Public Health England

Protecting and improving the nation's health

National congenital anomaly and rare disease registration service

Congenital anomaly statistics 2015

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Foreword

It is a great pleasure to be writing a foreword to the first report on congenital anomaly statistics released by the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS).

PHE launched NCARDRS on 1 April 2015. Prior to this date, regional congenital anomaly registers existed and they reported data to the benefit of clinicians, epidemiologists, researchers and most importantly patients. Three new regional teams have now been established covering London, the South East, the North West and the East of England. Moving forward we will be expanding the geographical coverage of these reports. 2017/18 will be the first year that we will have national coverage of congenital anomalies, a major step forward.

The quality of these reports depends not only on the geographical completeness but more importantly on the willingness and enthusiasm of healthcare workers to report congenital anomalies. Hopefully, the usefulness of the data in this document will provide the necessary encouragement to continue submitting all relevant findings going forward leading to more comprehensive and valuable reports in the future.

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Executive summary

This is the first congenital anomaly statistics report to be published by the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS). It reports on data collected in 2014 and 2015. During this time PHE took over responsibility for congenital anomaly registration in England. In establishing NCARDRS we worked closely with the British Isles Network of Congenital Anomaly Registers (BINOCAR) and would like to thank them for all their guidance, help and support. To aid consistency, and given that this was a transition period, this report follows a similar format to previous reports released by BINOCAR.

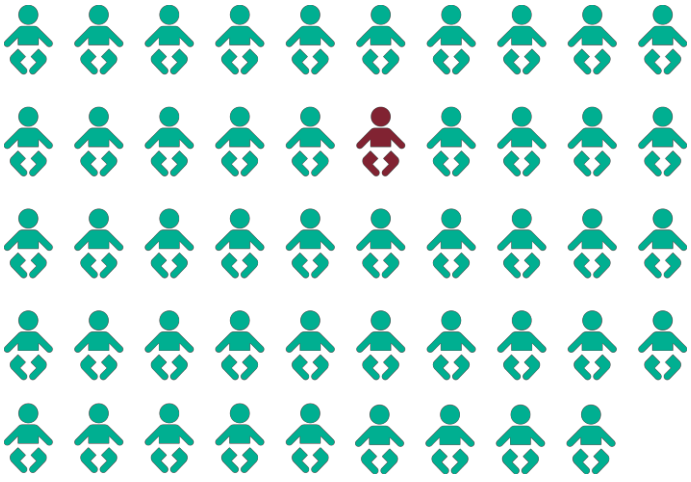
Data are presented from four NCARDRS regions, representing coverage of 21% of the total births in England to provide an estimate of birth prevalence of congenital anomalies nationally for 2015. Information from the Congenital Anomaly Register and Information Service for Wales is reported separately by Public Health Wales.

In addition, this report includes a focus on Down's syndrome, Edwards' syndrome and Patau's syndrome presenting data for all cases occurring in England up to 2014.

What does the data tell us?

In 2015, there were a total of 2,905 cases with one or more congenital anomaly notified to the four NCARDRS reporting regions, covering 141,474 total births.

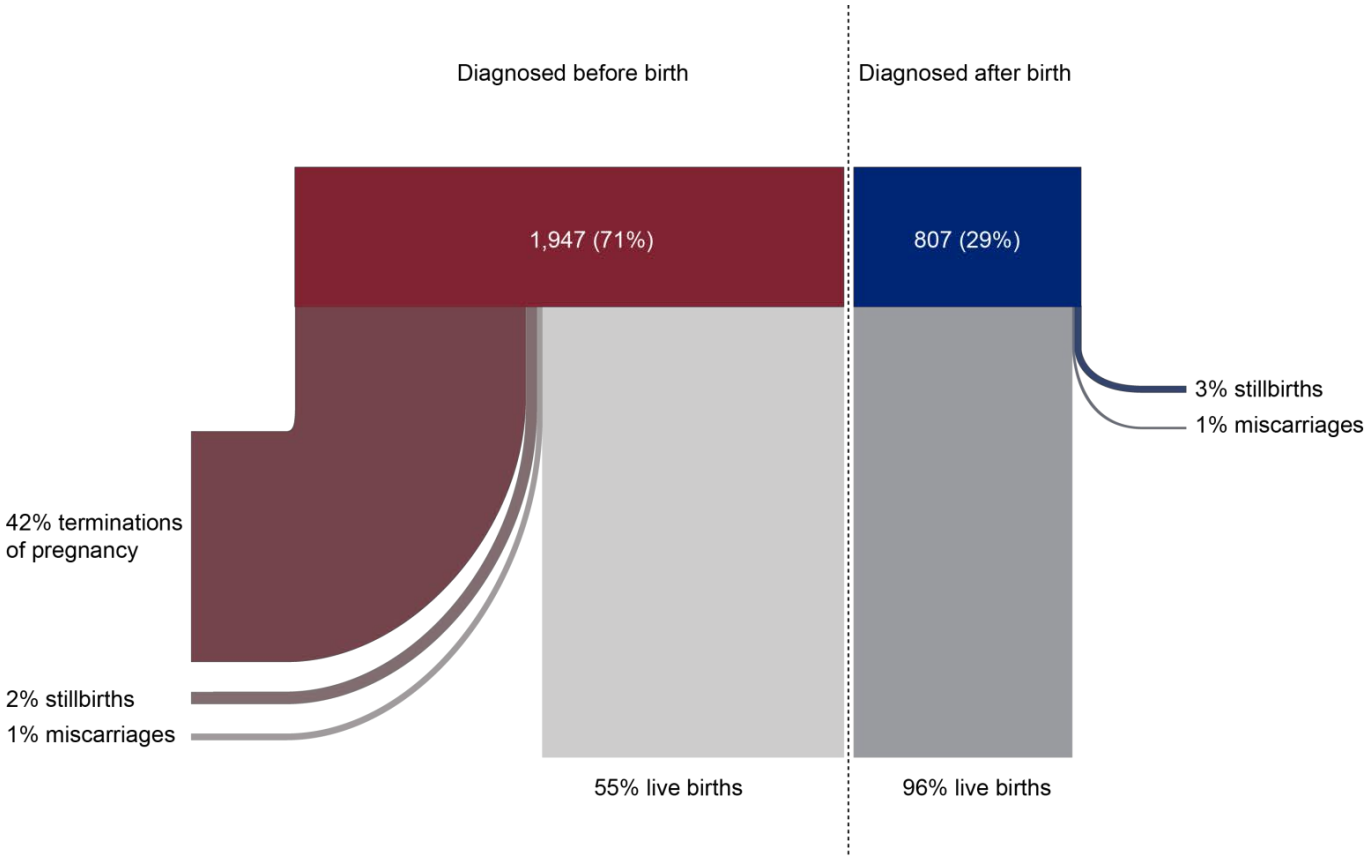
This gives an estimated overall birth prevalence of 205 per 10,000 total births or 1 in 49 births.



The most common congenital anomaly subgroups were those that were chromosomal in origin (eg Down's, Edwards', Patau's syndrome) with a prevalence of 50.2 per 10,000 total births, congenital heart defects with 49.9 per 10,000 total births and limb anomalies, 29.8 per 10,000 total births. Just over a quarter of congenital anomalies were known to be associated with genetic conditions.

In terms of the timing of diagnosis and outcome, of the 2,905 cases with one or more congenital anomaly, the timing of diagnosis was known for 95% of cases. Just over two

thirds of these were diagnosed prenatally (at any gestation) and nearly a third were diagnosed postnatally in 2015.



In 2015, the infant mortality rate in England was 39 per 10,000 live births, of which an estimated 17% had a congenital anomaly, based on the mortality rate in the four NCARDRS reporting regions.

Mothers aged between 25 and 29 at delivery had the lowest birth prevalence of all anomalies. The birth prevalence was significantly higher in the under-20 age group and in the 35-39 and 40 and over age groups.

The birth prevalence of the NCARDRS regions for all anomalies was not statistically significantly different to the prevalence of other EUROCAT registries. This reporting year was the first year of NCARDRS, and differences in the processing of cases and the sources by which cases were notified were still evident.

Future plans

Our aim is that NCARDRS acts as a much-needed resource to develop clinical research in the field of congenital anomalies and rare diseases, to improve patient care and inform healthcare planning and public health. To achieve this aim we are

committed to improving our data outputs and will continue to release data on both a greater geography and a wider number of rare diseases as we expand.

We now have national coverage in place for congenital anomaly registration. We plan to report statistics on congenital anomalies for the whole of England for the first time in 2019 (reporting on 2017/18 data).

The NCARDRS still has a long way to go but we now have a national infrastructure in place and our goal is to ensure that by 2020 clinicians and patients have access to information about congenital anomalies and rare diseases, their prevalence and trends in a clear, accessible and useful format. This report is a step towards that aim.

Thank you for your interest in NCARDRS. We welcome your feedback and suggestions on how to improve in the future. For comments and suggestions, please contact us at **ncardrs@phe.gov.uk**

Glossary

Term	Definition
18+0 to 20+6 weeks' fetal anomaly scan	A detailed ultrasound scan offered to all pregnancy women for the purpose of assessing the fetus for structural anomalies. The optimal period for undertaking the scan is 18^{+0} to 20^{+6} weeks of pregnancy with screening completed by 23^{+0} weeks where one further scan is required to complete examination of the fetal anatomy due to fetal lie or maternal factors (eg high BMI).
95% confidence interval	This provides a range of values in which the true underlying birth prevalence will fall 95% of the time.
Amniocentesis	A method of prenatal diagnosis where a small amount of amniotic fluid is taken and then tested for chromosomal abnormalities.
Antenatal/prenatal	The period from conception to birth.
Birth prevalence	The total number of cases of congenital anomaly (live births, stillbirths, late miscarriages and terminations of pregnancy with fetal anomaly) compared to the total number of births (live births and stillbirths).
Births/total births	Live births and stillbirths.
Case	A baby/fetus with one or more congenital anomaly. Includes live births, stillbirths, late miscarriages and terminations of pregnancy with fetal anomaly.
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)	A method of prenatal diagnosis where a sample of the chorionic villus (placental tissue) is taken and then tested for chromosomal abnormalities.
Combined Test	Screening test for trisomies 21, 18 and 13; available between 10 and 14 weeks of pregnancy. It involves a blood test and an ultrasound scan, and uses mother's age.

Congenital anomaly	Any defect present at delivery, probably originating before birth, and includes structural, chromosomal, genetic and biochemical defects and malformations.
Congenital hydronephrosis	An obstruction of the urinary flow from kidney to bladder. Cases are registered where the renal pelvis is ≥10 mm after birth.
Cytogenetics	The study of chromosomes. Clinical cytogenetics is the study of the relationship between chromosome aberrations and disease.
Infant mortality rate	The number of deaths of babies less than one year of age per 1,000 live births.
Karyotyping	A test to examine chromosomes and help to identify genetic problems as a cause of disease.
Late miscarriage	Late fetal deaths from 20-23 completed weeks of gestation.
Live birth	Delivery of an infant, which, after complete separation from its mother, shows signs of life.
Non-invasive prenatal test (NIPT)	Non-invasive cell free DNA blood test for Down's, Edwards' and Patau's syndrome
Nuchal translucency (NT)	Ultrasound measurement of the fluid at the back of the baby's neck.
Prenatal diagnosis	A diagnosis made in a live fetus at any gestation.
Quadruple test	Screening test for trisomy 21; available between 14 and 20 weeks of pregnancy. It involves a blood test and uses mother's age.

Severe congenital heart defects (CHD)	This includes the following congenital heart defects: - 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.
Stillbirths	Late fetal deaths from 24 completed weeks of gestation, The baby is born showing no signs of life.
Termination of pregnancy with fetal anomaly (TOPFA)	Term used to describe the deliberate ending of a pregnancy with the intention that the fetus will not survive and which is carried out when the fetus is diagnosed prenatally as having a major congenital anomaly.
Ultrasound scan	A medical, non-invasive investigative screening examination which uses ultrasound to create real-time images on a monitor.

Incidence and birth prevalence

Incidence is the total number of 'new' cases of disease occurring in a population in a specified time period, whereas prevalence is the total number of 'all' cases in a population at one point in time. Conventionally, as in this report, congenital anomaly registers report prevalence estimates. This is because it is not possible to ascertain all 'new' cases of any particular anomaly, as a proportion of pregnancies affected with an anomaly will miscarry spontaneously before being diagnosed. We also do not have a population estimate of the total number of pregnancies at risk of being affected by an anomaly due to miscarriages and terminations of pregnancy. Therefore congenital anomaly registers report prevalence estimates per 1,000 or 10,000 total births (live and stillbirths). By convention these are referred to as birth prevalence estimates even though the pregnancy may not result in a 'birth' because of late miscarriage or termination of pregnancy.

