



Public Health  
England

Protecting and improving the nation's health

# **National Congenital Anomaly and Rare Disease Registration Service**

## **Congenital anomaly statistics 2018**

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# Contents

Executive summary	4
Chapter 1: Introduction	6
Chapter 2: Prevalence of congenital anomalies	11
Chapter 3: Timing of diagnosis and outcome	21
Chapter 4: Important public health indicators	24
Chapter 5: Down's syndrome, Edwards' syndrome and Patau's syndrome	30
References	38
Appendix 1: Glossary of terms	39

## Executive summary

This is the fourth 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 and for the first time, reporting is based on 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 this fourth 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 2018, there were a total of 13,400 babies' with one or more congenital anomalies notified to NCARDRS, covering 628,171 total births (**live births** and **stillbirths**). This gives an overall birth prevalence for these regions of 213.3 per 10,000 total births – or 1 for every 47 births.

Some congenital anomalies are detectable during pregnancy and others are not. In 2018, the timing of first diagnosis was known for 11,601 (86.6%) babies and of these, 73.5% were diagnosed antenatally. Where a congenital anomaly was diagnosed **antenatally**, 61.0% of these resulted in a live birth. Where a baby was diagnosed with a congenital anomaly postnatally, 96.5% of these were diagnosed following a live birth.

Of the 13,400 babies with a confirmed or probable congenital anomaly reported to NCARDRS, 699 died in their first year, giving an **infant mortality** rate of 11.2 (95% CI 10.4 – 12.0) per 10,000 live births. Of all the deaths associated with a congenital anomaly, congenital heart anomalies were most frequently identified in 50.2% of reported infant deaths, followed by chromosomal anomalies (22.2%) and digestive system anomalies (18.0%).

Data recorded in 2018 shows that the prevalence of **genetic** 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).

Data on Down's syndrome, Edwards' syndrome and Patau's syndrome (full **trisomies**) is presented for England for 2018. The **prevalence** per 10,000 total births for Down's syndrome was 25.0 (95% CI: 23.8-26.3), or 1 in 400 total births, 7.2 (95% CI:6.5-7.9), or 1 in 1,389 for Edwards' syndrome and 2.4 (95% CI: 2.0-2.8), or 1 in 4,167 total births for Patau's syndrome respectively.

# Chapter 1: Introduction

This report is the National Congenital Anomaly and Rare Disease Registration Service's (NCARDRS) fourth report on congenital anomalies and the first report describing national data for England. It describes the number of babies delivered between 1 January and 31 December 2018 in England with one or more congenital anomalies.

Readers who are interested in congenital anomalies prior to 2018 are directed to our previous reports on data from 2015, 2016 and 2017 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.

This means, that for the first time, national coverage of congenital anomaly reporting on 2018 births is possible.

For the first time, congenital anomaly data for 2018 for the whole of England was submitted to the European Surveillance of Congenital Anomalies (EUROCAT) in February 2020, with new regions meeting the European data quality thresholds that EUROCAT set

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 and patient groups/ voluntary 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.

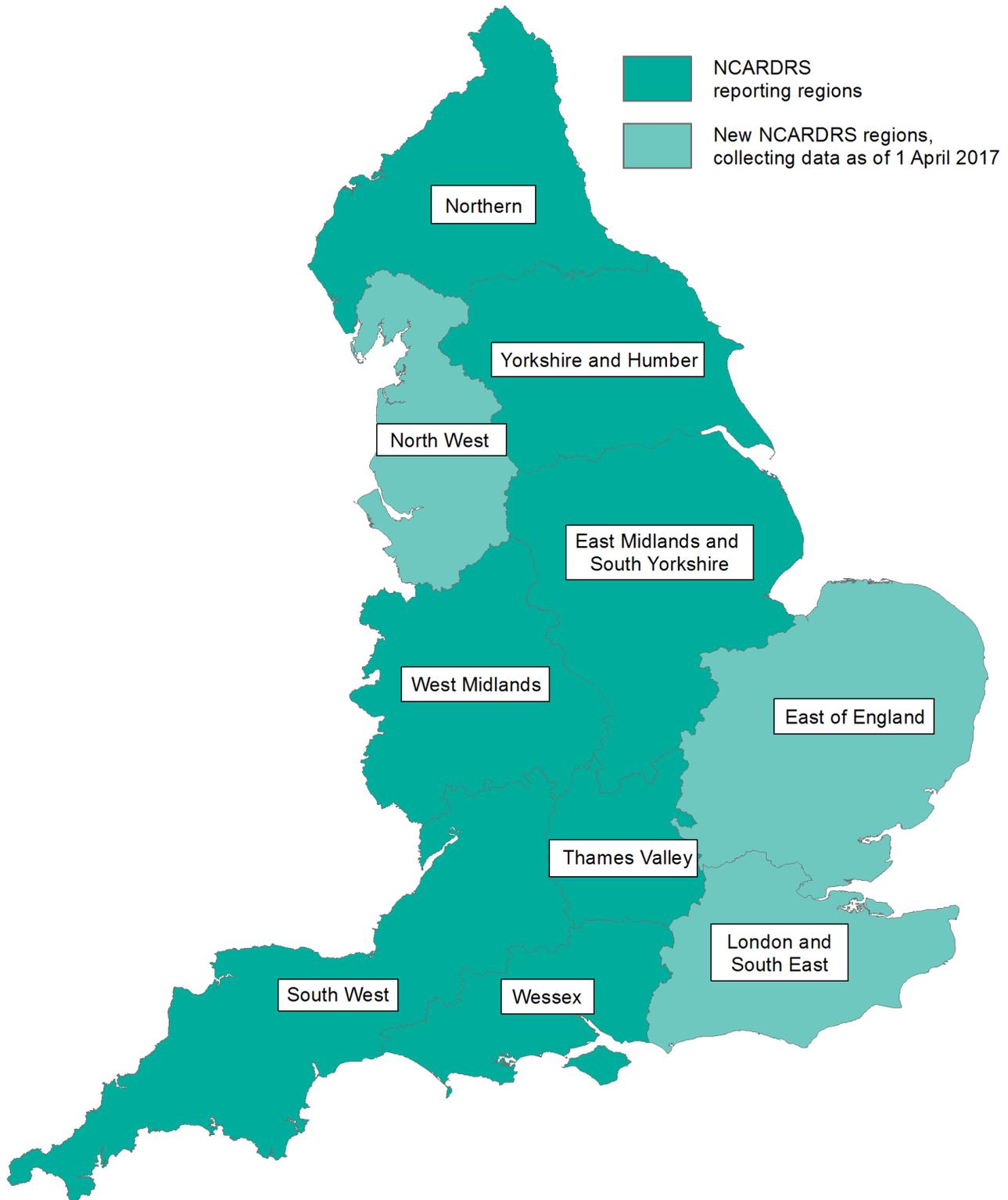
It is thanks to the dedication of these notifying healthcare professionals that this important and reliable information is available for clinicians, researchers, patients and their families. More information about the data collection process can be found in the accompanying technical details document.

## 1.1 NCARDRS reporting regions in 2018

NCARDRS is made up of 10 reporting regions; 7 regions which were collecting congenital anomaly data for some time, and 3 which began congenital anomaly registration for births expected from 1 April 2017 (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 2017 took coverage to 49% of births. 2018 is the first year of 100% congenital anomaly coverage for England.

**Figure 1: Map of NCARDS reporting regions England, 2018**



## 1.2 Data in this report

Congenital anomalies are defined as being present at delivery, probably originating before birth, and include structural, chromosomal and genetic anomalies. Data is collected according to definitions and guidelines of the European Surveillance of Congenital Anomalies (**EUROCAT**) and the World Health Organisation (WHO) 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 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 is required to consider trend analysis
- data is not directly comparable as regional coverage increased in 2016 and in 2018, and ascertainment is increasing annually as a result of improved data collection.
- comparing year on year data could lead to unreliable conclusions based on small numbers

This 2018 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 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 2018, diagnosed with Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13).

A separate summary, 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.

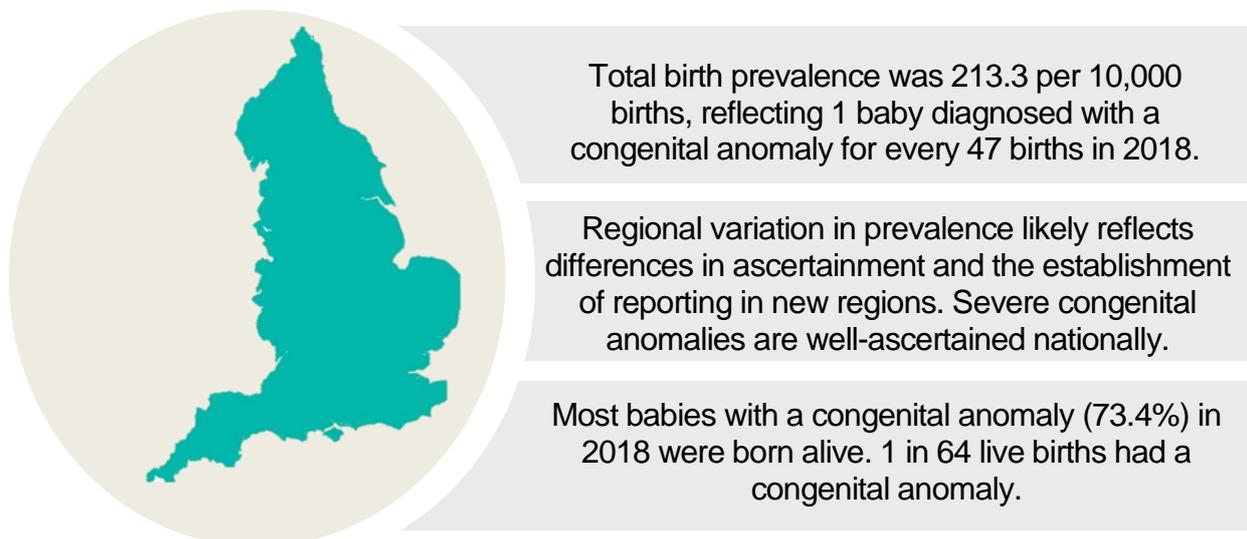
### Data source update for 2018

Since publication of the 2017 report, there have been additions to the data sources for the registration of babies with congenital anomalies including:

- the inclusion of Office for National Statistics (ONS) death certificate information to the database (2018 and retrospectively to the 2017 data)
- the ascertainment of selected anomalies using Hospital Episode Statistics (HES). Babies born in 2018 with polydactyl, congenital cataract and talipes equinovarus with an appropriate procedure code were extracted from HES and validated according to a methodology developed by NCARDRS

These developments sit 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



In 2018, there were a total of 13,400 babies with one or more congenital anomalies notified to NCARDRS out of 628,171 total births (live births and stillbirths) in England. This gives an overall birth prevalence of 213.3 per 10,000 total births (95% CI: 209.72-216.96). This reflects 1 for every 47 births (**live births** and **stillbirths**) (Table 1).

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

Prevalence was highest in regions with long-established registers (Northern, South West, Thames Valley and Wessex) and lowest in regions reporting their first year of data (London and the South East, East of England).

Prevalence in the North-West region – also reporting its first year of data – was consistent with the national prevalence and with some existing regions.

Geographical variation in congenital anomaly prevalence could be a result of disease clustering, exposure to **teratogens**, demographic variation including age and deprivation profiles between regions and the genetic composition of the local population.

However, given the infancy of the service, it is likely that most of the differences in prevalence across regions reflect **case ascertainment**.

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.

In the 2017 report, prevalence of chromosomal, abdominal wall anomalies and severe congenital heart anomalies was significantly higher in the NCARDRS data compared to the pan-European overall rate reported by EUROCAT for European registries.

