

**The National Down Syndrome Cytogenetic Register
for England and Wales:
2010 Annual Report**

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Foreword

This 2010 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 2010, and Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) from 2004 to 2010.

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 2010 there were 1,868 diagnoses of Down syndrome, 64% of which were made prenatally.
- In 2010 there were an estimated 715 Down syndrome live births, a live birth rate of 1.0 per 1,000 live births.
- In 2010 there were 213 diagnoses of Patau and 514 diagnoses of Edwards syndrome, of which an estimated 21 and 56 respectively were live births.
- The percentage of prenatal diagnoses with missing outcomes is 8% over all years, with only 2009 and 2010 above 10%.
- The type of screening that a woman received in 2009 was associated with her age. Older women were more likely to have received a prenatal diagnosis due to a first trimester screening test, were more likely to have a CVS compared to an amniocentesis and consequently received their diagnosis at younger gestational ages.
- Amongst women receiving prenatal diagnoses a greater proportion had 1st trimester screening in 2010 compared to 2009.
- There were regional differences in the type of screening that women received in 2010.
- The NDSCR is approved to use Section 251 of the NHS Act 2006 and has ethics approval from Trent MREC.
- Data collection for the NDSCR is funded by the Healthcare Quality Improvement Partnership (HQIP) until March 2012.

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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. HQIP (Healthcare Quality Improvement Partnership) is funding the NDSCR until March 2012. Further funding has not yet been identified. 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 2010 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 91% of affected pregnancies are terminated and 9% 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 the National Statistics Congenital Anomaly System and 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 2007 combined, and separately for 2008, 2009 and 2010. 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 National Information Governance Board for Health and Social Care (NIGB) 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. 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. 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.

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 special studies

In-house studies

- Are twin pregnancies more likely to be affected with Down syndrome?
- Are mosaic trisomies less likely to be detected by prenatal screening?
- What are the prevalences of cytogenetic variants of Down, Patau and Edwards syndromes (for example translocations)?

Collaborative studies

- Children with Down's Syndrome Study (St James' University Hospital in Leeds and the Epidemiology & Genetics Unit at the University of York).
- We are investigating whether the births in the Down syndrome register can be identified on the National Audiological Database to ascertain if they were automatically recalled for hearing tests at nine months, as is the current recommendation.
- Data on all amniocentesis and chorionic villus sampling procedures on all women in England and Wales for 2008 have been obtained from the majority of 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.

The Data in the NDSCR

Down syndrome cases diagnosed in 2010

Outcomes of Down syndrome cases

In 2010, 1,868 Down syndrome diagnoses were made, 1,188 (64%) prenatally and 680 (36%) postnatally (Table 1). The outcome of 167 of the prenatal diagnoses is unknown. Assuming that the proportion terminated remains as before 2010, the likely number of Down syndrome live births in England and Wales in 2010 would have been 715 (54 + 651+ 6% of 167), a prevalence of 1.0 per 1,000 live births occurring in England and Wales in 2010.

Table 1: Down syndrome cases diagnosed in England and Wales in 2010* according to time of diagnosis and outcome

| | | Number | % |
|-----------|------------------------------|--------|-------|
| Prenatal | Termination of pregnancy | 942 | 50.4 |
| | Live Birth | 54 | 2.9 |
| | Still Birth / Miscarriage | 25 | 1.3 |
| | Unknown outcome [†] | 167 | 8.9 |
| | | 1,188 | 63.6 |
| Postnatal | Live Birth | 651 | 34.9 |
| | Still Birth / Miscarriage | 29 | 1.6 |
| | | 680 | 36.4 |
| Total | | 1,868 | 100.0 |

* 2010 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. Twenty-two 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 2010*

| | Stage at diagnosis | | | |
|--------------------------|--------------------|-------|-----------|-------|
| | Prenatal | | Postnatal | |
| | Number | % | Number | % |
| Screened | 1,092 | 91.9 | 242 | 35.6 |
| No indication | .. | .. | 87 | 12.8 |
| Declined further testing | .. | .. | 142 | 20.9 |
| Unknown | .. | .. | 13 | 1.9 |
| Declined screening | 41 | 3.5 | 147 | 21.6 |
| No information | 55 | 4.6 | 291 | 42.8 |
| Total | 1,188 | 100.0 | 680 | 100.0 |

* 2010 data are provisional.

Indication for prenatal diagnosis according to maternal age

Table 3 shows the indication for prenatal diagnosis separately for younger and older women. The integrated test, (serum and NT measured in first trimester, and serum measured in the second trimester) is classified as a '2nd trimester' screening test because the final serum measurement is made in the 2nd trimester. 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.

A 1st trimester test was the most likely indication in all women. A greater percentage of younger than older women gave an ultrasound examination (usually the anomaly scan) as the indication. Nine 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 2010* according to maternal age

| Indication for prenatal diagnosis | Maternal Age | | | |
|-------------------------------------|--------------|-------|------------|-------|
| | < 35 years | | ≥ 35 years | |
| | Number | % | Number | % |
| 1 st Trimester screening | 202 | 57.5 | 562 | 68.5 |
| 2 nd Trimester screening | 111 | 31.6 | 205 | 25.0 |
| Ultrasound | 34 | 9.7 | 32 | 3.9 |
| Age | - | - | 14 | 1.7 |
| Other reasons / No information | 4 | 1.1 | 7 | 0.9 |
| Total | 351 | 100.0 | 820 | 100.0 |

* 2010 data are provisional; 17 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 older women (62%) having a CVS than younger women (50%), and a smaller percentage of older women having an amniocentesis (36%) than younger women (46%). The tissue was either unspecified or not from an amniocentesis or CVS in 4% of younger women and 3% in older women.

For all women, the median time from CVS or amniocentesis to termination of pregnancy was eight days. Ninety-one 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. Fifty-one percent of terminations in older mothers took place before 15 weeks gestation, compared to only 41% in younger mothers. Five percent of terminations in older mothers took place after 20 weeks gestation, compared to 12% in younger mothers.