Calculation of birth prevalence and their 95% confidence intervals:

$$\text{Birth prevalence} = \frac{\text{Number of cases (live births + stillbirths + late miscarriages + TOPFAs)}}{\text{Number of births (live births+stillbirths)}} \times 10{,}000$$

$$\text{Lower 95\% confidence limit} = \frac{\left(\frac{1.96}{2} - \sqrt{\text{number of cases} + 0.02}\right)^2}{\text{number of births}} \times 10{,}000$$

$$\text{Upper 95\% confidence limit} = \frac{\left(\frac{1.96}{2} + \sqrt{\text{number of cases} + 0.96}\right)^2}{\text{number of births}} \times 10{,}000$$

The confidence intervals are calculated using the Poisson distribution.[1]

[1] Bégaud B, Martin K, Abouelfath A, Tubert-Bitter P, Moore N, Moride Y. An easy to use method to approximate Poisson confidence limits. European Journal of Epidemiology 2005; 20:213-216.

Background

In response to the UK Rare Disease Strategy and the Chief Medical Officers' recommendation to ensure nationwide coverage of congenital anomaly registration, Public Health England committed to the expansion of congenital anomaly and rare disease registration in England and launched NCARDRS on 1 April 2015. Prior to that only half of the country collected data on congenital anomalies.

A wide public consultation was conducted and the creation of the NCARDRS supports the request from patients and their carers for the formation of a national register of rare diseases. We continue to work closely with patients and patient groups.

This national service incorporated the existing regional congenital anomaly registers[2], the National Down Syndrome Cytogenetic Register (NDSCR) and the BINOCAR hub. In those parts of the country where there was no data collection – London, the South East, East of England and the North West – three new regional teams have been established and for the first time we now have a national infrastructure in place.

Our aim is to provide a comprehensive national registration service for all congenital anomalies and rare diseases diagnosed and treated in England in order to:

- provide a resource for clinicians to support high quality clinical practice.
- support and empower patients and their carers, through the provision of information relevant to their disease or disorder.
- provide epidemiology and monitoring of the frequency, nature, cause and outcomes of these disorders.
- support all research into congenital anomalies, rare diseases and precision medicine including basic science, cause, prevention, diagnostics, treatment and management.
- inform the planning and commissioning of public health and health and social-care provision.
- provide a resource to monitor, evaluate and audit health and social-care services, including the efficacy and outcomes of screening programmes.

Data collection

A congenital anomaly is defined as any defect present at delivery, probably originating before birth, and includes structural, chromosomal, genetic and biochemical defects and malformations. Some congenital anomalies are detected during pregnancy, some are found at birth, while others become obvious only as a baby grows older.

[2] CAROBB; Congenital Anomaly Register for Oxfordshire, Berkshire and Buckinghamshire, EMSYCAR; East Midlands and South Yorkshire Congenital Anomalies Register, NorCAS: Northern Congenital Abnormality Survey, SWCAR; South West Congenital Anomaly Register, WANDA; Wessex Antenatally Detected Anomalies Register, WMCAR: West Midlands Congenital Anomaly Register and YHCAR; Yorkshire and the Humber Congenital Anomalies Register

Congenital anomaly data are collected from a number of different sources including:

- Maternity units
- Neonatal units
- Diagnostic departments (paediatric, neonatal, clinical genetics, antenatal ultrasound, fetal medicine, pathology)
- Genetic laboratories
- NHS Trust IT departments
- Child health systems
- Local audit schemes
- Disease-specific registers
- Neighbouring national registers

This multiple source reporting enables NCARDRS to achieve the highest possible ascertainment of congenital anomalies in the population. Much of the focus to date has been on ensuring high ascertainment and completeness of cases and ensuring consistency and standardisation across the country.

A single data management system has been developed and we have a team of around 35 dedicated registration officers and analysts. We currently take data from over 500 NHS providers across the country and have moved entirely to electronic notifications, ceasing all paper notifications, in order to improve information governance, efficiency and reporting.

Data are collected on all suspected and confirmed congenital anomalies identified in utero, at birth or at any point in childhood. In addition to live births and stillbirths affected by congenital anomalies, information about terminations of pregnancy with a diagnosed fetal anomaly at any gestation (TOPFA) and late miscarriages (20-23 weeks' gestation) where an anomaly is present, are also collected.

NCARDRS collects information about the mother and child, including postcode of residence, mother's age, pregnancy length, pregnancy outcome, when and how the anomaly was identified and the details of each anomaly. Some identifiable information is collected on the mother and child but only enough information to avoid duplicate registrations and for the validations of cases, ensuring accurate matching between antenatally diagnosed anomalies and postnatal notifications.

Data confidentiality

NCARDRS is authorised under Section 251 of the NHS Act 2006 to collect personal information without individual consent (CAG 10-02(d)2015). This exemption was granted by the Confidentiality Advisory Group (CAG) and is renewed each year following an annual review. Details of our current approval can be found on the Health Research Authority website. CAG reference CAG 10-02(d)/2015.

Recognising the extraordinary privilege of Section 251, NCARDRS has very strict policies approved by PHE and HRA that cover data collection, storage and release. Patients have an absolute right of opt-out from the register.

In line with the Disclosure Control Guidance where appropriate, statistics in this report will be disclosure-controlled to protect confidentiality. Data at the national, combined regional and individual regional level are considered to be at low risk of deductive disclosure, due to the large size of the
at-risk populations reported, so no suppression has been applied.

Data quality

As with all surveillance data, the numbers, percentages and prevalence rates presented in this report depend on ascertainment, detection of cases at all stages of diagnosis and notification to the service. Although we use a multiple source approach, maternity services are the most common source, and postnatal ascertainment is known to be lower than antenatal ascertainment. This means it is likely there is a reporting bias towards severity of congenital anomalies and against postnatal cases that manifest beyond the first year of life. All four reporting regions submitted data to the European Surveillance of Congenital Anomalies (EUROCAT) and followed their data quality procedures. In addition, NCARDRS has established national processes and systems for data collection, processing and quality assurance, adopting internationally approved methods of coding, recording, and analysis.

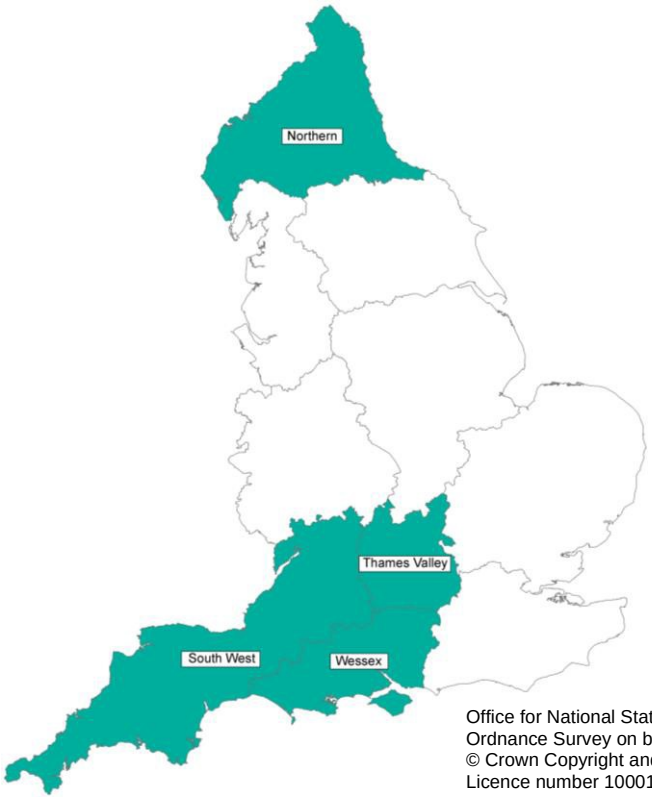
Chapter 1: Prevalence of congenital anomalies

1.1 Prevalence of congenital anomalies in 2015

This report describes cases with at least one congenital anomaly, born between 1 January and 31 December 2015, that were resident in the following NCARDRS regions: Northern, South West, Thames Valley and Wessex (see Figure 1.1 for a map of the geographical reporting and see Appendix A for a list of the geographical coverage of each region). Although two other regions were operational in 2015 these are the four regions that submitted data to EUROCAT for that period. From the 1 April 2017 we have national coverage for congenital anomaly registration and will be able to provide data for the whole of England from 2019. Information from the Congenital Anomaly Register and Information Service for Wales is reported separately.

In 2015, there were a total of 2,905 cases with one or more congenital anomaly notified to the four NCARDRS reporting regions covering 141,474 total births. This represents coverage of 21% of the total births in England. This gives a provisional overall birth prevalence of 205 per 10,000 total births (95% CI: 198, 213) or 1 in 49 births.

Figure 1.1: Map of England showing geographical coverage of the NCARDRS regions included in this report



Of the 2,905 cases with one or more anomaly, 1,998 were live births, 73 were stillbirths, 21 were late miscarriages and 813 were TOPFA. The TOPFAs include those cases civilly registered as live birth or stillbirths – stillborn after 24 weeks of pregnancy, or where parents have opted not to have fetocide performed prior to delivery and the TOPFA procedure resulted in a live birth. The TOPFA rate presented here may be an underestimate as some parents are using private screening services for NIPT and this is likely to have resulted in TOPs outside the NHS that are not captured in this data.

The most common congenital anomaly subgroups in the four reporting NCARDRS regions were those that were chromosomal in origin (eg Down's/Edwards'/Patau's syndrome), with 710 cases and congenital heart defects with 706 cases in 2015 (both with a prevalence of 50 per 10,000 total births, Table 1.1). For ease, table 1.2 identifies the conditions screened for by the fetal anomaly screening programme.

Just over a quarter (28%) of congenital anomalies were known to be associated with genetic conditions (for example, congenital heart defects are often detected in babies with Down's syndrome) but this proportion varied according to the type of anomaly (the true percentage is likely to be higher as not all babies with congenital anomalies are routinely karyotyped). For example, a larger proportion of abdominal wall (23%) and congenital heart defects (23%) were detected in cases with underlying genetic conditions, compared with oro-facial clefts (11%), urinary (8%) and genital anomalies (7%) (Figure 1.2).

Figure 1.2: Number and percentage of cases according to congenital anomaly subgroup, classified by those including and excluding genetic conditions; four reporting NCARDRS regions (coverage: 21% of births in England): 2015

