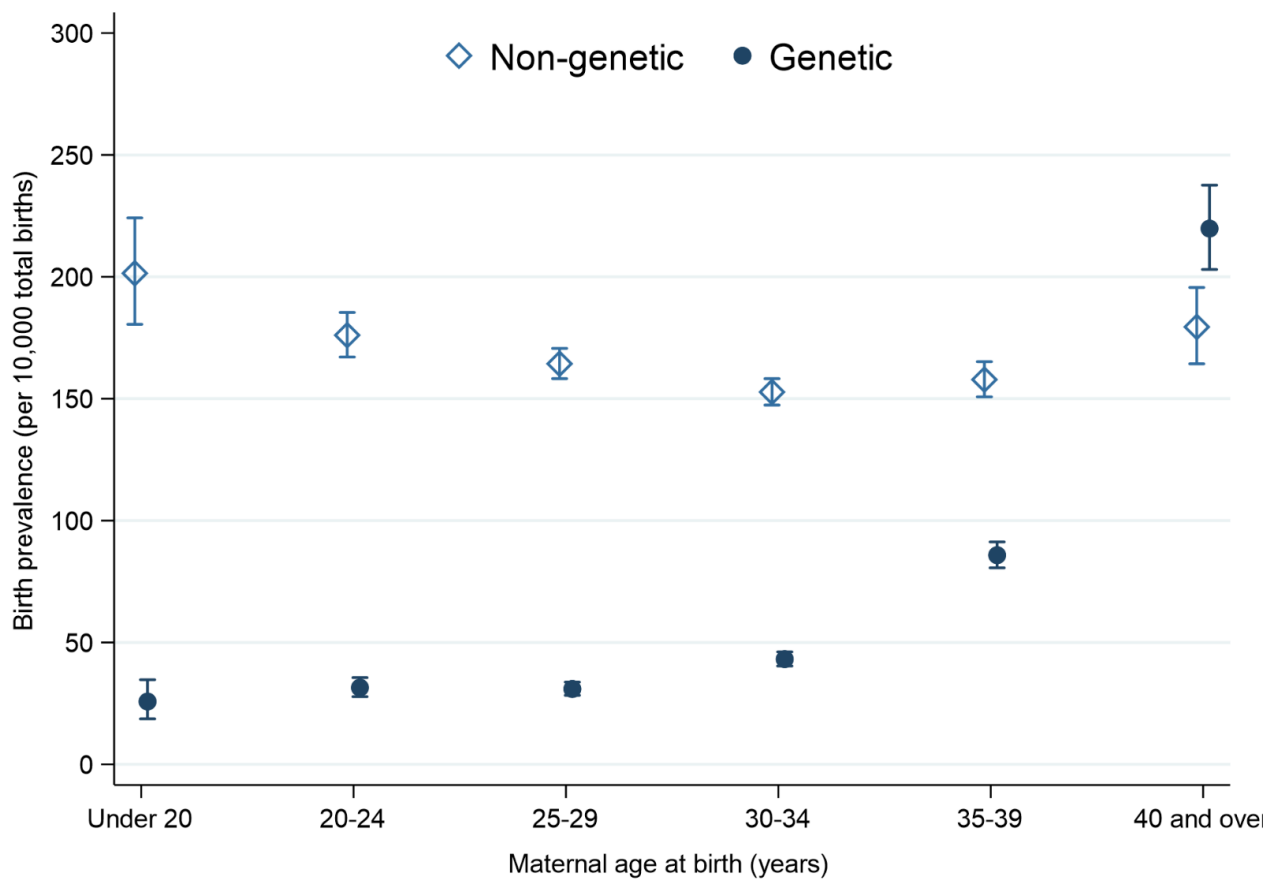
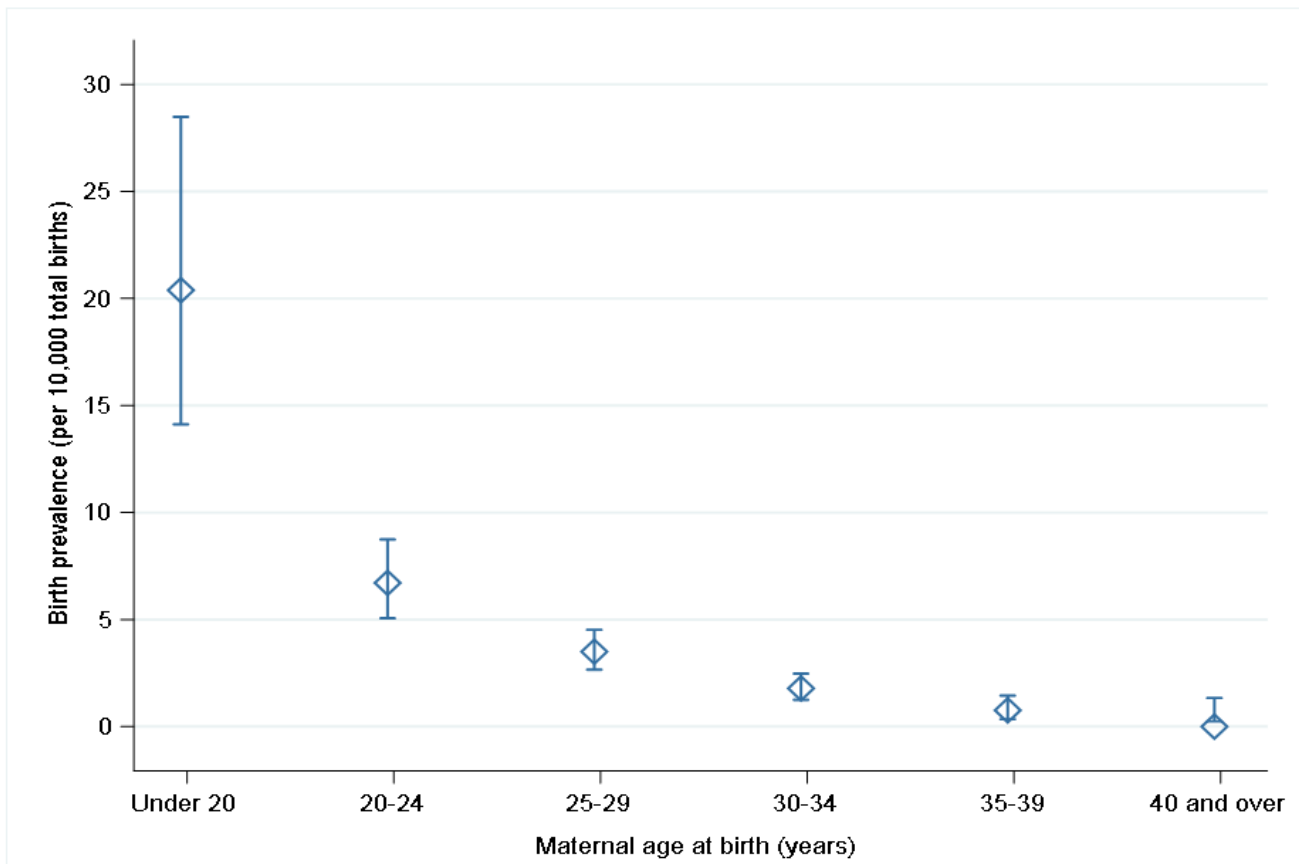
