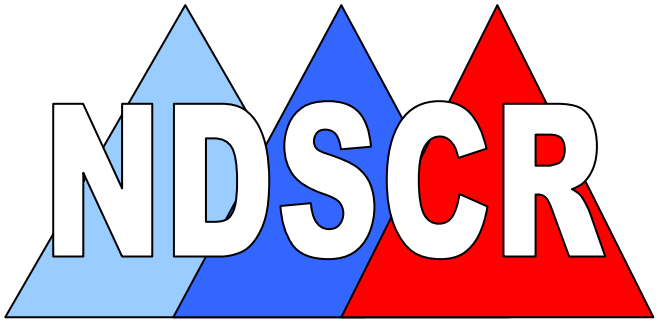

The National Down Syndrome Cytogenetic Register for England and Wales: 2012 Annual Report

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National Down Syndrome Cytogenetic Register

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Public Health England

Foreword

This 2012 annual report contains information about the NDSCR as well as detailed data on all reported cytogenetically diagnosed cases of Down syndrome (trisomy 21) from 1989 to 2012, and Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) from 2004 to 2012.

We would like to thank all the individuals who contribute to the NDSCR to make it such a valuable resource. We hope that we can continue to count on their collaboration.

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Executive Summary

- In 2012 there were 1,982 diagnoses of Down syndrome, 64% of which were made prenatally, a rate of 2.7 per 1,000 births.
- In 2012 there were an estimated 775 Down syndrome live births, a live birth rate of 1.1 per 1,000 live births.
- In 2012 there were 229 diagnoses of Patau and 526 diagnoses of Edwards syndrome, of which an estimated 22 and 68 respectively were live births. A rate of 0.3 per 1,000 births for Patau syndrome and a rate of 0.7 per 1,000 births for Edwards syndrome.
- The proportion of women under 35 receiving a prenatal diagnosis of Down syndrome has increased from 54% in 2008 to 66% in 2012. The proportion for women 35 and over remained constant at 71% from 2008 to 2012.
- The proportion of women receiving prenatal diagnoses of Down syndrome after 1st trimester screening increased from 45% in 2008 to 77% in 2012 for women under 35 and from 68% in 2008 to 80% in 2012 for women 35 and over.
- The proportion of women having a termination after a prenatal diagnosis of Down syndrome has decreased from 92% in 1989-2010 to 90% in 2011 and 2012.
- There were regional differences in the type of screening that the women were offered in 2012. In all of the English regions the majority of women were diagnosed after 1st trimester screening (81%), compared to 31% in Wales.
- The proportions of Down, Patau and Edwards syndrome diagnosed prenatally between 2007 and 2011 in England and Wales (62%, 89% and 90% respectively) is similar to the average for all European registers.

Suggested citation of this report:

Morris JK, Springett A. The National Down Syndrome Cytogenetic Register for England and Wales 2012 Annual Report. Queen Mary University of London, Barts and The London School of Medicine and Dentistry 2014.

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The NDSCR

Introduction

The NDSCR is based at the Centre for Environmental and Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London. Data collection for the NDSCR is funded by Public Health England. This report refers to Down syndrome (named after Dr Langdon Down), Patau syndrome (named after Dr Klaus Patau) and Edwards syndrome (named after Dr John Edwards).

Aims of the NDSCR

The NDSCR was started in 1989 and we aim to collect all cytogenetic or DNA reports of trisomies 21, 18 and 13 and their cytogenetic variants occurring in England and Wales. These data can then be used to:

- monitor the Down syndrome prenatal screening and diagnostic services, and the impact they have on the diagnosis of trisomies 18 (Edwards syndrome) and 13 (Patau syndrome);
- provide data on annual numbers of affected births to help those planning for their health, education and social care;
- provide information for research into Down, Edwards and Patau syndromes.

How the NDSCR works

All cytogenetic laboratories in England and Wales collaborate with the NDSCR and provide, on standard forms, a notification of all prenatal and postnatal diagnoses of Down, Edwards and Patau syndromes. (A copy of the form used in 2012 is shown in Appendix B). The form is self-copying and has four pages. The top (white) copy is sent to the NDSCR by the laboratory, the 2nd (blue) and 3rd (green) are sent to the referring clinician and the 4th (pink) sheet is retained by the laboratory. The clinicians are asked to complete the blue form and send it to the NDSCR and to forward the 3rd (green) copy to the local screening co-ordinator, who is usually based within the Antenatal Unit at the referring hospital. **No direct contact is ever made with the women by the NDSCR.**

What data are collected

The notification form (see Appendix B) contains details of the chromosome analysis and some information on the mother and child, including postcode of residence, mother's age, length of pregnancy, the reason for referral for diagnosis and prenatal screening information. To preserve anonymity, the data do not include full names or addresses, but do include enough information to enable us to identify duplicate registrations and link to other congenital anomaly registers.

Data completion and processing

Postnatal diagnoses

Postnatal diagnoses include all diagnoses made after the birth of the child (both live and still) and following a miscarriage occurring after 20 weeks gestation. Diagnoses following a miscarriage occurring before 20 weeks are not included, because not all early miscarriages are karyotyped. This is consistent with the practice of other congenital anomaly registers.

Follow-up of prenatal diagnoses

For all prenatal diagnoses we request the referring physicians to inform us of the date and gestational age at the outcome of the pregnancy (birth, termination or miscarriage). The data on outcome show that after the prenatal diagnosis of Down syndrome 92% of affected pregnancies are terminated and 8% are continued. Some of the continued pregnancies miscarry naturally, some end as still births, and approximately 6% of prenatal diagnoses are live births. There is often a time lapse before we are informed of these outcomes (see below).

Validation of data

In order to ensure high levels of ascertainment, the data are matched with those held by some of the Regional Congenital Anomaly Registers. In previous years this has shown the NDSCR data to be over 94% complete. Annual lists are sent to the laboratories for them to check that all cases have been registered.

Data quality

The Table in Appendix A gives the percentage of data on forms that is complete for the years up to 2009 combined, and separately for 2010, 2011 and 2012. This is always lowest in the most recent data where not all the clinicians have been contacted. Requests for missing data are sent out regularly. The major problem is ascertaining the outcome of prenatally diagnosed pregnancies, particularly where the referral was from a centre other than that at which the mother was booked. This occurs for private referrals, which have risen sharply over the years. Missing data for variables other than outcome are rare, with the exception of the numbers of previous pregnancies, a question that may not be seen as relevant by the clinicians although it is important in terms of risk of recurrence. There have been many changes in health authority definitions since the start of the register and regular recoding is carried out to keep these up-to-date.

Speed of reporting

Most laboratories provide data within six months of the diagnosis. The outcomes of prenatal diagnoses cannot be confirmed until a minimum of six months has elapsed to allow for any births to have occurred.

Data security, confidentiality and informed consent

Personal information held on a computer system is safeguarded by the Data Protection Act 1998 and the NDSCR is registered under this Act. Paper forms are kept in locked filing cabinets and electronic data are entered onto password-protected computers kept in locked offices. The full data are accessible only to the research team. The Government has made it clear that informed consent is a fundamental principle governing the use of patient identifiable information. However it also recognises that situations arise where informed consent cannot practicably be obtained. Section 251 of the NHS Act 2006 (originally enacted under Section 60 of the Health and Social Care Act 2001) provides a power to ensure that patient identifiable information needed to support essential NHS activity can be used without the consent of patients. The Act requires that the Confientiality Advisory Group (CAG) consider applications to use patient identifiable information without full informed consent. Since 2003, the NDSCR as a part of the British Isles Network of Congenital Anomaly Registers (BINOCAR) has been given permission to operate without informed consent (2-08(e)/2002). In 2006 the application of the NDSCR for ethics approval from the Trent multi-centre research ethics committee (MREC), as part of BINOCAR, was also approved (09/H0405/48). In 2011 this approval was renewed.

In line with the Code of Practice for Official Statistics, all statistics in this report have been risk assessed for disclosure-control to protect confidentiality. The BINOCAR Management Committee have agreed that in data for the whole population no suppression of small numbers is required.