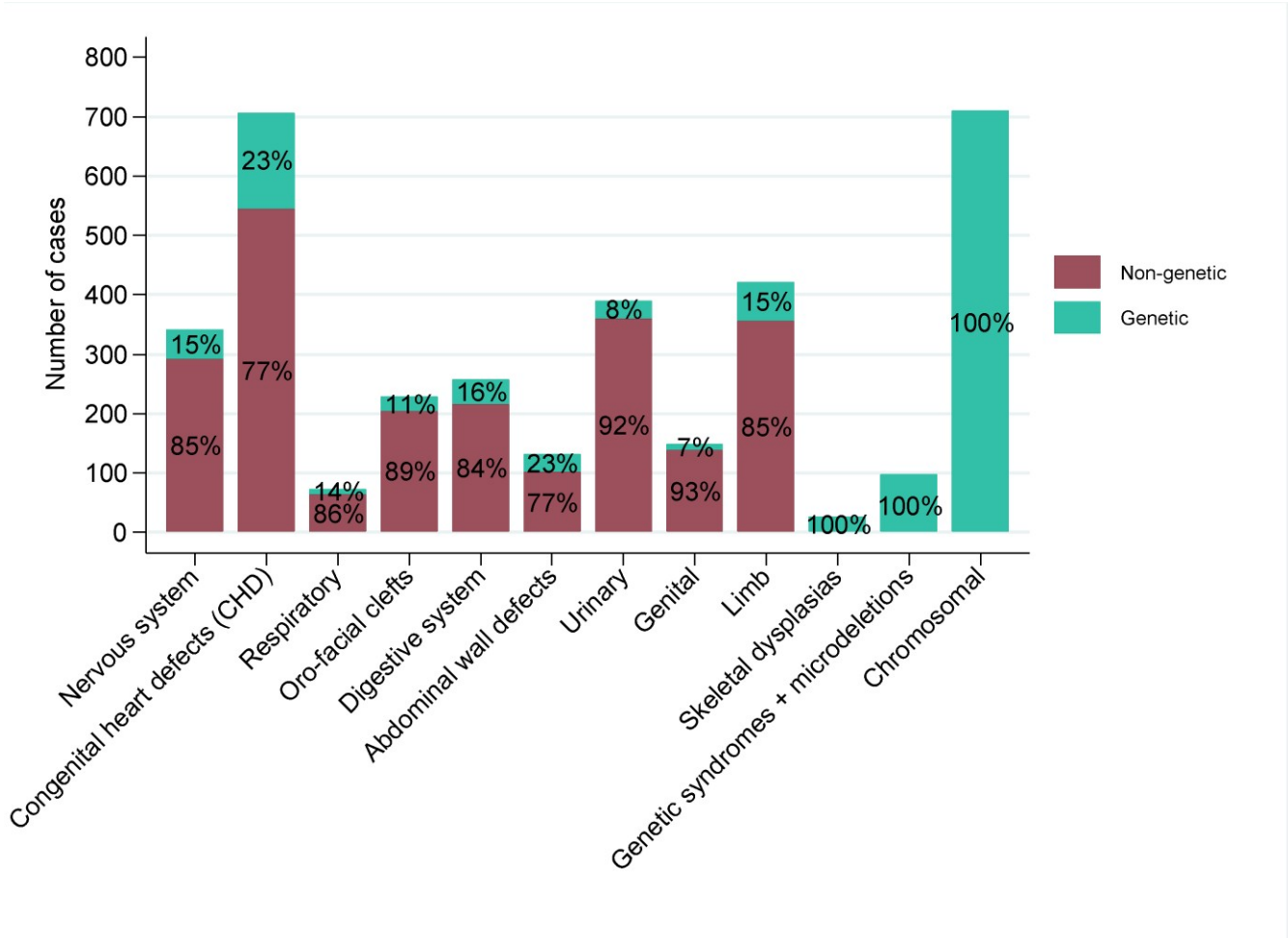


Table 1.1: Number of cases, birth prevalence (per 10,000 total births) and 95% CIs according to congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	Including genetic conditions						Excluding genetic conditions[2]	
	Number					Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]
	LB	SB	Misc	TOPFA	Total		Total	
Total births	**140,928**	**546**	**..**	**..**	**141,474**	**..**	**..**	**..**
All cases	**1,998**	**73**	**21**	**813**	**2,905**	**205.3 [197.9, 212.9]**	**2,086**	**147.4 [141.2, 153.9]**
Nervous system	**102**	**11**	**-**	**228**	**341**	**24.1 [21.6, 26.8]**	**291**	**20.6 [18.3, 23.1]**
Neural tube defects	21	3	-	140	164	11.6 [9.9, 13.5]	153	10.8 [9.2, 12.7]
Anencephaly and similar malformations	1	3	-	68	72	5.1 [4.0, 6.4]	69	4.9 [3.8, 6.2]
Encephalocele	1	-	-	16	17	1.2 [0.7, 1.9]	15	1.1 [0.6, 1.7]
Spina bifida	19	-	-	56	75	5.3 [4.2, 6.6]	69	4.9 [3.8, 6.2]
Hydrocephalus	44	2	-	35	81	5.7 [4.5, 7.1]	68	4.8 [3.7, 6.1]
Severe microcephaly	7	3	-	3	13	0.9 [0.5, 1.6]	8	0.6 [0.2, 1.1]
Arhinencephaly/holoprosencephaly	7	2	-	25	34	2.4 [1.7, 3.4]	23	1.6 [1.0, 2.4]
Congenital heart defects (CHD)	**573**	**18**	**4**	**111**	**706**	**49.9 [46.3, 53.7]**	**545**	**38.5 [35.4, 41.9]**
Severe CHD	239	9	1	78	327	23.1 [20.7, 25.8]	249	17.6 [15.5, 19.9]
Common arterial truncus	4	-	-	2	6	0.4 [0.2, 0.9]	3	0.2 [0.0, 0.6]
Double outlet right ventricle	23	3	-	10	36	2.5 [1.8, 3.5]	29	2.0 [1.4, 2.9]
Transposition of great vessels	48	1	-	8	57	4.0 [3.1, 5.2]	52	3.7 [2.7, 4.8]
Single ventricle	7	1	-	4	12	0.8 [0.4, 1.5]	11	0.8 [0.4, 1.4]
Ventricular septal defect	277	4	3	36	320	22.6 [20.2, 25.2]	255	18.0 [15.9, 20.4]
Atrial septal defect	115	3	1	6	125	8.8 [7.4, 10.5]	86	6.1 [4.9, 7.5]
Atrioventricular septal defect	33	2	-	25	60	4.2 [3.2, 5.5]	27	1.9 [1.3, 2.8]
Tetralogy of Fallot	42	1	-	8	51	3.6 [2.7, 4.7]	39	2.8 [2.0, 3.8]
Tricuspid atresia and stenosis	8	-	-	1	9	0.6 [0.3, 1.2]	9	0.6 [0.3, 1.2]
Ebstein's anomaly	2	2	-	1	5	0.4 [0.1, 0.8]	5	0.4 [0.1, 0.8]
Pulmonary valve stenosis	46	-	-	3	49	3.5 [2.6, 4.6]	43	3.0 [2.2, 4.1]
Pulmonary valve atresia	13	-	-	6	19	1.3 [0.8, 2.1]	17	1.2 [0.7, 1.9]
Aortic valve atresia/stenosis	16	-	-	5	21	1.5 [0.9, 2.3]	16	1.1 [0.6, 1.8]
Mitral valve anomalies	11	-	-	4	15	1.1 [0.6, 1.7]	10	0.7 [0.3, 1.3]
Hypoplastic left heart	22	1	1	20	44	3.1 [2.3, 4.2]	35	2.5 [1.7, 3.4]
Hypoplastic right heart	6	-	-	4	10	0.7 [0.3, 1.3]	10	0.7 [0.3, 1.3]
Coarctation of aorta	44	1	-	4	49	3.5 [2.6, 4.6]	39	2.8 [2.0, 3.8]
Aortic atresia/interrupted aortic arch	8	1	-	1	10	0.7 [0.3, 1.3]	6	0.4 [0.2, 0.9]

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Genetic conditions include chromosomal, skeletal dysplasias, genetic syndromes and microdeletions.
- = 0
.. = Not applicable
LB = Live birth, SB = Stillbirth (24+ weeks), Misc = Late miscarriage (20-23 weeks), TOPFA = Termination of pregnancy with fetal anomaly

Table 1.1 cont'd: Number of cases, birth prevalence (per 10,000 total births) and 95% CIs according to congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	Including genetic conditions						Excluding genetic conditions[2]	
	Number					Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]
	LB	SB	Misc	TOPFA	Total		Total	
Total anomalous pulmonary venous return	12	-	-	1	13	0.9 [0.5, 1.6]	13	0.9 [0.5, 1.6]
Patent ductus arteriosus as only CHD in term infants (GA 37+ weeks)	14	-	-	-	14	1.0 [0.5, 1.7]	9	0.6 [0.3, 1.2]
Respiratory	**61**	**1**	**-**	**11**	**73**	**5.2 [4.0, 6.5]**	**63**	**4.5 [3.4, 5.7]**
Choanal atresia	7	-	-	2	9	0.6 [0.3, 1.2]	8	0.6 [0.2, 1.1]
Cystic adenomatous malformation of lung	28	-	-	-	28	2.0 [1.3, 2.9]	28	2.0 [1.3, 2.9]
Oro-facial clefts	**202**	**1**	**2**	**23**	**228**	**16.1 [14.1, 18.3]**	**204**	**14.4 [12.5, 16.5]**
Cleft lip with or without cleft palate	125	1	1	21	148	10.5 [8.8, 12.3]	134	9.5 [7.9, 11.2]
Cleft palate	77	-	1	2	80	5.7 [4.5, 7.0]	70	4.9 [3.9, 6.3]
Digestive system	**194**	**8**	**3**	**52**	**257**	**18.2 [16.0, 20.5]**	**215**	**15.2 [13.2, 17.4]**
Oesophageal atresia with or without trachea-oesophageal fistula	39	-	1	6	46	3.3 [2.4, 4.3]	39	2.8 [2.0, 3.8]
Duodenal atresia or stenosis	19	1	1	4	25	1.8 [1.1, 2.6]	16	1.1 [0.6, 1.8]
Atresia or stenosis of other parts of small intestine	17	-	-	-	17	1.2 [0.7, 1.9]	14	1.0 [0.5, 1.7]
Ano-rectal atresia and stenosis	29	1	-	10	40	2.8 [2.0, 3.8]	35	2.5 [1.7, 3.4]
Hirschsprung's disease	12	-	-	-	12	0.8 [0.4, 1.5]	10	0.7 [0.3, 1.3]
Diaphragmatic hernia	39	2	1	12	54	3.8 [2.9, 5.0]	48	3.4 [2.5, 4.5]
Abdominal wall defects	**80**	**6**	**1**	**44**	**131**	**9.3 [7.7, 11]**	**101**	**7.1 [5.8, 8.7]**
Gastroschisis	53	2	-	6	61	4.3 [3.3, 5.5]	60	4.2 [3.2, 5.5]
Exomphalos (omphalocele)	27	3	1	36	67	4.7 [3.7, 6.0]	39	2.8 [2.0, 3.8]
Urinary	**305**	**5**	**3**	**77**	**390**	**27.6 [24.9, 30.4]**	**360**	**25.4 [22.9, 28.2]**
Bilateral renal agenesis including Potter syndrome	-	2	1	22	25	1.8 [1.1, 2.6]	22	1.6 [1.0, 2.4]
Multicystic renal dysplasia	72	1	-	10	83	5.9 [4.7, 7.3]	80	5.7 [4.5, 7.0]
Congenital hydronephrosis	128	-	-	6	134	9.5 [7.9, 11.2]	133	9.4 [7.9, 11.1]
Bladder exstrophy and/or epispadias	3	-	-	3	6	0.4 [0.2, 0.9]	5	0.4 [0.1, 0.8]
Posterior urethral valve and/or prune belly	11	-	-	6	17	1.2 [0.7, 1.9]	16	1.1 [0.6, 1.8]
Genital	**138**	**3**	**-**	**8**	**149**	**10.5 [8.9, 12.4]**	**138**	**9.8 [8.2, 11.5]**
Hypospadias	110	1	-	2	113	8.0 [6.6, 9.6]	109	7.7 [6.3, 9.3]
Indeterminate sex	13	-	-	1	14	1.0 [0.5, 1.7]	13	0.9 [0.5, 1.6]
Limb	**305**	**14**	**6**	**96**	**421**	**29.8 [27.0, 32.7]**	**356**	**25.2 [22.6, 27.9]**
Limb reduction defects	37	3	1	27	68	4.8 [3.7, 6.1]	48	3.4 [2.5, 4.5]
Club foot – talipes equinovarus	139	9	4	33	185	13.1 [11.3, 15.1]	173	12.2 [10.5, 14.2]

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Genetic conditions include chromosomal, skeletal dysplasias, genetic syndromes and microdeletions.
- = 0
LB = Live birth, SB = Stillbirth (≥24 weeks), Misc = Late miscarriage (20-23 weeks), TOPFA = Termination of pregnancy with fetal anomaly
CHD = Congenital heart defects, GA = Gestational age

Table 1.1 cont'd: Number of cases, birth prevalence (per 10,000 total births) and 95% CIs according to congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	Including genetic conditions						Excluding genetic conditions[2]	
	Number					Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]
	LB	SB	Misc	TOPFA	Total		Total	
Hip dislocation and/or dysplasia	24	-	-	1	25	1.8 [1.1, 2.6]	23	1.6 [1.0, 2.4]
Polydactyly	72	-	1	9	82	5.8 [4.6, 7.2]	67	4.7 [3.7, 6.0]
Syndactyly	17	-	-	4	21	1.5 [0.9, 2.3]	15	1.1 [0.6, 1.7]
Other anomalies/syndromes								
Skeletal dysplasias	11	1	1	14	27	1.9 [1.3, 2.8]	..	..
Genetic syndromes and microdeletions	75	4	1	17	97	6.9 [5.6, 8.4]	..	..
Chromosomal	**274**	**25**	**6**	**405**	**710**	**50.2 [46.6, 54.0]**	**..**	**..**
Down's syndrome[3]	138	8	2	199	347	24.5 [22.0, 27.2]	..	..
Patau's syndrome/trisomy 13[3]	6	1	-	32	39	2.8 [2.0, 3.8]	..	..
Edwards' syndrome/trisomy 18[3]	8	5	-	80	93	6.6 [5.3, 8.1]	..	..
Turner's syndrome	11	1	2	32	46	3.3 [2.4, 4.3]	..	..
Klinefelter's syndrome	7	1	-	4	12	0.8 [0.4, 1.5]	..	..