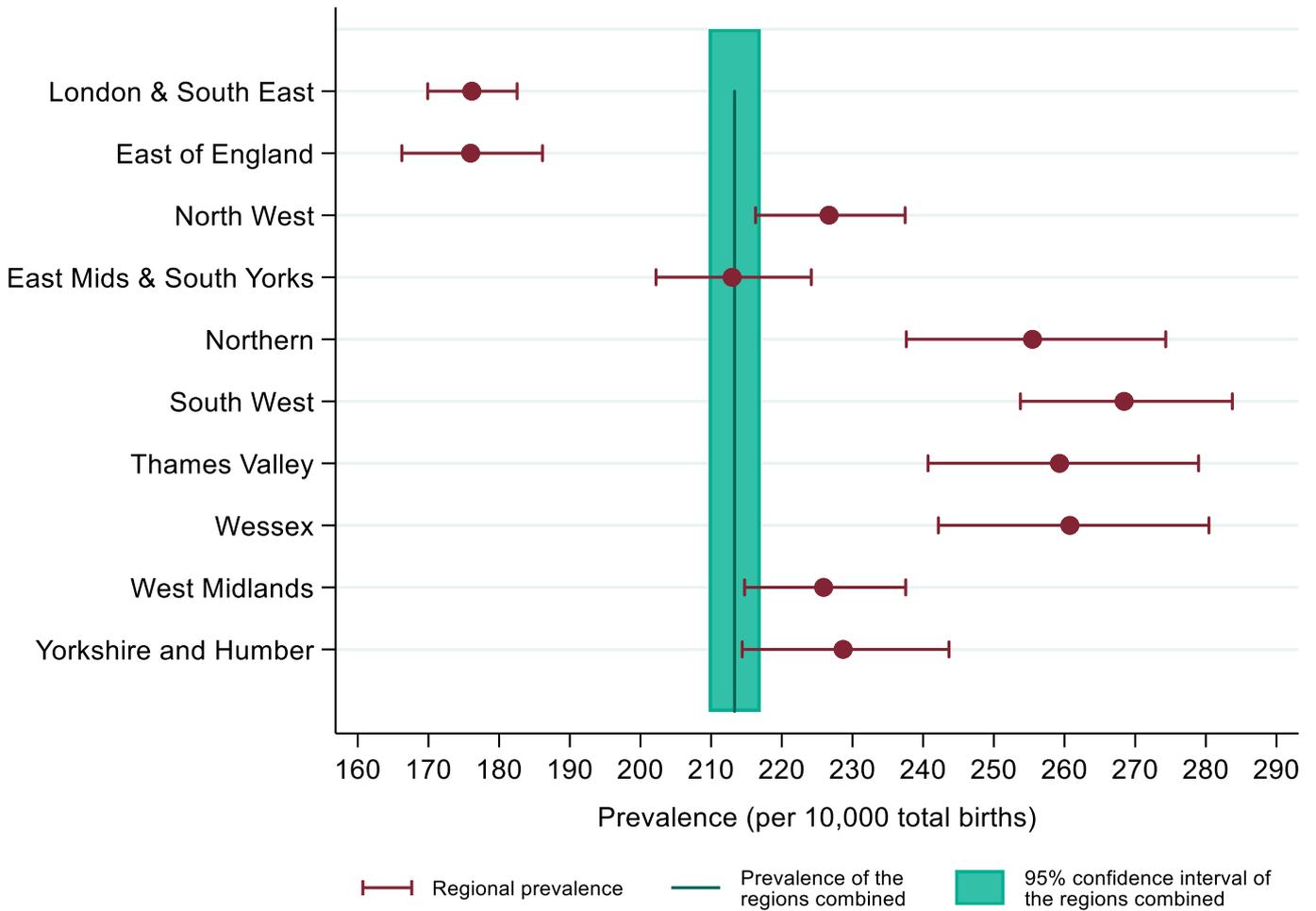
These more severe anomalies, along with spina bifida, lethal skeletal dysplasia, cleft lip+/palate, bilateral renal agenesis and congenital diaphragmatic hernia are audited in NCARDRS' work with the NHS Fetal Anomaly Screening Programme (FASP). As part of this work, these conditions are subject to more intensive reporting, resulting in higher data quality and ascertainment.

The reporting of EUROCAT prevalence data for 2018 has been delayed due to COVID-19 and is unavailable for comparison at time of publication.

While there is regional variation in the overall prevalence of congenital anomalies, if regional prevalence is restricted to babies with one of the 11 FASP conditions, prevalence across NCARDRS regions was more consistent (Figure 2a).

All but one of the regions (London and the South East) were consistent with the national rate and with each other.

**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 regions combined, 2018**



**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 NCARDS regions compared to regions combined, 2018**

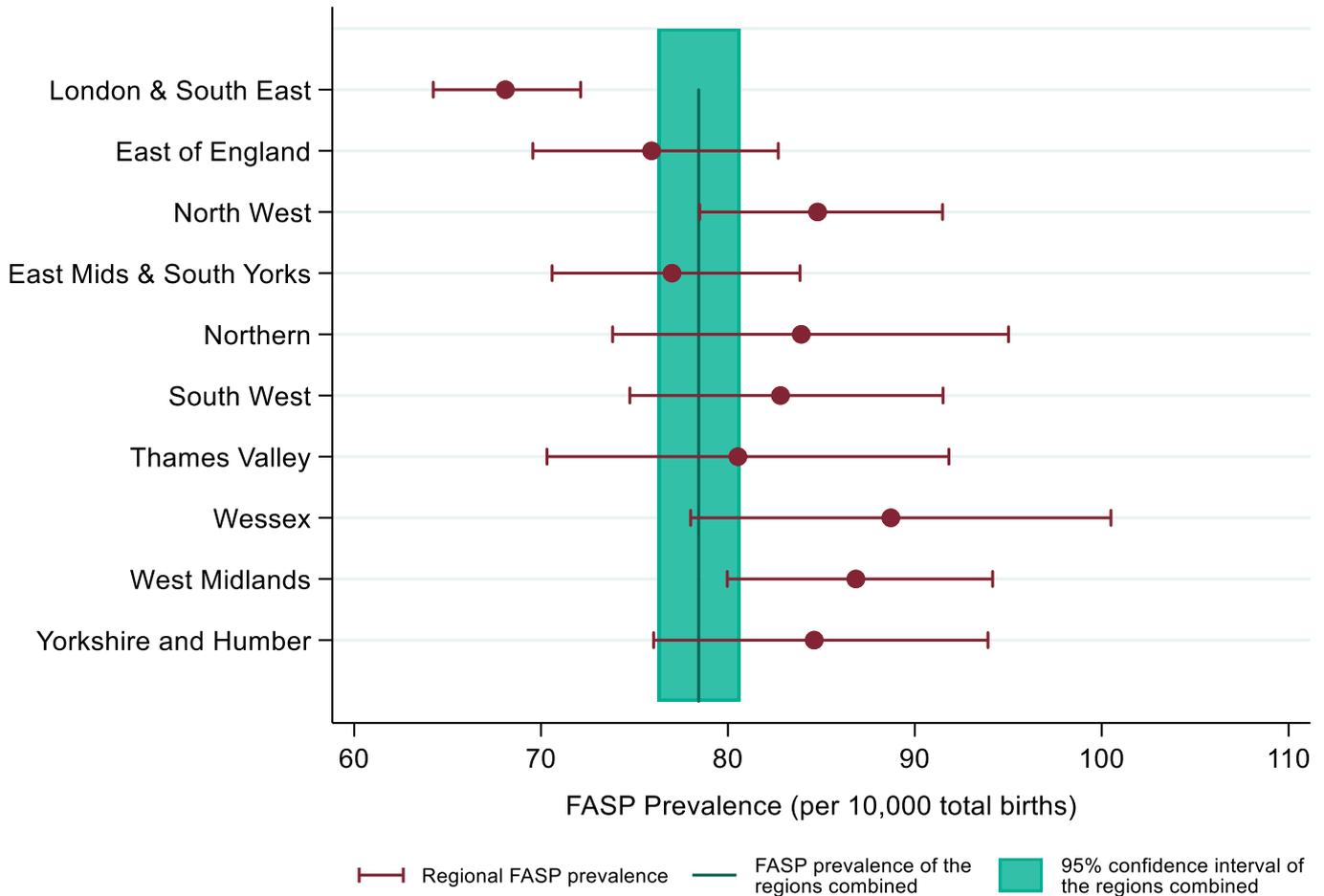


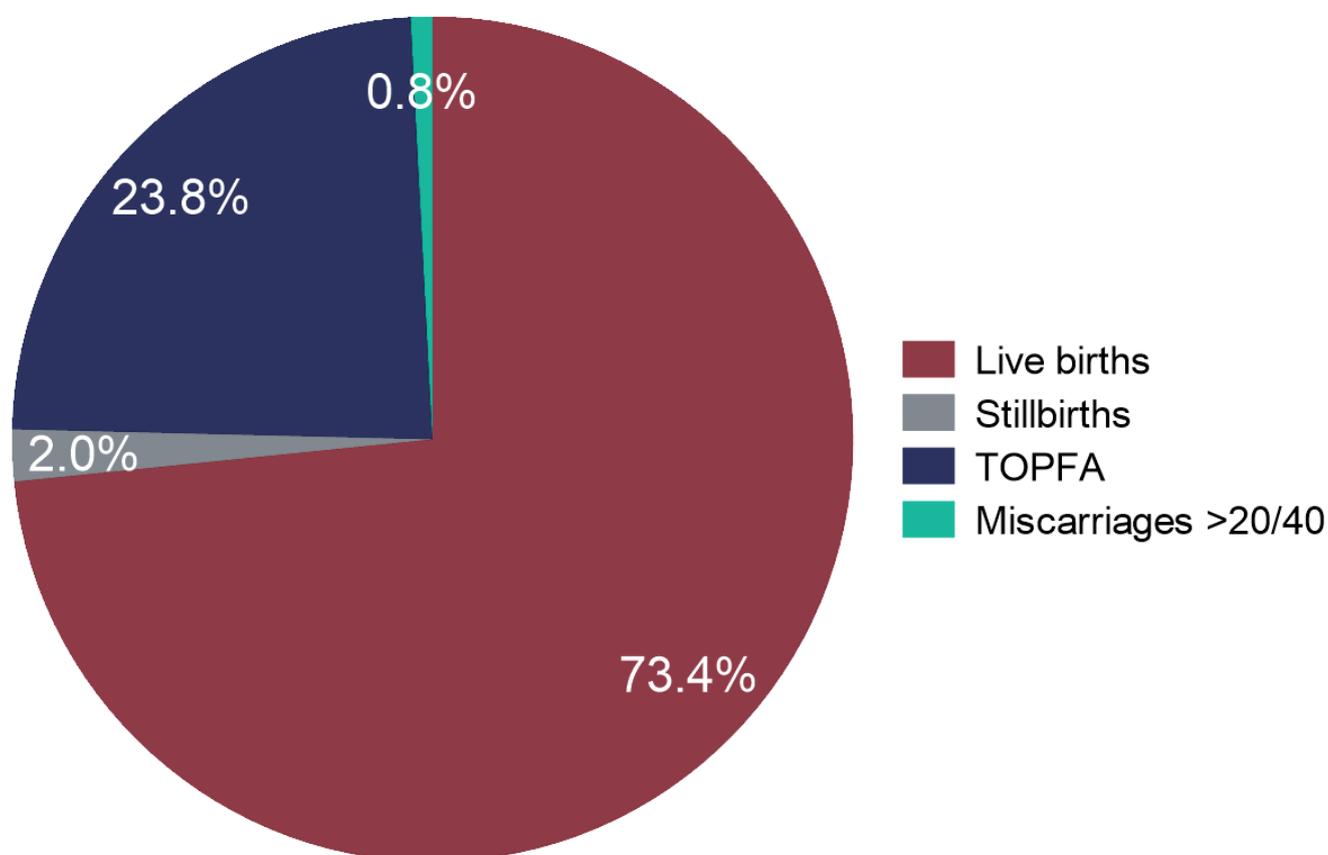
Figure 3 shows that of the 13,400 babies with one or more congenital anomalies, the majority (9,836, 73.4%) resulted in a **live birth**.

Of the remaining 3,564 babies, 265 (2.0%) were **stillbirths** (24+ weeks' gestation), 111 (0.8%) were **late miscarriages** (20 to 23 weeks' gestation) and 3,188 (23.8%) 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.