Table 4: Gestation at termination following prenatal diagnosis of Down Syndrome in 2010* according to maternal age

| Gestation at termination (following prenatal diagnosis) | Maternal Age | | | |
|--|--------------|-------|------------|-------|
| | < 35 years | | ≥ 35 years | |
| | Number | % | Number | % |
| <15 weeks | 115 | 40.8 | 327 | 50.7 |
| 15 to 20 weeks | 132 | 46.8 | 283 | 43.9 |
| ≥21 weeks | 35 | 12.4 | 35 | 5.4 |
| Total | 282 | 100.0 | 645 | 100.0 |

* 2010 data are provisional; two cases had no maternal age. 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 mother at observed or expected date of delivery was 36.0 (95% CI: 35.7 - 36.3) years. The mean age for women with a prenatal diagnosis was 36.7 (95% CI: 36.4 - 37.1) compared to 34.3 (95% CI: 33.8 – 34.9) for those with a postnatal diagnosis. Overall 65% (1115/1722) of the women of known age were 35 or older (Table 5).

Table 5: Down syndrome cases diagnosed in 2010* according to maternal age at observed or expected date of delivery

| Maternal age (years) | Number | % |
|----------------------|--------|-------|
| < 20 | 29 | 1.6 |
| 20-24 | 95 | 5.1 |
| 25-29 | 162 | 8.7 |
| 30-34 | 321 | 17.2 |
| 35-39 | 623 | 33.4 |
| 40-44 | 456 | 24.4 |
| ≥ 45 | 36 | 1.9 |
| missing | 146 | 7.8 |
| Total | 1,868 | 100.0 |

*2010 data are provisional.

Patau and Edwards syndrome cases diagnosed in 2010

Outcomes of Patau and Edwards syndrome cases

In 2009, 90% of Patau and 91% of Edwards syndrome diagnoses were made prenatally. A large proportion of births were still births, due to the severity of the syndromes. The outcome of 21 Patau and 65 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 21 and 56 respectively.

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

Table 6a: Patau syndrome cases in 2010* according to outcome

| | | Number | % |
|-----------|------------------------------|--------|-------|
| Prenatal | Termination of pregnancy | 151 | 70.9 |
| | Live Birth | 3 | 1.4 |
| | Still Birth / Miscarriage | 16 | 7.5 |
| | Unknown outcome [†] | 21 | 9.9 |
| Postnatal | Live Birth | 17 | 8.0 |
| | Still Birth / Miscarriage | 5 | 2.3 |
| Total | | 213 | 100.0 |

Table 6b: Edwards syndrome cases in 2010* according to time of diagnosis and outcome

| | | Number | % |
|-----------|------------------------------|--------|-------|
| Prenatal | Termination of pregnancy | 344 | 66.9 |
| | Live Birth | 13 | 2.5 |
| | Still Birth / Miscarriage | 44 | 8.6 |
| | Unknown outcome [†] | 65 | 12.6 |
| Postnatal | Live Birth | 41 | 8.0 |
| | Still Birth / Miscarriage | 7 | 1.4 |
| Total | | 514 | 100.0 |

* 2010 data are provisional; [†] Approximately 4% of Patau and 3% of Edwards syndrome with unknown outcomes are likely to result in a live birth.

Indication for prenatal diagnosis

The two main indications for a prenatal diagnosis of Patau and Edwards syndromes were 1st trimester tests (for Down syndrome) and late ultrasounds (Table 7). Approximately 14% of prenatal diagnoses of Patau syndrome in younger women were made at 21 weeks gestation or later, compared to 13% in older women.

Approximately 20% of prenatal diagnoses of Edwards syndrome in younger women were made at 21 weeks gestation or later, compared to 12% in older women.

Table 7: Indication for prenatal diagnosis of Patau and Edwards syndrome cases in 2010*

| Indication for prenatal diagnosis | Patau syndrome | | Edwards syndrome | |
|-------------------------------------|----------------|--------------|------------------|--------------|
| | Number | % | Number | % |
| 1 st Trimester screening | 106 | 55.5 | 310 | 66.5 |
| 2 nd Trimester screening | 34 | 17.8 | 54 | 11.6 |
| Ultrasound | 44 | 23.0 | 87 | 19.5 |
| Age and other reasons | 2 | 1.0 | 4 | 0.9 |
| No information | 5 | 2.6 | 11 | 2.4 |
| Total | 191 | 100.0 | 466 | 100.0 |

* 2010 data are provisional.

Maternal age at observed or expected date of delivery

The mean age of the mother at expected or observed date of delivery was 33.6 years for Patau syndrome and 36.7 years for Edwards syndrome, compared to 36.0 years for Down syndrome. For Patau syndrome 49% of women with known maternal age were aged 35 or over, and for Edwards syndrome 68% of women with known maternal age were aged 35 or over (Table 8).

Table 8: Patau and Edwards syndrome cases diagnosed in 2010* according to maternal age at observed or expected date of delivery

| Maternal age (years) | Patau syndrome | | Edwards syndrome | |
|----------------------|----------------|--------------|------------------|--------------|
| | Number | % | Number | % |
| < 25 | 22 | 10.3 | 35 | 6.8 |
| 25-29 | 36 | 16.9 | 53 | 10.3 |
| 30-34 | 47 | 22.1 | 71 | 13.8 |
| 35-39 | 60 | 28.2 | 164 | 31.9 |
| ≥ 40 | 39 | 18.3 | 180 | 35.0 |
| missing | 9 | 4.2 | 11 | 2.1 |
| Total | 213 | 100.0 | 514 | 100.0 |

* 2010 data are provisional.

Regional differences in cases diagnosed in 2010

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 mothers 35 years of age or over tend to have lower proportions of prenatal diagnoses. The highest proportions of prenatal diagnoses occur in London and the South East of England.