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Genetic conditions include chromosomal, skeletal dysplasias, genetic syndromes and microdeletions.
3 Information on Down's syndrome, Patau's syndrome and Edwards' syndrome for the whole of England can be found in Chapter 5.
- = 0
.. = Not applicable
LB = Live birth, SB = Stillbirth (≥24 weeks), Misc = Late miscarriage (20-23 weeks), TOPFA = Termination of pregnancy with fetal anomaly

Table 1.2: Number of cases, birth prevalence (per 10,000 total births) and 95% CIs according to the FASP conditions; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

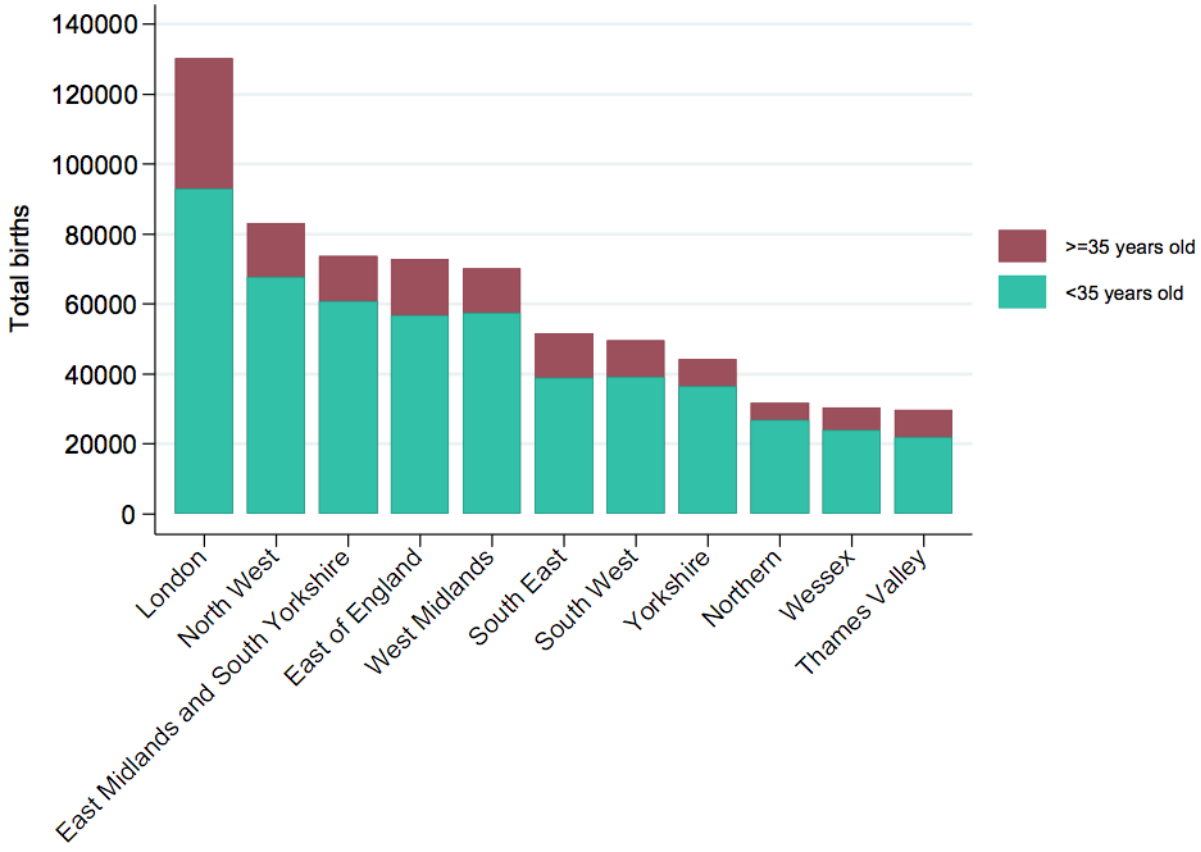
Congenital anomaly[1]	Including genetic conditions						Excluding genetic conditions[2]	
	Number					Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]
	LB	SB	Misc	TOPFA	Total		Total	
Total births	**140,928**	**546**	**..**	**..**	**141,474**	**..**	**..**	**..**
Anencephaly and similar malformations	1	3	-	68	72	5.1 [4.0, 6.4]	69	4.9 [3.8, 6.2]
Open spina bifida	10	-	-	18	28	2.0 [1.3, 2.9]	27	1.9 [1.3, 2.8]
Serious cardiac anomalies	144	4	1	59	208	14.7 [12.8, 16.8]	150	10.6 [9.0, 12.4]
Transposition of great vessels	48	1	-	8	57	4.0 [3.1, 5.2]	52	3.7 [2.7, 4.8]
Atrioventricular septal defect	33	2	-	25	60	4.2 [3.2, 5.5]	27	1.9 [1.3, 2.8]
Tetralogy of Fallot	42	1	-	8	51	3.6 [2.7, 4.7]	39	2.8 [2.0, 3.8]
Hypoplastic left heart	22	1	1	20	44	3.1 [2.3, 4.2]	35	2.5 [1.7, 3.4]
Cleft lip with or without cleft palate	125	1	1	21	148	10.5 [8.8, 12.3]	134	9.5 [7.9, 11.2]
Diaphragmatic hernia	39	2	1	12	54	3.8 [2.9, 5.0]	48	3.4 [2.5, 4.5]
Gastroschisis	53	2	-	6	61	4.3 [3.3, 5.5]	60	4.2 [3.2, 5.5]
Exomphalos (omphalocele)	27	3	1	36	67	4.7 [3.7, 6.0]	39	2.8 [2.0, 3.8]
Bilateral renal agenesis	-	2	1	21	24	1.7 [1.1, 2.5]	21	1.5 [0.9, 2.3]
Lethal skeletal dysplasias	6	1	-	7	14	1.0 [0.5, 1.7]	..	..
Down's syndrome[3]	138	8	2	199	347	24.5 [22.0, 27.2]	..	..
Patau's syndrome/trisomy 13[3]	6	1	-	32	39	2.8 [2.0, 3.8]	..	..
Edwards' syndrome/trisomy 18[3]	8	5	-	80	93	6.6 [5.3, 8.1]	..	..

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Genetic conditions include chromosomal, skeletal dysplasias, genetic syndromes and microdeletions.
3 Information on Down's syndrome, Patau's syndrome and Edwards' syndrome for the whole of England can be found in Chapter 5.
- = 0
.. = Not applicable
LB = Live birth, SB = Stillbirth (≥24 weeks), Misc = Late miscarriage (20-23 weeks), TOPFA = Termination of pregnancy with fetal anomaly

1.2 Estimated numbers of cases in England

The approximate number of congenital anomalies in the whole of England in 2015 can be estimated by applying the birth prevalence estimated from the four NCARDRS reporting regions for 2015 to the total number of births in England in 2015 (667,351) assuming that the birth prevalence was consistent over the whole of England. This is currently the best measure that we have, but it is presented here with the awareness that there is likely to be significant differences in prevalence across England due to differences in demographics, and that underpins the need to establish true national coverage. For example, in some of the new NCARDRS regions (particularly London), there were larger proportions of older mothers (≥35, see Figure 1.3) and so the birth prevalence of most chromosomal anomalies is likely to have been higher in these areas. Therefore, the estimated number of cases of chromosomal anomalies is likely to be an underestimate.

Figure 1.3: Total births according to mothers' age group; NCARDRS regions: 2015



Source: Office for National Statistics

Table 1.3: Estimated numbers of cases of congenital anomalies in England: 2015

Congenital anomaly[1]	Birth prevalence per 10,000 total births [95% CI]	Estimated number of cases in England
All cases	**205.3 [197.9, 212.9]**	**13,703**
Nervous system	24.1 [21.6, 26.8]	1,609
Congenital heart defects	49.9 [46.3, 53.7]	3,330
Respiratory	5.2 [4.0, 6.5]	344
Oro-facial clefts	16.1 [14.1, 18.3]	1,076
Digestive system	18.2 [16.0, 20.5]	1,212
Abdominal wall defects	9.3 [7.7, 11.0]	618
Urinary	27.6 [24.9, 30.4]	1,840
Genital	10.5 [8.9, 12.4]	703
Limb	29.8 [27.0, 32.7]	1,986
Chromosomal[2]	50.2 [46.6, 54.0]	3,349

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Information on Down's syndrome, Patau's syndrome and Edwards' syndrome for the whole of England can be found in Chapter 5.

Chapter 2: Timing of diagnosis and outcome

Of the 2,905 cases with one or more congenital anomaly, the timing of diagnosis was known for 2,754 (95%) cases. Of these, 71% were diagnosed prenatally in 2015.

Of the 1,947 cases diagnosed prenatally, 813 (42%) pregnancies resulted in a TOPFA (Table 2.1). On average, a prenatal diagnosis occurred at 19 weeks' gestation, which is as expected as the screening window is between 18 – 20 weeks. Every hospital trust in England will receive a report over the summer with detailed information on the timing and prenatal diagnosis of individual FASP conditions for their patients. In future a national and regional summary of that data will be provided as part of this report.

Just under a third (n=775) of congenital anomalies were diagnosed postnatally in a live birth. The time of diagnosis was known for 353 (46%) of these; 65% were diagnosed at birth, 15% in the 1st week, 7% in the 2nd to 4th week and 12% after the 1st postnatal month. Of the live births with congenital anomalies detected in the four NCARDRS reporting regions in 2015, less than 1% were diagnosed after 1 year of age (as of the time of writing this report).

Table 2.1: Timing of first diagnosis and pregnancy outcome for all cases; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Time of diagnosis	Pregnancy outcome	Number	Percentage [95% CI]
All cases n=2,905 (100%)		**2,905**	..
Prenatal n=1,947 (67%)	**Total**	**1,947**	**100.0**
	Termination of pregnancy	813	41.8 [39.6, 44.0]
	Miscarriage (20-23 weeks)	15	0.8 [0.5, 1.3]
	Stillbirth (≥24 weeks)	44	2.3 [1.7, 3.0]
	Live birth	1,075	55.2 [53, 57.4]
Postnatal n=807 (28%)	**Total**	**807**	**100.0**
	Miscarriage (20-23 weeks)	5	0.6 [0.3, 1.4]
	Stillbirth (≥24 weeks)	27	3.3 [2.3, 4.8]
	Live birth	775	96.0 [94.5, 97.2]
	At birth	230	28.5 [25.5, 31.7]
	Less than 1 week	54	6.7 [5.2, 8.6]
	1-4 weeks	25	3.1 [2.1, 4.5]
	Over 1 month	44	5.5 [4.1, 7.2]
	Age at diagnosis not known	422	52.3 [48.8, 55.7]
Timing of diagnosis not known n=151 (5%)	**Total**	**151**	**100.0**
	Miscarriage (20-23 weeks)	1	0.7 [0.1, 3.7]
	Stillbirth (≥24 weeks)	2	1.3 [0.4, 4.7]
	Live birth	148	98.0 [94.3, 99.3]

Abdominal wall defects, nervous system anomalies and urinary anomalies were the conditions most frequently diagnosed prenatally. These groups include conditions that are looked for as part of the 18-20 week fetal anomaly scan.

Table 2.2: Timing of diagnosis according to major congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly	Total number of cases	Number prenatally diagnosed	Percentage [95% CI]
Nervous system	341	300	88.0 [84.1, 91.0]
Congenital heart defects	706	337	47.7 [44.1, 51.4]
Respiratory	73	40	54.8 [43.4, 65.7]
Oro-facial clefts	228	117	51.3 [44.9, 57.7]
Digestive system	257	89	34.6 [29.1, 40.6]
Abdominal wall defects	131	127	96.9 [92.4, 98.8]
Urinary	390	322	82.6 [78.5, 86.0]
Genital	149	6	4.0 [1.9, 8.5]
Limb	421	220	52.3 [47.5, 57.0]
Chromosomal	710	432	60.8 [57.2, 64.4]

Timing of diagnosis is affected by the provision of health services including the availability and performance of prenatal screening procedures and maternal factors such as choice regarding screening. It is also dependent on how amenable anomalies are to diagnosis/detection by ultrasound or other screening, eg cleft palate, hypospadias and syndactyly are common conditions in which diagnosis prenatally by ultrasound is rare.

2.1 Rates of termination of pregnancy with fetal anomaly

Rates of TOPFA varied by gestational age (Table 2.3). The overall rate of TOPFA for the four NCARDRS reporting regions was 31 per 10,000 total births but before 20 weeks' gestation this was 20 per 10,000 total births, falling to 11 per 10,000 total births from 20 weeks' gestation onwards.

The highest rate of TOPFA was associated with chromosomal anomalies (16 per 10,000 total births), followed by nervous system anomalies (9 per 10,000 total births) and CHDs (4 per 10,000 total births) (Table 2.3). The majority of cases with chromosomal anomalies underwent a TOPFA before 20 weeks' gestation. This followed screening for Down's syndrome which generally took place much earlier then 18 weeks' gestation. The majority of prenatally detected cases with CHDs underwent a TOPFA from 20 weeks' gestation as they are structural anomalies which will be primarily detected at the 18^{+0} to 20^{+6} weeks fetal anomaly scan and usually require a referral to a tertiary provider. In the majority of pregnancies affected with an abdominal wall defect, the TOPFA occurred before 20 weeks' gestation as these are frequently diagnosed on early ultrasound scans.

Table 2.3: Rates of termination of pregnancy (per 10,000 total births) and 95% CIs according to major congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	TOPFA <20 weeks rate per 10,000 total births [95% CI]	TOPFA 20+ weeks rate per 10,000 total births [95% CI]	Total TOPFA rate per 10,000 total births [95% CI]
All cases	**19.5 [17.9, 21.3]**	**10.7 [9.5, 12.0]**	**31.2 [29.1, 33.4]**
Nervous system	4.8 [4.0, 5.7]	3.8 [3.1, 4.6]	8.7 [7.6, 9.9]
Congenital heart defects	1.2 [0.8, 1.7]	3.0 [2.4, 3.8]	4.3 [3.5, 5.1]
Respiratory	0.2 [0.0, 0.4]	0.3 [0.1, 0.6]	0.4 [0.2, 0.8]
Digestive system	0.9 [0.6, 1.4]	1.1 [0.7, 1.6]	2.0 [1.5, 2.6]
Abdominal wall defects	1.6 [1.1, 2.1]	0.1 [0.0, 0.3]	1.7 [1.2, 2.3]
Urinary	1.1 [0.8, 1.6]	1.8 [1.3, 2.4]	3.0 [2.3, 3.7]
Genital	0.1 [0.0, 0.3]	0.2 [0.1, 0.4]	0.3 [0.1, 0.6]
Limb	1.5 [1.1, 2.1]	2.1 [1.6, 2.7]	3.7 [3.0, 4.5]
Chromosomal	12.3 [11.0, 13.7]	2.6 [2.0, 3.3]	15.5 [14.0, 17.1]

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table, ie the pregnancy may not have been terminated because of that anomaly.