How the data are used

Audit of Down Syndrome Screening

- The NDSCR is the only national source of the numbers of pre- and postnatal diagnoses of Down, Patau and Edwards syndrome cases in England and Wales. The National Congenital Anomaly System (NCAS) which previously also estimated these numbers no longer collects this data.
- Annual reports are produced describing numbers of prenatal and postnatal diagnoses, and the methods of prenatal screening which led to prenatal diagnoses.
- More detailed information is regularly published in medical journals (see appendix C).
- All local screening co-ordinators should receive the green copy of the NDSCR form to assist them in their audit requirements.
- Data on prenatal diagnosis of Down, Patau and Edwards syndrome are provided to EUROCAT for use in their interactive website tables (www.eurocat-network.eu/prenatalscreeninganddiagnosis/prenataldetection(pd)rates).

Feedback

- NDSCR leaflets giving information on the trends in Down syndrome diagnosis are produced annually and distributed to cytogenetic laboratories, local screening co-ordinators and clinicians.
- The NDSCR website (www.wolfson.qmul.ac.uk/ndscr) is regularly updated.
- Information is provided on request to medical professionals, researchers, journalists, charities and other interested parties.

- NDSCR leaflets are provided to the Down Syndrome Association and to SOFT (Support Organisation for trisomy 13/18 and related disorders).

Recent collaborative studies

- Children with Down's Syndrome Study (St James' University Hospital in Leeds and the Epidemiology & Genetics Unit at the University of York).
- The treatment received and the outcomes for babies with Down syndrome compared with babies without Down syndrome who are admitted to a neonatal unit; a case-control study analysing data from the National Neonatal Research Database.
- The treatment received and the outcomes for babies with Patau and Edwards syndrome who are admitted to a neonatal unit: Analysing data from the National Neonatal Research Database.
- Data on all amniocentesis and chorionic villus sampling procedures on all women in England and Wales will be obtained annually from 2012 onwards from cytogenetic laboratories in England and Wales in order to investigate how many women are having these invasive diagnostic tests and the reasons why.

Publications

- A list of selected publications based on or using NDSCR data is provided in Appendix C.
- Copies of this report and previous NDSCR reports can be found on the NDSCR website (www.wolfson.qmul.ac.uk/ndscr).
- There is a chapter using the data from the NDSCR within the BINOCAR annual report which can be found on the BINOCAR website (www.binocar.org/publications/reports).
- Data from the NDSCR are included in some interactive graphs and tables on prenatal diagnosis of selected congenital anomalies (including Down, Edwards and Patau syndrome) on the EUROCAT website (www.eurocat-network.eu/prenatalscreeninganddiagnosis/prenataldetection(pd)rates).

The Data in the NDSCR

Down syndrome cases diagnosed in 2012

Outcomes of Down syndrome cases

In 2012, 1,982 Down syndrome diagnoses were made, 1,259 (64%) prenatally and 723 (36%) postnatally (Table 1). This gives a prevalence of 2.7 (95% CI: 2.6-2.8) per 1,000 births. The outcome of 166 of the prenatal diagnoses is unknown. Assuming that the proportion terminated remains as before 2012, the likely number of Down syndrome live births in England and Wales in 2012 would have been 775 (76 + 689 + 6% of 166), giving a live birth prevalence of 1.1 (95% CI: 1.0 – 1.1) per 1,000 live births occurring in England and Wales in 2012.

Table 1: Down syndrome cases diagnosed in England and Wales in 2012* according to time of diagnosis and outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	983	50 (47 - 52)
	Live Birth	76	4 (3 - 5)
	Still Birth / Miscarriage	34	2 (1 - 2)
	Unknown outcome†	166	8 (7 - 10)
		1,259	64 (61 - 66)
Postnatal	Live Birth	689	35 (33 - 37)
	Still Birth / Miscarriage	34	2 (1 - 2)
		723	36 (34 - 39)
Total		1,982	100

* 2012 data are provisional. † About 6% of those with unknown outcomes are likely to result in a live birth.

Acceptance of screening

Table 2 shows the percentage of women who declined prenatal screening, where 'prenatal screening' includes 1st trimester and 2nd trimester tests. Women who decided to proceed directly to a diagnostic test due to age were classified as declining screening. Women classified as "no information" 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. Nineteen percent of women with a postnatal diagnosis had declined to be screened. The true percentage is likely to be higher as we have no information on 47% of women with a postnatal diagnosis.

Table 2: Acceptance of prenatal screening tests among women with a Down syndrome diagnosis in 2012*

	Stage at diagnosis			
	Prenatal		Postnatal	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
Screened	1,107	88 (86 - 90)	246	34 (31 - 38)
No indication	..	..	73	10 (8 - 13)
Declined further testing	..	..	160	22 (19 - 25)
Unknown	..	..	13	2 (1 - 3)
Declined screening	41	3 (2 - 4)	139	19 (17 - 22)
No information	111	9 (7 - 11)	338	47 (43 - 50)
Total	1,259	100	723	100

* 2012 data are provisional.

Indication for prenatal diagnosis according to maternal age

In 2012, 64% of Down syndrome diagnoses were made prenatally, 66% (95% CI: 62 – 69) in younger women and 71% (95% CI: 68 – 73) in older women.

Table 3 shows the indication for prenatal diagnosis separately for younger and older women. First trimester screening includes the dating scan, NT measurement alone and the combined test (serum and NT measurement). Second trimester screening includes 2nd trimester serum only and the integrated test, (serum and NT measured in first trimester, and serum measured in the second trimester). The ultrasound includes the 18-21 week anomaly scan and other includes anxiety, previous affected pregnancy and 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 (e.g. CVS or amniotic fluid) was obtained was used to classify it as 1st trimester or 2nd trimester screening.

A 1st trimester test was the indication in 78% of women. A greater percentage of younger (13%) than older women (6%) gave an ultrasound examination as the indication. Ten percent of prenatal diagnoses in younger women occurred at 21 weeks gestation or later, compared to only 5% of prenatal diagnoses in older women (data not shown).

Table 3: Indication for prenatal diagnosis of Down Syndrome in 2012* according to maternal age

Indication for prenatal diagnosis	Maternal Age			
	< 35 years		≥ 35 years	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
1st Trimester screening	315	77 (73 - 81)	660	80 (77 - 83)
2nd Trimester screening	35	9 (6 - 12)	95	12 (10 - 14)
Ultrasound	52	13 (10 - 16)	47	6 (4 - 8)
Age	-	-	6	1 (0 - 2)
Other reasons / No information	7	2 (1 - 3)	15	2 (1 - 3)
Total	409	100	823	100

* 2012 data are provisional; 27 cases had no maternal age.

Tissue used for prenatal diagnosis and gestational age at termination following prenatal diagnosis

The tissue used for prenatal diagnosis reflects the type of screening that led to the prenatal diagnosis, with a greater percentage of women (58%, 95% CI: 55 - 61) having a CVS than amniocentesis (36%, 95% CI: 34 - 39). The tissue was either unspecified or not from an amniocentesis or CVS in 5% of women.

The median time from CVS or amniocentesis to termination of pregnancy was eight days. Eighty-eight percent of all terminations following CVS and 89% following amniocentesis were within 14 days of the procedure.

The gestation at termination following a prenatal diagnosis also reflects the indication for prenatal diagnosis, and differs by maternal age, as shown in Table 4. The proportions of terminations taking place before 15 weeks is similar for younger and older women, however the proportions after 20 weeks were very different with 6% in older women compared to 12% in younger women.

Table 4: Gestation at termination following prenatal diagnosis of Down Syndrome in 2012* according to maternal age

Gestation at termination (following prenatal diagnosis)	Maternal Age			
	< 35 years		≥ 35 years	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
<15 weeks	142	46 (40 - 51)	324	50 (46 - 54)
15 to 20 weeks	133	43 (37 - 48)	287	44 (41 - 48)
≥21 weeks	37	12 (9 - 16)	36	6 (4 - 8)
Total	312	100	647	100

* 2012 data are provisional; six cases had no maternal age and eighteen cases had no gestation at sample or outcome. Outcomes were assumed to occur one week after diagnostic sample if gestation was missing.

Maternal age at observed or expected date of delivery

The mean age of the woman at observed or expected date of delivery was 36.1 (95% CI: 35.8 - 36.4) years. The mean age for women with a prenatal diagnosis was 36.5 (95% CI: 36.2 – 36.8) compared to 35.3 (95% CI: 34.8 – 35.9) for those with a postnatal diagnosis. Overall 65% (1163/1786) of the women of known age were 35 or older (Table 5).