Table 9: All live births and all Down syndrome diagnoses according to region of maternal residence in 2010*

| Region | All Live Births † | | Down syndrome diagnoses | |
|------------------------|-------------------|----------------------------------|-------------------------|--|
| | Number (1,000) | Percentage of mothers ≥35 (%) | Number | Percentage prenatally diagnosed (%) |
| North East | 31 | 15.0 | 72 | 55.6 |
| North West | 89 | 17.0 | 205 | 50.2 |
| Yorkshire & Humberside | 67 | 15.9 | 157 | 58.0 |
| East Midlands | 55 | 17.8 | 112 | 58.0 |
| West Midlands | 72 | 16.8 | 180 | 57.8 |
| East England | 73 | 20.5 | 188 | 63.3 |
| London | 133 | 24.9 | 407 | 74.2 |
| South East | 106 | 23.3 | 277 | 73.6 |
| South West | 60 | 20.8 | 185 | 62.2 |
| Wales | 36 | 16.0 | 75 | 49.3 |
| Total | 723 | 19.9 | 1,868 | 63.6 |

* 2010 data are provisional. Ten cases have unknown region † National data are for calendar year 2010.

Indication for prenatal diagnosis according to maternal region of residence

Table 10 shows the indication for a prenatal diagnosis according to region of residence. London and the South East had the highest proportions of women having a diagnostic test due to a 1st trimester screening test result, whereas the Yorkshire & Humberside had the highest proportion of women having a diagnostic test due to an ultrasound. 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. Thirteen cases with missing gestation at termination have been excluded. However, the number of terminations in some regions is small. Women in London and the South East are the most likely to have a

termination before 15 weeks gestation, and women in the North East, North West and Wales are the least likely.

Table 10: Indication for prenatal diagnosis of Down syndrome according to region of maternal residence in 2010*

| Region | Number of prenatal diagnoses | Indication for prenatal diagnosis (%) | | | | | Total |
|------------------------|------------------------------|---------------------------------------|----------------------------------|------------|--------------|----------------|-------|
| | | 1 st trimester screen | 2 nd trimester screen | Ultrasound | Maternal Age | Other/ Missing | |
| North East | 40 | 37.5 | 57.5 | 5.0 | 0.0 | 0.0 | 100.0 |
| North West | 103 | 39.8 | 44.7 | 8.7 | 2.9 | 3.9 | 100.0 |
| Yorkshire & Humberside | 91 | 51.7 | 33.0 | 14.3 | 1.1 | 0.0 | 100.0 |
| East Midlands | 65 | 58.5 | 30.8 | 4.6 | 0.0 | 6.2 | 100.0 |
| West Midlands | 104 | 45.2 | 43.3 | 7.7 | 1.9 | 1.9 | 100.0 |
| East England | 119 | 74.8 | 20.2 | 4.2 | 0.8 | 0.0 | 100.0 |
| London | 302 | 77.8 | 17.6 | 4.0 | 0.3 | 0.3 | 100.0 |
| South East | 204 | 83.8 | 11.8 | 3.4 | 0.0 | 1.0 | 100.0 |
| South West | 115 | 62.6 | 28.7 | 4.4 | 2.6 | 1.7 | 100.0 |
| Wales | 37 | 21.6 | 59.5 | 8.1 | 8.1 | 2.7 | 100.0 |
| Total | 1,180 | 64.6 | 27.3 | 5.6 | 1.2 | 1.4 | 100.0 |

* 2010 data are provisional; ten cases have unknown region.

Table 11: Gestation at termination after prenatal diagnosis of Down syndrome according to region of maternal residence in 2010*

| Region | Number of terminations | Gestation at termination (%) | | | |
|------------------------|------------------------|------------------------------|----------------|-----------|-------|
| | | <15 weeks | 15 to 20 weeks | 21+ weeks | Total |
| North East | 36 | 47.2 | 47.2 | 5.6 | 100.0 |
| North West | 73 | 31.9 | 59.7 | 8.3 | 100.0 |
| Yorkshire & Humberside | 68 | 47.8 | 44.8 | 7.5 | 100.0 |
| East Midlands | 51 | 34.0 | 56.0 | 10.0 | 100.0 |
| West Midlands | 94 | 42.4 | 47.1 | 10.6 | 100.0 |
| East England | 88 | 45.5 | 44.3 | 10.2 | 100.0 |
| London | 223 | 56.3 | 36.9 | 6.8 | 100.0 |
| South East | 175 | 58.9 | 36.6 | 4.6 | 100.0 |
| South West | 100 | 44.0 | 49.0 | 7.0 | 100.0 |
| Wales | 32 | 18.8 | 68.8 | 12.5 | 100.0 |
| Total | 942 | 47.8 | 44.7 | 17.6 | 100.0 |

* 2010 data are provisional; ten cases have unknown region; 13 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 2010*

| Region | Patau Syndrome (%) | Edwards Syndrome (%) |
|------------------------|--------------------|----------------------|
| | Prenatal | Prenatal |
| North East | 83.3 | 76.5 |
| North West | 100.0 | 85.4 |
| Yorkshire & Humberside | 86.4 | 93.8 |
| East Midlands | 94.1 | 92.3 |
| West Midlands | 94.7 | 76.9 |
| East England | 95.0 | 90.0 |
| London | 77.8 | 94.9 |
| South East | 92.3 | 95.4 |
| South West | 100.0 | 85.7 |
| Wales | 100.0 | 92.3 |
| Total | 90.0 | 90.6 |

*2010 data are provisional. Three cases of Patau syndrome and four 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 2010. However, some of these differences may arise due to the different maternal age distributions (Table 9). Many screening tests (for fixed risk cut-offs) have higher detection rates for older women and these women may also be more likely to present in time to have first trimester screening than younger women. 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 1989-2010

