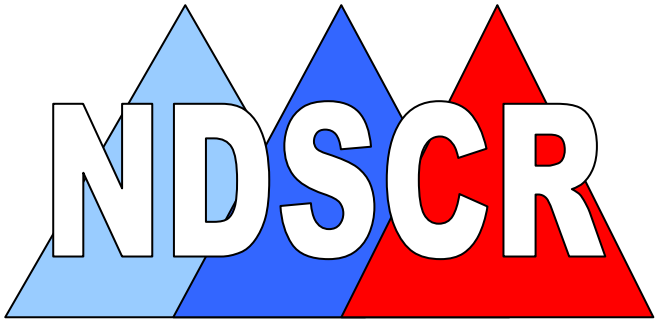

The National Down Syndrome Cytogenetic Register for England and Wales: 2013 Annual Report

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National Down Syndrome Cytogenetic Register

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Foreword

This 2013 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 2013, and Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) from 2004 to 2013. We would like to thank all the individuals who contribute to the NDSCR to make it such a valuable resource.

This will be the last report to be published in its current format. Public Health England's (PHE) current remit is to establish a national congenital anomaly data collection system using established regional and disease specific registers and to develop new registers in those areas in England not currently covered. As part of this process the NDSCR register staff will move to PHE from 1st April 2015. The NDSCR is working closely with PHE to help facilitate this process and to ensure that the high quality data in the NDSCR is maintained.

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Executive Summary

- In 2013 there were 1,872 diagnoses of Down syndrome, 65% of which were made prenatally, a rate of 2.7 per 1,000 births.
- In 2013 there were an estimated 717 Down syndrome live births, a live birth rate of 1.0 per 1,000 live births.
- In 2013 there were 179 diagnoses of Patau and 473 diagnoses of Edwards syndrome, of which an estimated 18 and 33 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 55% in 2009 to 62% in 2013. The proportion for women 35 and over remained fairly constant at around 70%-75% from 2009 to 2013.
- The proportion of women receiving prenatal diagnoses of Down syndrome after 1st trimester screening increased from 56% in 2009 to 74% in 2013 for women under 35 and from 71% in 2009 to 79% in 2013 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, 2012 and 2013.
- There were regional differences in the type of screening that the women were offered in 2013. In all of the English regions the majority of women were diagnosed after 1st trimester screening (78%), compared to 26% in Wales.

Suggested citation of this report:

Morris JK, Springett A. The National Down Syndrome Cytogenetic Register for England and Wales 2013 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 until April 2015. In April 2015 the NDSCR register staff will move to 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 aims 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 2013 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 2010 combined, and separately for 2011, 2012 and 2013. 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 2009 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 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/current-projects/downs-syndrome-register) 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.

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/current-projects/downs-syndrome-register).
- 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 2013

Outcomes of Down syndrome cases

In 2013, 1,886 Down syndrome diagnoses were made, 1,232 (65%) prenatally and 654 (35%) postnatally (Table 1). This gives a prevalence of 2.7 (95% CI: 2.6-2.8) per 1,000 births. The outcome of 205 of the prenatal diagnoses is unknown. Assuming that the proportion terminated remains as before 2013, the likely number of Down syndrome live births in England and Wales in 2013 would have been 728 (82 + 634 + 6% of 205), giving a live birth prevalence of 1.0 (95% CI: 1.0 – 1.1) per 1,000 live births occurring in England and Wales in 2013.

Table 1: Down syndrome cases diagnosed in England and Wales in 2013* according to time of diagnosis and outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	925	49 (47 - 51)
	Live Birth	82	4 (4 - 5)
	Still Birth / Miscarriage	20	1 (1 - 2)
	Unknown outcome†	205	11 (10 - 12)
		1,232	65 (63 - 67)
Postnatal	Live Birth	634	34 (32 - 36)
	Still Birth / Miscarriage	20	1 (1 - 2)
		654	35 (33 - 37)
Total		1,886	100

* 2013 data are provisional due to late reporting of cases. † 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 43% of women with a postnatal diagnosis.