Table 5: Down syndrome cases diagnosed in 2012* according to maternal age at observed or expected date of delivery

Maternal age (years)	Number	Percentage (95% CI)
< 20	34	2 (1 - 2)
20-24	78	4 (3 - 5)
25-29	161	8 (7 - 9)
30-34	350	18 (16 - 19)
35-39	620	31 (29 - 33)
40-44	501	25 (23 - 27)
≥ 45	40	2 (1 - 3)
missing	198	10 (9 - 11)
Total	1,982	100

*2012 data are provisional.

Patau and Edwards syndrome cases diagnosed in 2012

Outcomes of Patau and Edwards syndrome cases

In 2012, 229 Patau syndrome diagnoses were made, of which 93% were made prenatally and 526 Edwards syndrome diagnoses were made, of which 88% were made prenatally. This gives a prevalence of 0.3 (95% CI: 0.3-0.4) per 1,000 births for Patau syndrome and a prevalence of 0.7 (95% CI: 0.7-0.8) per 1,000 births for Edwards syndrome.

A large proportion of births were still births, due to the severity of the syndromes. The outcome of 24 Patau and 67 Edwards syndrome prenatal diagnoses is unknown. Approximately 4% of Patau and 3% of Edwards syndrome with unknown outcomes are likely to result in a live birth (rather than a termination or miscarriage), therefore the total number of live births is estimated to be 22 and 68 respectively, giving a live birth prevalence of 0.03 (95% CI: 0.02-0.05) per 1,000 live births for Patau syndrome and a prevalence of 0.09 (95% CI: 0.07-0.12) per 1,000 live births for Edwards syndrome.

Table 6a and 6b present outcomes for Patau syndrome and Edwards syndrome cases according to time at diagnosis.

Table 6a: Patau syndrome cases in 2012* according to outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	177	77 (71 - 82)
	Live Birth	7	3 (1 - 6)
	Still Birth / Miscarriage	5	2 (1 - 5)
	Unknown outcome†	24	10 (7 - 15)
		213	93 (89 - 96)
Postnatal	Live Birth	14	6 (4 - 10)
	Still Birth / Miscarriage	2	1 (0 - 3)
		16	7 (4 - 11)
	Total	229	100

* 2012 data are provisional; † Approximately 4% of Patau syndrome with unknown outcomes are likely to result in a live birth.

Table 6b: Edwards syndrome cases in 2012* according to time of diagnosis and outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	366	70 (66 - 73)
	Live Birth	12	2 (1 - 4)
	Still Birth / Miscarriage	20	4 (2 - 6)
	Unknown outcome†	67	13 (10 - 16)
		465	88 (85 - 91)
Postnatal	Live Birth	54	10 (8 - 13)
	Still Birth / Miscarriage	7	1 (1 - 3)
		61	12 (9 - 15)
	Total	526	100

* 2012 data are provisional; † Approximately 3% of Edwards syndrome with unknown outcomes are likely to result in a live birth.

Indication for prenatal diagnosis

A 1st trimester test (for Down syndrome) was the indication in 73% of women. A further 20% were picked up by the fetal anomaly ultrasound (Table 7). A greater percentage of younger women (97%) had a prenatal diagnosis of Patau syndrome than older women (94%), whereas a greater percentage of older women (92%) had a prenatal diagnosis of Edwards syndrome than younger women (90%) (data not shown).

Table 7: Indication for prenatal diagnosis of Patau and Edwards syndrome cases in 2012*

Indication for prenatal diagnosis	Patau syndrome		Edwards syndrome	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
1st Trimester screening	156	73 (67 - 79)	340	73 (69 - 77)
2nd Trimester screening	7	3 (2 - 7)	18	4 (2 - 6)
Ultrasound	46	22 (17 - 28)	91	20 (16 - 23)
Age and other reasons	0	0 (0 - 2)	1	0 (0 - 1)
No information	4	2 (1 - 5)	15	3 (2 - 5)
Total	213	100	465	100

* 2012 data are provisional.

Maternal age at observed or expected date of delivery

The mean age of the woman at expected or observed date of delivery was 35.2 years for Patau syndrome and 36.3 years for Edwards syndrome, compared to 36.1 years for Down syndrome. For Patau syndrome 57% of women with known maternal age were aged 35 or over, and for Edwards syndrome 64% of women with known maternal age were aged 35 or over (Table 8).

Table 8: Patau and Edwards syndrome cases diagnosed in 2012* according to maternal age at observed or expected date of delivery

Maternal age (years)	Patau syndrome		Edwards syndrome	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
< 25	13	6 (3 - 9)	30	6 (4 - 8)
25-29	30	13 (9 - 18)	58	11 (9 - 14)
30-34	51	22 (17 - 28)	93	18 (15 - 21)
35-39	74	32 (27 - 39)	149	28 (25 - 32)
≥ 40	50	22 (17 - 28)	167	32 (28 - 36)
missing	11	5 (3 - 8)	29	6 (4 - 8)
Total	229	100	526	100

* 2012 data are provisional.

Geographical variation in cases diagnosed in 2012

Down syndrome diagnoses and maternal age according to maternal region of residence

Table 9 shows the numbers of diagnoses of Down syndrome across England and Wales, according to the maternal region of residence. Areas with a lower proportion of women 35 years of age or over, tend to have lower proportions of prenatal diagnoses. The highest proportions of prenatal diagnoses occur in the North East of England, London and the South East of England.

Table 9: All live births and all Down syndrome diagnoses according to region of maternal residence in 2012*

Region	All Live Births		Down syndrome diagnoses	
	Number (1,000)	Percentage of women ≥35 (%)	Prevalence per 1,000 total births	Percentage prenatally diagnosed (95% CI)
North East	30	15	1.9	76 (64 - 85)
North West	89	17	2.6	55 (48 - 61)
Yorkshire & Humberside	67	16	2.0	53 (44 - 61)
East Midlands	56	17	2.7	62 (54 - 69)
West Midlands	74	17	2.4	48 (41 - 55)
East England	75	21	2.7	67 (60 - 73)
London	134	26	3.4	70 (66 - 74)
South East	108	23	2.7	73 (67 - 78)
South West	61	20	2.9	67 (60 - 74)
Wales	35	16	2.0	51 (40 - 63)
Total	730	20	2.7	64 (61 - 66)

* 2012 data are provisional. Twenty-one cases have unknown region

Indication for prenatal diagnosis according to maternal region of residence

Table 10 shows the indication for a prenatal diagnosis according to region of residence. North East England, East of England and the South East had the highest proportions of women having a diagnostic test due to a 1st trimester screening test result, whereas Wales had the highest proportion of women having a diagnostic test due to a 2nd trimester screening test result. Care must be taken in interpreting Table 10 as the "other/missing" category is large for some regions.

Gestational age at termination after prenatal diagnosis according to maternal region of residence

The gestational age at termination following prenatal diagnosis reflects the reason given for the diagnosis. Table 11 gives a more accurate reflection of regional variation than Table 10 does as there is no "other" category. Twenty-two cases with missing gestation at termination have been excluded. However, the number of terminations in some regions is small. Women in Wales are the least likely to have a termination before 15 weeks gestation.

Table 10: Indication for prenatal diagnosis of Down syndrome according to region of maternal residence in 2012*

Region	Number of prenatal diagnoses	Indication for prenatal diagnosis (%)					
		1st trimester screen	2nd trimester screen	Ultrasound	Maternal Age	Other/ Missing	Total
North East	45	89	11	0	0	0	100
North West	128	55	21	19	2	2	100
Yorkshire & Humberside	72	75	11	10	0	4	100
East Midlands	93	81	11	4	1	3	100
West Midlands	86	73	7	13	0	7	100
East England	135	87	7	5	0	1	100
London	321	84	7	7	1	2	100
South East	212	86	8	6	0	0	100
South West	120	85	8	7	0	1	100
Wales	36	31	47	22	0	0	100
Total	1,248	79	10	8	0	2	100

* 2012 data are provisional; eleven cases have unknown region.