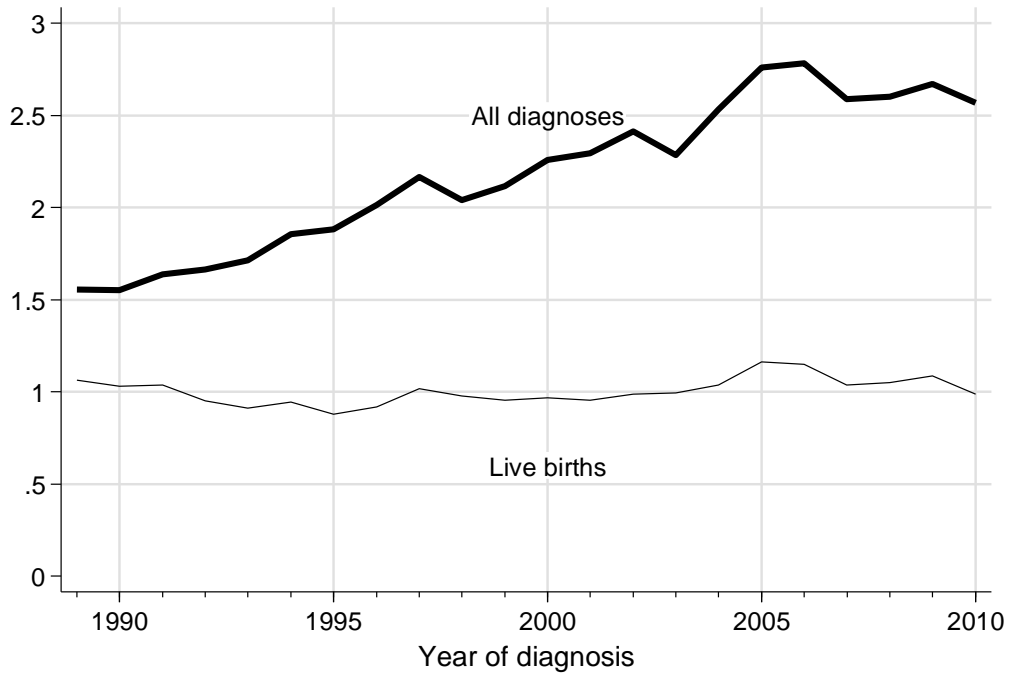
Since the register started collecting data on 1st January 1989 the annual number and prevalence of Down syndrome diagnoses has increased (Table 13 and Figure 1), firstly due to the considerable increases in maternal age, the major known risk factor, and secondly due to the increase in the numbers of 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 around 91% of women who receive a prenatal diagnosis decide to terminate the pregnancy (Table 13).

Table 13: Down syndrome diagnoses and outcomes in England and Wales from 1989 to 2010*

| Calendar year of diagnosis | Numbers of Diagnoses | | | | | Outcome of prenatal diagnoses ‡ (%) | | |
|----------------------------------|----------------------|--------------|--------------------------|-----------|---------------------|--|-----------------------------|----------------|
| | All | Prenatal (%) | Live births [†] | | Unknown outcomes | Termi- nation | Miscarriage /still birth | Live births |
| | | | Reported | Estimated | | | | |
| 1989 | 1,069 | 321 (30) | 750 | 750 | 8 | 93.6 | 2.9 | 3.5 |
| 1990 | 1,095 | 374 (34) | 738 | 739 | 12 | 90.6 | 3.3 | 6.1 |
| 1991 | 1,146 | 430 (38) | 736 | 737 | 9 | 87.7 | 5.2 | 7.1 |
| 1992 | 1,148 | 499 (43) | 662 | 663 | 18 | 91.7 | 2.9 | 5.4 |
| 1993 | 1,155 | 558 (48) | 621 | 621 | 8 | 92.2 | 2.5 | 5.3 |
| 1994 | 1,234 | 613 (50) | 638 | 640 | 25 | 92.2 | 2.9 | 4.9 |
| 1995 | 1,220 | 660 (54) | 579 | 581 | 25 | 91.0 | 3.3 | 5.7 |
| 1996 | 1,308 | 721 (55) | 606 | 607 | 13 | 92.4 | 2.4 | 5.2 |
| 1997 | 1,392 | 739 (53) | 666 | 667 | 19 | 92.2 | 2.8 | 5.0 |
| 1998 | 1,298 | 704 (54) | 631 | 633 | 26 | 91.2 | 2.2 | 6.6 |
| 1999 | 1,316 | 728 (55) | 602 | 604 | 29 | 92.7 | 2.0 | 5.3 |
| 2000 | 1,365 | 807 (59) | 592 | 596 | 63 | 91.9 | 0.9 | 7.1 |
| 2001 | 1,364 | 815 (60) | 571 | 576 | 82 | 92.4 | 2.2 | 5.5 |
| 2002 | 1,439 | 885 (62) | 585 | 591 | 104 | 90.8 | 3.1 | 6.2 |
| 2003 | 1,419 | 835 (59) | 616 | 620 | 72 | 90.9 | 2.5 | 6.7 |
| 2004 | 1,619 | 988 (61) | 659 | 664 | 83 | 89.9 | 3.3 | 6.7 |
| 2005 | 1,766 | 1,055 (60) | 733 | 741 | 141 | 90.8 | 3.5 | 5.7 |
| 2006 | 1,844 | 1,116 (61) | 751 | 760 | 142 | 91.0 | 3.6 | 5.4 |
| 2007 | 1,787 | 1,110 (62) | 706 | 713 | 119 | 91.5 | 2.7 | 5.8 |
| 2008 | 1,845 | 1,138 (62) | 736 | 742 | 100 | 90.2 | 2.8 | 7.0 |
| 2009 | 1,896 | 1,181 (62) | 759 | 769 | 165 | 89.0 | 4.0 | 6.9 |
| 2010 | 1,868 | 1,188 (64) | 705 | 715 | 167 | 92.1 | 2.5 | 5.3 |
| Total | 31,593 | 17,465 (55) | 14,642 | 14,729 | 1,428 | 91.2 | 2.9 | 5.9 |

* 2010 data are provisional. † Estimated live births includes 6% of unknown outcomes. ‡ Calculated as a percentage of all known outcomes.