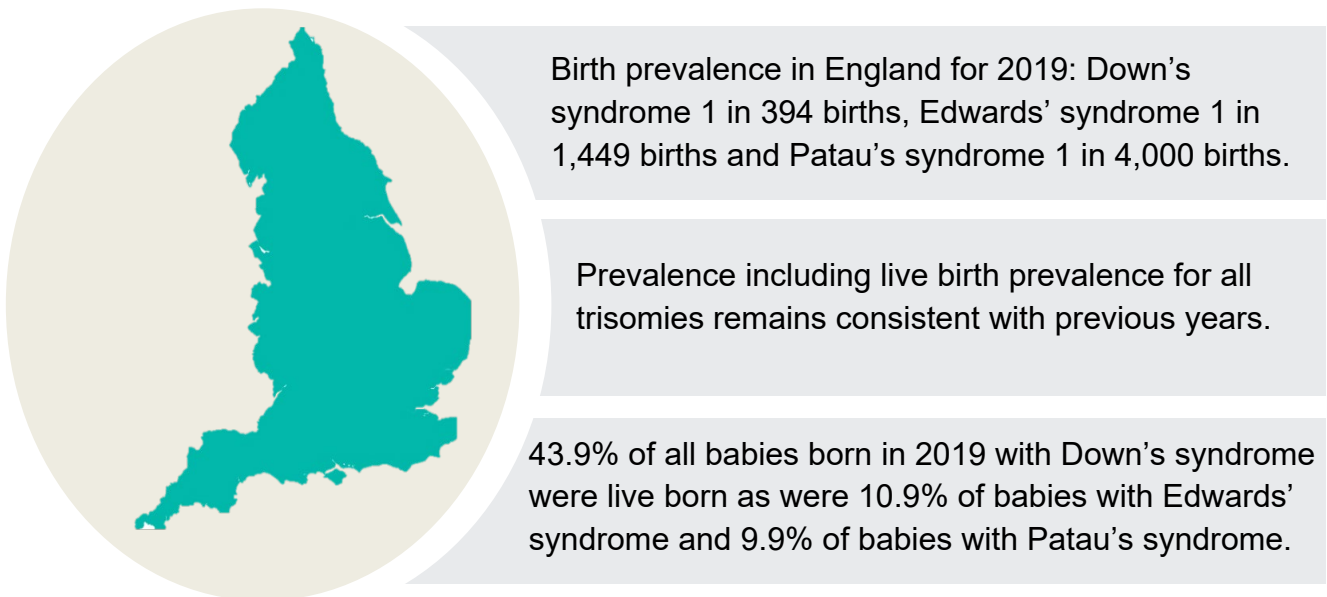