Table 2: Acceptance of prenatal screening tests among women with a Down syndrome diagnosis in 2013*

	Stage at diagnosis			
	Prenatal		Postnatal	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
Screened	1,097	89 (87 - 91)	248	38 (34 - 42)
No indication	..	..	76	12 (9 - 14)
Declined further testing	..	..	150	23 (20 - 26)
Unknown	..	..	22	3 (2 - 5)
Declined screening	32	3 (2 - 4)	124	19 (16 - 22)
No information	103	8 (7 - 10)	282	43 (39 - 47)
Total	1,232	100	654	100

* 2013 data are provisional due to late reporting of cases.

Indication for prenatal diagnosis according to maternal age

In 2013, 65% of Down syndrome diagnoses were made prenatally, 62% (95% CI: 58 – 66) in younger (<35 years) women and 75% (95% CI: 72 – 77) in older (≥35 years) women.

Table 3 shows the indication for prenatal diagnosis separately for younger and older women. First trimester screening includes the dating scan, nuchal translucency (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 18-20 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 77% of women. A greater percentage of younger (11%) than older women (5%) gave an ultrasound examination as the indication. Eleven percent of prenatal diagnoses in younger women occurred at 21 weeks gestation or later, compared to only 4% of prenatal diagnoses in older women (data not shown).

Table 3: Indication for prenatal diagnosis of Down Syndrome in 2013* 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	273	73 (68 - 77)	653	79 (76 - 82)
2nd Trimester screening	46	12 (9 - 16)	100	12 (10 - 15)
Ultrasound	41	11 (8 - 15)	42	5 (4 - 7)
Maternal age	-	-	5	1 (0 - 1)
Other reasons / No information	13	3 (2 - 6)	25	3 (2 - 4)
Total	373	100	825	100

* 2013 data are provisional due to late reporting of cases; 34 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 (35%, 95% CI: 33 - 38). The tissue was either unspecified or not from an amniocentesis or CVS in 7% of women.

The median time from CVS to termination of pregnancy was eight days and from amniocentesis was nine days. Eighty-six percent of all terminations following CVS and 84% 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 2013* 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	126	45 (40 - 51)	287	47 (43 - 51)
15 to 20 weeks	120	42 (37 - 48)	289	47 (43 - 51)
≥21 weeks	35	12 (9 - 16)	36	6 (4 - 8)
Total	281	100	612	100

* 2013 data are provisional due to late reporting of cases; fourteen 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 36.8 (95% CI: 36.5 – 37.1) compared to 34.4 (95% CI: 33.8 – 35.0) for those with a postnatal diagnosis. Overall 65% (1,104/1,708) of the women of known age were 35 or older (Table 5).

Table 5: Down syndrome cases diagnosed in 2013* according to maternal age at observed or expected date of delivery

Maternal age (years)	Number	Percentage (95% CI)
< 20	21	1 (1 - 2)
20-24	81	4 (3 - 5)
25-29	175	9 (8 - 11)
30-34	327	17 (16 - 19)
35-39	603	32 (30 - 34)
40-44	457	24 (22 - 26)
≥ 45	42	2 (2 - 3)
missing	180	10 (8 - 11)
Total	1,886	100

*2013 data are provisional due to late reporting of cases.

Patau and Edwards syndrome cases diagnosed in 2013

Outcomes of Patau and Edwards syndrome cases

In 2013, 180 Patau syndrome diagnoses were made, of which 91% were made prenatally, and 474 Edwards syndrome diagnoses were made, of which 93% were made prenatally. This gives a prevalence of 0.3 (95% CI: 0.2-0.3) per 1,000 births for Patau syndrome and a prevalence of 0.7 (95% CI: 0.6-0.7) 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 19 Patau and 55 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, still birth or miscarriage), therefore the total number of live births is estimated to be 19 and 40 respectively, giving a live birth prevalence of 0.03 (95% CI: 0.02-0.04) per 1,000 live births for Patau syndrome and a prevalence of 0.06 (95% CI: 0.04-0.08) 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 2013* according to outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	130	72 (65 - 78)
	Live Birth	4	2 (1 - 6)
	Still Birth / Miscarriage	10	6 (3 - 10)
	Unknown outcome†	19	11 (7 - 16)
		163	91 (85 - 94)
Postnatal	Live Birth	14	8 (5 - 13)
	Still Birth / Miscarriage	3	2 (1 - 5)
		17	9 (6 - 15)
	Total	180	100

* 2013 data are provisional due to late reporting of cases; † Approximately 4% of Patau syndrome with unknown outcomes are likely to result in a live birth.