Chapter 3: Key public health indicators

3.1 Infant mortality

In 2015, the infant mortality rate in England was 39 per 10,000 live births,[3] of which an estimated 17% had a congenital anomaly, based on the mortality rate in the four NCARDRS reporting regions.

There were 93 infant deaths with one or more congenital anomaly present among 141,474 live births in 2015, giving an infant mortality rate of 7 per 10,000 live births (Table 3.1). The main types of congenital anomaly in which infant mortality was highest were CHDs (51% of anomaly related infant mortality rate), chromosomal anomalies (28%) and digestive system anomalies (27%).

Table 3.1: Numbers of infant deaths, mortality rates (per 10,000 live births) and 95% CIs according to congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	Number of infant deaths	Infant mortality rate (per 10,000 live births) [95% CI]
All cases	**93**	**6.6 [5.3, 8.1]**
All cases excluding genetic anomalies	**67**	**4.7 [3.7, 6.0]**
Nervous system	12	0.8 [0.4, 1.5]
Congenital heart defects	47	3.3 [2.4, 4.4]
Respiratory	8	0.6 [0.2, 1.1]
Digestive system	25	1.8 [1.1, 2.6]
Abdominal wall defects	3	0.2 [0.0, 0.6]
Urinary	12	0.8 [0.4, 1.5]
Limb	15	1.1 [0.6, 1.7]
Chromosomal	26	1.8 [1.2, 2.7]

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table. Caution should be taken when interpreting these data as some cases may have died from one anomaly but will also appear in the data for the other (possibly less severe) anomalies.

3.2 Maternal age

Mothers aged between 25 and 29 at delivery had the lowest birth prevalence of all anomalies (169 per 10,000 total births, Table 3.2). The birth prevalence was significantly higher in the under 20 age group (243 per 10,000 total births) and in the 35-

39 and 40 and over age groups (247 per 10,000 total births and 375 per 10,000 total births respectively).

[3] Office for National Statistics (ONS) Statistical Bulletin: Deaths registered in England and Wales: 2015

The birth prevalence of non-genetic anomalies also varied by maternal age (Figure 3.1; Table 3.2). It was highest among younger mothers (<20 years) and lowest in the 25-29 age group (Table 3.2). The higher rate of non-genetic malformation among the under-20s appears to be driven by comparatively higher rates of nervous system, abdominal wall, limb and cardiac anomalies in this age category (Table 3.2). In all age categories above 20 years, the rate of non-genetic anomalies was relatively stable.

As expected, the birth prevalence of chromosomal anomalies increased significantly as maternal age increased (Figure 3.1). The birth prevalence was almost 7 [6.5; 95% CI: 4.0, 10.6] times higher for the oldest (40+) mothers compared with the youngest (<20) age group (Table 3.2). It is known that Down's syndrome is more common in older mothers and accounted for over half of the chromosomal anomalies. The birth prevalence in the under 20's and 20-24 age categories was non-significantly higher compared to the 25-29 age category, in which the lowest prevalence was recorded (22 per 10,000 births).

Figure 3.1: Birth prevalence and 95% CIs according to maternal age for genetic and non-genetic anomalies; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

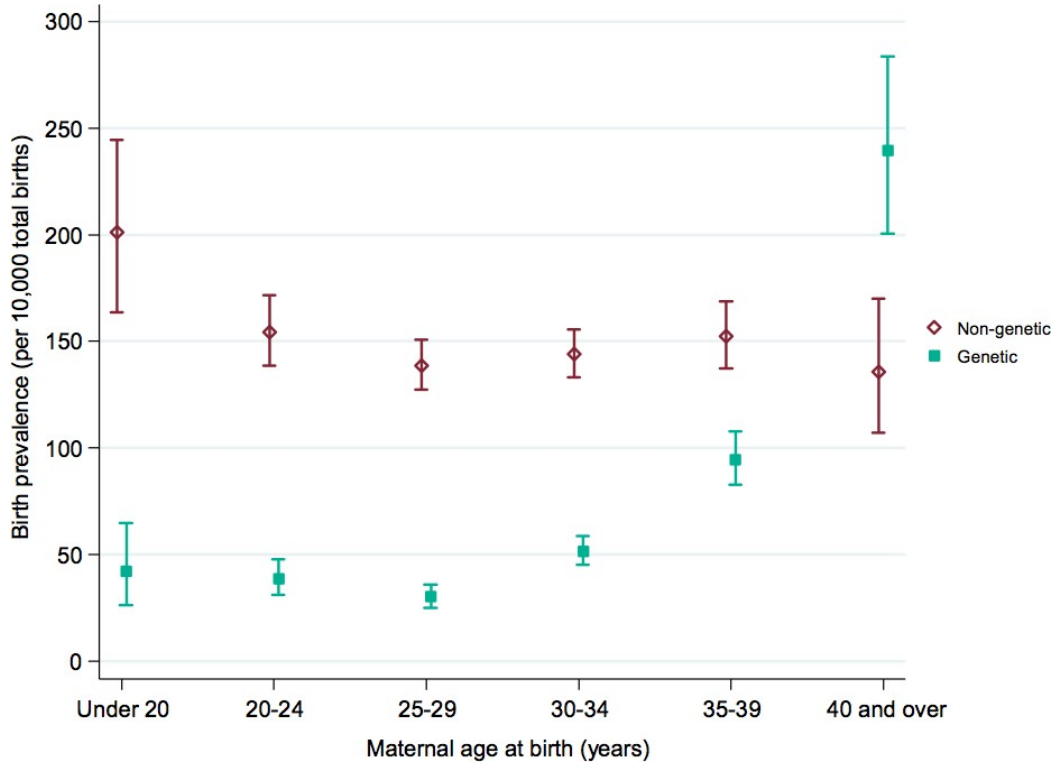


Table 3.2: Birth prevalence (per 10,000 total births) and 95% CIs according to maternal age for each congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly	Total	Under 20	20-24	25-29	30-34	35-39	40 and over
Total births	**141,474**	**4,970**	**22,275**	**40,166**	**44,264**	**24,203**	**5,596**
Total number of cases	**2,905**[1]	**121**	**430**	**678**	**866**	**598**	**210**
Birth prevalence per 10,000 total births							
All cases	**205 [198, 213]**	**243 [202, 291]**	**193 [175, 212]**	**169 [156, 182]**	**196 [183, 209]**	**247 [228, 268]**	**375 [326, 430]**
Non-genetic anomalies[2]	**147 [141, 154]**	**201 [164, 245]**	**154 [139, 172]**	**139 [127, 151]**	**144 [133, 156]**	**152 [137, 169]**	**136 [107, 170]**
Nervous system	21 [18, 23]	44 [28, 67]	24 [18, 31]	21 [17, 26]	18 [14, 22]	16 [11.5, 22]	20 [10, 35]
Congenital heart defects	39 [35, 42]	58 [39, 84]	33 [26, 42]	34 [29, 41]	43 [37, 50]	38 [30.6, 47]	36 [22, 55]
Respiratory	4 [3, 6]	2 [0, 11]	5 [3, 9]	4 [3, 7]	5 [3, 7]	3 [1.4, 7]	5 [1, 16]
Oro-facial clefts	14 [13, 17]	16 [7, 32]	16 [11, 22]	13 [9, 17]	13 [10, 17]	18 [13.2, 24]	11 [4, 23]
Digestive system	15 [13, 17]	16 [7, 32]	15 [11, 21]	15 [12, 20]	12 [9, 16]	19 [13.6, 25]	20 [10, 35]
Abdominal wall defects	7 [6, 9]	20 [10, 37]	13 [8, 18]	6 [4, 9]	5 [3, 8]	3 [1.4, 7]	11 [4, 23]
Urinary	25 [23, 28]	22 [11, 40]	28 [22, 36]	24 [20, 29]	26 [21, 31]	25 [19.3, 32]	27 [15, 44]
Genital	10 [8, 12]	12 [4, 26]	10 [6, 15]	9 [7, 13]	10 [8, 14]	10 [6.7, 15]	2 [0, 10]
Limb	25 [23, 28]	40 [25, 62]	26 [20, 34]	23 [19, 28]	24 [20, 29]	26 [20, 33]	29 [16, 46]
Genetic anomalies	**58 [54, 62]**	**42 [26, 65]**	**39 [31, 48]**	**30 [25, 36]**	**52 [45, 59]**	**95 [82.8, 108]**	**239 [201, 284]**
Skeletal dysplasias	2 [1, 3]	2 [0, 11]	2 [0, 5]	2 [1, 4]	2 [1, 4]	2 [0.4, 4]	0 [1, 7]
Genetic syndromes and microdeletions	7 [6, 8]	6 [1, 18]	8 [4, 12]	7 [4, 10]	6 [4, 9]	9 [5.7, 14]	4 [0, 13]
Chromosomal	50 [47, 54]	36 [21, 57]	30 [23, 38]	22 [18, 28]	45 [39, 51]	85 [73.9, 98]	236 [197, 280]

1 Includes age not known (0.1% of all cases)
2 Excluding cases with known genetic anomalies (skeletal dysplasias, genetic syndromes and microdeletions and chromosomal)

Chapter 4: Geographical variations and comparison with EUROCAT registries

This chapter compares the prevalence of NCARDRS regions with the combined NCARDRS regional birth prevalence and with the EUROCAT birth prevalence. EUROCAT is a European network of population based congenital anomaly registries. Started in 1979 it collects data from 43 registries in 23 countries with coverage of a third of the European birth population at 1.7 million births per year.

Geographical variation in congenital anomaly prevalence can be the result of disease clustering, exposure to teratogens, demographic variation including age profiles of areas and also genetic composition of the local population, but it can also be a result of variation in case ascertainment, diagnosis and reporting. The reporting year was the first year of NCARDRS, and differences in the processing of cases and the sources by which cases were notified were still evident.

The birth prevalence of the NCARDRS regions for all anomalies was not statistically significantly different to the prevalence of other EUROCAT registries (Table 4.1). For specific anomaly groups, the birth prevalence estimates for oro-facial clefts, digestive system anomalies, abdominal wall defects and chromosomal anomalies are statistically significantly higher in the NCARDRS regions compared to the EUROCAT registries. For anomalies of the heart, genital organs and limbs, the prevalence was statistically significantly lower in the NCARDRS regions compared to the EUROCAT registries. However, as this comparator comprises only 11 of 43 full member registries this may change when further data is available.

The Thames Valley region had the lowest overall birth prevalence of the NCARDRS reporting regions (Figure 4.1 and Table 4.1) however this is more likely to be due to lower ascertainment than the other regions than evidence of regional variation. There are no statistically significant differences between the overall birth prevalence for the other regions however there were more limb anomalies reported in the South West region than any other region (Table 4.1). There are also slightly more genital anomalies in the South West than the average for NCARDRS regions however this may also be due to low ascertainment in the Thames Valley region for this anomaly group.

