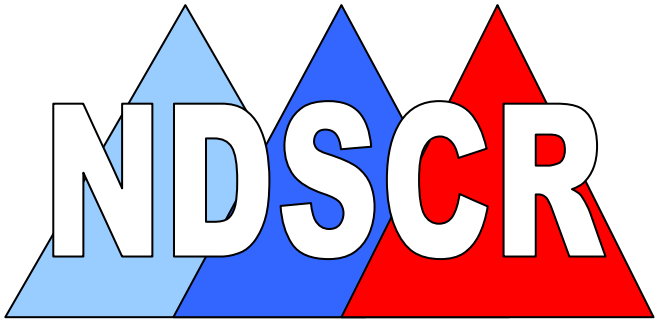


# The National Down Syndrome Cytogenetic Register

# 2007/8 Annual Report

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February 2009

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# Foreword

This 2007/8 annual report contains information about the NDSCR – who we are and what we do as well as detailed data on all reported cytogenetically diagnosed cases of Down syndrome from 1989/90 to 2007/8 and Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) from 2004/5 to 2007/8.

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.

Joan Morris – Director NDSCR
Eva Alberman
David Mutton
Haiyan Wu
Annabelle Stapleton
Beth de Souza
Khadeeja Wahid

# Executive Summary

- This report is based on financial years for the first time, due to a request by the National Fetal Anomaly Screening Programme.
- In 2007/8 there were 1843 diagnoses of Down syndrome, of which 60% were prenatally diagnosed.
- In 2007/8 there were an estimated 743 Down syndrome live births, a live birth rate of 1.2 per 1000.
- In 2007/8 there were 209 diagnoses of Patau and 488 diagnoses of Edwards syndrome of which an estimated 29 and 59 respectively were live births.
- The number of missing outcomes for the whole register is under 5%, with only 2007/8 above 10% (12%).
- The type of screening that a woman received in 2007/8 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.
- There were regional differences in the type of screening that women received in 2007/8.
- The NDSCR is approved to gain support under Section 60 of the Health and Social Care Act 2001 and has ethics approval from Trent MREC.
- Data collection by the NDSCR was funded by the National Fetal Anomaly Screening Programme until March 2009. The Department of Health is funding the NDSCR for only 1 year until March 2010.

**Suggested citation of this report:**
Morris JK, The National Down Syndrome Cytogenetic Register 2007/8 Annual Report. Barts and The London School of Medicine and Dentistry. Queen Mary University of London 2009.

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## 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. The register is funded by the National Fetal Anomaly Screening Programme until March 2009. The Department of Health is then funding the NDSCR for only 1 year until March 2010. 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 diagnoses of trisomies 18 (Edwards syndrome) and 13 (Patau syndrome);
- provide data on annual numbers of affected births to help those planning for their health, educational 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 2007 is shown in Appendix B). The form is self-copying and has 4 pages. The top copy is sent to the NDSCR by the laboratory, the 2$^{nd}$ (blue) and 3$^{rd}$ (green) are sent to the referring clinician and the 4$^{th}$ (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 3$^{rd}$ (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 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 as 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 we have on outcome show that after the prenatal diagnosis of Down syndrome 92% of affected pregnancies are terminated and 8% are continued, some miscarry naturally, some end as still births resulting in around 6% being 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 proportion of missing data on forms for the years up to 2004/5 combined and separately for 2005/6, 2006/7 and 2007/8. This is always highest in the most recent data where the clinicians have not yet been contacted. Requests for missing data are sent out regularly. The major problem is to ascertain the outcome of prenatally diagnosed pregnancies, particularly where the referral was from a centre other than that where 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 postcodes since the start of the register and the same is true for health authority definitions. 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 6 months has elapsed. We are developing a web site to enable the laboratories to complete the forms online in the future if they wish.

## 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 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 Patient Information Advisory Group (PIAG) 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.

## How the data are used

**Audit of Down Syndrome Screening**

- All local screening co-ordinators should receive the green copy of the NDSCR form to assist them in their audit requirements.

- 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).

**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 web site is regularly updated.

- Information is provided on request to journalists, charities and other interested parties.

**Recent special studies**

**In-house studies**

1) We are investigating the risk of a woman having a Down, Edwards or Patau syndrome pregnancy given that she has already had a pregnancy affected with Down, Edwards or Patau syndrome.

2) By combining data from the NDSCR and data from registries who are members of BINOCAR we are estimating the prevalence of trisomies 13 and 18 according to maternal age and gestational age.