Table 6b: Edwards syndrome cases in 2013* according to time of diagnosis and outcome

		Number	Percentage (95% CI)
Prenatal	Termination of pregnancy	358	76 (71 - 79)
	Live Birth	11	2 (1 - 4)
	Still Birth / Miscarriage	17	4 (2 - 6)
	Unknown outcome†	55	12 (9 - 15)
		441	93 (90 - 95)
Postnatal	Live Birth	27	6 (4 - 8)
	Still Birth / Miscarriage	6	1 (1 - 3)
		33	7 (5 - 10)
	Total	474	100

* 2013 data are provisional due to late reporting of cases; † 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 19% were picked up by the fetal anomaly ultrasound (Table 7). A greater percentage of older women (95%) had a prenatal diagnosis of Patau syndrome than younger women (87%), whereas there was little difference between younger and older women for Edwards syndrome (94% for both) (data not shown).

Table 7: Indication for prenatal diagnosis of Patau and Edwards syndrome cases in 2013*

Indication for prenatal diagnosis	Patau syndrome		Edwards syndrome	
	Number	Percentage (95% CI)	Number	Percentage (95% CI)
1st Trimester screening	122	75 (68 - 81)	321	73 (68 - 77)
2nd Trimester screening	8	5 (3 - 9)	13	3 (2 - 5)
Ultrasound	28	17 (12 - 24)	85	19 (16 - 23)
Maternal age	0	0 (0 - 2)	0	0 (0 - 1)
Other reasons / No information	5	3 (1 - 7)	22	5 (3 - 7)
Total	163	100	441	100

* 2013 data are provisional due to late reporting of cases.

Maternal age at observed or expected date of delivery

The mean age of the woman at expected or observed date of delivery was 35.4 years for Patau syndrome and 36.2 years for Edwards syndrome, compared to 36.2 years for Down syndrome. For Patau syndrome 59% of women with known maternal age were aged 35 or over, and for Edwards syndrome 61% of women with known maternal age were aged 35 or over (Table 8).

Table 8: Patau and Edwards syndrome cases diagnosed in 2013* 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	12	7 (4 - 11)	36	8 (6 - 10)
25-29	24	13 (9 - 19)	44	9 (7 - 12)
30-34	33	18 (13 - 25)	92	19 (16 - 23)
35-39	61	34 (27 - 41)	99	21 (17 - 25)
≥ 40	40	22 (17 - 29)	171	36 (32 - 40)
missing	10	6 (3 - 10)	32	7 (5 - 9)
Total	180	100	474	100

* 2013 data are provisional due to late reporting of cases.

Geographical variation in cases diagnosed in 2013

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 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 2013*

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	29	15	2.0	40 (29 - 53)
North West	86	17	2.3	56 (49 - 63)
Yorkshire & Humberside	65	16	2.4	58 (50 - 65)
East Midlands	53	17	2.2	60 (51 - 68)
West Midlands	71	17	2.4	59 (51 - 66)
East England	71	21	2.7	72 (65 - 77)
London	128	27	3.5	72 (68 - 76)
South East	102	23	2.9	76 (70 - 80)
South West	59	20	2.7	63 (55 - 70)
Wales	34	16	1.9	60 (48 - 71)
Total	699	20	2.7	65 (63 - 67)

* 2013 data are provisional due to late reporting of cases. Eight 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. East of England, London, the South East and the South West 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-eight 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 2013*

Region	Number of prenatal diagnoses	Indication for prenatal diagnosis (%)					
		1st trimester screening	2nd trimester screening	Ultrasound	Maternal age	Other/ Missing	Total
North East	23	70	22	4	0	4	100
North West	111	56	25	16	2	1	100
Yorkshire & Humberside	91	71	9	11	0	9	100
East Midlands	74	73	19	4	0	4	100
West Midlands	99	70	13	8	0	9	100
East England	138	82	9	7	0	3	100
London	327	86	7	3	0	4	100
South East	226	81	8	7	0	4	100
South West	100	82	11	5	1	1	100
Wales	39	23	49	26	0	3	100
Total	1,232	76	12	7	0	4	100

* 2013 data are provisional due to late reporting of cases; four cases had unknown region.