Figure 4.1: Prevalence (per 10,000 total births) and 95% CIs according NCARDRS reporting region compared to the prevalence of the regions combined; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

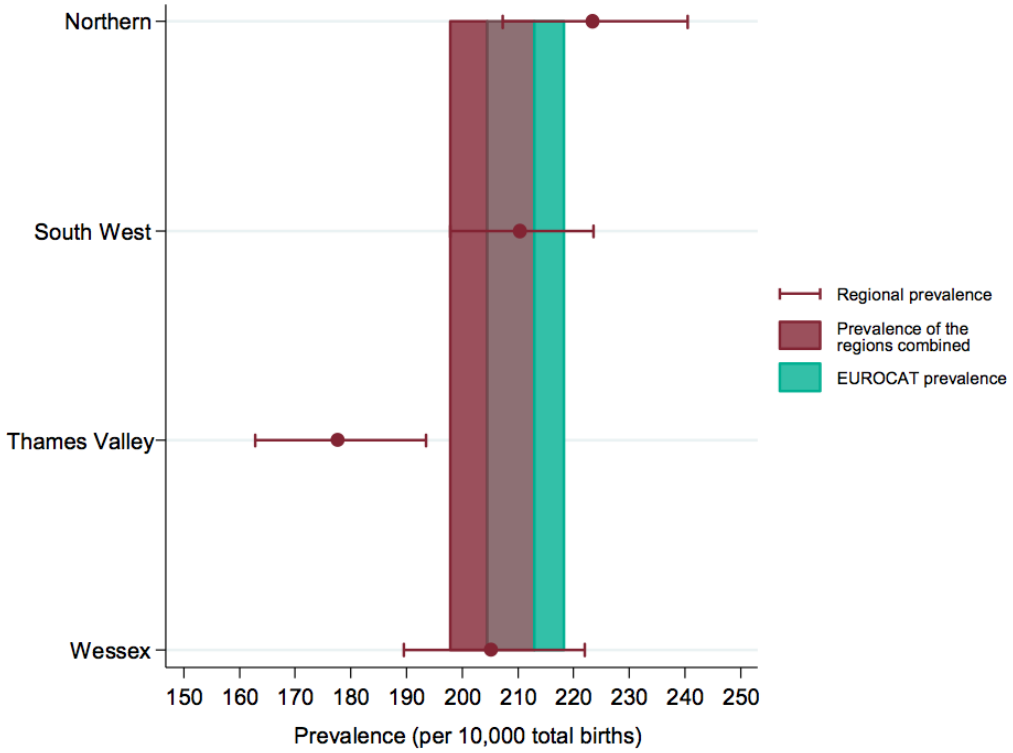


Table 4.1: Birth prevalence (per 10,000 total births) and 95% CIs by NCARDRS region according to congenital anomaly subgroup; four NCARDRS reporting regions (coverage: 21% of births in England): 2015

Congenital anomaly[1]	Birth prevalence per 10,000 total births [95% CI]					
	Northern	South West	Thames Valley	Wessex	NCARDRS regions	EUROCAT Registries[2] (excluding NCARDRS regions)
Total births	**31,726**	**49,569**	**29,777**	**30,402**	**141,474**	**172,798**
Total number of cases	**709**	**1,043**	**529**	**624**	**2,907**	**3,652**
Birth prevalence per 10,000 total births						
All cases	**223 [207, 241]**	**210 [198, 224]**	**178 [163, 193]**	**205 [189, 222]**	**205 [198, 213]**	**211 [205, 218]**
Nervous system	24 [19, 30]	25 [20, 29]	23 [17, 29]	25 [20, 31]	24 [22, 27]	21 [19, 24]
Congenital heart defects	62 [53, 71]	53 [46, 59]	49 [41, 58]	34 [28, 41]	50 [46, 54]	71 [67, 75]
Respiratory	6 [3, 9]	6 [4, 8]	3 [2, 6]	6 [3, 9]	5 [4, 6]	3 [2, 4]
Oro-facial clefts	17 [13, 23]	16 [13, 20]	13 [9, 18]	18 [13, 23]	16 [14, 18]	10 [9, 12]
Digestive system	20 [16, 26]	19 [15, 23]	12 [8, 16]	22 [17, 28]	18 [16, 21]	12 [11, 14]
Abdominal wall defects	13 [10, 18]	7 [5, 10]	6 [4, 10]	11 [7, 15]	9 [8, 11]	4 [3, 5]
Urinary	30 [25, 37]	28 [24, 33]	26 [21, 33]	25 [20, 32]	28 [25, 30]	29 [27, 32]
Genital	11 [8, 15]	17 [13, 21]	3 [2, 6]	7 [5, 11]	11 [9, 12]	16 [14, 18]
Limb	21 [16, 26]	43 [37, 49]	18 [14, 24]	30 [24, 36]	30 [27, 33]	36 [33, 39]
Chromosomal	57 [49, 66]	47 [41, 53]	48 [41, 57]	50 [42, 59]	50 [47, 54]	33 [30, 36]

1 Some of the cases shown in this table will have multiple anomalies and appear in more than one row of the table.
2 Includes 11 EUROCAT Full Member Registries (excluding the NCARDRS Regions) who had provided data to EUROCAT by 07/04/2017.

Chapter 5: National data on Down's, Edwards' and Patau's syndromes (2014)

This chapter contains detailed data on all reported cases of Down's syndrome (trisomy 21), Edwards' syndrome (trisomy 18) and Patau's syndrome (trisomy 13) occurring in England up to 2014 that have a prenatal or postnatal cytogenetic diagnosis[4]). Cases with non-invasive prenatal testing (NIPT, cell free DNA) results and/or suspected by ultrasound but without cytogenetic diagnosis were excluded from this analysis.

Unlike in previous chapters, the time period in which cases were detected was 1 January to 31 December 2014. NCARDRS brought together the existing regional anomaly registration of trisomy cases and the national registration of Down's, Edwards' and Patau's syndromes (trisomies 21, 18 and 13, formerly the National Down Syndrome Cytogenetic Register, NDSCR). During 2016, the notification methods for trisomy diagnoses changed from individual paper notifications to bulk electronic files from cytogenetic laboratories reducing the burden on clinical teams and improving the timeliness and completeness of data. A report on 2015 trisomy data from the electronic data feeds is planned for later in 2017/18.

5.1 Diagnoses of Down's, Edwards' and Patau's syndromes

In 2014, 1,698 Down's syndrome, 508 Edwards' syndrome and 165 Patau's syndrome cases were diagnosed in England. The prevalence of these trisomies in 2014 was 1 in 391 (Down's Syndrome), 1 in 1,316 (Edwards' syndrome), and 1 in 4,000 (Patau's syndrome).

Of the 1,698 Down's syndrome cases, the majority (64%) were diagnosed by prenatal cytogenetic diagnosis (Table 5.1). The birth prevalence of Down's syndrome in England in 2014 was 25.6 per 10,000 total births (Table 5.2). It is expected that about 6% of those with unknown outcomes are likely to result in a live birth; therefore the live birth prevalence of Down's syndrome for England in 2014 is estimated to have been 10.1 per 10,000 live births, around 1 in 990 live births.

Edwards' and Patau's syndromes occur less frequently than Down's syndrome, but a higher proportion of cases were diagnosed antenatally. In England in 2014, the birth prevalence of Edwards' syndrome was 7.6 per 10,000 total births and Patau's syndrome was 2.5 per 10,000 total births (Table 5.2).

Of the 508 Edwards' syndrome cases, 91% were diagnosed prenatally and 90% of the 165 Patau's syndrome cases were diagnosed prenatally (Table 5.1). Edwards' and

[4] full karyotype, rapid result (eg FISH or QF-PCR), or microarray diagnosis on a prenatal (following amniocentesis, chorionic villus sampling (CVS) or fetal blood sampling or postnatal (blood/tissue) sample

Patau's syndrome cases are likely to have other structural anomalies eg cardiac anomalies, exomphalos or spina bifida, which may be detected by ultrasound.

Table 5.1: Down's, Edwards' and Patau's syndrome cases diagnosed and notified according to time of diagnosis and outcome; England: 2014

Time of diagnosis	Outcome	Number (Percentage)		
		Down's syndrome	Edwards' syndrome	Patau's syndrome
Prenatal	Miscarriage (20-23 weeks)	4 (0.2)	3 (0.6)	1 (0.6)
	Termination of pregnancy	800 (47.1)	359 (70.7)	114 (69.1)
	Stillbirth (≥24 weeks)	19 (1.1)	21 (4.1)	2 (1.2)
	Live birth	97 (5.7)	14 (2.8)	8 (4.8)
	Unknown outcome	171 (10.1)	64 (12.6)	24 (14.5)
	Total	**1,091 (64.3)**	**461 (90.7)**	**149 (90.3)**
Postnatal	Miscarriage (20-23 weeks)	6 (0.4)	2 (0.4)	3 (1.8)
	Stillbirth (≥24 weeks)	27 (1.6)	12 (2.4)	1 (0.6)
	Live birth	574 (33.8)	33 (6.5)	12 (7.3)
	Total	**607 (35.7)**	**47 (9.3)**	**16 (9.7)**
Total		**1,698 (100.0)**	**508 (100.0)**	**165 (100.0)**

The birth prevalence of Down's and Patau's syndromes has remained constant over the last ten years, however Edwards' syndrome showed a significant increasing trend of 1.2% (95% CI: 0.2-2.3%) per year (Table 5.2 and Figures 5.1 and 5.2). All three trisomies occur more frequently in older mothers. The prevalence of these conditions is therefore affected by the age profile of the maternal population.

The live birth prevalence of Down's syndrome showed a significant decreasing trend of 1.0% (95% CI: 0.2-1.8%) per year, however the proportion of Down's syndrome cases ending in a TOPFA has remained constant over the last ten years.Fifteen percent of trisomy cases diagnosed prenatally did not have pregnancy outcomes reported.

Table 5.2: Trends over time (per 10,000 total births) and 95% CIs in Down's, Edwards' and Patau's syndromes; England: 2005-2014

Year	Down's syndrome		Down's syndrome live births		Edwards' syndrome		Patau's syndrome	
	Number	Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 live births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]	Number	Birth prevalence per 10,000 total births [95% CI]
2005	1,665	27.0 [25.7, 28.3]	703	11.5 [10.6, 12.3]	407	6.6 [6.0, 7.3]	145	2.4 [2.0, 2.8]
2006	1,762	27.6 [26.3, 28.9]	724	11.4 [10.6, 12.2]	439	6.9 [6.2, 7.5]	186	2.9 [2.5, 3.4]
2007	1,705	25.9 [24.7, 27.1]	682	10.4 [9.6, 11.2]	455	6.9 [6.3, 7.6]	203	3.1 [2.7, 3.5]
2008	1,774	26.2 [25.0, 27.5]	714	10.6 [9.8, 11.4]	463	6.8 [6.2, 7.5]	179	2.6 [2.3, 3.1]
2009	1,836	27.2 [26.0, 28.5]	752	11.2 [10.4, 12.0]	505	7.5 [6.8, 8.2]	170	2.5 [2.2, 2.9]
2010	1,831	26.5 [25.3, 27.8]	689	10.0 [9.3, 10.8]	514	7.4 [6.8, 8.1]	213	3.1 [2.7, 3.5]
2011	1,871	27.0 [25.8, 28.3]	716	10.4 [9.7, 11.2]	526	7.6 [7.0, 8.3]	189	2.7 [2.4, 3.2]
2012	1,909	27.4 [26.2, 28.6]	740	10.7 [9.9, 11.5]	512	7.3 [6.7, 8.0]	222	3.2 [2.8, 3.6]
2013	1,845	27.6 [26.4, 28.9]	699	10.5 [9.8, 11.3]	467	7.0 [6.4, 7.7]	181	2.7 [2.3, 3.1]
2014	1,698	25.6 [24.4, 26.8]	671	10.1 [9.4, 10.9]	508	7.6 [7.0, 8.3]	165	2.5 [2.1, 2.9]

The prevalence of all three trisomies was lower in 2014 compared to 2013. This finding is unlikely to arise from changes in the maternal age population, and may reflect a drop in ascertainment, or the effect of NIPT in the private sector on the uptake of invasive diagnostic testing.

Figure 5.1: Birth prevalence (per 10,000 births) and 95% CIs of Down's syndrome; England: 2005-2014

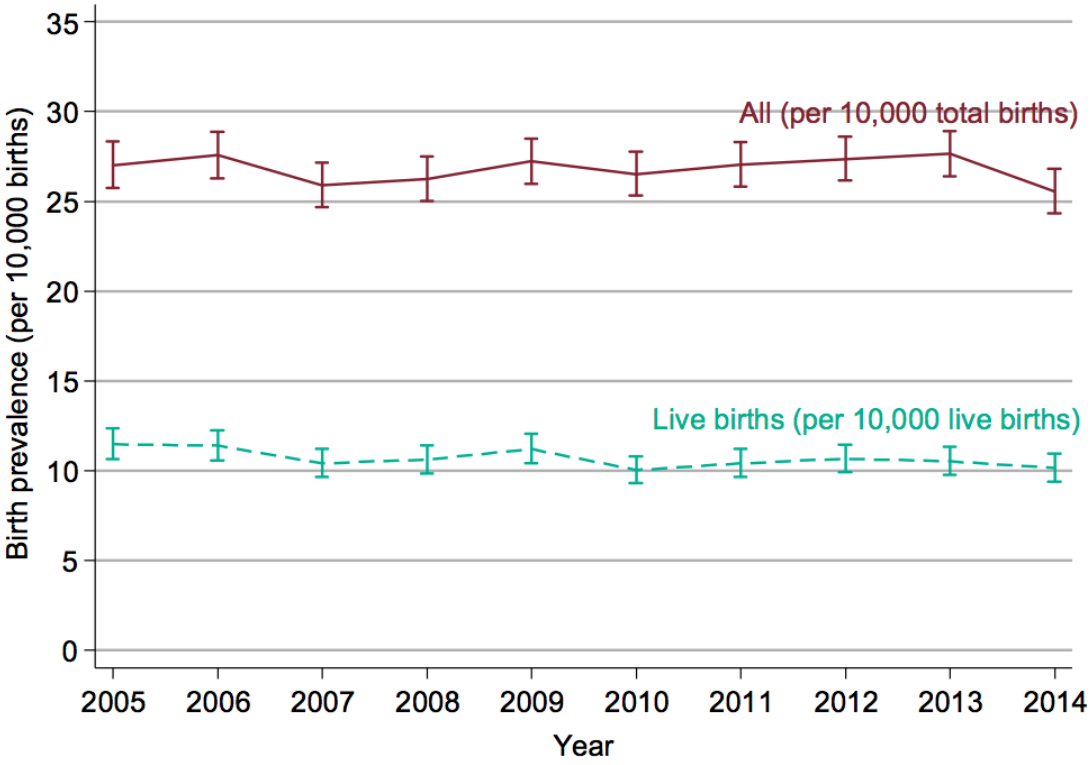
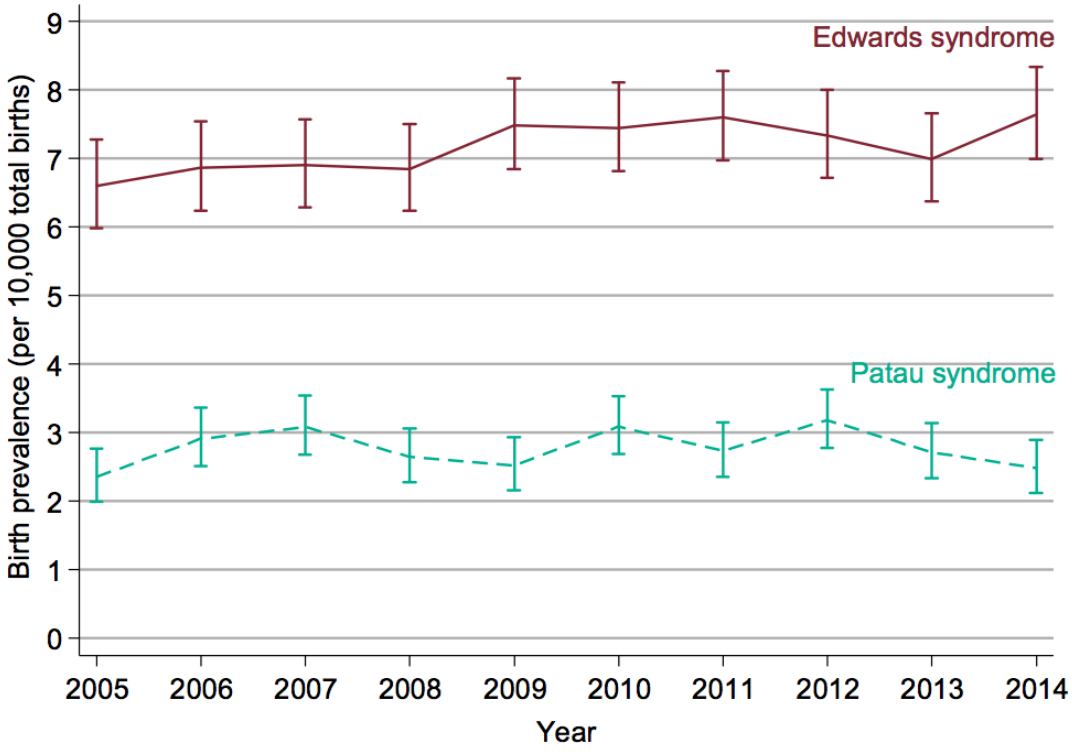