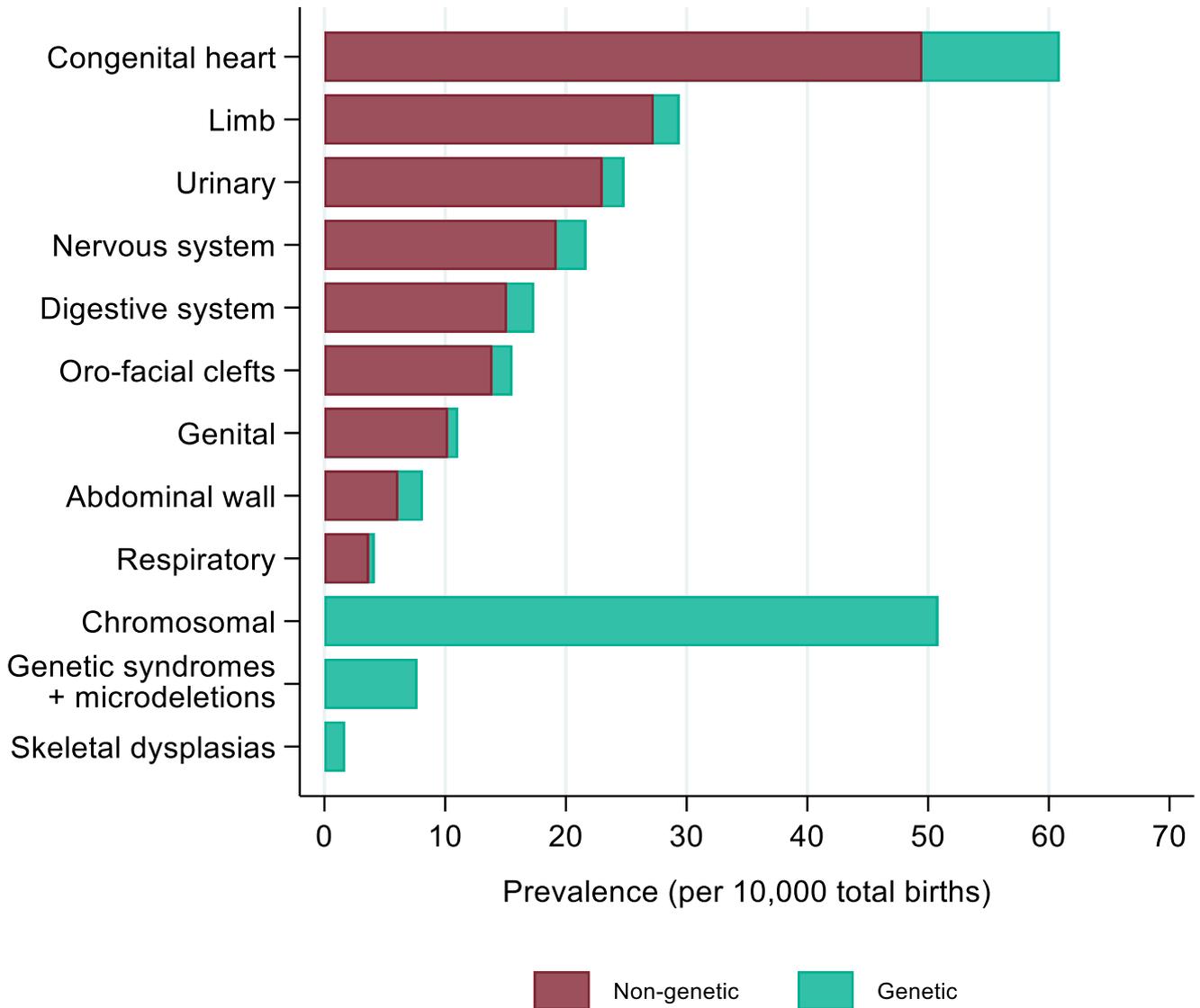
**Figure 3: Percentage of babies with one or more reported congenital anomalies by outcome of pregnancy in England, 2018**



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 2018, the prevalence for total births (Figure 4a and Table 1) was highest in the congenital heart anomalies subgroup (60.9 per 10,000, 95% CI 59.0-62.8), followed by those that are chromosomal in origin (50.8 per 10,000, 95% CI 49.1-52.6) (Table 1). The prevalence for those who are live born (Figure 4b and Table 3) was also highest in congenital heart anomalies (49.4 per 100,000, 95% CI 47.7-51.2), followed by the limb anomalies subgroup (25.9 per 100,000, 95% CI 24.6-27.2) and then those that are **chromosomal** in origin (22.5 per 10,000, 95% CI 21.4-23.7). Not all babies undergo genetic testing, 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, 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.

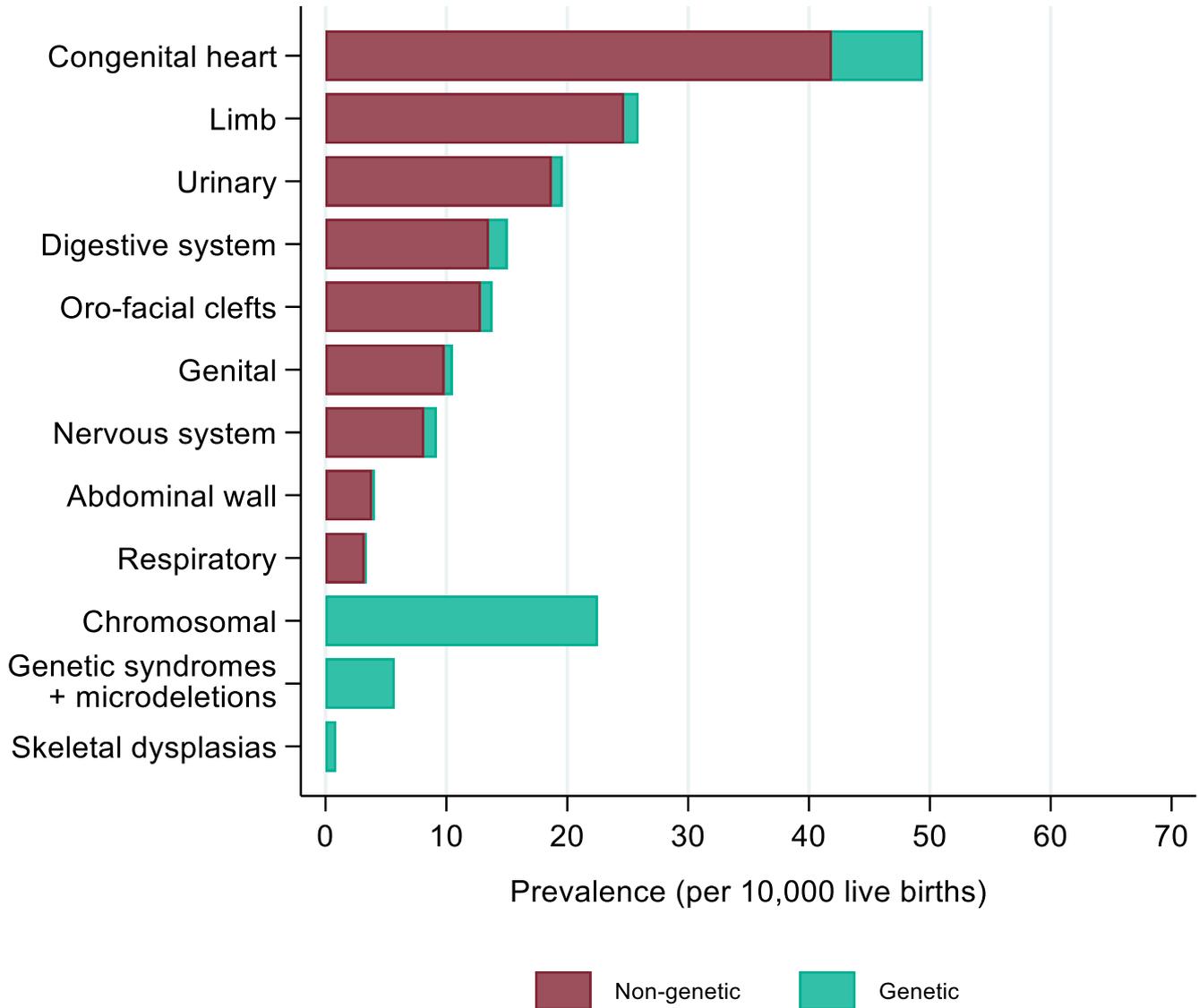
**Figure 4a: Total birth prevalence: The number<sup>1</sup> of babies diagnosed with each congenital anomaly per 10,000 total births by congenital anomaly subgroup<sup>2</sup> in England, 2018**



<sup>1</sup> Babies with multiple anomalies will be counted in each applicable bar in Figures 4a, b and c.

<sup>2</sup> Conditions categorised as “Genetic” include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-chromosomal 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 4b: Live birth prevalence: The number of babies<sup>3</sup> diagnosed with each congenital anomaly<sup>4</sup> per 10,000 live births, by congenital anomaly subgroup<sup>2</sup> in England, 2018**



<sup>3</sup> Babies with multiple anomalies will be counted in each applicable bar in Figures 4a, b and c.

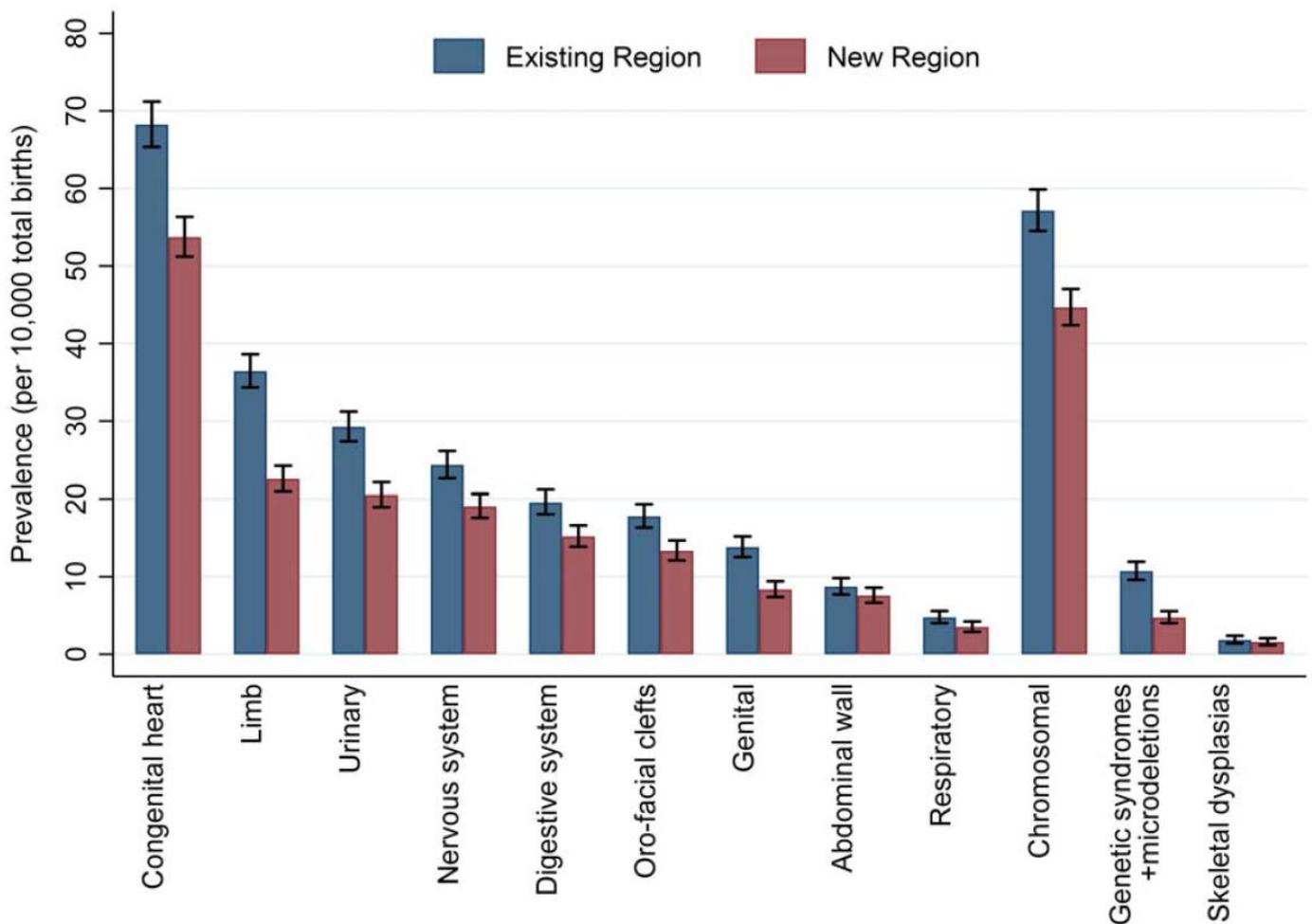
<sup>4</sup> Conditions categorised as “Genetic” include those babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-chromosomal conditions include babies with one or more congenital anomaly with no identified anomalies that are chromosomal, skeletal dysplasias, genetic syndromes or microdeletions. Not all babies undergo genetic testing and it is likely some of these are of genetic origin.

### Impact of the addition of 3 new regions

The addition of the 3 new regions has resulted in a slight fall in overall congenital heart anomaly prevalence compared to 2017, reflecting developing ascertainment in these new regions (68.2 per 10,000 95% CI 65.4-71.2 in existing regions vs 53.7 per 10,000 95% CI 51.2-56.3 in new regions).