Table 11: Gestation at termination after prenatal diagnosis of Down syndrome according to region of maternal residence in 2013*

Region	Number of terminations	Gestation at termination (%)			
		<15 weeks	15 to 20 weeks	21+ weeks	Total
North East	21	43	48	10	100
North West	76	29	59	12	100
Yorkshire & Humberside	55	41	51	8	100
East Midlands	62	32	60	8	100
West Midlands	79	41	53	6	100
East England	95	48	45	8	100
London	230	59	32	9	100
South East	185	52	41	7	100
South West	88	44	53	2	100
Wales	33	15	67	18	100
Total	924	46	46	8	100

* 2013 data are provisional due to late reporting of cases; one case had unknown region and 28 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 2013*

Region	Percentage (95% CI)	
	Patau Syndrome	Edwards Syndrome
	Prenatal	Prenatal
North East	100 (68 - 100)	90 (70 - 97)
North West	77 (57 - 90)	92 (80 - 97)
Yorkshire & Humberside	100 (76 - 100)	93 (80 - 97)
East Midlands	100 (68 - 100)	100 (89 - 100)
West Midlands	83 (55 - 95)	91 (79 - 96)
East England	92 (67 - 99)	98 (88 - 100)
London	93 (81 - 97)	91 (84 - 95)
South East	95 (83 - 99)	95 (88 - 98)
South West	81 (60 - 92)	90 (75 - 97)
Wales	100 (51 - 100)	94 (73 - 99)
Total	91 (85 - 94)	93 (90 - 95)

*2013 data are provisional due to late reporting of cases. One case of Patau syndrome does not have region data.

Summary of regional differences

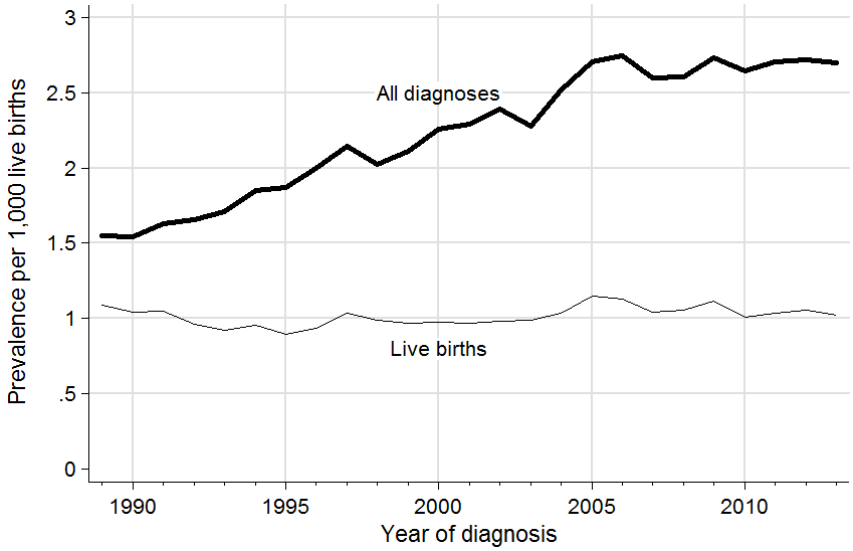
There are clear regional differences in screening for Down syndrome in England and Wales in 2013. These differences may arise not only due to service factors, but also maternal factors including age, social deprivation and cultural beliefs influencing the take up of screening and diagnostic tests. More 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.

Trends over time in Down syndrome diagnoses

Outcomes of Down syndrome cases from 1989-2013

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 1), 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, 2012 and 2013.

Figure 1: Prevalence of Down syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2013 data are provisional due to late reporting of cases.