Table 11: Gestation at termination after prenatal diagnosis of Down syndrome according to region of maternal residence in 2012*

Region	Number of terminations	Gestation at termination (%)			
		<15 weeks	15 to 20 weeks	21+ weeks	Total
North East	29	48	41	10	100
North West	86	34	49	17	100
Yorkshire & Humberside	51	46	54	0	100
East Midlands	78	47	46	7	100
West Midlands	76	51	45	4	100
East England	106	44	46	10	100
London	242	56	37	7	100
South East	181	52	41	8	100
South West	106	52	42	6	100
Wales	28	18	79	4	100
Total	983	49	44	8	100

* 2012 data are provisional; 22 cases had no gestation at outcome.

Patau and Edwards syndrome diagnoses according to maternal region of residence

Table 12: Proportion of Patau and Edwards syndrome that are prenatally diagnosed according to region of maternal residence in 2012*

Region	Percentage (95% CI)	
	Patau Syndrome	Edwards Syndrome
	Prenatal	Prenatal
North East	100 (68 - 100)	85 (58 - 96)
North West	91 (72 - 97)	91 (81 - 96)
Yorkshire & Humberside	90 (60 - 98)	86 (72 - 93)
East Midlands	93 (70 - 99)	91 (79 - 96)
West Midlands	86 (67 - 95)	77 (58 - 89)
East England	91 (76 - 97)	89 (77 - 95)
London	95 (85 - 98)	92 (86 - 96)
South East	100 (88 - 100)	91 (83 - 96)
South West	96 (80 - 99)	80 (67 - 89)
Wales	100 (70 - 100)	95 (76 - 99)
Total	93 (89 - 96)	88 (85 - 91)

*2012 data are provisional. Two cases of Patau syndrome and eight cases of Edwards syndrome do not have region data.

Summary of regional differences

There are clear regional differences in screening for Down syndrome in England and Wales in 2012. These differences may arise not only due to service factors, but also maternal factors including age, social deprivation and cultural beliefs influencing the take up of screening and diagnostic tests. More detailed analyses are required to investigate these apparent regional differences. The numbers of Patau and Edwards syndrome diagnoses are smaller, so regional variations are harder to assess.

Prenatal diagnosis compared to other European registers 2007-2011

Figures 1, 2 and 3 are taken from the EUROCAT website (www.eurocat-network.eu/prenatalscreeeningand diagnosis/prenataldetection(pd)rates) and show the proprotions of Down, Patau and Edwards syndrome diagnosed prenatally across European registers between 2007 and 2011. The proportion of Down syndrome prenatally diagnosed in England and Wales (62%) is average for all European registers, with Paris having the highest proportion prenatally diagnosed (84%) and South East Ireland having the lowest (6%, Figure 1).

Similarly the proportions of Patau and Edwards syndrome prenatally diagnosed in England and Wales (89% and 90% respectively) were again average for all European registers.

Figure 1: Proportion of Down syndrome cases prenatally diagnosed by gestation at diagnosis in European registers, 2007-2011

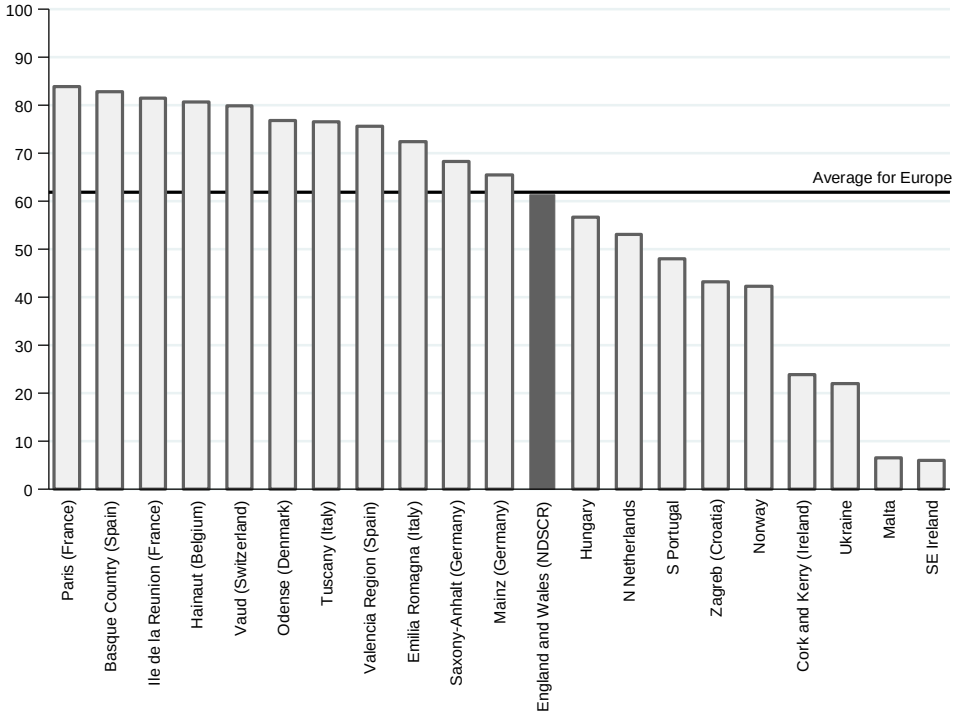


Figure 2: Proportion of Patau syndrome cases prenatally diagnosed by gestation at diagnosis in European registers, 2007-2011

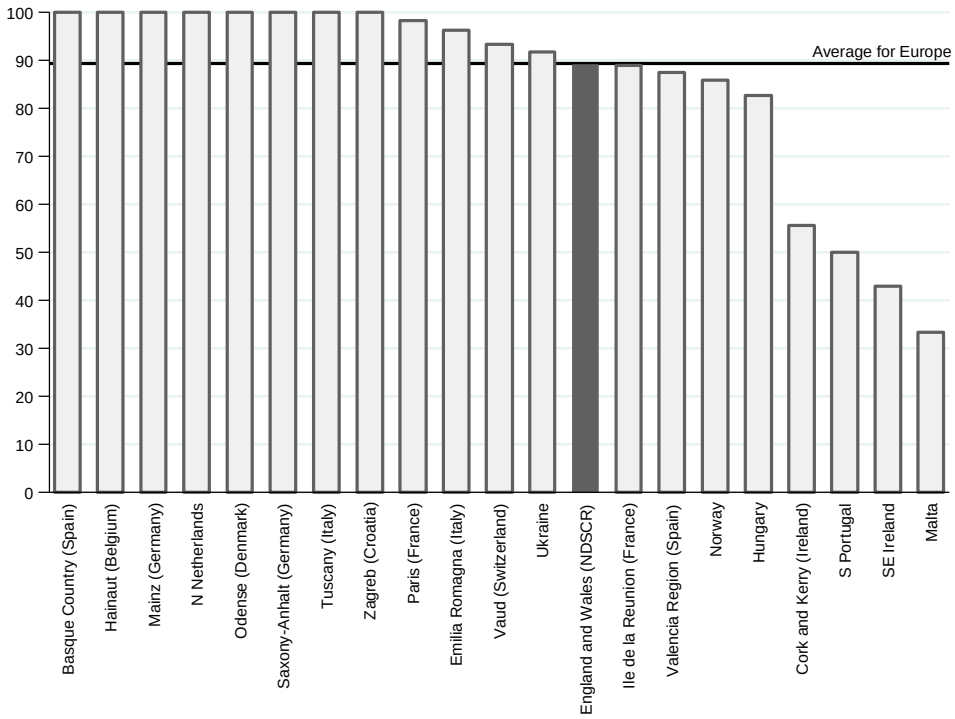
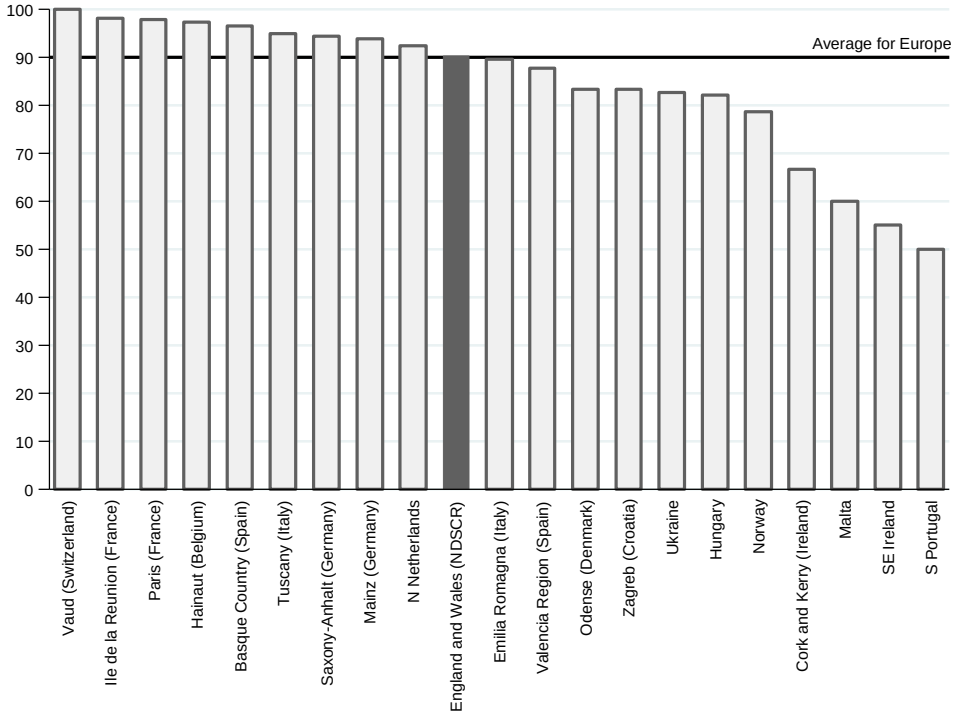