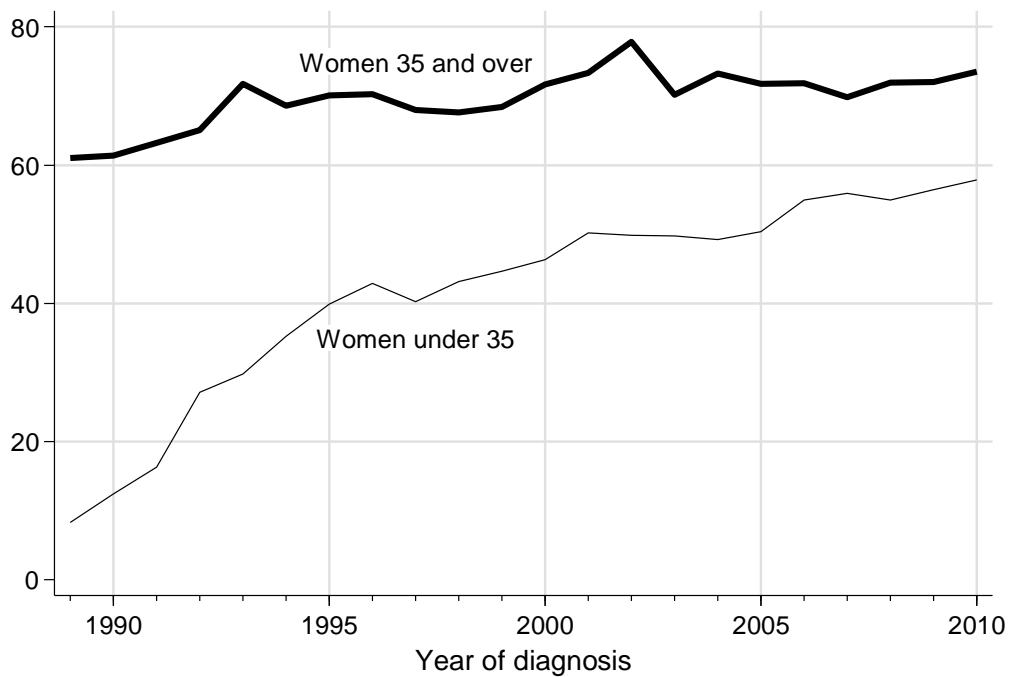
Figure 1: Prevalence of Down syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2010 data are provisional.

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.

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

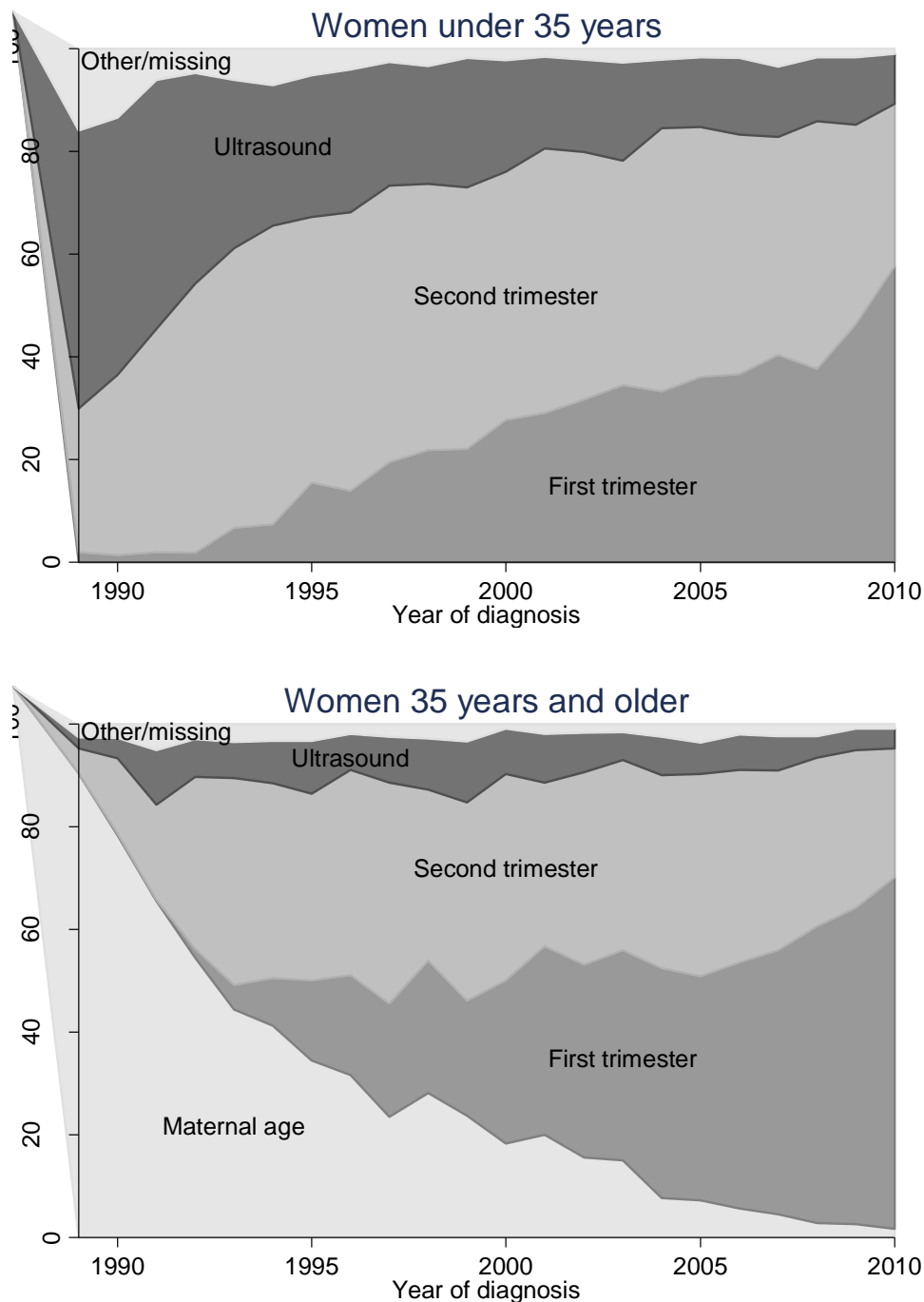


* 2010 data are provisional.