Table 13 shows that the percentages of prenatal diagnoses have increased over time, however, Figure 2 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 2013*

	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	5
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	1,313	725 (55)	602	604	27	93	1	5
2000	1,363	805 (59)	591	594	43	92	1	7
2001	1,361	811 (60)	576	580	63	93	1	6
2002	1,427	874 (61)	585	589	74	92	2	6
2003	1,417	831 (59)	613	616	58	92	2	6
2004	1,612	979 (61)	661	665	67	91	2	7
2005	1,749	1,038 (59)	741	747	104	92	2	6
2006	1,836	1,109 (60)	758	764	101	91	3	6
2007	1,791	1,107 (62)	718	723	77	92	2	6
2008	1,844	1,127 (61)	750	754	62	91	2	7
2009	1,928	1,193 (62)	788	793	79	90	3	8
2010	1,912	1,219 (64)	731	737	94	92	1	7
2011	1,959	1,274 (65)	752	758	108	89	2	9
2012	1,983	1,257 (63)	772	779	111	90	3	7
2013	1,886	1,232 (65)	716	728	205	90	2	8
Total	37,379	21,134 (57)	16,980	17,068	1,435	92	2	6

* 2013 data are provisional due to late reporting of cases. † Estimated live births includes 6% of unknown outcomes. ‡ Calculated as a percentage of all known outcomes.

Indication for prenatal diagnosis 1989-2013

Figure 3 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, 2012 and 2013 there was a much greater proportion of younger women having first trimester screening.

Figure 2: Percentage of Down syndrome cases which were prenatally diagnosed according to maternal age and year of diagnosis*

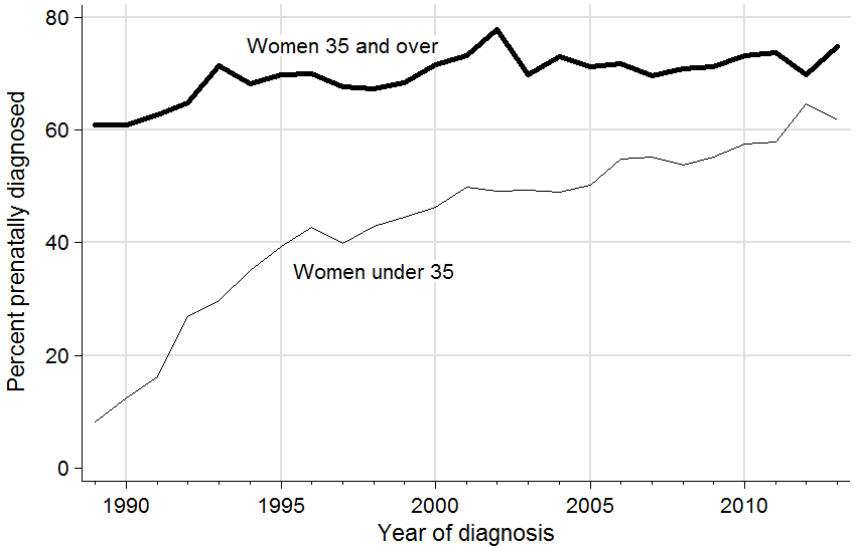
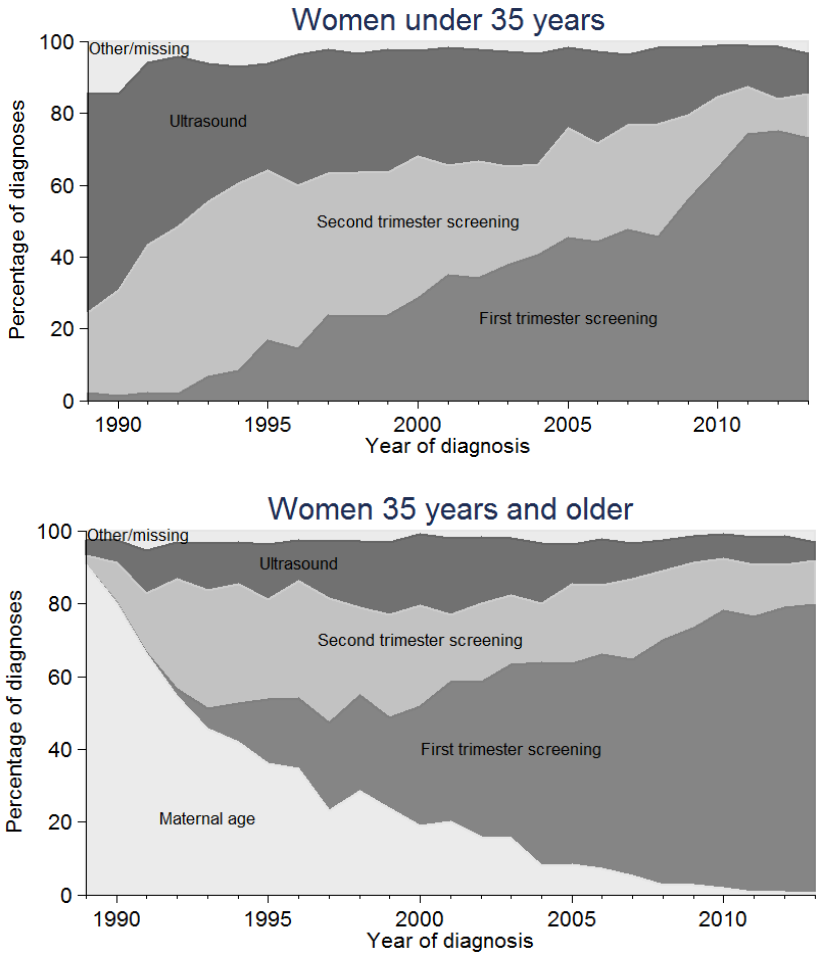