Figure 11: Prevalence (per 10,000 total births) and 95% confidence intervals of gastroschisis by maternal age in England, 2019



Chapter 5: Down's syndrome, Edwards' syndrome and Patau's syndrome



5.1 Diagnoses and prevalence of Down's syndrome, Edwards' syndrome and Patau's syndrome

Figure 12 shows that there were 1,559 babies with Down's syndrome, 423 babies with Edwards' syndrome and 152 babies with Patau's syndrome delivered in England in 2019. This represents a prevalence of 25.4 per 10,000 total births or one in every 394 births for Down's syndrome, 6.9 per 10,000 births or one in every 1,449 births for Edwards syndrome and 2.5 per 10,000 births or one in every 4,000 births for Patau's syndrome, figures which are consistent with those reported for 2018.

Table 13 shows that the live birth prevalence remains consistent with previous years' data, with 11.2 per 10,000 live births or one in 893 live births for Down's syndrome, 0.8 per 10,000 live births or one in 12,500 for Edwards' syndrome and 0.2 per 10,000 births, or one in 50,000 for Patau's syndrome respectively.

Trisomy definitions

Trisomy

Babies normally inherit 2 copies of each chromosome, one from their mother and one 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 one chromosome. This occurs randomly but is more common in older mothers.

Translocation trisomy

This is rarer and occurs when 2 different chromosomes are physically joined together, so are inherited as a single unit. One of the parents may carry 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. Babies with partial trisomies are not included in the data for chapter 5 as, depending on the size of the partial trisomy, the outcomes and timing of diagnosis may vary. This means that prevalence estimates for Down's syndrome, Edwards' syndrome and Patau's syndrome presented in this chapter vary slightly to those displayed in Table 1.

Figure 12: The number of babies with Down’s syndrome, Edwards’s syndrome and Patau’s syndrome born in England in 2019, and categorised by the timing of diagnosis