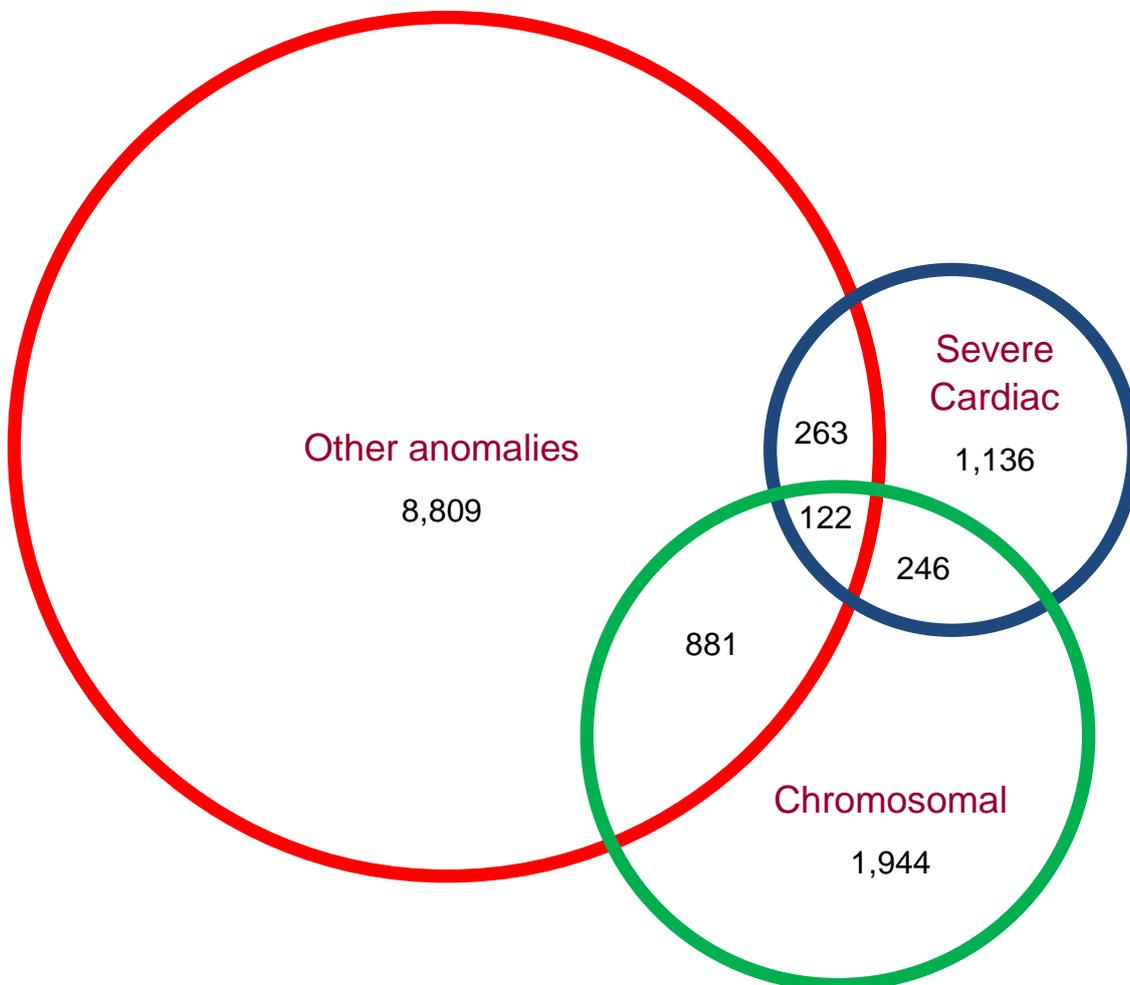
The prevalence of urinary, limb and chromosomal anomalies are also significantly lower in new regions compared to those with long-standing registration (Figure 4c). However, the prevalence of abdominal wall, respiratory anomalies and skeletal dysplasia were consistent, at least in part reflecting work with the FASP programme. As registration becomes embedded and ascertainment increases, differences in prevalence as a result of data collection will dissipate, revealing true regional differences, if they exist.

**Figure 4c: A comparison of total birth prevalence (the number<sup>1</sup> of babies diagnosed with each anomaly per 10,000 total births) by congenital anomaly subgroup<sup>2</sup> in the existing regions and new reporting regions in England, 2018**



More than a third (35.9%) of babies had more than one registered anomaly in 2018. 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 1,767 babies with severe cardiac anomalies (Box 1) in 2018 births; 1,136 (64.3%) occurred in isolation, 263 (14%) also had another structural anomaly, 246 (13.9%) also had a chromosomal anomaly, and 122 (6.9%) babies had both a chromosomal anomaly and another structural anomaly in addition to their severe cardiac anomaly.

**Figure 5: Multiple anomalies: babies with severe cardiac, chromosomal and/or other anomalies, in England, 2018**



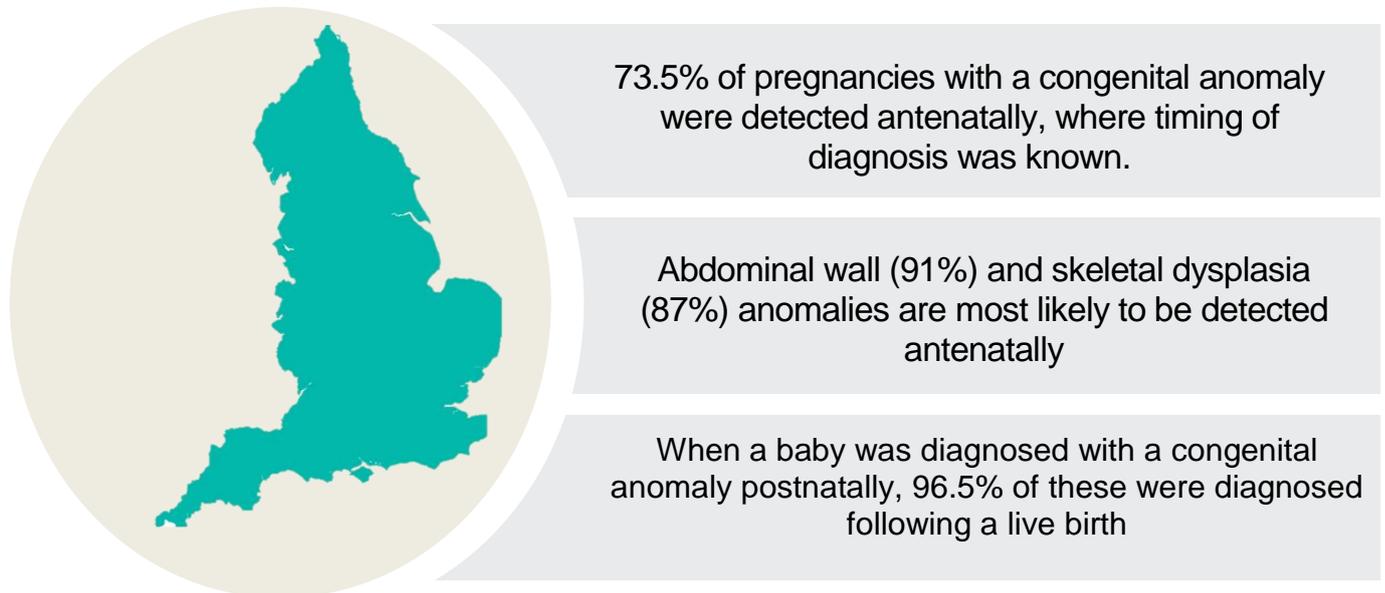
### Box 1: Severe cardiac anomalies

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 \(2013\)](#)

## Chapter 3: Timing of diagnosis and outcome



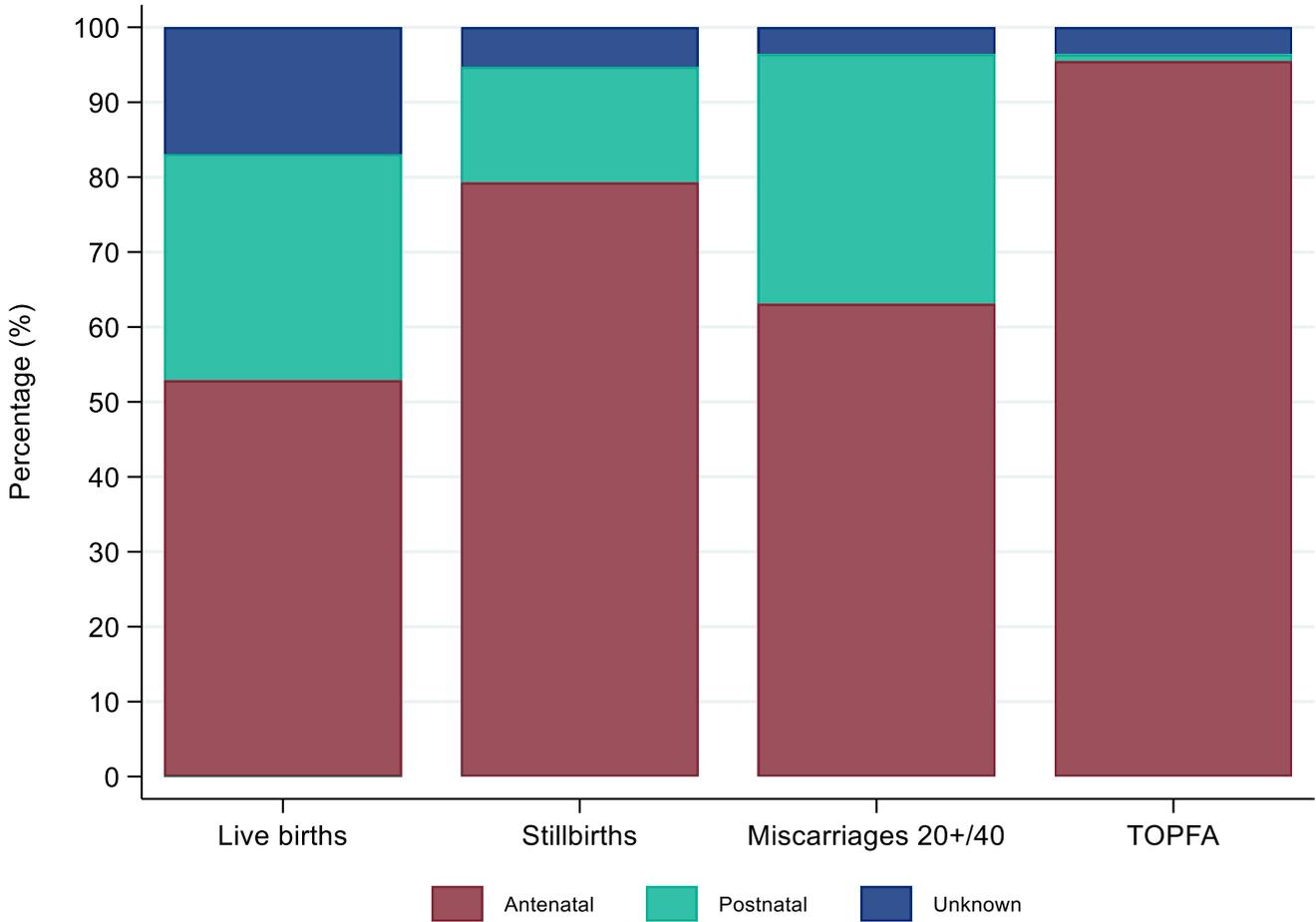
Some **congenital anomalies** are detectable during pregnancy and others are not. Screening is offered by NHS maternity services to maximise antenatal detection of specified conditions where women choose, and present in time. NCARDRS provides a separate annual audit of the NHS **Fetal Anomaly Screening 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.

The timing of first diagnosis of a congenital anomaly was known for 11,601 (86.5%) babies. Where the timing of diagnosis was known, 73.5% of babies were diagnosed antenatally in 2018. Of the 8,521 babies where a congenital anomaly was diagnosed antenatally, 5,198 (61.1%) were born alive and 3,043 (37.7%) resulted in **termination of pregnancy for fetal anomaly** (TOPFA) (Table 4). Where a congenital anomaly was first diagnosed postnatally, 96.5% were diagnosed following a live birth (Table 4).

Figure 6 shows that where a baby was liveborn 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 was detected antenatally in 79.2% of cases.