Indication for prenatal diagnosis 1989-2010

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 2010 there was a much greater proportion of younger women having first trimester screening.

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



* 2010 data are provisional

Table 14: Indication for Down syndrome prenatal diagnosis according to maternal age from 1989 to 2010*

| Calendar Year of diagnosis | Women under 35 (%) | | | | Women 35+ (%) | | | | |
|----------------------------------|------------------------------|------------------------------|-----------------|-------------------|---------------|------------------------------|------------------------------|-----------------|-------------------|
| | 1 st Trimester | 2 nd Trimester | Ultra- sound | Other/ Missing | Age alone | 1 st Trimester | 2 nd Trimester | Ultra- sound | Other/ Missing |
| 1989 | 2.0 | 28.0 | 54.0 | 16.0 | 90.4 | 0.0 | 4.8 | 2.2 | 2.6 |
| 1990 | 1.4 | 35.1 | 50.0 | 13.5 | 78.3 | 0.3 | 14.7 | 4.0 | 2.7 |
| 1991 | 2.0 | 43.4 | 48.5 | 6.1 | 65.5 | 0.3 | 18.5 | 10.6 | 5.2 |
| 1992 | 1.8 | 52.4 | 41.0 | 4.8 | 54.4 | 1.8 | 33.5 | 7.3 | 3.0 |
| 1993 | 6.7 | 54.4 | 32.8 | 6.1 | 44.4 | 4.8 | 40.2 | 7.1 | 3.4 |
| 1994 | 7.4 | 58.1 | 27.4 | 7.0 | 41.2 | 9.3 | 37.9 | 8.3 | 3.3 |
| 1995 | 15.5 | 51.7 | 27.6 | 5.2 | 34.5 | 15.5 | 36.4 | 10.3 | 3.3 |
| 1996 | 13.9 | 54.2 | 27.8 | 4.0 | 31.6 | 19.5 | 39.9 | 7.0 | 2.0 |
| 1997 | 19.5 | 53.8 | 24.1 | 2.7 | 23.5 | 22.0 | 43.1 | 8.9 | 2.5 |
| 1998 | 21.8 | 51.8 | 23.0 | 3.5 | 28.1 | 25.8 | 33.3 | 9.9 | 2.9 |
| 1999 | 22.0 | 51.0 | 25.1 | 1.9 | 23.7 | 22.4 | 38.6 | 11.9 | 3.5 |
| 2000 | 27.7 | 48.3 | 21.7 | 2.2 | 18.3 | 31.7 | 40.3 | 8.8 | 0.9 |
| 2001 | 29.1 | 51.4 | 17.9 | 1.6 | 20.0 | 36.7 | 31.8 | 9.5 | 2.0 |
| 2002 | 31.6 | 48.3 | 17.9 | 2.3 | 15.6 | 37.5 | 37.5 | 7.7 | 1.8 |
| 2003 | 34.5 | 43.7 | 19.1 | 2.8 | 15.0 | 40.9 | 37.1 | 5.4 | 1.6 |
| 2004 | 33.2 | 51.3 | 13.3 | 2.2 | 7.7 | 44.7 | 37.6 | 7.5 | 2.5 |
| 2005 | 36.1 | 48.6 | 13.6 | 1.7 | 7.3 | 43.6 | 39.3 | 6.2 | 3.8 |
| 2006 | 36.6 | 46.7 | 14.9 | 1.8 | 5.7 | 47.9 | 37.4 | 6.9 | 2.1 |
| 2007 | 40.4 | 42.4 | 13.7 | 3.5 | 4.6 | 51.3 | 35.0 | 6.7 | 2.4 |
| 2008 | 37.6 | 48.3 | 12.4 | 1.7 | 2.9 | 57.7 | 32.8 | 4.2 | 2.3 |
| 2009 | 46.3 | 38.9 | 13.1 | 1.7 | 2.6 | 61.6 | 30.7 | 4.2 | 1.0 |
| 2010 | 57.6 | 31.6 | 9.7 | 1.1 | 1.7 | 68.5 | 25.0 | 3.9 | 0.9 |

* 2010 data are provisional.

Gestational age at termination following prenatal diagnosis 1989-2010

The shift towards earlier screening has increased the percentage of prenatal diagnoses with terminations before 15 weeks gestation, for younger and older women (Table 15). The percentage of terminations taking place at 21 weeks gestation or later has decreased for younger and older women but it remains higher for younger women.