Figure 5.2: Birth prevalence (per 10,000 total births) and 95% CIs of Edwards' and Patau's syndromes; England: 2005-2014



5.2 Acceptance of screening

Up to 2014, the National Fetal Anomaly Screening Programme (FASP) offered combined[5] and quadruple[6] test screening for Down's syndrome; both tests involve the calculation of an individual risk of being affected based on maternal age, blood test , and ultrasound measurement (combined test only). For Edwards' and Patau's syndrome, ultrasound screening at 18^{+0}-20^{+6} weeks' gestation was offered. By March 2016, combined test screening was extended to include screening for Edwards' and Patau's syndromes. NIPT has been available within the private sector since 2012, an evaluation of its introduction into the fetal anomaly screening pathway will take place from 2018/19. However, given that some women are currently choosing to access this test privately this may be affecting the update of screening and prenatal diagnosis within the NHS.

Table 5.3 shows the percentage of women with affected pregnancies who declined prenatal screening, where 'prenatal screening' includes 1st trimester and 2nd trimester tests. In this analysis, women who decided to proceed directly to a diagnostic test due to age were classified as declining screening. Women classified as 'no information' on screening include those women with a late ultrasound for whom we do not know if they had had an earlier screening test, and women with postnatal diagnoses for whom we have no screening information. A total of 62% of women with a postnatal diagnosis of Down's syndrome had declined to be screened, compared to 77% of women with a postnatal diagnosis of Edwards' syndrome and 88% of women with a postnatal diagnosis of Patau's syndrome. The true percentage is likely to be higher as we have no information on 8% of women with a postnatal diagnosis of Down's syndrome, 12% with a postnatal diagnosis of Edwards' syndrome and 6% with a postnatal diagnosis of Patau's syndrome.

During 2017 NCARDRS plans to link data on affected trisomy cases with electronic data feeds from biochemistry laboratories who offer trisomy screening (combined or quadruple test screening). This will ensure screening data are validated, but will also allow NCARDRS to provide laboratories with detection rates for their screened population, and provide PHE Screening Programmes with national estimates. Data on NIPT will also be collected to support monitoring and evaluation of its implementation as an additional option in the fetal anomaly screening pathway.

[5] Combined test: screening test for trisomies 21, 18 and 13; available between 10 and 14 weeks of pregnancy. It involves a blood test and an ultrasound scan, and uses mother's age.
[6] Quadruple test: Screening test for trisomy 21; available between 14 and 20 weeks of pregnancy. It involves a blood test and uses mother's age.

Table 5.3: Acceptance of prenatal screening tests among women with a Down's, Edwards', Patau's syndrome diagnosis; England: 2014

	Number (Percentage)					
	Down's syndrome		Edwards' syndrome		Patau's syndrome	
	Prenatal	Postnatal	Prenatal	Postnatal	Prenatal	Postnatal
Screened	942 (86.3)	221 (36.4)	338 (73.3)	11 (23.4)	103 (69.1)	1 (6.3)
No indication	..	87 (14.3)	..	7 (14.9)	..	-
Declined further testing	..	98 (16.1)	..	4 (8.5)	..	-
Unknown	..	36 (5.9)	..	-	..	1 (6.3)
Declined screening	62 (5.7)	378 (62.3)	68 (14.8)	36 (76.6)	22 (14.8)	14 (87.5)
No information	87 (8.0)	8 (1.3)	55 (11.9)	-	24 (16.1)	1 (6.3)
Total	1,091 (100.0)	607 (100.0)	461 (100.0)	47 (100.0)	149 (100.0)	16 (100.0)

5.3 Indication for prenatal karyotype diagnosis according to maternal age

In 2014, 64% of Down's syndrome diagnoses were made prenatally, 83% of karyotype diagnoses followed 1st or 2nd trimester screening (53% of all cases). In Edwards' and Patau's syndrome, a higher proportion of prenatal karyotype diagnoses were made following ultrasound abnormalities; 17% of prenatal diagnoses of Edwards' and Patau's syndrome.

Table 5.4 shows the indication for prenatal diagnosis separately for younger and older women. The first trimester screening category includes structural anomalies identified at the dating scan, by nuchal translucency (NT)[7] measurement alone and the combined test (maternal age, blood test and NT measurement). It is worth noting that screening by NT alone is not part of fetal anomaly screening programme, and may reflect inaccurate terminology for combined test screening in notifications. Second trimester screening includes 2nd trimester blood test only (eg quadruple test screening in the NHS) The ultrasound includes the 18^{+0}-20^{+6} week anomaly scan and 'other' includes those reported as due to maternal anxiety, previous affected pregnancy, and with no indication. If there was no indication as to the type of screening (for example if only a risk was given) then the gestation at which the sample for diagnosis (eg CVS or amniotic fluid) was obtained was used to classify it as 1st trimester or 2nd trimester screening.

[7] Nuchal translucency: ultrasound measurement of the fluid at the back of the baby's neck.

Table 5.4: Indication for prenatal diagnosis of Down's, Edwards' and Patau's syndromes according to maternal age; England: 2014

	Number (Percentage)					
	Down's syndrome		Edwards' syndrome		Patau's syndrome	
	< 35 years	≥35 years	< 35 years	≥35 years	< 35 years	≥35 years
1st trimester screening	247 (76.0)	577 (76.5)	113 (71.1)	201 (67.7)	49 (69.0)	48 (61.5)
2nd trimester screening	30 (9.2)	76 (10.1)	4 (2.5)	15 (5.1)	1 (1.4)	6 (7.7)
Ultrasound	22 (6.8)	43 (5.7)	32 (20.1)	54 (18.2)	17 (23.9)	14 (17.9)
Maternal age	-	4 (0.5)	-	-	-	-
Other reasons/no information	26 (8.0)	54 (7.2)	10 (6.3)	27 (9.1)	4 (5.6)	10 (12.8)
Total	325 (100.0)	754 (100.0)	159 (100.0)	297 (100.0)	71 (100.0)	78 (100.0)

The percentage of Down's syndrome cases prenatally diagnosed in both younger (<35) and older (35+) mothers showed a significant increasing trend of 5.4% (95% CI: 3.5-7.3%) per year and 2.2% (95% CI: 0.7-3.7%) per year respectively. There was also a significant increasing trend in the percentage of Edwards' syndrome cases prenatally diagnosed in younger (<35) mothers of 9.0% (95% CI: 2.8-15.6%) per year, however the percentage for older (35+) mothers has remained constant over the last ten years. The percentage of Patau's syndrome cases prenatally diagnosed has remained constant over the last ten years in both younger (<35) and older (35+) mothers.

The percentage of prenatally diagnosed Down's syndrome cases was 30% in younger (<35 years) women and 70% in older (≥35 years) women; 64.3% in all age groups. Thirty-five percent of Edwards' syndrome prenatal diagnoses and 48% of Patau's syndrome diagnoses were made in women who were 35 or younger.

Figure 5.3: Percentage of Down's syndrome cases which were prenatally diagnosed according to maternal age and year of diagnosis; England: 2005-2014