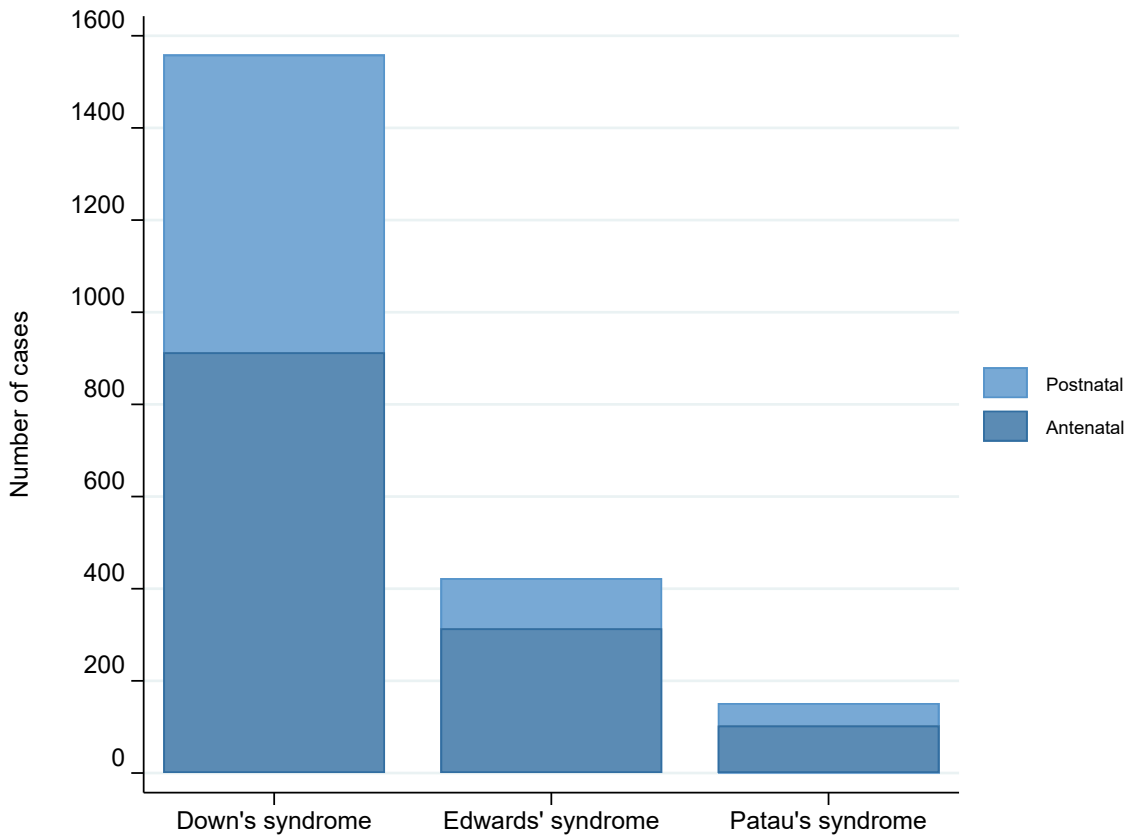


Figure 12 and Tables 10, 11 and 12 show that most babies with a trisomy were diagnosed **antenatally**; 58.6% of Down’s syndrome, 74.2% of Edwards’ syndrome and 67.8% of Patau’s syndrome diagnoses were antenatal. For pregnancies with a trisomy that were diagnosed antenatally, the TOPFA rate was broadly similar across all 3 conditions, at 88% for Down’s syndrome, 86.9% for Edwards’ syndrome and 86.4% for Patau’s syndrome.

Postnatal diagnoses include babies where a woman has chosen to decline antenatal tests, whether this is screening or diagnostic cytogenetic tests, but will also include testing performed following a miscarriage, TOPFA or stillbirth. In a proportion of postnatal diagnoses, the presence of a trisomy may have been clinically suspected due to a structural anomaly seen on ultrasound scan, for example a heart anomaly or a higher chance screening result, but the presence of the trisomy was not confirmed until after the baby was delivered.

Considering both antenatal and postnatal diagnoses for babies born in 2019, 43.9% with Down’s syndrome were live born as were 10.9% of babies with Edwards syndrome and 9.9% of babies with Patau’s syndrome.

Figure 13 shows that for both antenatal and postnatal diagnoses, in the majority a **full karyotype** was the most definitive test recorded, with **rapid aneuploidy testing** being the second most frequently recorded test method. However, this does not necessarily represent all completed tests as some babies will have received both antenatal and postnatal testing by multiple

methods but only one test is included for these purposes, prioritising antenatal over postnatal testing and karyotyping or microarray over rapid aneuploidy testing.

Figure 13: Timing of diagnosis and laboratory test method for babies born with Down’s syndrome, Edwards’ syndrome and Patau’s syndrome in 2019