Maternal age at observed or expected date of delivery 1989-2010

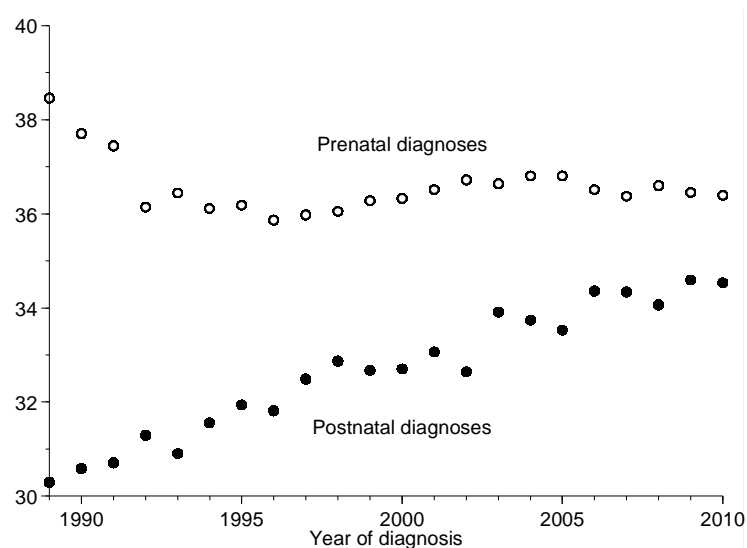
At the start of the register, the main prenatal screening test available was a mother's age and so the majority of prenatal diagnoses occurred in older women. As more screening tests became more available and detection rates for younger women improved, more younger women received prenatal diagnoses. This is reflected in the average maternal age (Figure 4). 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 2010*

| Calendar 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 | 2.4 | 45.2 | 52.4 | 17.6 | 63.7 | 18.8 |
| 1990 | 8.3 | 45.0 | 46.7 | 12.9 | 64.8 | 22.4 |
| 1991 | 1.3 | 52.0 | 46.7 | 14.0 | 66.4 | 19.6 |
| 1992 | 2.3 | 61.7 | 36.1 | 8.9 | 69.9 | 21.3 |
| 1993 | 10.9 | 42.2 | 46.9 | 13.5 | 61.8 | 24.7 |
| 1994 | 6.3 | 54.6 | 39.2 | 17.8 | 65.6 | 16.6 |
| 1995 | 17.9 | 49.0 | 33.2 | 21.0 | 62.8 | 16.1 |
| 1996 | 14.2 | 52.1 | 33.8 | 24.5 | 61.9 | 13.6 |
| 1997 | 19.2 | 53.9 | 26.9 | 27.5 | 58.9 | 13.6 |
| 1998 | 23.2 | 50.0 | 26.9 | 28.1 | 59.0 | 13.0 |
| 1999 | 21.5 | 52.1 | 26.5 | 29.1 | 58.1 | 12.8 |
| 2000 | 27.3 | 48.2 | 24.5 | 34.6 | 54.2 | 11.2 |
| 2001 | 28.0 | 48.3 | 23.7 | 41.9 | 47.5 | 10.6 |
| 2002 | 31.8 | 46.8 | 21.4 | 41.5 | 50.8 | 7.7 |
| 2003 | 31.4 | 47.1 | 21.4 | 43.8 | 49.6 | 6.7 |
| 2004 | 31.1 | 48.9 | 20.0 | 45.0 | 46.5 | 8.6 |
| 2005 | 33.8 | 47.6 | 18.6 | 44.2 | 46.8 | 9.1 |
| 2006 | 33.6 | 45.4 | 21.0 | 42.4 | 48.4 | 9.2 |
| 2007 | 40.1 | 42.4 | 17.6 | 50.7 | 41.5 | 7.8 |
| 2008 | 33.3 | 50.2 | 16.5 | 54.7 | 38.6 | 6.7 |
| 2009 | 36.7 | 46.2 | 17.1 | 49.1 | 44.5 | 6.4 |
| 2010 | 40.8 | 46.8 | 12.4 | 50.7 | 43.9 | 5.4 |

* 2010 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 4: Mean maternal age according to year of diagnosis* and stage at diagnosis



* 2010 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) due to increases in maternal age, the major known risk factor, and due to the increase in the number of pregnancies diagnosed prenatally (due to screening for Down syndrome), many of which were non-viable and would have miscarried and therefore remained undiagnosed in the absence of prenatal screening. The number of diagnoses of Patau syndrome in 2009 is lower than in the previous three years, the reason for which is unclear.

Table 16: Patau syndrome diagnoses and outcomes in England and Wales from 2004 to 2010*

| Year of diagnosis | Patau syndrome: Numbers of Diagnoses | | | | |
|-------------------|--------------------------------------|--------------|-------------|------------------------|------------------|
| | All | Prenatal (%) | Live births | | Unknown outcomes |
| | | | Reported | Estimated [†] | |
| 2004 | 152 | 139 (91.4) | 15 | 15 | 8 |
| 2005 | 159 | 138 (86.8) | 25 | 25 | 11 |
| 2006 | 193 | 175 (90.7) | 24 | 25 | 14 |
| 2007 | 205 | 184 (89.8) | 24 | 24 | 8 |
| 2008 | 189 | 170 (89.9) | 25 | 25 | 11 |
| 2009 | 165 | 144 (87.3) | 19 | 20 | 17 |
| 2010 | 213 | 191 (89.7) | 20 | 21 | 20 |
| Total | 1,276 | 1,141 (89.4) | 152 | 155 | 89 |

* 2010 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 2010*

| Year of diagnosis | Edwards syndrome: Numbers of Diagnoses | | | | |
|-------------------|--|--------------|-------------|------------------------|------------------|
| | All | Prenatal (%) | Live births | | Unknown outcomes |
| | | | Reported | Estimated [†] | |
| 2004 | 369 | 332 (90.0) | 40 | 41 | 47 |
| 2005 | 434 | 389 (89.6) | 41 | 43 | 54 |
| 2006 | 455 | 393 (86.4) | 65 | 66 | 47 |
| 2007 | 483 | 442 (91.5) | 52 | 53 | 41 |
| 2008 | 493 | 458 (92.9) | 40 | 41 | 36 |
| 2009 | 506 | 460 (90.1) | 42 | 44 | 70 |
| 2010 | 514 | 466 (90.7) | 54 | 56 | 64 |
| Total | 3,254 | 2,940 (90.7) | 334 | 344 | 359 |

* 2010 data are provisional. [†] Estimated live births include 3% of unknown outcomes.