Figure 3: Proportion of Edwards syndrome cases prenatally diagnosed by gestation at diagnosis in European registers, 2007-2011

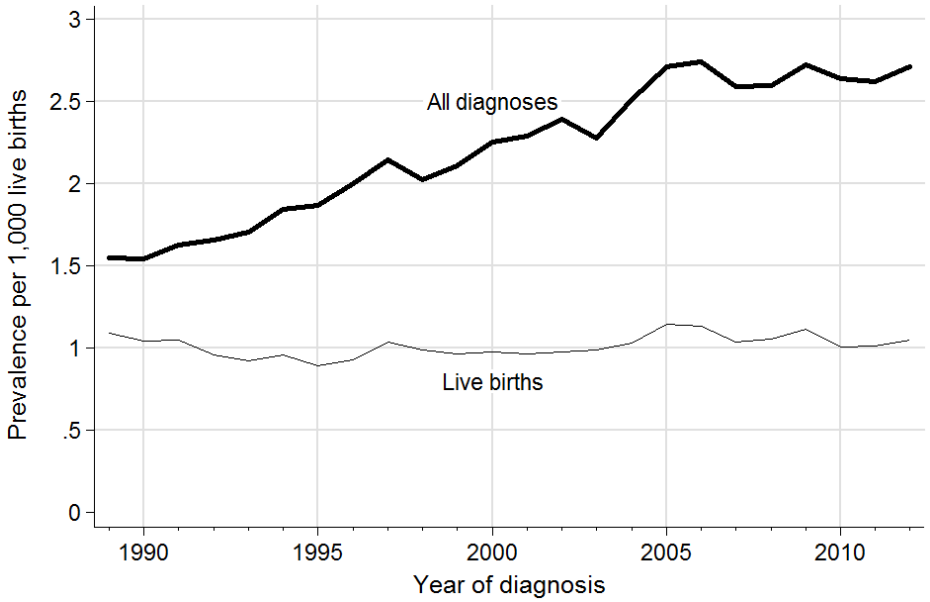


Trends over time in Down syndrome diagnoses

Outcomes of Down syndrome cases from 1989-2012

Since the register started collecting data on 1st January 1989 the annual number and prevalence of Down syndrome diagnoses has increased (Table 13 and Figure 4), firstly due to the considerable increases in maternal age, the major known risk factor, and secondly due to the increase in the numbers of Down syndrome pregnancies diagnosed prenatally, many of which were non-viable and would have miscarried and therefore remained undiagnosed in the absence of prenatal screening. The number and prevalence of Down syndrome live births has not changed significantly, this reflects the fact that an increasing proportion of Down syndrome diagnoses are occurring prenatally and that over 90% of women who receive a prenatal diagnosis decide to terminate the pregnancy (Table 13). The proportion of women having a termination after a prenatal diagnosis of Down syndrome has decreased from 92% in 1989-2010 to 90% in 2011 and 2012.

Figure 4: Prevalence of Down syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2012 data are provisional.

Table 13 shows that the percentages of prenatal diagnoses have increased over time, however, Figure 5 shows that the increases have been greatest amongst women under 35 years of age.

Table 13: Down syndrome diagnoses and outcomes in England and Wales from 1989 to 2012*

	Numbers of Diagnoses					Outcome of prenatal diagnoses ‡ (%)		
Calendar year of diagnosis	All	Prenatal (%)	Live births†		Unknown outcomes	Termi-nation	Miscarriage /still birth	Live births
			Reported	Estimated				
1989	1,066	318 (30)	750	750	8	95	2	4
1990	1,091	370 (34)	738	739	12	92	2	6
1991	1,139	423 (37)	736	737	9	89	4	7
1992	1,143	494 (43)	662	663	18	93	2	6
1993	1,150	553 (48)	621	621	8	93	2	5
1994	1,228	607 (49)	637	639	25	93	2	5
1995	1,212	652 (54)	579	581	25	92	2	6
1996	1,299	713 (55)	606	607	13	93	1	5
1997	1,381	728 (53)	666	667	19	94	1	5
1998	1,289	695 (54)	631	633	25	92	1	7
1999	1,311	723 (55)	602	604	26	93	1	5
2000	1,363	805 (59)	591	594	43	92	1	7
2001	1,361	811 (60)	576	580	63	93	2	6
2002	1,427	874 (61)	584	589	75	92	2	6
2003	1,418	832 (59)	614	617	58	92	2	6
2004	1,610	978 (61)	660	664	67	91	2	7
2005	1,751	1,040 (59)	740	746	104	92	2	6
2006	1,836	1,109 (60)	758	764	102	91	3	6
2007	1,789	1,106 (62)	716	721	78	92	2	6
2008	1,844	1,128 (61)	750	754	63	91	2	7
2009	1,927	1,193 (62)	787	792	83	90	3	8
2010	1,911	1,219 (64)	728	734	101	92	1	6
2011	1,901	1,232 (65)	733	739	100	89	2	9
2012	1,982	1,259 (64)	765	775	166	90	3	7
Total	35,429	19,862 (56)	16,230	16,310	1,291	92	2	6

* 2012 data are provisional. † Estimated live births includes 6% of unknown outcomes. ‡ Calculated as a percentage of all known outcomes.

Indication for prenatal diagnosis 1989-2012

Figure 6 and Table 14 show the changes in the indications for a prenatal diagnosis of Down syndrome. For older women there has been a clear shift from having a diagnostic test due to advanced maternal age to having a diagnostic test due to a high risk predicted from screening. For younger women, at the start of the register the majority of prenatal diagnoses were due to anomalies seen during the fetal anomaly scan. A greater proportion is now detected due to screening. In 2011 and 2012 there was a much greater proportion of younger women having first trimester screening.

Figure 5: Percentage of Down syndrome cases which were prenatally diagnosed according to maternal age and year of diagnosis*