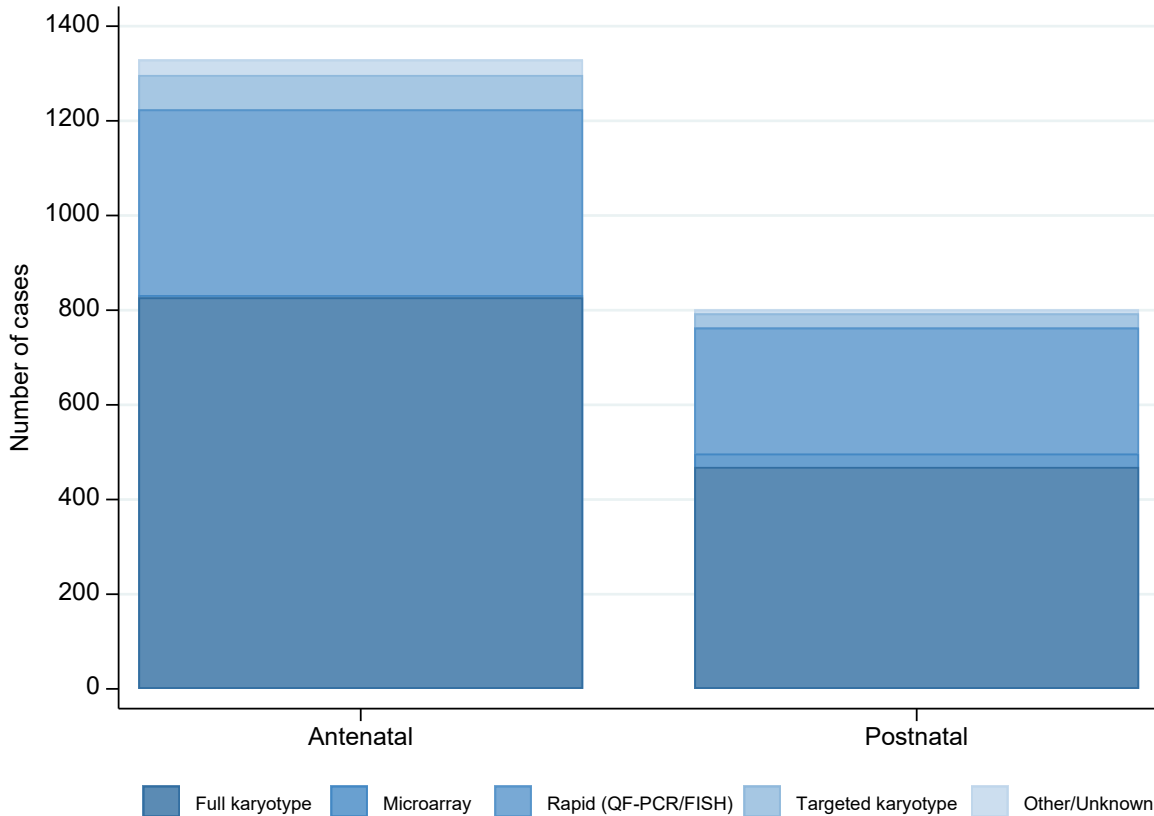
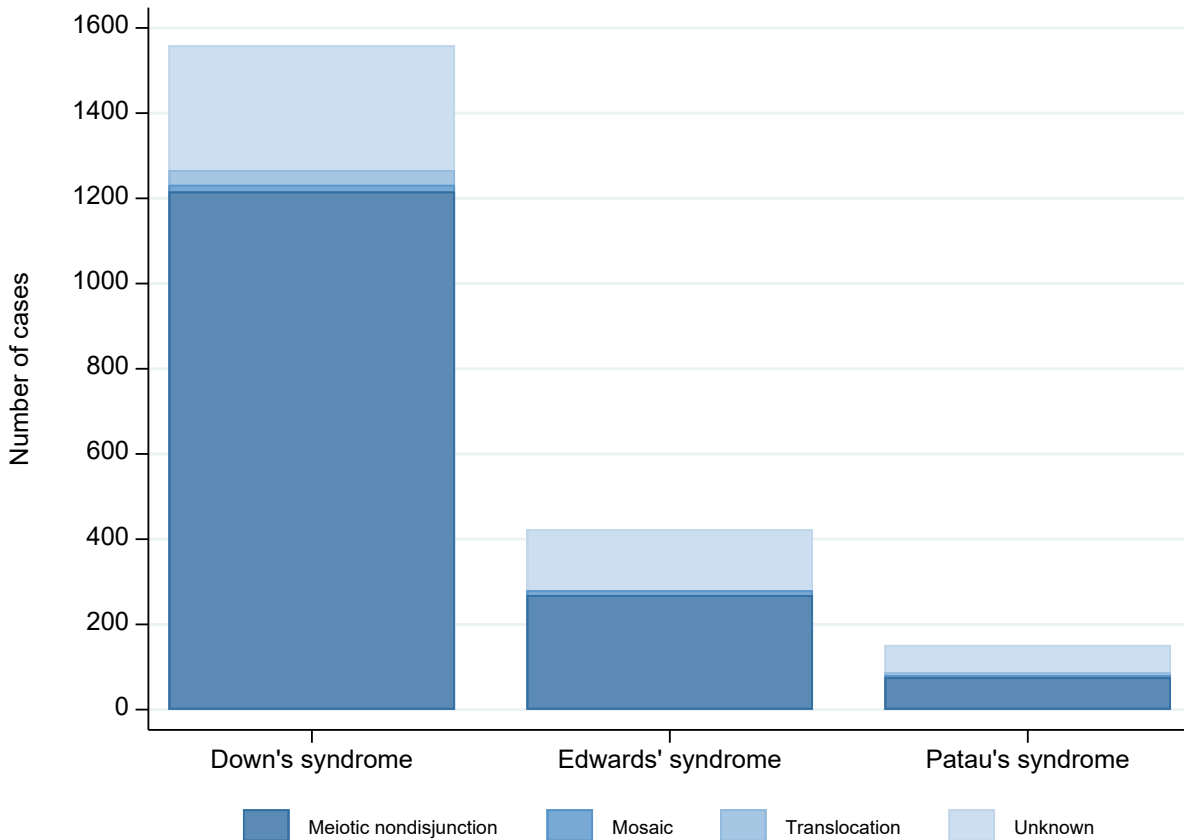