Figure 3: Indication for Down syndrome prenatal diagnosis according to year of diagnosis* and maternal age



* 2013 data are provisional due to late reporting of cases.

Table 14: Indication for Down syndrome prenatal diagnosis according to maternal age from 1989 to 2013*

Calandar Year of diagnosis	Women under 35 (%)				Women 35+ (%)				
	1st trimester screening	2nd trimester screening	Ultra-sound	Other/ Missing	Maternal age	1st trimester screening	2nd trimester screening	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	16	12	5
1992	2	47	47	4	54	2	30	10	3
1993	7	49	39	6	46	5	33	13	3
1994	8	52	33	7	42	11	33	12	3
1995	17	47	30	6	36	18	27	15	4
1996	14	45	37	4	35	19	32	11	3
1997	24	40	35	2	23	24	34	16	3
1998	24	40	33	4	29	26	24	18	3
1999	24	40	34	2	24	25	28	20	3
2000	29	39	29	3	19	33	28	20	1
2001	35	31	33	2	20	38	19	21	2
2002	34	32	31	2	16	43	22	18	2
2003	38	27	32	3	16	48	19	16	2
2004	41	25	31	3	8	56	16	16	4
2005	45	30	23	2	8	55	22	11	4
2006	44	27	25	3	7	59	19	13	2
2007	48	29	19	4	5	60	22	10	3
2008	46	31	21	2	3	67	19	8	3
2009	56	23	19	2	3	71	18	7	2
2010	65	20	14	1	2	76	14	7	1
2011	74	13	12	1	1	75	14	7	2
2012	75	9	14	1	1	78	12	8	2
2013	73	12	11	3	1	79	12	5	3

* 2013 data are provisional due to late reporting of cases.

Gestational age at termination following prenatal diagnosis 1989-2013

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 2013 for younger women.

Table 15: Gestation at termination after prenatal diagnosis of Down syndrome according to maternal age from 1989 to 2013*

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	22	52	26	29	58	13
2000	27	48	25	35	55	11
2001	27	49	24	42	48	10
2002	31	47	21	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	39	44	17	51	42	7
2008	34	49	17	54	39	7
2009	40	45	16	50	44	6
2010	42	46	12	53	42	5
2011	46	38	15	44	49	7
2012	45	43	12	51	44	5
2013	45	43	12	47	47	6

* 2013 data are provisional due to late reporting of cases. 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.