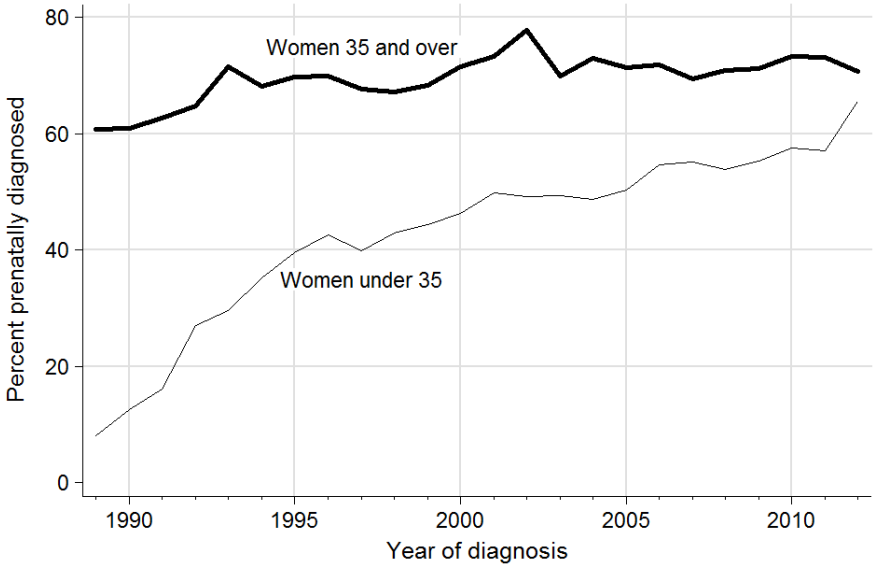
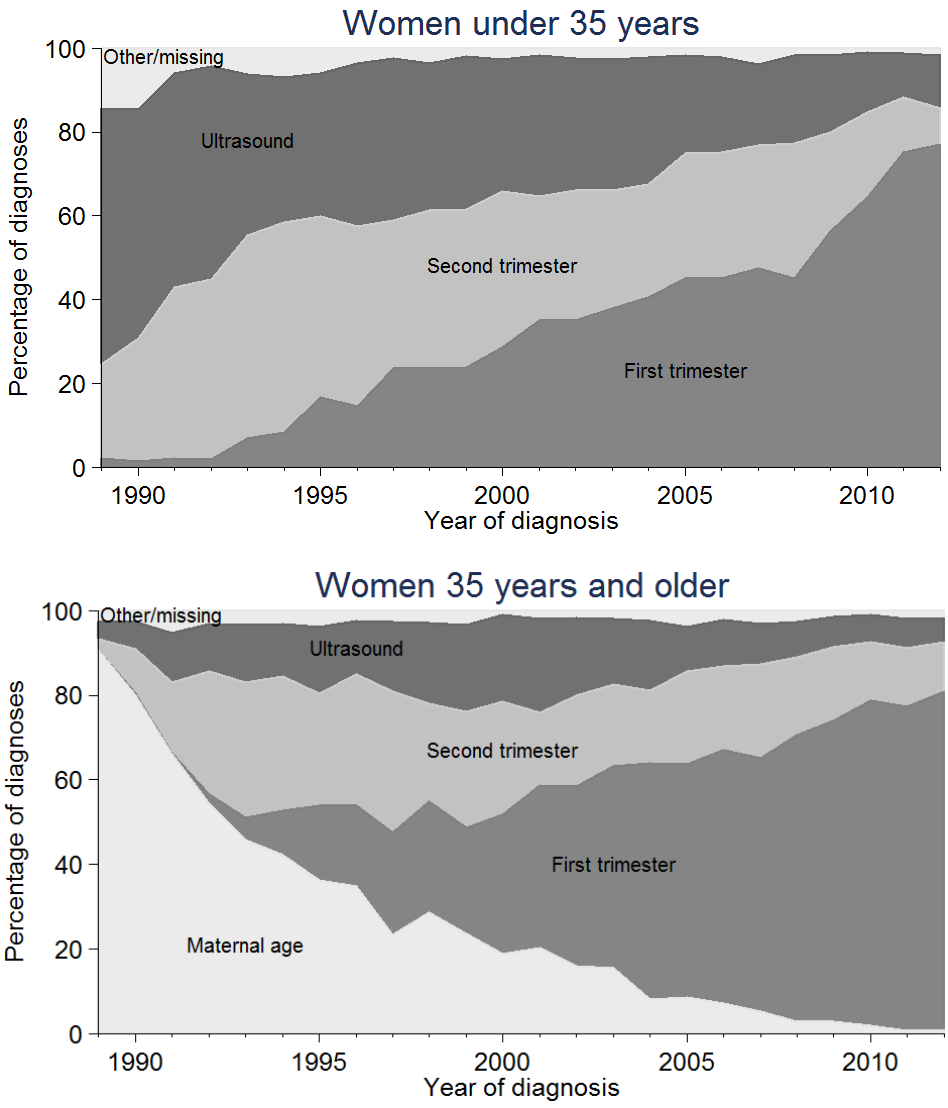


Figure 6: Indication for Down syndrome prenatal diagnosis according to year of diagnosis* and maternal age



* 2012 data are provisional

Table 14: Indication for Down syndrome prenatal diagnosis according to maternal age from 1989 to 2012*

Calandar Year of diagnosis	Women under 35 (%)				Women 35+ (%)				
	1st Trimester	2nd Trimester	Ultra-sound	Other/ Missing	Age alone	1st Trimester	2nd Trimester	Ultra-sound	Other/ Missing
1989	2	22	61	14	91	0	3	4	3
1990	1	29	55	15	80	0	11	6	3
1991	2	41	51	6	66	0	17	12	5
1992	2	43	51	4	54	2	29	11	3
1993	7	49	39	6	46	5	32	14	3
1994	8	50	35	7	42	11	32	13	3
1995	17	43	34	6	36	18	26	16	4
1996	14	43	39	4	35	19	31	13	2
1997	24	35	39	2	23	24	33	16	3
1998	24	38	35	4	29	26	23	19	3
1999	24	38	37	2	24	25	28	20	3
2000	29	37	32	3	19	33	27	21	1
2001	35	30	34	2	20	38	17	22	2
2002	35	31	32	2	16	42	22	18	2
2003	38	28	31	3	15	48	19	16	2
2004	40	27	30	2	8	56	17	16	3
2005	45	30	23	2	8	55	22	11	4
2006	45	30	23	2	7	60	20	11	2
2007	47	29	19	4	5	60	22	10	3
2008	45	32	21	2	3	68	19	8	3
2009	56	24	18	2	3	71	17	7	2
2010	64	20	14	1	2	77	14	6	1
2011	75	13	10	1	1	77	14	7	2
2012	77	9	13	2	1	80	12	6	2

* 2012 data are provisional.

Gestational age at termination following prenatal diagnosis 1989-2012

The shift towards earlier screening has increased the percentage of prenatal diagnoses with terminations before 15 weeks gestation for younger women, and is back up to the pre-2011 proportions for older women (Table 15). The percentage of terminations taking place at 21 weeks gestation or later has continued to decrease in 2012 for younger and older women, though it remains higher for younger women.

Maternal age at observed or expected date of delivery 1989-2012

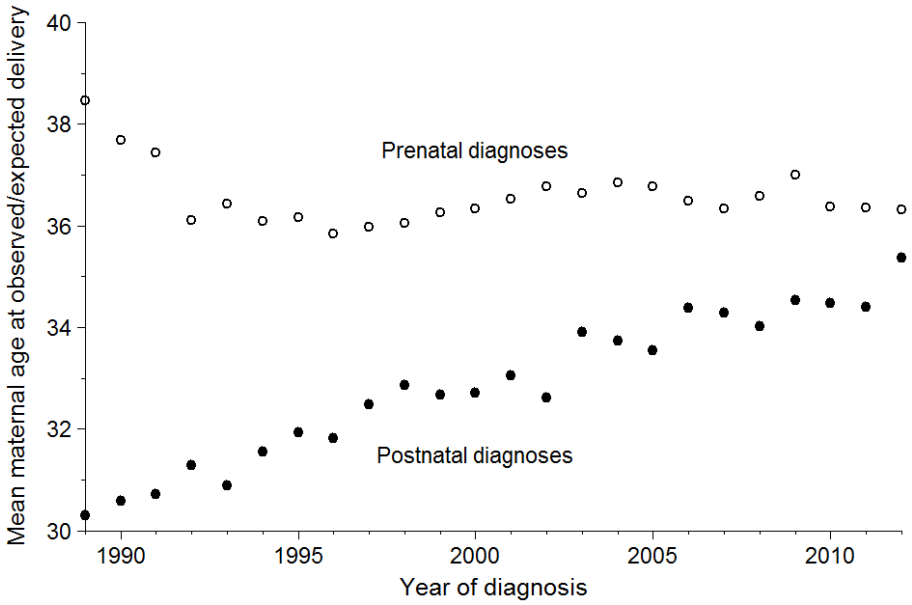
At the start of the register, the main prenatal screening test available was a mother's age and so the majority of prenatal diagnoses occurred in older women. As more screening tests became more available and detection rates for younger women improved, more younger women received prenatal diagnoses. This is reflected in the average maternal age (Figure 5). The average age for prenatal diagnoses is declining, whilst the average age for postnatal diagnosis is increasing. This has important implications for the long term care of these children, by increasingly older parents.