Table 14 shows that antenatal diagnoses were primarily made from **chorionic villus sampling (CVS)** (54.9%) or **amniocentesis** (42.9%), with fetal blood sampling less commonly. Postnatal diagnoses include blood or saliva taken after a live birth, with venous blood representing 76.7% of all postnatal samples, and post-mortem tissue specimens tested following a **late miscarriage, TOPFA, or a stillbirth also seen frequently in the data.**

5.2 Origin of trisomies

Down’s syndrome, Edwards’ syndrome and Patau’s syndrome can arise by several different mechanisms, outlined in Box 3. As expected, figure 14 shows that meiotic non-disjunction (which is strongly associated with maternal age) accounted for the majority of babies diagnosed with Down’s syndrome, Edwards’ syndrome or Patau’s syndrome, with fewer translocation and mosaic cases being observed. Mosaic trisomies are likely to be under-ascertained as low-level mosaicism (especially of trisomy 21) may result only in mild or sub-clinical features and so may be diagnosed much later or remain undiagnosed. Babies where the genetic type of trisomy is unspecified are those where conventional karyotyping failed or was not performed, that is, they were diagnosed only by a rapid aneuploidy test or microarray; these latter tests cannot distinguish between standard and translocation trisomies.

Figure 14: The number of babies diagnosed with Down’s syndrome, Edwards’ syndrome and Patau’s syndrome born in England in 2019 categorised by chromosome and underlying genetic mechanism¹⁰