**Collaborative studies**

1) We are collaborating with the Children with Down's Syndrome Study (St James' University Hospital in Leeds and the Epidemiology & Genetics Unit at the University of York).

**Future studies**

1) In 2006 we started collecting data on whether women had been offered screening and whether they had accepted or rejected the offer. When more data is available we will be reporting on the completeness and efficacy of screening for Down syndrome in England and Wales.

**Publications**

A list of publications based on, or using NDSCR data, are given in Appendix C.

## The NDSCR Steering Committee

A steering committee was established in 2004 to be an independent source for:

a) Monitoring the progress of the register towards its overall objectives;
b) Advising on the strategies for the use and development of the register;
c) Advising on the undertaking and conduct of new research projects;
d) Providing technical advice.

The membership is:

| | |
|---|---|
| Prof Joan Morris (chair) | NDSCR |
| Dr Jenny Kurinczuk | National Perinatal Epidemiology Unit. |
| Dr Karl Murphy | St Mary's Hospital, Imperial College Healthcare NHS Trust. |
| Ms Susannah Seyman | The Down's Syndrome Association. |
| Dr Jonathan Waters | NE London Regional Cytogenetics Laboratory. |

# The Data in the NDSCR

## Down syndrome cases diagnosed in 2007/8

### Outcomes of Down syndrome cases

1843 Down syndrome diagnoses were made in 2007/8, 1112 (60%) prenatally and 731 (40%) postnatally (Table 1). The outcome of 214 of the prenatal diagnoses is unknown. Assuming that the proportion terminated remains as before 2007/8, the likely number of Down syndrome live births in England and Wales in 2007/8 would have been 743 (43 + 687 + 6% of 214), a prevalence of 1.2 per 1000 live births occurring in England and Wales in 2007/8.

Table 1: Down syndrome cases diagnosed in England and Wales in 2007/8* by time of diagnosis and outcome

| | | Number | % |
|---|---|---|---|
| Prenatal | Termination of pregnancy | 833 | 45 |
| | Live Birth | 43 | 2 |
| | Still Birth / Miscarriage | 22 | 1 |
| | Unknown outcome† | 214 | 12 |
| | | 1112 | 60 |
| Postnatal | Live Birth | 687 | 38 |
| | Still Birth / Fetal death | 44 | 2 |
| | | 731 | 40 |
| Total | | 1843 | 100 |

* 2007/8 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 proportion of women who accepted or declined “prenatal screening”, where “prenatal screening” includes 1st trimester combined test and 2nd trimester serum and integrated tests. Women who decided to proceed directly to a diagnostic test, due to age or other reasons, were classified as declining screening. Women classified as “unknown” 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. It is of interest that 22% of women with a postnatal diagnosis had declined to be screened. The proportion is likely to be higher as we have no information on 42% of women with a postnatal diagnosis.

Table 2: Acceptance of prenatal screening tests among women with a Down syndrome diagnosis in 2007/8*

| | Stage at diagnosis | | | |
|---|---|---|---|---|
| | Prenatal | | Postnatal | |
| | Number | % | Number | % |
| Screened | 970 | 87 | 263 | 36 |
| Declined screening | 68 | 6 | 158 | 22 |
| No information | 74 | 7 | 310 | 42 |
| Total | 1112 | 100 | 731 | 100 |

* 2007/8 data are provisional.

**Indication for prenatal diagnosis**

Table 3 shows the indication for prenatal diagnosis, separately for younger and older women. A 1st trimester combined test was the most likely indication given. A greater proportion of older than younger women gave a 1st trimester combined test as the indication, whereas a greater proportion of younger than older women gave an ultrasound examination (usually the anomaly scan) as the indication.

Table 3: Indication for prenatal diagnosis of Down Syndrome in 2007/8* according to maternal age

| Indication for prenatal diagnosis | Maternal Age | | | |
|---|---|---|---|---|
| | < 35 years | | ≥ 35 years | |
| | Number | % | Number | % |
| 1st Trimester : Combined | 145 | 42 | 392 | 51 |
| 2nd Trimester : Serum | 59 | 17 | 82 | 11 |
| 2nd Trimester : Integrated | 5 | 1 | 21 | 3 |
| Screen +ve (no info) | 59 | 17 | 99 | 13 |
| Ultrasound | 68 | 19 | 81 | 11 |
| Age | - | - | 39 | 5 |
| Other reasons | 2 | 1 | 16 | 2 |
| No information | 11 | 3 | 29 | 4 |
| Total | 349 | 100 | 759 | 100 |

* 2007/8 data are provisional; 4 cases had no maternal age.