Appendix A

Data Completeness

The following Table shows the completeness of the different data items for the years 1989 to 2007, 2008, 2009 and 2010. We are still following up the missing data from 2008 onwards. The data from 1989 to 2007 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 2010*

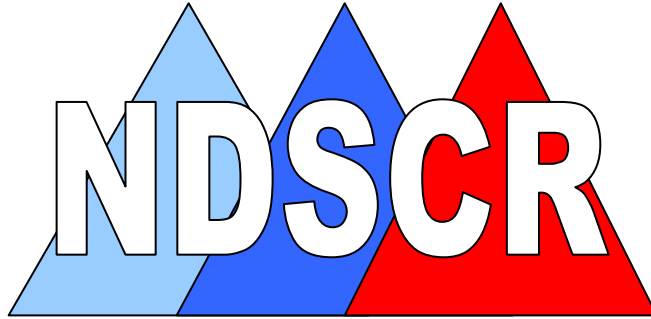
| Data Item | 1989-2007 | Percentage complete | | |
|---|-----------|---------------------|------|------|
| | | 2008 | 2009 | 2010 |
| Reason for referral for diagnosis | 99 | 98 | 98 | 99 |
| Type of tissue karyotyped | 99 | 96 | 97 | 98 |
| Sex of fetus (some DNA based diagnoses such as FISH and q-PCR do not include sex chromosome analysis) | 100 | 100 | 99 | 92 |
| Maternal age | 95 | 94 | 93 | 94 |
| Gestational age at sample for prenatal diagnosis | 98 | 96 | 95 | 95 |
| Outcome of pregnancy if prenatal diagnosis | 93 | 91 | 86 | 86 |
| Post Codes (some information) | 93 | 96 | 95 | 96 |
| Maternal NHS number (requested from 2005) | N/A | 71 | 64 | 70 |

* 2010 data are provisional.

Appendix C: Selected NDSCR Publications

1. 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.
2. Savva GM, Morris JK. Ascertainment and accuracy of Down syndrome cases reported in congenital anomaly registers in England and Wales. *Arch Dis Child Fetal Neonatal Ed* 2009; **94**:F23-7.
3. Morris JK, Mutton DE, Alberman E. The proportions of Down's syndrome pregnancies detected prenatally in England and Wales from 1989 to 2004. *J Med Screen* 2006; **13**:163-5.
4. Crane B, Morris JK. Changes in maternal age in England and Wales – Implications for Down syndrome. *Down syndrome research and practice* 2006; **10**:41-43.
5. Savva GM, Morris JK, Mutton DE, Alberman E. Maternal age-specific fetal loss rates in Down syndrome pregnancies. *Prenat Diagn.* 2006; **26**:499-504.
6. 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.
7. 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.
8. Kovaleva NV, Mutton DE. Epidemiology of double aneuploidies involving chromosome 21 and the sex chromosomes. *Am J Med Genet* 2006; **134A (1)**:24-32.
9. 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.
10. Smith-Bindman R, Chu P, Bacchetti P, Waters JJ, Mutton D, Alberman E. Prenatal screening for Down syndrome in England and Wales and population-based birth outcomes. *Am J Obstet Gynecol* 2003; **189**:980-5.
11. 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.
12. Morris JK, Mutton DE, Alberman E. Revised estimates of the maternal age specific live birth prevalence of Down's syndrome. *J Med Screen* 2002; **9**:2-6
13. Vrijheid M, Dolk H et al. Chromosomal congenital anomalies and residence near hazardous waste landfill sites. *Lancet* 2002; **359**:320-3.
14. Smith-Bindman R, Waters J, Mutton D, Alberman E. Trends in the effectiveness and efficiency of prenatal Down syndrome (DS) screening in England and Wales, 1989-1999. *J Med Genet* 2001: Supplement 1 SP33.
15. Hook EB, Cross PK, Mutton DE. Female predominance (low sex ratio) in 47, +21 mosaics. *Am J Med Genet* 1999; **84**:316-319.
16. Morris JK, Wald NJ, Watt HC. Fetal loss in Down's syndrome pregnancies. *Prenat Diagn* 1999; **19**:142-145.
17. Morris JK, Alberman E, Mutton D. Is there evidence of clustering in Down syndrome? *Int J Epid* 1998; **27**:495-8.

18. Mutton D, Bunch K, Draper G, Alberman E. Children's cancer and Down syndrome. *J Med Genet* 1997; **34**:S65.
19. Huang T, Watts HC et al. Reliability of statistics on DS notifications. *J Med Screen* 1997; **4**:94-97.
20. Hook EB, Mutton DE, Ide R, Alberman ED, Bobrow M. The natural history of Down syndrome conceptuses diagnosed prenatally which are not electively terminated. *Am J Hum Genet* 1995; **57**:875-881.
21. Mutton DE, Alberman ED, Hook EB. Cytogenetic and epidemiological findings in Down syndrome: 1993. *J Med Genet* 1996; **33**:387-394.
22. Williamson P, Harris R, Church S, Fiddler M, Rhind J. Prenatal genetic services for Down's syndrome: access and provision. *Br J Obstet Gynaecol* 1996; **103**:676-83.
23. Alberman E, Mutton D, Ide R, Nicholson A, Bobrow M. Down's syndrome births and pregnancy terminations in 1989 to 1993: preliminary findings. *Br J Obstet Gynaecol* 1995; **102**:445-7.
24. Mutton DE, Ide R, Alberman E, Bobrow M. Analysis of National Register of Down's syndrome in England and Wales: trends in prenatal diagnosis. *BMJ* 1993; **306**:431-2.
25. Mutton DE, Alberman E, Ide R, Bobrow M. Results of first year (1989) of a national register of Down's syndrome in England and Wales. *BMJ* 1991; **303**:1295-7.



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