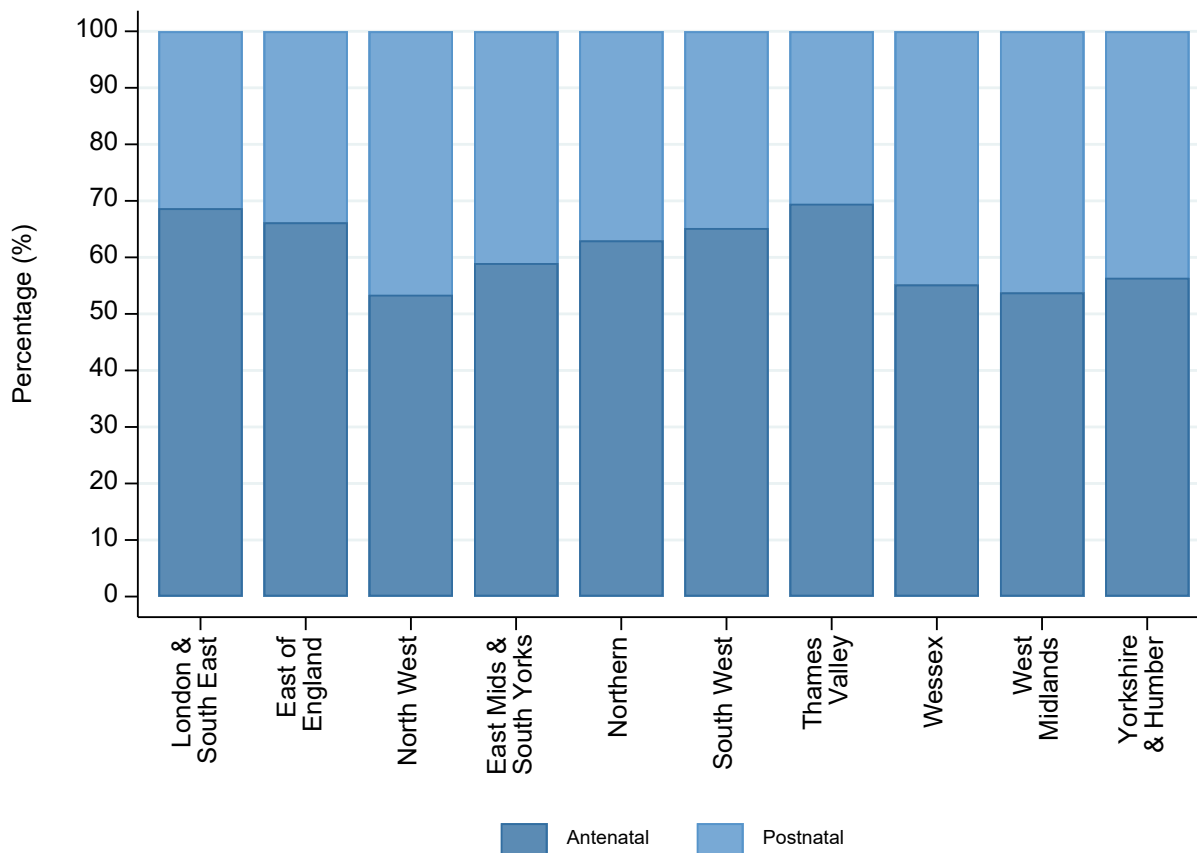


5.4 Regional differences in outcomes

Figures 15 and 16 show timing of diagnosis and differences in outcome split by geographical region. Where a baby has had both a prenatal and a postnatal diagnostic test, the earlier diagnosis is taken as the point of ascertainment. There is variation in both the timing of diagnosis and outcomes of pregnancy across the regions. There is likely to be several reasons behind this, including differences in the population, differences in maternal age and uptake of screening. There may also be some regional variation in ascertainment and data completeness, which could underestimate the number of miscarriages and TOPFAs.

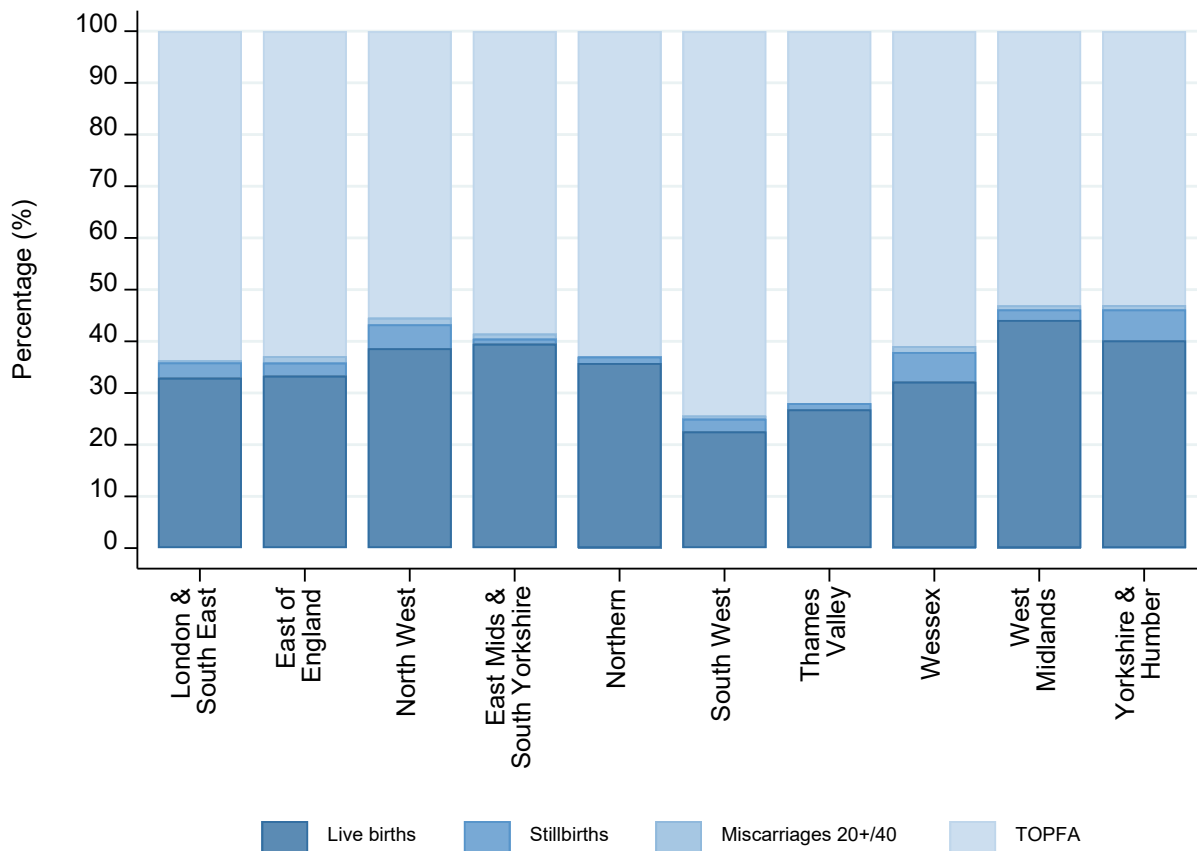
¹⁰ See box 3 for explanatory notes. Babies where the genetic type of trisomy is unspecified are those where conventional karyotyping failed or was not performed, that is, they were diagnosed only by a rapid aneuploidy test or microarray; these latter tests cannot distinguish between standard and translocation trisomies.

Figure 15: Timing of diagnosis for babies with Down’s syndrome, Edwards’ syndrome and Patau’s syndrome delivered in 2019, by NCARDS region¹¹



¹¹ Where a baby has had both a prenatal and a postnatal diagnostic test, the earlier diagnosis is taken as the point of ascertainment.