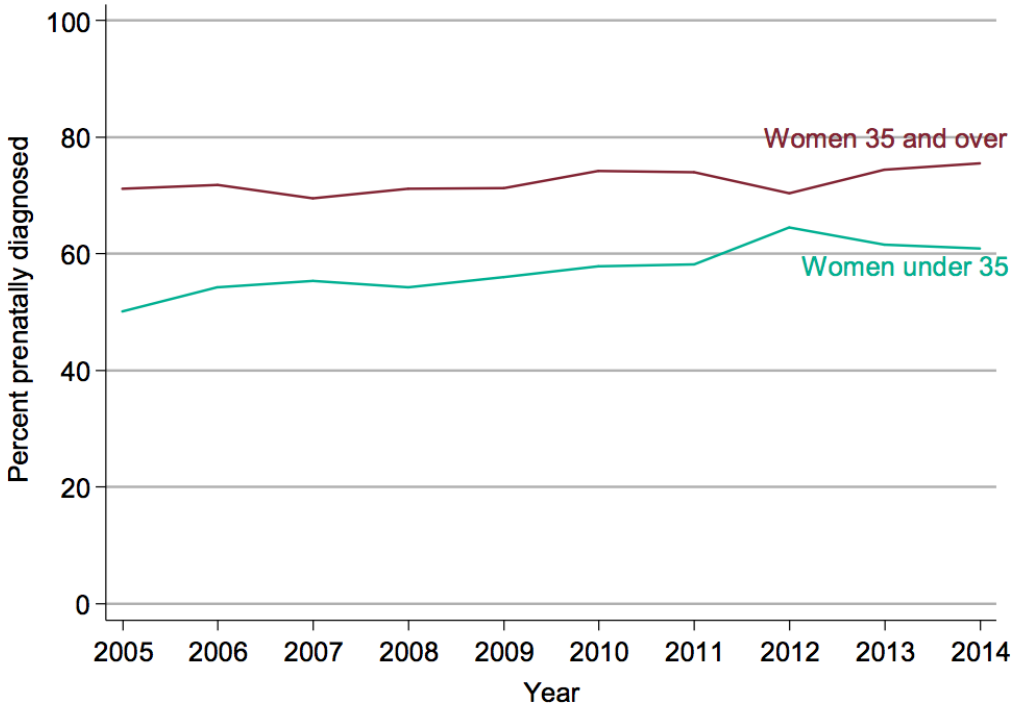
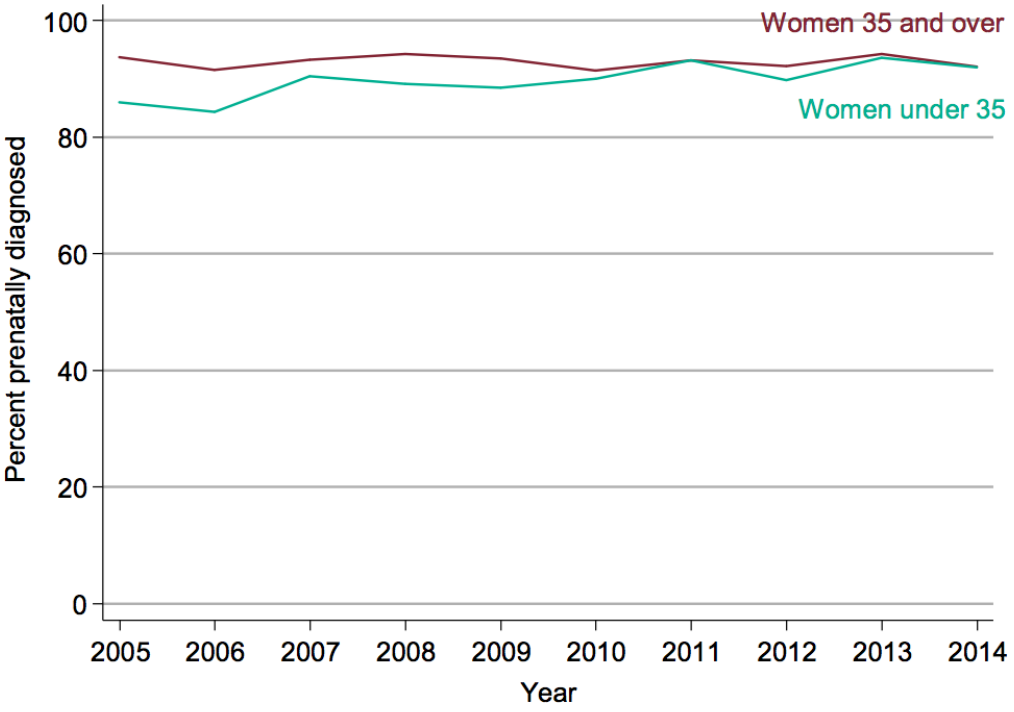
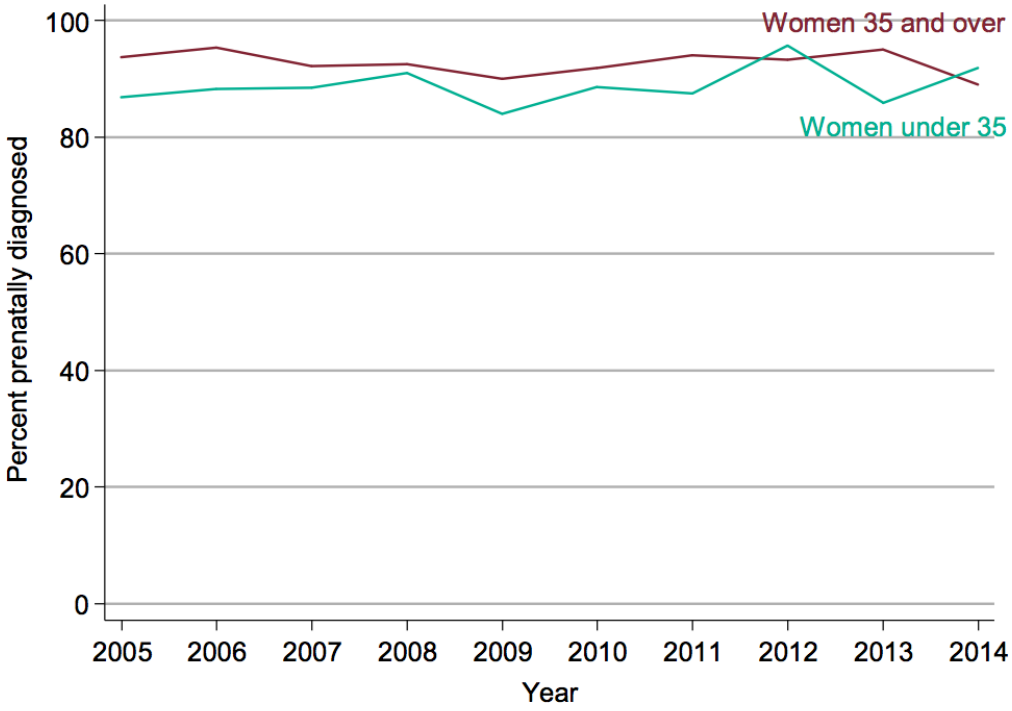


Figure 5.4: Percentage of Edwards' syndrome cases which were prenatally diagnosed according to maternal age and year of diagnosis; England: 2005-2014



Figures 5.5: Percentage of Patau's syndrome cases which were prenatally diagnosed according to maternal age and year of diagnosis; England: 2005-2014

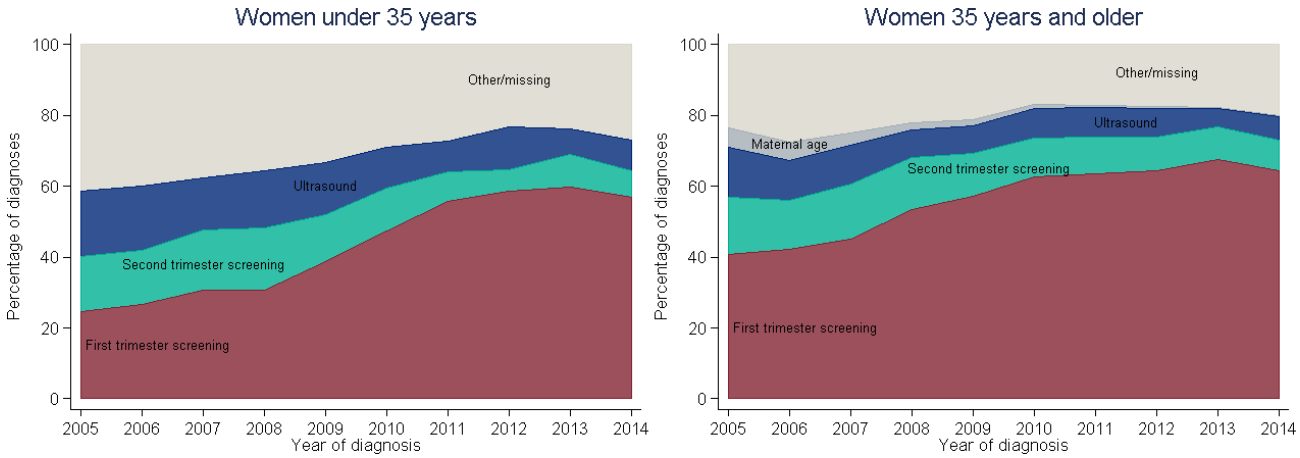


Figures 5.6 to 5.8 show the trends in the indications for a prenatal diagnosis of Down's, Edwards' and Patau's syndromes over time.

For both younger and older women there has been a clear shift towards earlier diagnoses following first trimester screening (Table 5.4).

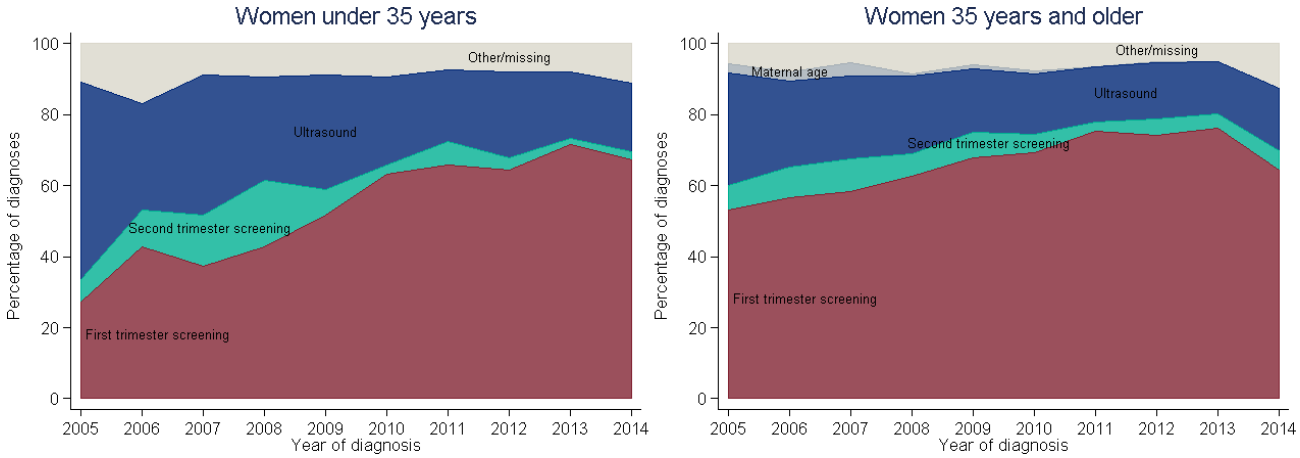
The percentage of prenatally diagnosed Down's syndrome cases where the indication for karyotyping was first trimester screening showed a significant increasing trend of 22% (95% CI: 19-24%) per year in younger mothers and of 14% (95% CI: 12-15%) per year in older mothers. The other indication categories shown in Figure 5.6 show significant decreasing trends over the last ten years.

Figure 5.6: Indication for Down's syndrome prenatal diagnosis according to maternal age and year of diagnosis; England: 2005-2014



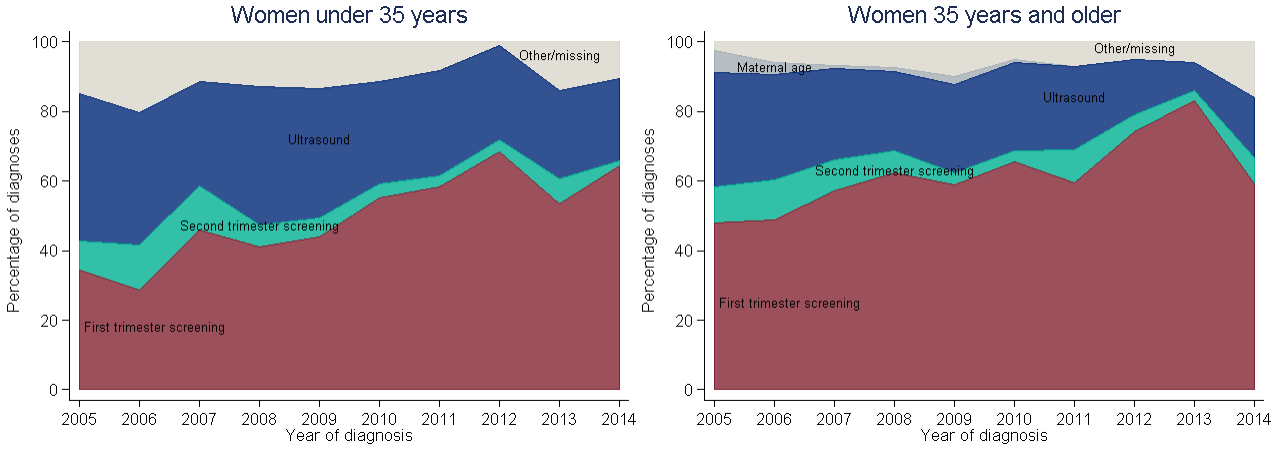
The percentage of prenatally diagnosed Edwards' syndrome cases where the indication for karyotyping was first trimester screening showed a significant increasing trend of 22% (95% CI: 17-26%) per year in younger mothers and of 10% (95% CI: 7.1-13%) per year in older mothers. The other indication categories shown in Figure 5.7 apart from the 'Other/missing' category show significant decreasing trends over the last ten years.

Figure 5.7: Indication for Edwards' syndrome prenatal diagnosis according to maternal age and year of diagnosis; England: 2005-2014



The percentage of prenatally diagnosed Patau's syndrome cases where the indication for karyotyping was first trimester screening showed a significant increasing trend of 18% (95% CI: 12-24%) per year in younger mothers and of 14% (95% CI: 8.2-19%) per year in older mothers. The other indication categories shown in Figure 5.8 apart from the 'Second trimester screening' and 'Other/missing' category for older mother show significant decreasing trends over the last ten years.

Figure 5.8: Indication for Patau's syndrome prenatal diagnosis according to maternal age and year of diagnosis; England: 2005-2014



Appendix A: Geographical coverage of the NCARDRS regions in this report

NCARDRS region	Local Authorities	
Northern	Allerdale	Middlesbrough
	Carlisle	Newcastle upon Tyne
	Copeland	North Tyneside
	County Durham	Northumberland
	Darlington	Redcar and Cleveland
	Eden	South Tyneside
	Gateshead	Stockton-On-Tees
	Hartlepool	Sunderland
South West	Bath and North East Somerset	Plymouth
	Bristol, City of	Sedgemoor
	Cheltenham	South Gloucestershire
	Cornwall	South Hams
	Cotswold	South Somerset
	East Devon	Stroud
	Exeter	Swindon
	Forest of Dean	Taunton Deane Teignbridge
	Gloucester	Tewkesbury
	Isles of Scilly	Torbay
	Mendip	Torridge
	Mid Devon	West Devon
	North Devon	West Somerset
	North Somerset	Wiltshire (excluding Salisbury)
Thames Valley	Aylesbury Vale	South Bucks
	Bracknell Forest	South Oxfordshire
	Cherwell	Vale of White Horse
	Chiltern	West Berkshire
	Milton Keynes	Windsor & Maidenhead
	Oxford	Wokingham
	Reading	Wycombe
	Slough	
Wessex	Basingstoke and Deane	North Dorset
	Bournemouth	Poole
	Christchurch	Portsmouth
	East Dorset	Purbeck
	East Hampshire	Rushmoor
	Eastleigh	Southampton
	Fareham	Test Valley
	Gosport	West Dorset
	Hart	Weymouth and Portland
	Havant	Wiltshire (Salisbury only)
	Isle of Wight	Winchester
	New Forest	