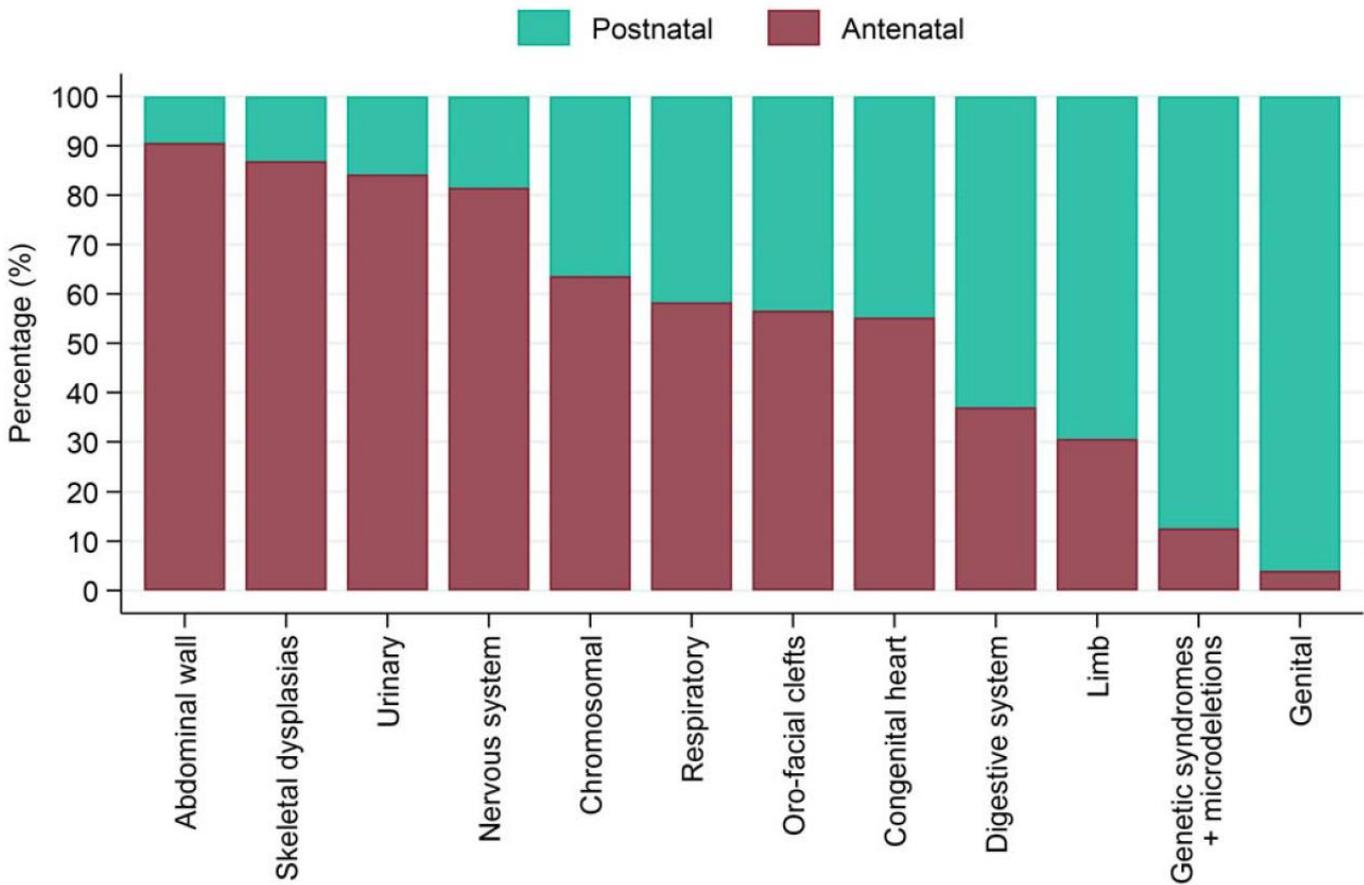
**Figure 6: Timing of first diagnosis<sup>5</sup> and pregnancy outcome (percentage) in England, 2018**



Some types of congenital anomalies are more likely to be diagnosed antenatally than others. Figure 7 shows that abdominal wall, skeletal dysplasia, 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 5.

<sup>5</sup> Identification of any congenital anomaly

**Figure 7: Timing of diagnosis by congenital anomaly subgroup – based on individual anomaly (percentage) in England, 2018**



The overall rate of TOPFA for England was 50.8 per 10,000 total births. The rate of TOPFA at over 20 weeks’ gestation was 17.1 per 10,000 total births (Table 6).

The data in Table 6 shows the highest rate of TOPFA was associated with chromosomal anomalies (25.8 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. 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 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: 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 699 infant deaths among babies with one or more **congenital anomalies** in the 625,651 live births in 2018, giving an **infant mortality** rate of 11.2 per 10,000 live births. The rate of **perinatal mortality** was lower, at 9.1 per 10,000 births (Table 8).

#### Box 2: Mortality definitions

**Infant mortality:** Deaths under 1 year of age

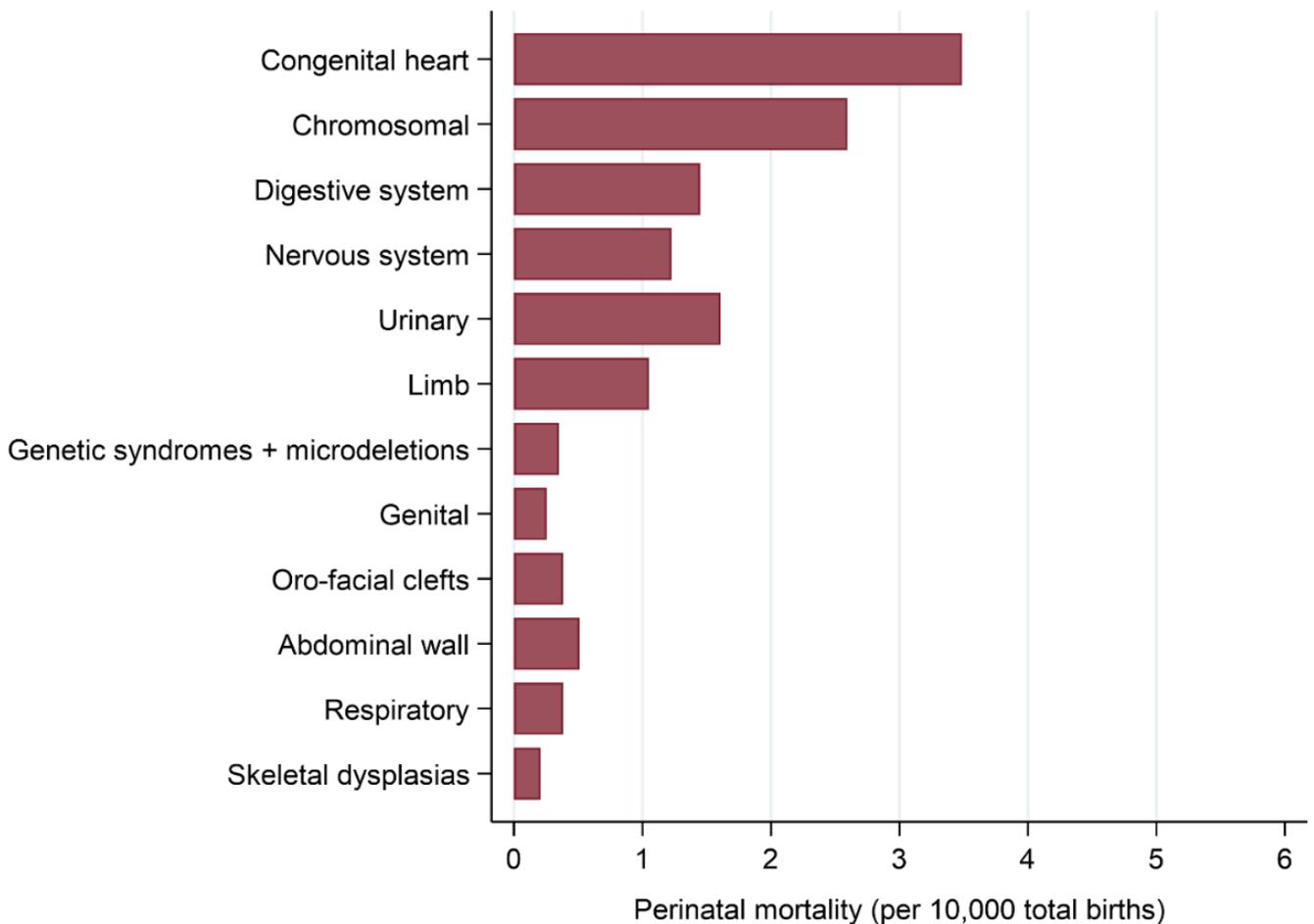
**Perinatal mortality:** Stillbirths and deaths under 7 days of age

Figures 9a and 9b show that in cases of both perinatal and infant mortality, the most frequently recorded anomalies were the same; congenital heart anomalies (3.5, 5.6 per 10,000 births) followed by chromosomal (2.6, 2.5 per 10,000 births).

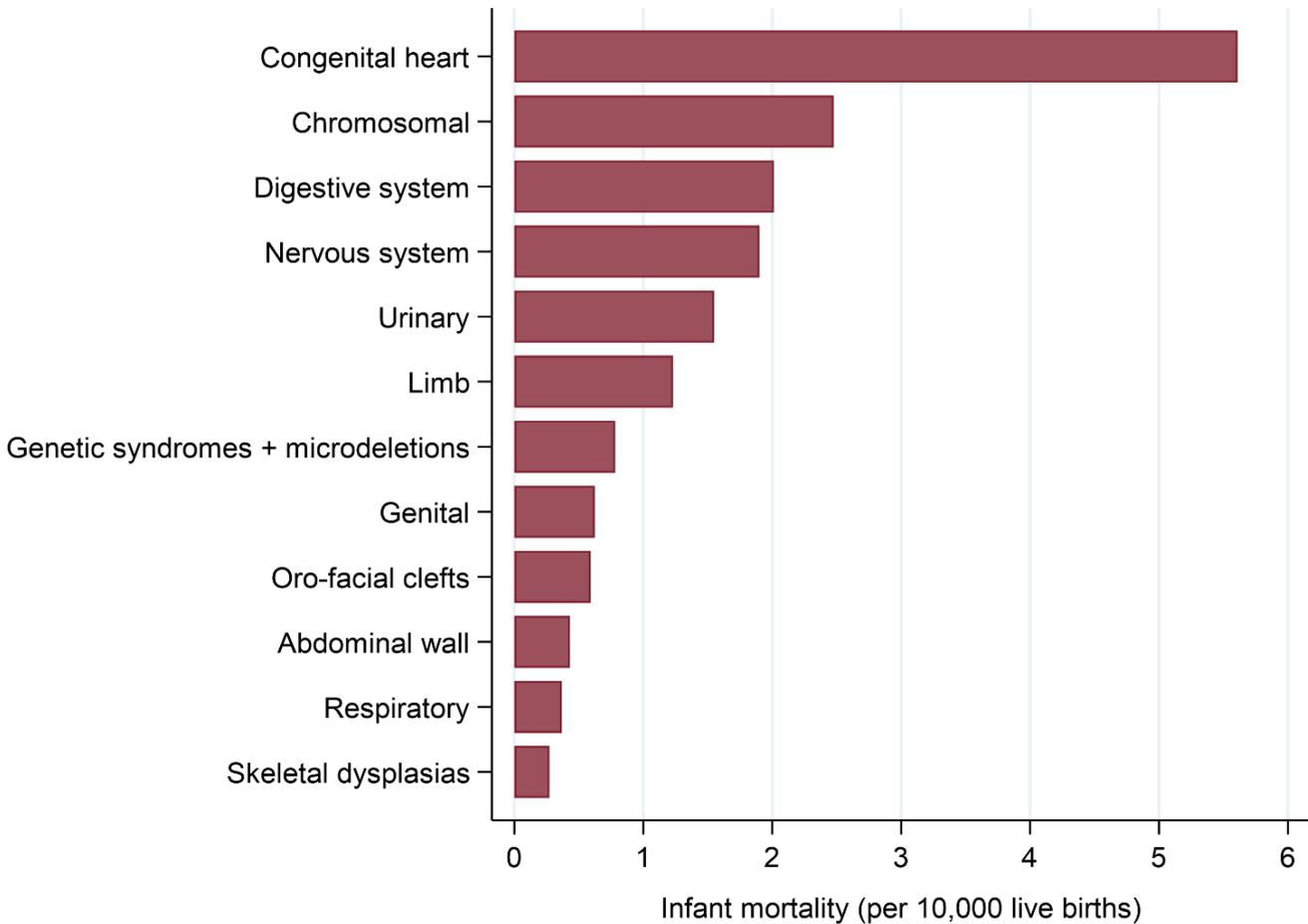
The data presented here should be viewed with some caution, as babies with more than one anomaly will appear in each anomaly subgroup. Additionally, a link between the presence of a congenital anomaly and the cause of death has not been established, therefore it is possible that the identified congenital 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.