Table 15: Gestation at termination after prenatal diagnosis of Down syndrome according to maternal age from 1989 to 2012*

Calandar year of diagnosis	Women under 35 (%)			Women ≥35 (%)		
	<15 weeks	15 to 20 weeks	≥21 weeks	<15 weeks	15 to 20 weeks	≥21 weeks
1989	2	45	52	18	64	19
1990	8	45	47	13	65	22
1991	1	52	47	14	66	20
1992	2	61	37	9	70	21
1993	11	42	47	14	62	25
1994	6	55	39	18	66	17
1995	18	49	33	21	63	16
1996	14	52	34	25	62	14
1997	19	54	27	28	59	14
1998	23	50	27	28	59	13
1999	21	52	26	29	58	13
2000	27	48	25	35	55	11
2001	27	49	24	42	48	10
2002	31	47	22	41	51	8
2003	32	47	21	44	49	7
2004	31	49	20	45	46	9
2005	34	48	18	44	47	9
2006	34	46	20	43	48	9
2007	40	43	17	51	42	8
2008	34	50	17	55	39	7
2009	40	44	16	50	44	6
2010	42	46	12	53	42	5
2011	46	39	15	44	49	7
2012	46	43	12	50	44	6

* 2012 data are provisional. Gestation at termination was estimated where necessary using the median time between diagnostic sample and termination according to year of diagnosis and tissue used for diagnosis.

Figure 5: Mean maternal age according to year of diagnosis* and stage at diagnosis



* 2012 data are provisional

Trends over time in Patau and Edwards syndromes diagnoses

The number of diagnoses of Patau and Edwards syndromes has risen since data started being collected in 2004 (Tables 16 and 17). However, after excluding the data in 2004, which may have been subject to under-reporting, the prevalence of these syndromes has not increased significantly (Figures 6 and 7).

Table 16: Patau syndrome diagnoses and outcomes in England and Wales from 2004 to 2012*

Year of diagnosis	Patau syndrome: Numbers of Diagnoses				
	All	Prenatal (%)	Live births		Unknown outcomes
			Reported	Estimated†	
2004	147	134 (91)	15	15	6
2005	154	135 (88)	24	24	8
2006	190	172 (91)	25	25	10
2007	213	188 (88)	27	27	3
2008	188	170 (90)	24	24	6
2009	176	150 (85)	27	27	9
2010	221	198 (90)	28	28	10
2011	196	172 (88)	23	23	10
2012	229	213 (93)	21	22	24
Total	1,714	1,532 (89)	214	215	86

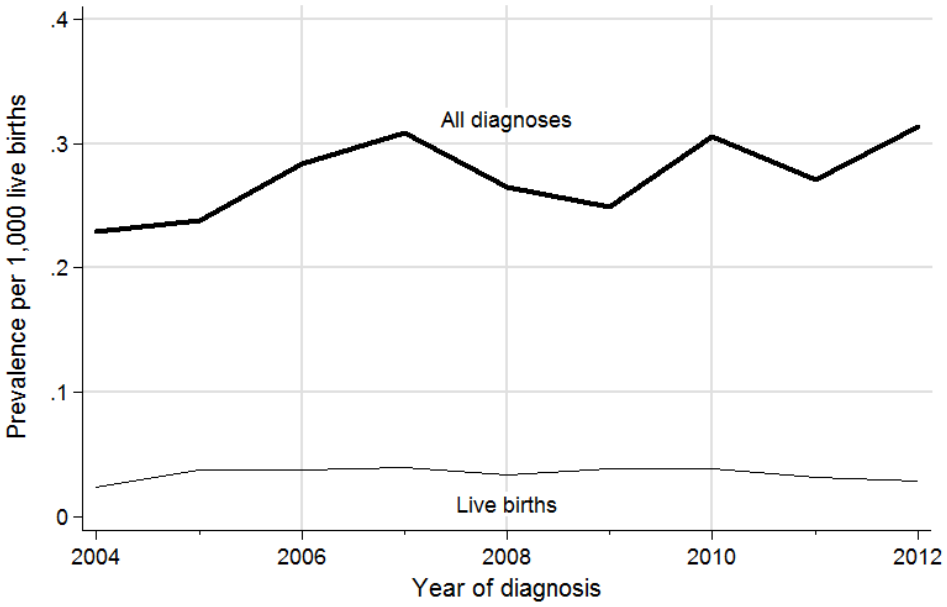
* 2012 data are provisional. † Estimated live births include 4% of unknown outcomes.

Table 17: Edwards syndrome diagnoses and outcomes in England and Wales from 2004 to 2012*

Year of diagnosis	Edwards syndrome: Numbers of Diagnoses				
	All	Prenatal (%)	Live births		Unknown outcomes
			Reported	Estimated†	
2004	356	320 (90)	38	39	35
2005	426	383 (90)	40	41	37
2006	451	394 (87)	67	68	37
2007	482	441 (91)	54	55	34
2008	488	450 (92)	46	47	22
2009	520	471 (91)	52	53	36
2010	538	484 (90)	65	66	40
2011	510	471 (92)	42	43	35
2012	526	465 (88)	66	68	67
Total	4,297	3,879 (90)	470	480	343

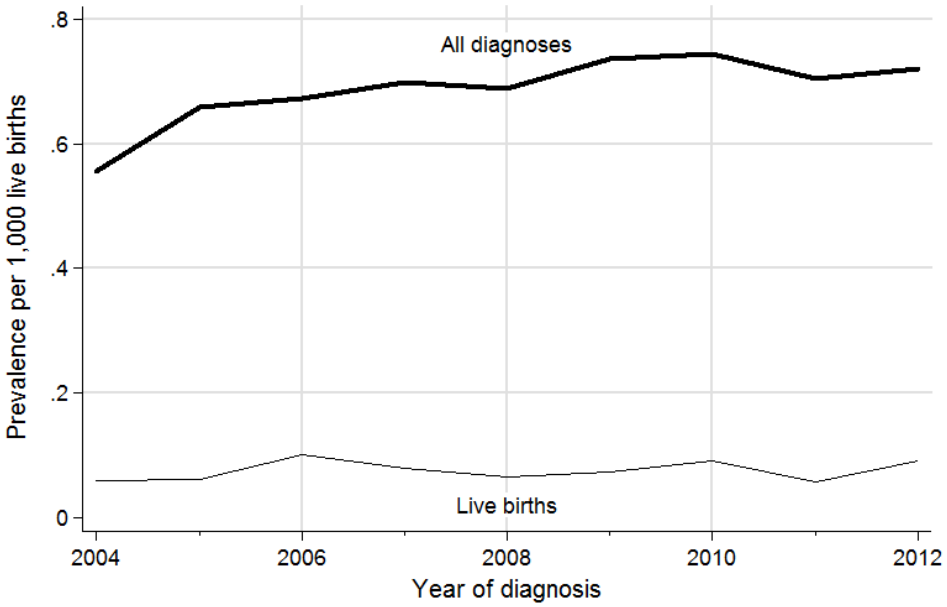
* 2012 data are provisional. † Estimated live births include 3% of unknown outcomes.

Figure 6: Prevalence of Patau syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2012 data are provisional.

Figure 7: Prevalence of Edwards syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2012 data are provisional.

Appendix A

Data Completeness

The following table shows the completeness of the different data items for the years 1989 to 2009, 2010, 2011 and 2012. We are still following up the missing data from 2010 onwards. The data from 1989 to 2009 are included for comparison purposes to demonstrate the levels we are aiming to achieve for the more recent data.

Table A1: Completeness of data from 1989 to 2012*

Data Item	Percentage complete			
	1989-2009	2010	2011	2012
Reason for referral for diagnosis	99	98	96	96
Type of tissue karyotyped	98	98	98	96
Sex of fetus (some DNA based diagnoses such as FISH and q-PCR do not include sex chromosome analysis)	98	94	94	92
Maternal age	95	95	95	91
Gestational age at sample for prenatal diagnosis	97	95	94	91
Outcome of pregnancy if prenatal diagnosis	94	92	92	87
Post Codes (some information)	94	96	96	93
Maternal NHS number (requested from 2005)	**68	77	83	80
Infants NHS number (requested from 2005)	**69	83	87	85

* 2012 data are provisional.