**Gestational age at prenatal diagnosis**

The gestational age at diagnosis reflects the type of screening that led to the prenatal diagnosis, and therefore older women had a greater proportion of diagnoses before 15 weeks gestation than younger women, whilst younger women had a higher proportion of diagnoses after 21 weeks gestation (Table 4).

Table 4: Down syndrome cases diagnosed prenatally according to gestational age at diagnosis in 2007/8*

| Gestational age (wks) | Maternal Age | | | |
|---|---|---|---|---|
| | < 35 years | | ≥ 35 years | |
| | Number | % | Number | % |
| <15 | 143 | 41 | 418 | 55 |
| 15-20 | 156 | 45 | 287 | 38 |
| 21+ | 47 | 14 | 50 | 7 |
| Total | 346 | 100 | 755 | 100 |

* 2007/8 data are provisional; 11 diagnoses have missing gestational or maternal ages.

**Tissue used for prenatal diagnosis**

The tissue used for prenatal diagnosis also reflects the type of screening that led to the prenatal diagnosis, with a greater proportion of women under 35 having an amniocentesis than older women ( 55% versus 42%) and a greater proportion of older women having a CVS than women under 35 (again 55% vs 42%) (The tissue was either unspecified or not from an amniocentesis or CVS in 3% of women in both age groups). For all women the median time from CVS sampling to termination of pregnancy was 7 days compared with 8 days for amniocentesis. 92% of all terminations following CVS and 89% following amniocentesis were within 14 days of the procedure.

**Maternal age at diagnosis**

The mean age of the mother at the time of diagnosis was 36, however the mean age for women with a prenatal diagnosis was 36.7 (95% CI: 36.4 – 37.0) compared to 34.6 (34.0 – 35.1) for those with a postnatal diagnosis. Overall 64% (1062/1660) of the women of known age were 35 or older (Table 5).

Table 5: Down syndrome cases diagnosed in 2007/8* according to maternal age at diagnosis

| Maternal age (years) | Number | % |
|---|---|---|
| <20 | 30 | 2 |
| 20- | 84 | 5 |
| 25- | 154 | 8 |
| 30- | 330 | 18 |
| 35- | 591 | 32 |
| 40- | 431 | 23 |
| 45+ | 40 | 2 |
| missing | 183 | 10 |
| Total | 1843 | 100 |

* 2007/8 data are provisional.

## Patau and Edwards syndrome cases diagnosed in 2007/8

### Outcomes of Patau and Edwards syndrome cases

Around 88% of Patau and Edwards syndrome diagnoses were made prenatally (Table 6). A large proportion of births were still births, due to the severity of the syndromes. The outcome of 24 Patau and 86 Edwards syndrome prenatal diagnoses is unknown. About 4% of Patau and 3% of Edwards syndrome with unknown outcomes are likely to result in a live birth, therefore the total number of live births is estimated to be 29 and 59 respectively.

Table 6: Patau and Edwards syndrome cases in 2007/8* by time of diagnosis and outcome

| | | Patau syndrome | | Edwards syndrome | |
|---|---|---|---|---|---|
| | | Number | % | Number | % |
| Prenatal | Termination of pregnancy | 144 | 69 | 302 | 62 |
| | Live Birth | 10 | 5 | 13 | 3 |
| | Still Birth / Miscarriage | 7 | 3 | 29 | 6 |
| | Unknown outcome† | 24 | 11 | 86 | 17 |
| Postnatal | Live Birth | 18 | 9 | 44 | 9 |
| | Still Birth / Fetal death | 6 | 3 | 14 | 3 |
| | Total | 209 | 100 | 488 | 100 |

* 2007/8 data are provisional; † About 4% of Patau and 3% of Edwards syndrome with unknown outcomes are likely to result in a live birth.

### Indication for prenatal diagnosis

The main indication for a prenatal diagnosis was a 1st trimester combined test for Down syndrome or a late ultrasound (Table 7).

Table 7: Indication for prenatal diagnosis of Patau and Edwards syndrome cases in 2007/8*

| Indication for prenatal diagnosis | Patau syndrome | | Edwards syndrome | |
|---|---|---|---|---|
| | Number | % | Number | % |
| 1st Trimester : Combined | 72 | 39 | 175 | 41 |
| 2nd Trimester : Serum | 11 | 6 | 27 | 6 |
| 2nd Trimester : Integrated | 1 | 1 | 7 | 2 |
| Screen +ve (no info) | 10 | 5 | 30 | 7 |
| Ultrasound | 78 | 42 | 148 | 34 |
| Age | 1 | 1 | 10 | 2 |
| Other reasons | 2 | 1 | 5 | 1 |
| No information | 10 | 5 | 28 | 7 |
| Total | 185 | 100 | 430 | 100 |

* 2007/8 data are provisional.