The rate of infant mortality has risen since the 2017 report, particularly for congenital heart anomalies, whereas perinatal mortality has remained relatively constant. In 2017, we reported the infant mortality rate for congenital heart anomalies as 3.4 per 10,000 births (95% CI 2.8-4.1) compared to 6.2 per 10,000 births (95% CI 5.4-7.2) in those same 7 regions in 2018 and 5.6 per 10,000 births (95% CI 5.0-6.2) in England as a whole. Congenital heart anomalies were associated with 50.2% of infant deaths, compared with 35% in the 2017 report. It is likely that this increase in infant mortality because of improved ascertainment of anomalies in babies that die later in their first year as a result of a new data source obtained in 2018: the ONS death certificate data. However, NCARDRS will continue to monitor this situation.

**Figure 9a: Perinatal mortality (stillbirths and deaths under 7 days of age) by congenital anomaly subgroup in England, 2018**



**Figure 9b: Infant mortality (deaths under 1 year of age) by congenital anomaly subgroup in England, 2018**



Child and infant mortality data from the ONS for 2018 shows that congenital anomalies were the most common cause of death in the **post neonatal period**, accounting for 33.9% of deaths. Congenital anomalies were also listed as the cause of 31.4% of **infant deaths** and 23.7% 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

The birth prevalence of all anomalies was slightly lower in mothers aged between 30 and 34 years at delivery compared to the prevalence in those aged between 25 and 29 years (187.1 and 192.2 per 10,000 total births respectively). Compared to these groups, the birth prevalence was significantly higher in mothers aged 35 to 39 years (229.9 per 10,000 total births) and those 40 years and over (399.6 per 10,000 total births). For mothers in the under 20 years and 20-24 years age groups, the rates were broadly similar to each other,

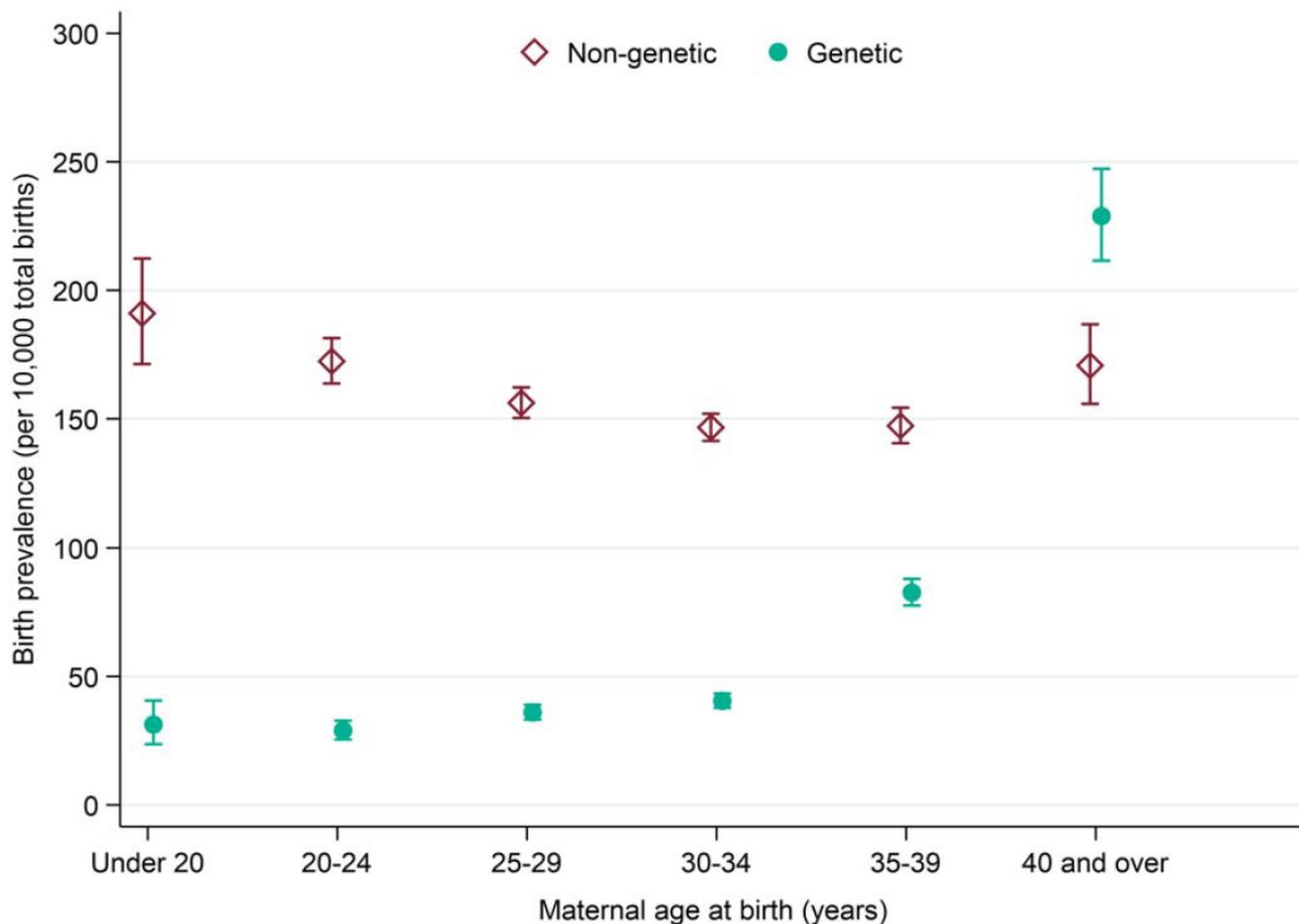
but those under 20 years had a significantly higher rate compared to those aged between 30 and 34 years (Table 9).

The association between higher maternal age and certain genetic disorders, including Down's syndrome, is well established. Mothers aged 40 and over had a significantly higher prevalence of **genetic anomalies** compared to all other age groups (Figure 10). The rate of genetic congenital anomalies in women over 40 years (n=642) was 7 times higher (7.3; 95% CI 5.6-9.8) relative to women under 20 years (n=56). Down's syndrome is the most common genetic anomaly (25.1 per 10,000 births) and is likely a primary factor in the higher rate in older age groups.

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 (Figure 10, Table 9). 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 (16.2 per 10,000 births) compared to 4.7 per 10,000 births in women aged 30 to 34 years.

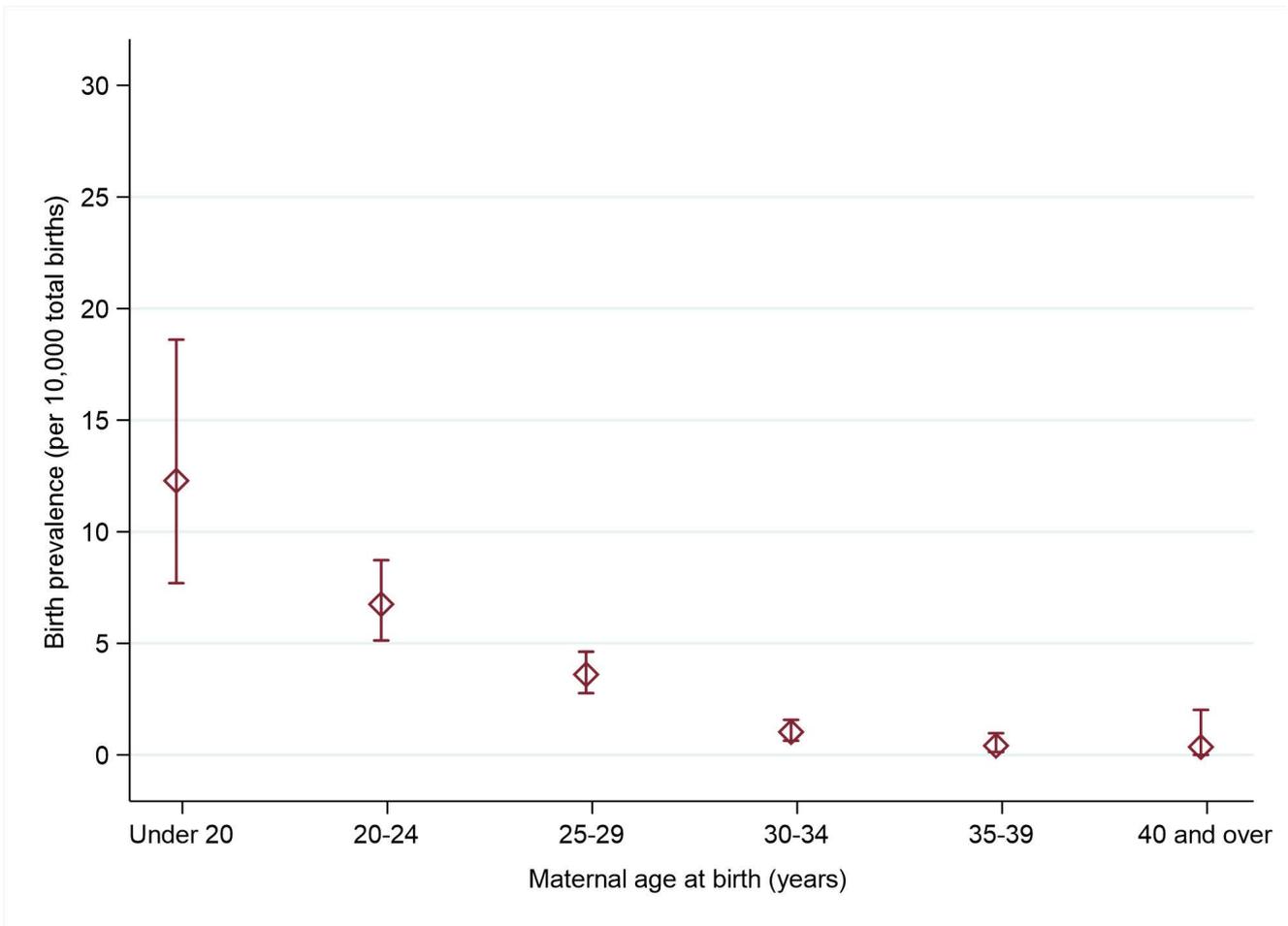
Gastroschisis, an abdominal wall anomaly, is known to be associated with lower maternal age (Baldacci et al, 2020; Fillingham & Rankin, 2008), and this relationship is demonstrated within this data as the prevalence among those under 20 is 19.9 per 10,000 births compared to 0.4 per 10,000 births in women aged over 40 (Figure 11).

**Figure 10: Prevalence (per 10,000 total births) and 95% confidence intervals of genetic and non-genetic<sup>6</sup> congenital anomalies by maternal age in England, 2018**



<sup>6</sup> Genetic conditions include babies with an identified chromosomal anomaly, skeletal dysplasia, genetic syndrome and/or microdeletion. Non-genetic conditions include babies with one 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 England, 2018**



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



Birth prevalence in England for 2018: Down's syndrome 1 in 400 births, Edwards' syndrome 1 in 1,389 births and Patau's syndrome 1 in 4,167 births

A change in inclusion criteria has seen a decrease in overall prevalence but livebirth prevalence remains stable with previous reports.

46.0% of all babies born in 2018 with Down's syndrome were live born as were 11.6% of babies with Edwards' syndrome and 8.1% of babies with Patau's syndrome

### 5.1 Background

The data relating to Down's syndrome (Trisomy 21), Edwards' syndrome (Trisomy 18) and Patau's syndrome (Trisomy 13) in the previous report for 2015 to 2017 used a definition including both date of delivery or date of confirmatory genetic test where date of delivery was not known. This was to account for less complete data in new regions, where data collection had just commenced, so as to include babies with a known trisomy diagnosis but where the date of delivery or outcome was not available. This may have resulted in the inclusion of some fetal losses at early gestations. Improvements in data cleaning and quality in new regions mean that this is no longer necessary, and in order to align data within this report, the data presented within this chapter follows the same criteria as the previous chapters; all livebirths, fetal deaths with gestational age  $\geq 20$  weeks and TOPFA (at any gestational age) with at least one registered anomaly (see technical details). As a consequence, the data from 2018 may not be directly comparable to data reported in previous years.

### Box 3: 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 Chapter 5 as, depending on the size of the partial trisomy, the outcomes and timing of diagnosis may vary.