Trends over time in Patau and Edwards syndromes diagnoses

After excluding the data in 2004, which may have been subject to under-reporting, the prevalence of Patau and Edwards syndromes have not increased significantly (Tables 16 and 17, Figures 4 and 5).

Table 16: Patau syndrome diagnoses and outcomes in England and Wales from 2004 to 2013*

Year of diagnosis	Patau syndrome: Numbers of Diagnoses				
	All	Prenatal (%)	Live births		Unknown outcomes
			Reported	Estimated†	
2004	145	133 (92)	14	14	6
2005	154	135 (88)	24	24	8
2006	189	171 (90)	25	25	10
2007	211	188 (89)	27	27	3
2008	189	171 (90)	24	24	5
2009	176	150 (85)	27	27	8
2010	221	198 (90)	28	28	11
2011	195	172 (88)	22	22	11
2012	232	215 (93)	22	23	25
2013	180	163 (91)	18	19	19
Total	1,892	1,695 (90)	231	233	106

* 2013 data are provisional due to late reporting of cases. † Estimated live births include 4% of unknown outcomes.

Table 17: Edwards syndrome diagnoses and outcomes in England and Wales from 2004 to 2013*

Year of diagnosis	Edwards syndrome: Numbers of Diagnoses				
	All	Prenatal (%)	Live births		Unknown outcomes
			Reported	Estimated†	
2004	356	319 (90)	39	40	34
2005	426	383 (90)	40	41	38
2006	454	395 (87)	68	69	37
2007	484	443 (92)	54	55	32
2008	489	450 (92)	47	48	20
2009	521	472 (91)	52	53	37
2010	542	487 (90)	65	66	38
2011	540	501 (93)	43	44	34
2012	532	473 (89)	66	68	57
2013	474	441 (93)	38	40	55
Total	4,818	4,364 (91)	512	524	382

* 2013 data are provisional due to late reporting of cases. † Estimated live births include 3% of unknown outcomes.

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

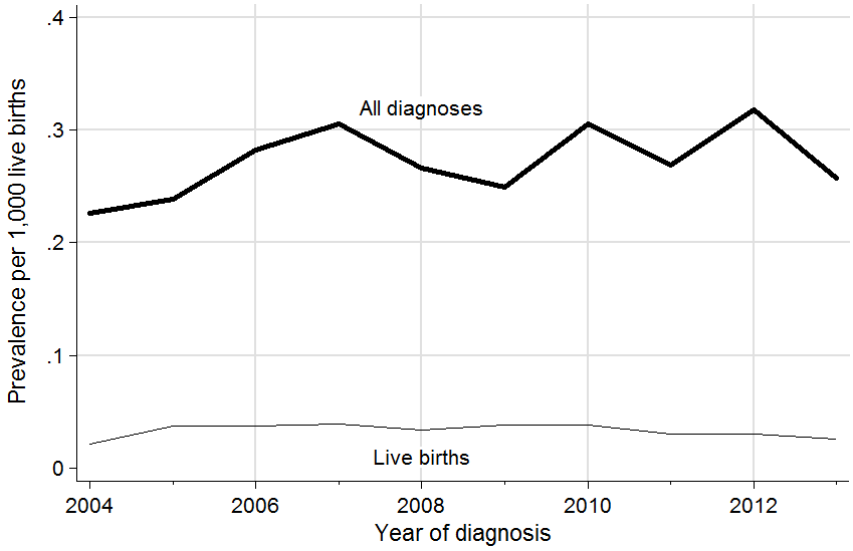
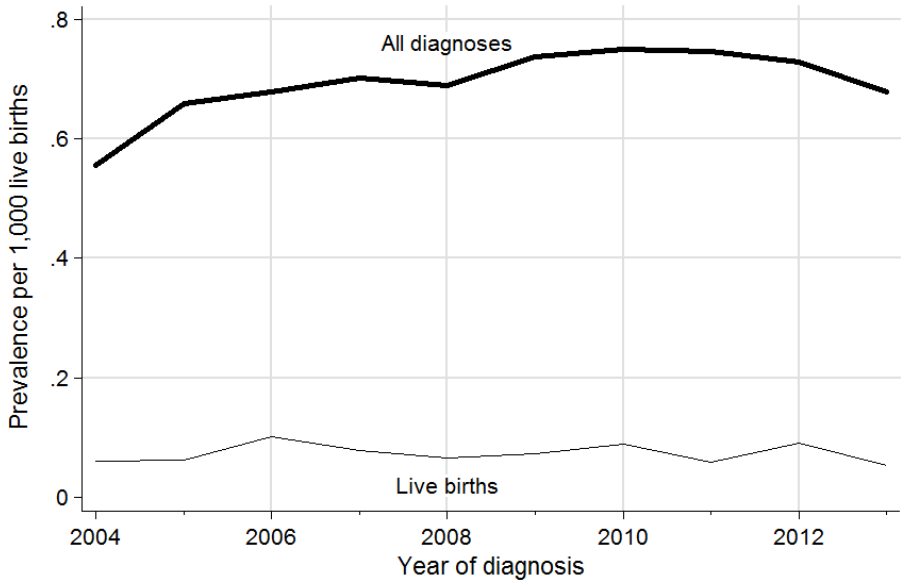