**Data for 2005-2009

Appendix B: Form in 2012

Reference No. NDSCR |__|__|__|__|__|

NATIONAL DOWN SYNDROME CYTOGENETIC REGISTER

Now including trisomies 13 and 18 *CONFIDENTIAL* NIGB ref: 2-08(e)/2002 Trent REC ref: 09/H0405/48

Please complete and return this form to:
Joan Morris, NDSCR, Wolfson Institute of Preventive Medicine, Barts and the London, Charterhouse Square, London, EC1M 6BQ
Telephone: 020 7882 6220 Fax: 020 7882 6221 (confidential) Website: http://www.wolfson.qmul.ac.uk/ndscr/
and forward blue copy to the referring clinician. Thank you for your help.

TRISOMY

Laboratory ID |__|__| 21 |__| 13 |__| 18 |__|

Specimen ID |__|__|__|__|__|__|__|__|__|__|

Date of LMP (D D M M Y Y) |__|__|__|__|__|__|

Best estimate of EDD |__|__|__|__|__|__|

Karyotype .....

Method of karyotyping Full |__| PCR |__| FISH |__|

PCR / FISH result .....

Date sample taken (D D M M Y Y) |__|__|__|__|__|__| gest |__|__| wks

Sample CVS |__| Amnio |__| Postnatal |__| Other .....

Confirmation of previous diagnosis Yes |__| No |__|

ID |__|__|__|__|__|__|__|__|__|

SCREENING TESTS

(Please complete all relevant sections below)

NHS |__| or Private |__|

Screening result : +ve |__| -ve |__| Risk 1 in .....

1st trimester (Tick all markers tested)

NT |__| .....mm PAPP-A |__| Freeβ-hCG |__| Other .....

2nd trimester (Tick all markers tested)

AFP |__| uE_3 |__| hCG (any) |__| Inhibin-A |__| Other .....

Please specify any other screening test performed and result:

.....

Not screened |__|

Too late |__| Not offered |__| Screening test declined |__|

Too early |__| Other |__| please specify .....

TIMING OF DIAGNOSIS AND INDICATIONS

Prenatal Screen result |__| Mat Age |__| Family history |__|

|__| U/S findings (please specify) |__| .....

Other .....

Postnatal No indication |__| Diagnostic test declined |__|

|__| Diagnosed after miscarriage |__| Other .....

IDENTIFYING INFORMATION

Mother's hospital ID |__|__|__|__|__|__|__|__|__|__|

First 3 letters of mother's surname |__|__|__| Initial |__|

Mother's NHS No. |__|__|__|__|__|__|__|__|__|__|

Infant's hospital ID |__|__|__|__|__|__|__|__|__|__|

Infant's NHS No. |__|__|__|__|__|__|__|__|__|__|

Mother's date of birth (D D M M Y Y) |__|__|__|__|__|__| age |__|__| (age at testing)

Father's date of birth |__|__|__|__|__|__| |__|__| (age at testing)

OUTCOME

Termination |__| Miscarriage |__| Stillbirth |__| Livebirth |__|

Date of outcome/ termination/ birth (D D M M Y Y) |__|__|__|__|__|__|

Gestation at outcome |__|__| wks

Infant's birth weight |__|__|__|__| gms

Name of referring clinician and hospital:

.....

If terminated or delivered elsewhere, name of clinician and hospital:

.....

Multiple pregnancy? No |__| Twin |__| Triplet |__| Other |__|

If yes, please give sex and outcome of all other fetuses / babies:

.....

Is this the first pregnancy? Yes |__| No |__|

If no, please give number of outcomes of previous pregnancies:

Terminations |__| Miscarriages |__| Stillbirths |__| Livebirths |__|

No. previous pregnancies with trisomies 21 |__| 13 |__| 18 |__|

If previous anomaly, please specify outcome .....

Other chromosomal anomaly, including parents' if known:

.....

Mother's usual town of residence:

.....

Postcode |__|__|__|__| |__|__|__|__| PCT |__|__|__|

Note: (e.g. condition of infant, previous family history, fertility problems, etc.)

.....

.....

.....

(Please continue overleaf)

FOR OFFICE USE ONLY C

Reference No. NDSCR |__|__|__|__|__|

Laboratory |__|__| Trisomy 21 13 18 pren/ postn/ misc

Specimen ID |__|__|__|__|__|__|__|__|__|__|

Appendix C: Selected NDSCR Publications

1. Boyle B, Morris JK, McConkey R, Garne E, Loane M, Addor MC, Gatt M, Haeusler M, Latos-Bielenska A, Lelong N, McDonnell R, Mullaney C, O'Mahony M, Dolk H. The prevalence and risk of Down syndrome in monozygotic and dizygotic multiple pregnancies in Europe: implications for prenatal screening. *BJOG* 2013 (in press).
2. Wu J, Springett A, Morris JK. Survival of trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome) in England and Wales: 2004-2011. *Am J Med Genet A* 2013; **161**:2512-8.
3. Wu J, Morris JK. Trends in maternal age distribution and the live birth prevalence of Down's syndrome in England and Wales: 1938-2010. *Eur J Hum Genet* 2013; **21**:943-7.
4. Wu J, Morris JK. The population prevalence of Down's syndrome in England and Wales in 2011. *Eur J Hum Genet* 2013; **21**:1016-9.
5. Morris JK. Trisomy 21 mosaicism and maternal age. *Am J Med Genet A* 2012; **158A**:2482-4.
6. Morris JK, Waters JJ, de Souza E. The population impact of screening for Down syndrome: audit of 19326 invasive diagnostic tests in England and Wales in 2008. *Prenat Diagn* 2012; **32**:596-601.
7. Alberman E, Mutton D, Morris JK. Cytological and epidemiological findings in trisomies 13, 18, and 21: England and Wales 2004-2009. *Am J Med Genet A* 2012; **158A**:1145-50.
8. Morris JK, Alberman E, Mutton D, Jacobs P. Cytogenetic and epidemiological findings in Down syndrome: England and Wales 1989-2009. *Am J Med Genet A* 2012; **158A**:1151-7.
9. De Souza E, Alberman E, Morris JK. Down's syndrome: screening and antenatal diagnosis regionally in England and Wales 1989-2008. *J Med Screen* 2010; **17**:170-5.
10. Morris JK, Alberman E. Trends in Down's syndrome live births and antenatal diagnoses in England and Wales from 1989 to 2008: analysis of data from the National Down Syndrome Cytogenetic Register. *BMJ* 2009; **339**:b3794.
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13. Crane B, Morris JK. Changes in maternal age in England and Wales – Implications for Down syndrome. *Down syndrome research and practice* 2006; **10**:41-3.
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15. Morris JK, Mutton DE, Alberman E. Recurrences of free trisomy 21: Analysis of data from the National Down Syndrome Cytogenetic Register. *Prenat Diagn* 2006; **25**:1120-8.
16. Morris JK, de Vigan C, Mutton DE, Alberman E. Risk of a Down syndrome live birth in women of 45 years of age and older. *Prenat Diagn* 2006; **25**:275-8.
17. Kovaleva NV, Mutton DE. Epidemiology of double aneuploidies involving chromosome 21 and the sex chromosomes. *Am J Med Genet* 2006; **134A:**24-32.
18. Alberman E, Huttly W, Hennessy E, McIntosh A. The use of record linkage for auditing the uptake and outcome of prenatal serum screening and prenatal diagnostic tests for Down syndrome. *Prenat Diagn* 2003; **23**:801-6.

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20. Morris JK, Wald NJ, Mutton DE, Alberman E. Comparison of models of maternal age-specific risk for Down syndrome live births. *Prenat Diagn* 2003; **23**:252-8.
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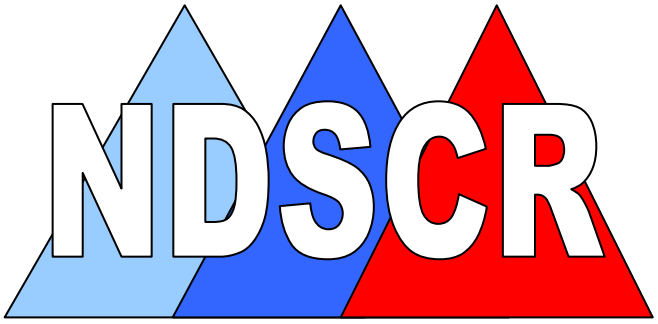

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