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

In 2018, there were 1,570 babies with Down's syndrome, 450 babies with Edwards' syndrome and 148 babies with Patau's syndrome delivered in England (Figure 12). This represents a **prevalence** of 25 per 10,000 total births or 1 in every 400 births for Down's syndrome, 7.2 per 10,000 births or one in every 1,389 births for Edwards syndrome and 2.4 per 10,000 births or 1 in every 4,167 births for Patau's syndrome.

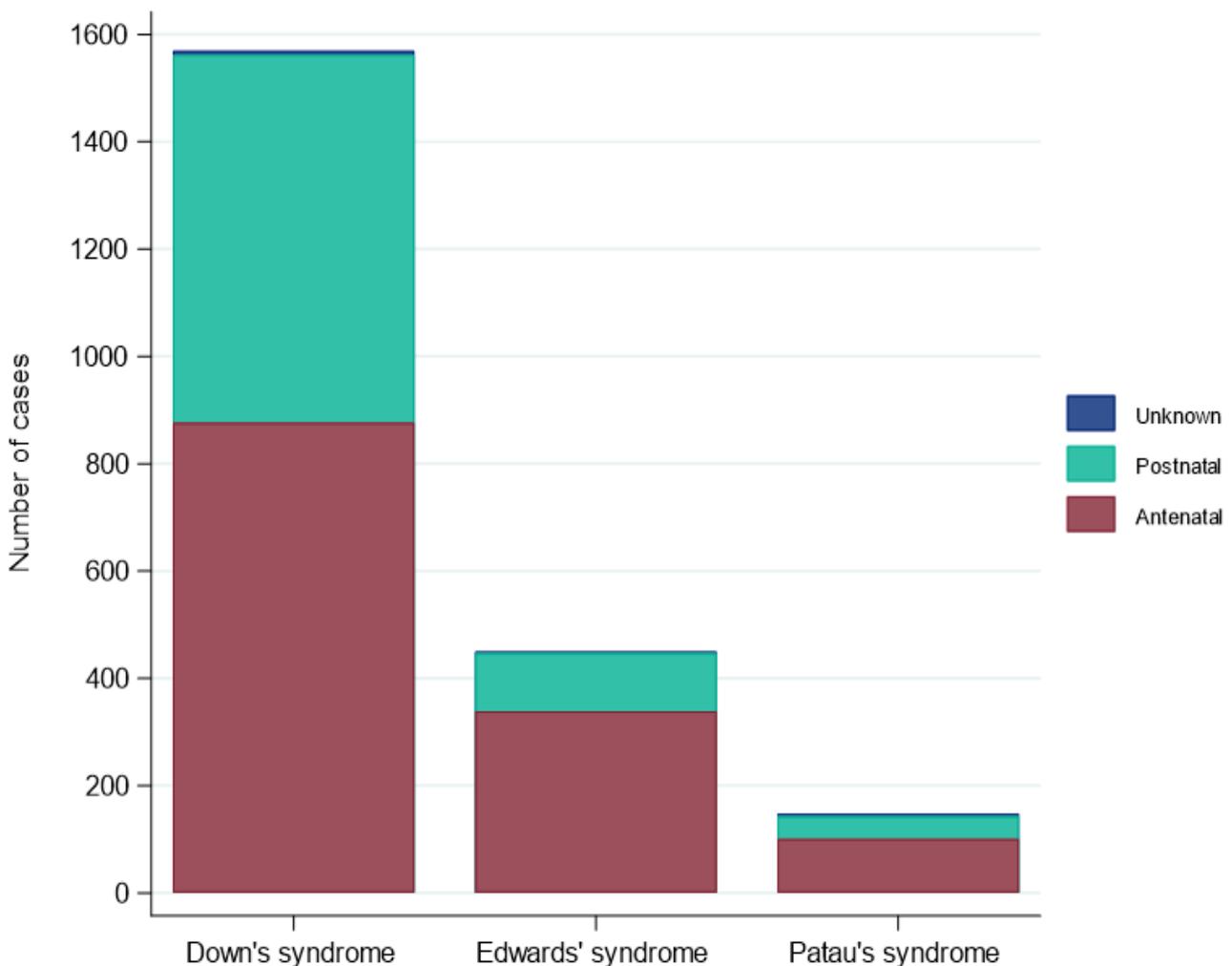
These figures are significantly lower than those reported from the 2015 to 2017 data, when the prevalences were 28.3 for Down's syndrome, 8.4 for Edwards' syndrome and 3.5 for Patau's syndrome. This is likely to have resulted from the change in the inclusion criteria, rather than a true change in the prevalence of these conditions. The previous inclusion of pregnancies with an unknown outcome or date of birth, which likely included

several early fetal losses, likely slightly artificially inflated 2015 to 2017 prevalence estimates, and these are now excluded from this report.

The **live birth prevalence** seems to confirm this, as this remains consistent with the 2015 to 2017 data, with 11.6 per 10,000 **live births** or 1 in 862 live births for Down's syndrome, 0.8 per 10,000 live births or 1 in 12,500 for Edwards' syndrome and 0.2 per 10,000 births, or 1 in 50,000 for Patau's syndrome respectively (Table 13).

Historical data from the **National Down Syndrome Cytogenetic Register (NDSCR)** presented in the NCARDRS 2015 and 2017 reports indicates that the live birth prevalence of Down's syndrome has remained largely stable since 2005, although it is important to note that the current and historical data are not directly comparable.

**Figure 12: The number of babies with Down's syndrome, Edwards's syndrome and Patau's syndrome born in England in 2018, and categorised by the timing of diagnosis**



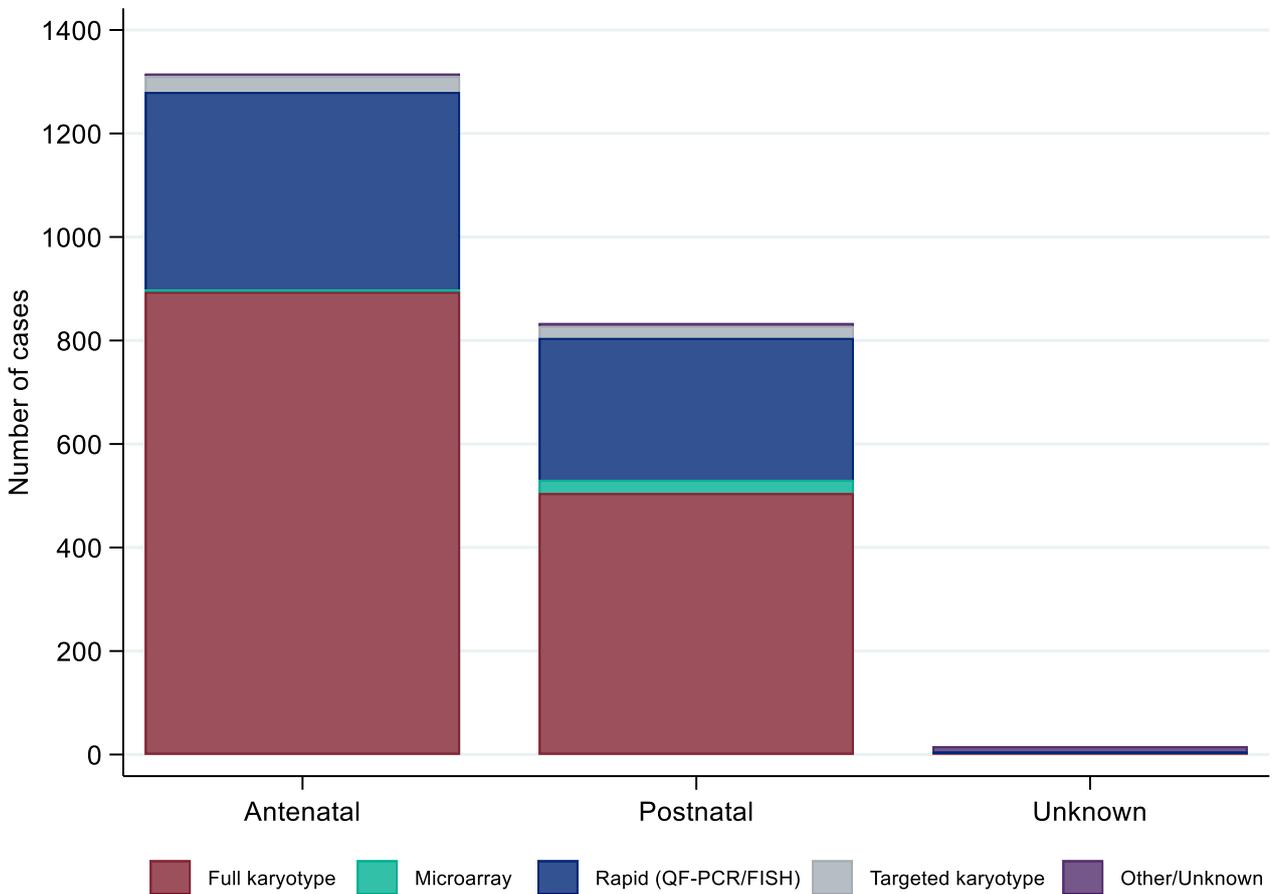
Most babies with a trisomy were diagnosed **antenatally** (Figure 12, Table 10, 11, 12), 55.9% of Down's syndrome, 75.3% of Edwards' syndrome and 68.2% of Patau's syndrome diagnoses were made antenatally. For pregnancies with a trisomy were diagnosed antenatally, the TOPFA rate was broadly similar across all 3 conditions, at 85.2% for Down's syndrome, 87.6% for Edwards' syndrome and 90.1% 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 2018, 46.0% with Down's syndrome were live born as were 11.6% of babies with Edwards syndrome and 8.1% of babies with Patau's syndrome.

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 (Figure 13). 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 2018**

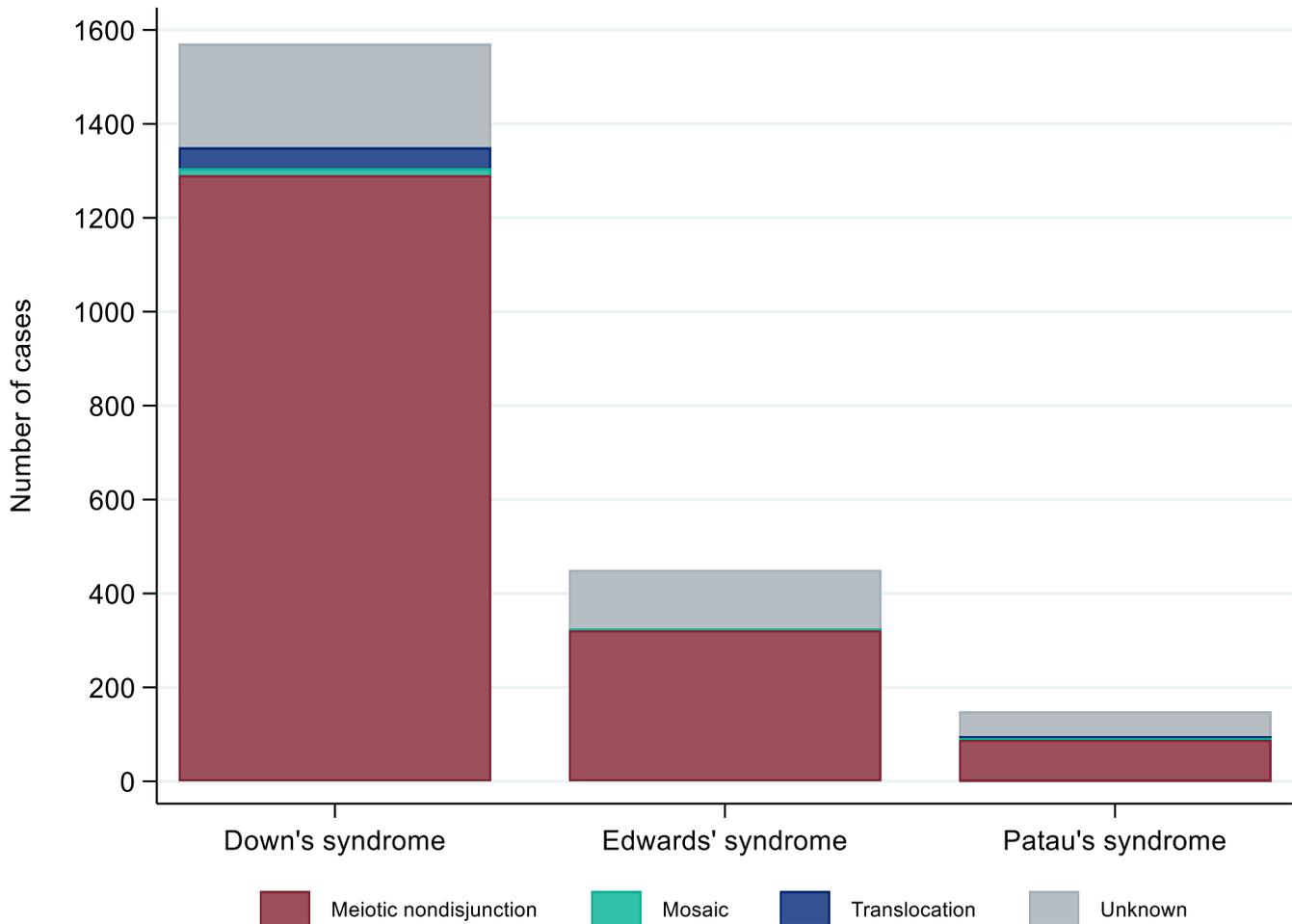


Antenatal diagnoses were primarily made from **chorionic villus sampling (CVS)** (54.1%) or **amniocentesis** (44.9%), with occasional fetal blood sampling (Table 14). Postnatal diagnoses include blood or saliva taken after a live birth, with venous blood representing 77% of all postnatal samples, and postmortem tissue specimens tested following a **late miscarriage, TOPFA, or a stillbirth.**

### 5.3 Origin of trisomies

Down’s syndrome, Edwards’ 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 syndrome, Edwards’ syndrome or Patau’s syndrome, with fewer translocation and mosaic cases being observed (Figure 14). 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.