Figure 5: Prevalence of Edwards syndrome diagnoses and live births per thousand live births in England and Wales according to year of diagnosis*



* 2013 data are provisional due to late reporting of cases.

Appendix A

Data Completeness

The following table shows the completeness of the different data items for the years 1989 to 2010, 2011, 2012 and 2013. We are still following up the missing data from 2011 onwards. The data from 1989 to 2010 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 2013*

Data Item	Percentage complete			
	1989-2010	2011	2012	2013
Reason for referral for diagnosis	99	97	98	97
Type of tissue karyotyped	98	97	97	95
Sex of fetus (some DNA based diagnoses such as FISH and q-PCR do not include sex chromosome analysis)	98	95	94	91
Maternal age	95	95	93	91
Gestational age at sample for prenatal diagnosis	97	95	94	90
Outcome of pregnancy if prenatal diagnosis	94	92	90	85
Post Codes (some information)	94	95	94	95
Maternal NHS number (requested from 2005)	**69	83	82	81
Infants NHS number (requested from 2005)	**73	88	87	84

* 2013 data are provisional due to late reporting of cases.

**Data for 2005-2010

Appendix B: Form in 2013

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 |__|__|__|__|__|__|__|__|__|__|

D D M M Y Y D D M M Y Y

LMP |__|__|__|__|__|__| EDD |__|__|__|__|__|__|

Method of karyotyping Result

Microarray |__| .....
qf - PCR |__| .....
FISH |__| .....
MLPA |__| .....
Conventional |__| .....

D D M M Y Y

Date sample taken |__|__|__|__|__|__| gest |__|__| wks

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

Confirmation of prenatal diagnosis Yes |__| No |__|

specimen ID |__|__|__|__|__|__|__|__|__|

SCREENING TESTS

NHS |__| or Private |__|

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

1st trimester

NT alone |__| Serum alone |__| Combined |__|

NT .....mm Other U/S findings : .....

2nd trimester

Triple |__| Quad |__|

Integrated |__| Serum Integrated |__|

Please specify any other screening test performed:

.....

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. |__|__|__|__|__|__|__|__|__|__|

D D M M Y Y age

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

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

OUTCOME

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

D D M M Y Y

Date of outcome/ termination/ birth |__|__|__|__|__|__|

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 E

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

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

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

Appendix C: Selected NDSCR Publications

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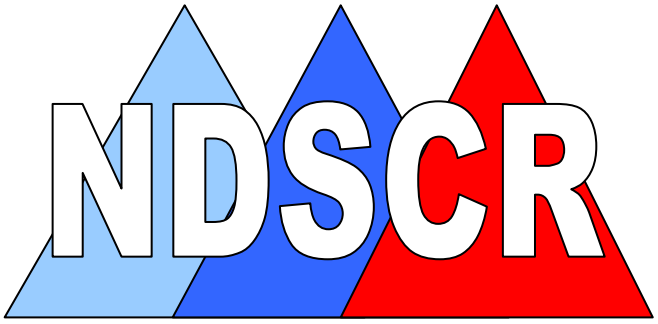

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