**Gestational age and maternal age at diagnosis**

The mean gestational age at prenatal diagnosis was 16 weeks for both syndromes compared to 15 weeks for Down syndrome. The mean age of the mother at the time of diagnosis was 34.2 years for Patau syndrome and 35.9 years for Edwards syndrome, compared to 36.0 years for Down syndrome.

## Regional differences in cases diagnosed in 2007/8

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

Table 8 shows the patterns of diagnoses of Down syndrome across England and Wales, according to the maternal region of residence. Areas with a lower proportion of mothers over 35 years of age tend to have lower proportions of prenatal diagnoses. The highest proportions of prenatal diagnoses occur in the East and South East of England.

Table 8: All births and all Down syndrome diagnoses according to region of maternal residence in 2007/08*

| Government Regional Office (GRO) | All Births | | Down syndrome diagnoses | |
|---|---|---|---|---|
| | Number (1000) | Percentage of mothers ≥35 (%) | Number | Percentage of prenatal diagnoses (%) |
| North East | 30 | 16 | 93 | 51 |
| North West | 86 | 18 | 194 | 55 |
| Yorkshire & Humberside | 64 | 17 | 136 | 53 |
| East Midlands | 52 | 18 | 126 | 56 |
| West Midlands | 70 | 18 | 200 | 59 |
| East England | 69 | 21 | 187 | 69 |
| London | 126 | 24 | 385 | 63 |
| South East | 101 | 24 | 276 | 67 |
| South West | 57 | 22 | 150 | 57 |
| Wales | 34 | 17 | 96 | 56 |
| Total | 690 | 20 | 1,843 | 60 |

* 2007/8 data are provisional.

**Indication for prenatal diagnosis according to maternal region of residence**

Table 9 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 Wales had the highest proportion of women having a diagnostic test due to an ultrasound. Care must be taken in interpreting Table 9 as the "other" category for some regions is large.

**Gestational age at prenatal diagnosis according to maternal region of residence**

The gestational age at diagnosis reflects the reason given for the diagnosis. Table 10 gives a more accurate reflection of regional variation than Table 9 does as there is no "other" category. Women in London and the

South East are more likely to have their diagnostic test under 15 weeks gestation than women in Wales or the North West.

Table 9: Indication for prenatal diagnosis of Down syndrome according to region of maternal residence in 2007/08*

| Government Regional Office | Indication for prenatal diagnosis (%) | | | | | |
|---|---|---|---|---|---|---|
| | 1st trimester screen | 2nd trimester screen | Screen +ve (no info) | Ultrasound | Other† | Total |
| North East | 49 | 19 | 2 | 26 | 4 | 100 |
| North West | 25 | 10 | 29 | 24 | 11 | 100 |
| Yorkshire & Humberside | 44 | 17 | 13 | 18 | 8 | 100 |
| East Midlands | 33 | 16 | 17 | 11 | 23 | 100 |
| West Midlands | 35 | 31 | 10 | 15 | 9 | 100 |
| East England | 49 | 19 | 15 | 11 | 6 | 100 |
| London | 64 | 8 | 11 | 8 | 8 | 100 |
| South East | 62 | 11 | 12 | 9 | 6 | 100 |
| South West | 50 | 20 | 13 | 9 | 8 | 100 |
| Wales | 24 | 11 | 22 | 30 | 13 | 100 |
| Total | 48 | 15 | 14 | 13 | 9 | 100 |

* 2007/8 data are provisional.

† Other includes maternal age and no information.

Table 10: Gestational age at prenatal diagnosis of Down syndrome according to region of maternal residence in 2007/08*

| Government Regional Office | Gestational age at diagnosis (%) | | | |
|---|---|---|---|---|
| | < 15 weeks | 15-20 weeks | 21 + weeks | All |
| North East | 47 | 36 | 17 | 100 |
| North West | 31 | 60 | 9 | 100 |
| Yorkshire & Humberside | 54 | 35 | 11 | 100 |
| East Midlands | 49 | 41 | 10 | 100 |
| West Midlands | 40 | 51 | 9 | 100 |
| East England | 47 | 42 | 11 | 100 |
| London | 65 | 28 | 7 | 100 |
| South East | 63 | 31 | 6 | 100 |
| South West | 48 | 43 | 9 | 100 |
| Wales | 30 | 64 | 6 | 100 |
| Total | 51 | 40 | 9 | 100 |

* 2007/8 data are provisional; 11 cases have no gestational age

**Patau and Edwards syndrome diagnoses according to maternal region of residence**

Table 11 reports the numbers of Patau and Edwards syndrome diagnoses and the proportion that are prenatal. There appear to be slightly different proportions detected prenatally, but the total numbers of diagnoses are small and therefore such differences are due to sampling errors.