**Figure 14: The number of babies diagnosed with Down’s syndrome, Edwards’ syndrome and Patau’s syndrome born in England in 2018 categorised by chromosome and underlying genetic mechanism<sup>7</sup>.**

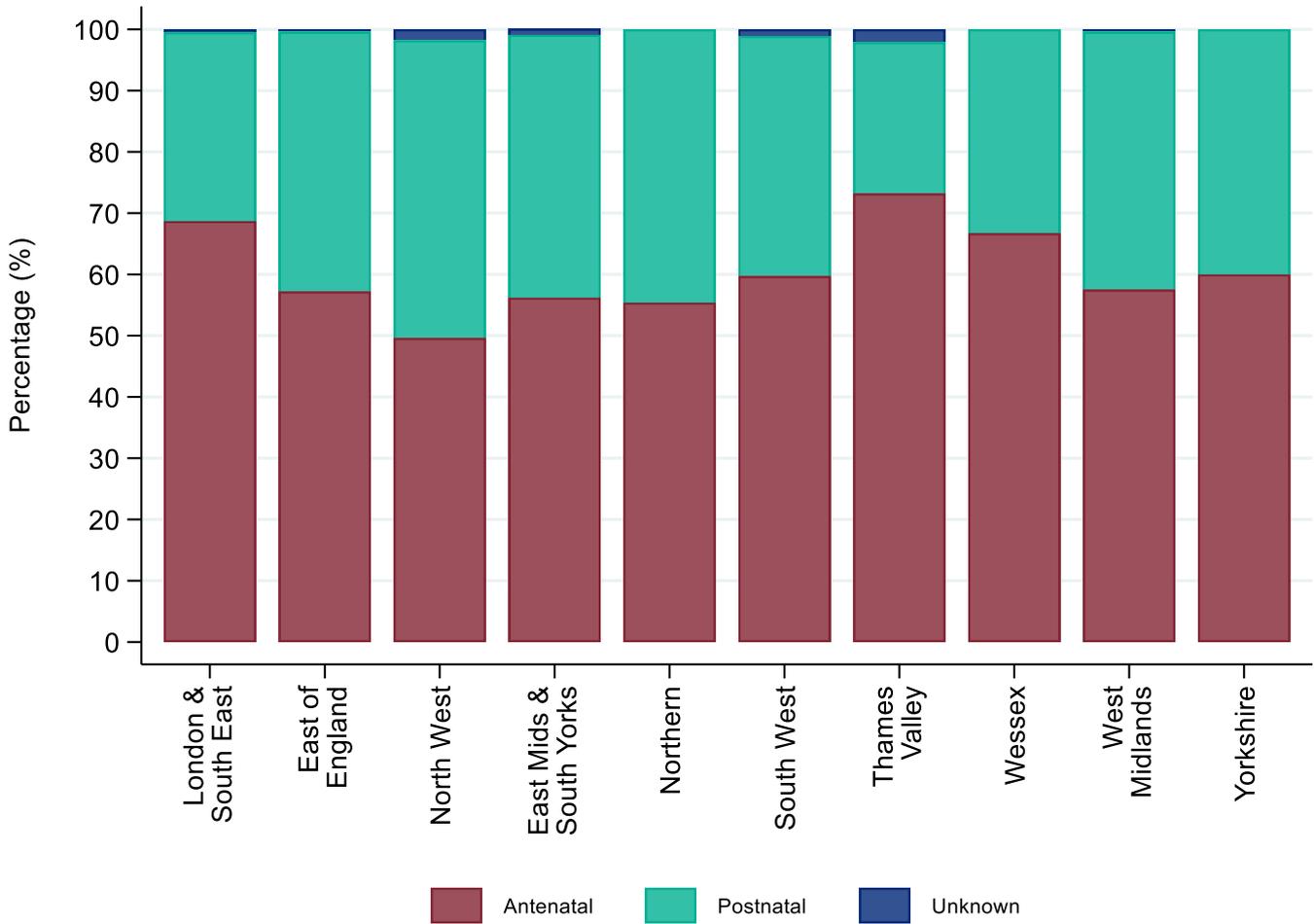


### 5.4 Regional differences in outcomes

Figures 15 and 16 show timing of diagnosis and differences in outcome split by geographical region. 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.

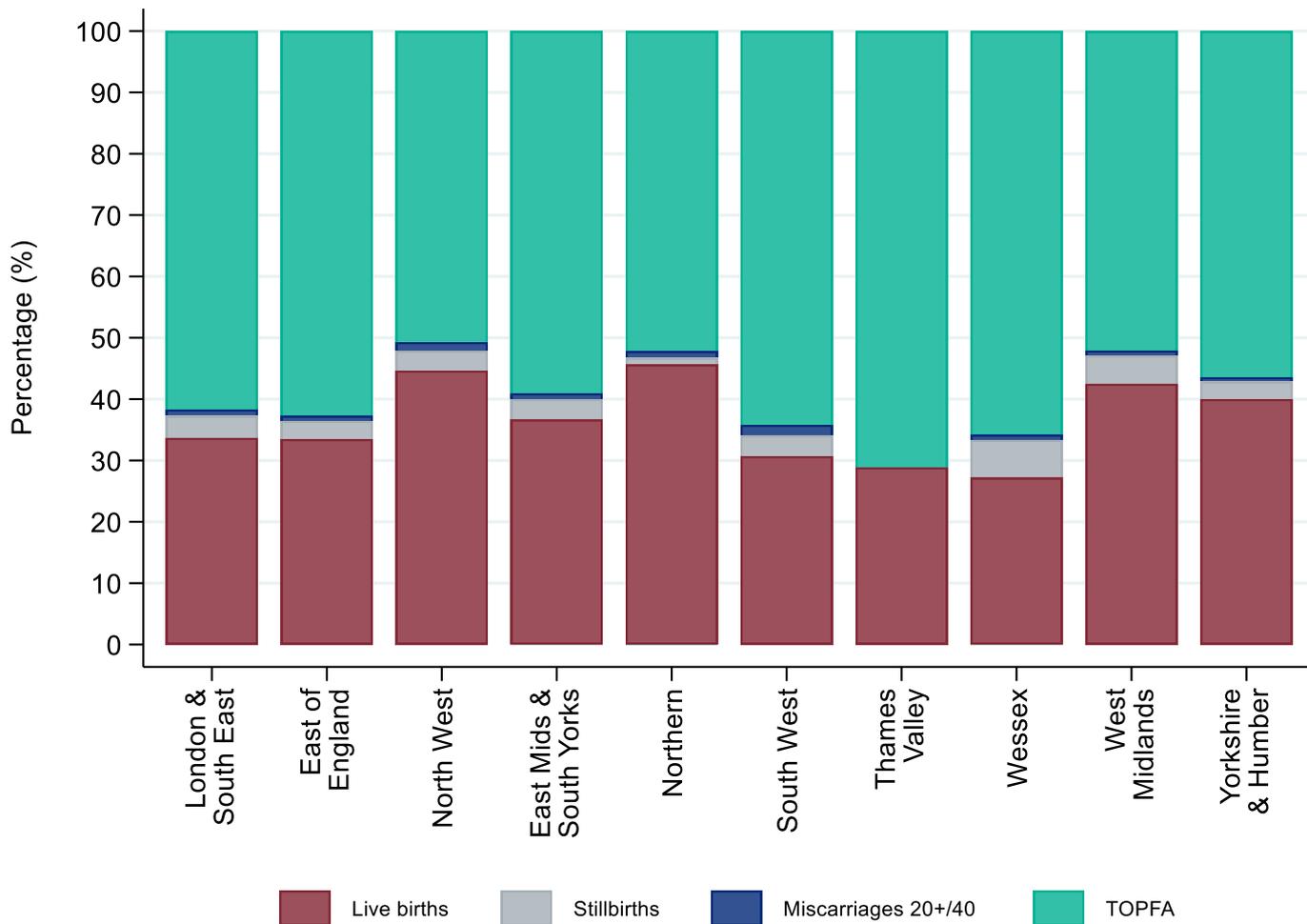
<sup>7</sup> See Box 3 for explanatory notes. Babies where the genetic type of trisomy is unspecified are those where conventional karyotyping failed or was not performed, i.e. they were diagnosed only by a rapid aneuploidy test or microarray; these latter tests cannot distinguish between standard and translocation trisomies.

**Figure 15: Timing of diagnosis for babies with Down’s syndrome, Edwards’ syndrome and Patau’s syndrome delivered in 2018, by NCARDRS region<sup>8</sup>**



<sup>8</sup> 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 2018, by NCARDRS 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). <sup>ii</sup>
Births/total births	Live births and stillbirths. <sup>iii</sup>
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.
Genetic anomalies	Includes chromosomal anomalies, skeletal dysplasias, genetic syndromes and microdeletions <sup>i</sup>
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 $\geq 10$ mm after birth. <sup>i</sup>
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).</p> <p>Anencephaly (Q00*)            Spina bifida (Q05*)            Transposition of great arteries (Q203)            Atrioventricular septal defect (Q212*)            Tetralogy of Fallot (Q213, Q2182)            Hypoplastic left heart (Q234)            Cleft lip +/- palate (Q36*, Q37*)            Bilateral renal agenesis (Q601)            Lethal skeletal dysplasia (Q770*, Q771, Q772, Q778*, Q780%)            Congenital diaphragmatic hernia (Q790*)            Exomphalos (Q792)            Gastroschisis (Q793)            Trisomy 21 (Q90*)            Trisomy 18 &amp; Trisomy 13 (Q91*)</p>
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. <sup>iv</sup>
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, procedures and outpatient appointments at NHS hospitals in England.
Infant deaths	Deaths from birth to under 1 year of age. <sup>ii</sup>
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. <sup>ii</sup>
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.

Term	Definition
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. <sup>i</sup>
National Down Syndrome Cytogenetic Register ( <b>NDSCR</b> ).	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. <sup>ii</sup>
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.

Term	Definition
Severe congenital heart disease (CHD)	<p>This includes the following congenital heart anomalies:</p> <ul style="list-style-type: none"> <li>• common arterial truncus</li> <li>• transposition of great vessels</li> <li>• single ventricle</li> <li>• atrioventricular septal defect</li> <li>• tetralogy of Fallot</li> <li>• tricuspid atresia and stenosis</li> <li>• Ebstein's anomaly</li> <li>• pulmonary valve atresia</li> <li>• aortic valve atresia/stenosis</li> <li>• hypoplastic left heart</li> <li>• hypoplastic right heart</li> <li>• coarctation of aorta</li> <li>• total anomalous pulmonary venous return</li> </ul>
Severe microcephaly	Where the head circumference is less than – 3 standard deviations for sex and gestational age. <sup>i</sup>
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. <sup>ii</sup>
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 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. 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.</p>

Term	Definition
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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<sup>i</sup> Data downloaded 29<sup>th</sup> June 2020

<sup>ii</sup> <http://www.eurocat-network.eu/>

<sup>iii</sup> <https://www.ons.gov.uk/>

<sup>iv</sup> Royal College of Obstetricians and Gynaecologists. The Future Workforce in Obstetrics and Gynaecology in England and Wales. Working Party Report. London: RCOG; 2009.