Figure 16: Outcome of pregnancy for Down's syndrome, Edwards' syndrome and Patau's syndrome delivered in delivered in 2019, by NCARDS region



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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 for fetal anomaly) compared to the total number of births (live births and stillbirths).
Births or total births	Live births and stillbirths as recorded by the Office for National Statistics
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 involving the removal of a sample of placental tissue for the purposes of chromosomal or genetic testing.
Confidence interval (see Technical Guidance document for more information)	Expresses the uncertainty of a statistic as a range in which the true value would be expected to be found on repeat sampling.
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 as defined by EUROCAT .
Estimated date of delivery (EDD)	The estimated delivery date of a pregnancy, calculated as 40 weeks gestation.
EUROCAT	European Surveillance of Congenital Anomalies – European network of population-based registries for the epidemiological surveillance of congenital anomalies.

Term	Definition
NHS Fetal Anomaly Screening Programme (FASP)	NHS screening for specified structural and chromosomal anomalies during pregnancy using laboratory and/or ultrasound tests.
FASP conditions	<p>The 11 auditable conditions screened under the Fetal Anomaly Screening Programme (FASP) are:</p> <ul style="list-style-type: none"> • Anencephaly (Q00*) • Spina bifida (Q05*) • Transposition of great arteries (Q20.3) • Atrioventricular septal defect (Q21.2*) • Tetralogy of Fallot (Q21.3, Q21.82) • Hypoplastic left heart (Q23.4) • Cleft lip +/- palate (Q36*, Q37*) • Bilateral renal agenesis (Q60.1) • Lethal skeletal dysplasia (Q77.0*, Q77.1, Q77.2, Q77.8*, Q78.0*) • Congenital diaphragmatic hernia (Q79.0*) • Exomphalos (Q79.2) • Gastroschisis (Q79.3) • Trisomy 21 (Q90*) • Trisomy 18 and Trisomy 13 (Q91*)
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 as defined by the Royal College of Obstetricians and Gynaecologists .
Full karyotype	Visual inspection of all chromosomes down the microscope, enabling assessment of chromosome number and integrity.
Genetic anomalies	Includes chromosomal anomalies, skeletal dysplasias, genetic syndromes and microdeletions as defined by EUROCAT .
Hospital Episode Statistics (HES)	Database of all admissions, A&E attendances, procedures, and outpatient appointments at NHS hospitals in England.
Infant deaths	Deaths from birth to under 1 year of age as recorded by Child and infant mortality data from the ONS

Term	Definition
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. In these tests, a needle is inserted directly into the uterus to take a sample.
Late miscarriage	Late fetal deaths from 20 to 23 completed weeks of gestation.
Live birth	A baby showing signs of life at birth as recorded by the Office for National Statistics
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 as defined by EUROCAT .
National Down Syndrome Cytogenetic Register (NDSCR).	The NDSCR collected cytogenetic or DNA reports of trisomies 21, 18 and 13, and their cytogenetic variants, occurring in England and Wales between 1989 and April 2015, when this function was transferred to NCARDS.
Non-genetic anomalies	Includes anomalies with no known genetic cause. Not all babies undergo genetic testing, so it is likely that some of these anomalies are of 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.
Outcome of pregnancy	Outcome of the end of the pregnancy, as distinct to the registerable nature of the birth. Still births or live births preceded by a termination are categorised as a termination.
Palliative care	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 as recorded

Term	Definition
	by the Office for National Statistics .
Perinatal mortality	The number of perinatal deaths per 10,000 total births.
Post-neonatal period	From 28 days of life 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.
Rare Diseases	Non-cancerous, usually non-infectious diseases that affect <1:2000 in the population at risk with an Orphanet Rare Disease classification.
Severe congenital heart disease (CHD)	<p>This includes the following congenital heart anomalies:</p> <ul style="list-style-type: none"> • 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 as defined by EUROCAT .
Stillbirths	A baby born after 24 or more completed weeks of gestation and which did not, at any time, breathe or show signs of life as recorded by the Office for National Statistics .
Statistical significance (see Technical details 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.

Term	Definition
Termination of pregnancy for fetal anomaly (TOPFA)	<p>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.</p> <p>This includes terminations of pregnancy for fetal anomaly as well as terminations of pregnancy for other medical reasons where a fetal anomaly was present.</p> <p>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.</p> <p>Depending on the gestation at which a TOPFA takes place (before or after 24 weeks), it may also be registered as a stillbirth.</p>
Tertiary service	A hospital which provides specialist care following referral from a local provider, this may include antenatal or postnatal specialities.
Total births	Total number of live births and stillbirths.

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