Table 11: Patau and Edwards syndrome diagnoses according to region of maternal residence in 2007/08*

| Government Regional Office | Patau Syndrome | | Edwards Syndrome | |
|---|---|---|---|---|
| | Number | Prenatal (%) | Number | Prenatal (%) |
| North East | 11 | 82 | 24 | 83 |
| North West | 18 | 83 | 50 | 86 |
| Yorkshire & Humberside | 17 | 88 | 35 | 83 |
| East Midlands | 12 | 100 | 25 | 88 |
| West Midlands | 28 | 75 | 44 | 86 |
| East England | 22 | 95 | 63 | 87 |
| London | 38 | 95 | 102 | 94 |
| South East | 35 | 94 | 85 | 88 |
| South West | 19 | 74 | 32 | 94 |
| Wales | 9 | 100 | 28 | 79 |
| Total | 209 | 89 | 488 | 88 |

*2007/8 data are provisional.

There are clear regional differences in screening for Down syndrome in England and Wales in 2007/08. However, some of these differences may arise due to the different maternal age distributions (Table 8). Many screening tests 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. These regional differences are not seen with Patau or Edwards syndrome as the numbers are much smaller.

## Trends over time in Down syndrome diagnoses

### Outcomes of Down syndrome cases from 1989-2008

Since the register started collecting data on 1st January 1989 the annual number of Down syndrome diagnoses has increased steadily (Table 12 and Figure 1), firstly due to the considerable increases in maternal age, the major known risk factor of the condition, and secondly due to the increase in the numbers of DS pregnancies diagnosed prenatally, many of whom were non-viable and would have miscarried and therefore remained undiagnosed in the absence of prenatal screening. The numbers 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 92% of women, on receipt of a prenatal diagnosis, decide to terminate the pregnancy (Table 12).

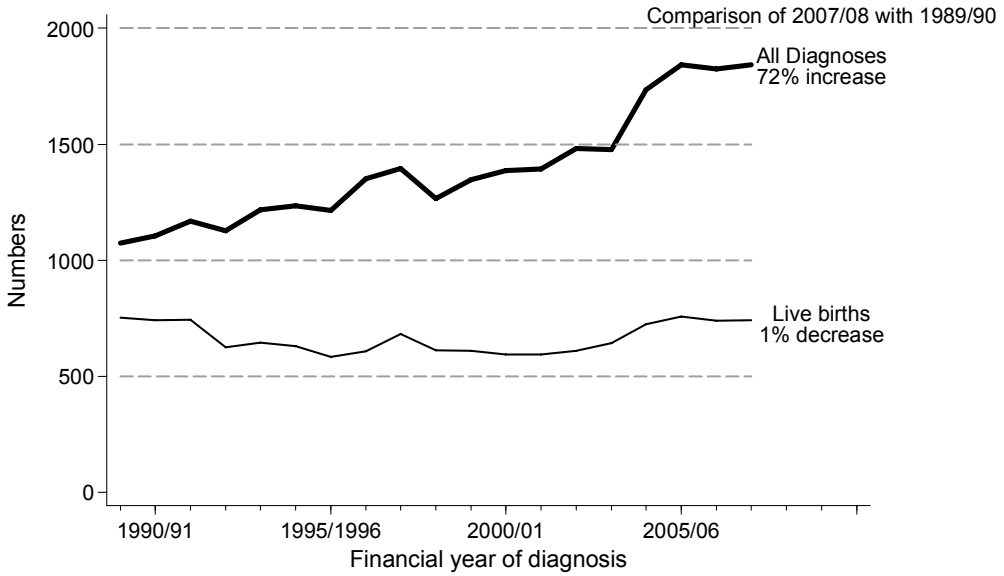
Table 12: Down syndrome diagnoses and outcomes in England and Wales from 1989 to 2007/8*

| Year of diagnosis | Numbers of Diagnoses | | | | | Outcomes of prenatal diagnoses ‡ (%) | | |
|---|---|---|---|---|---|---|---|---|
| | All | Prenatal | Live births | | Unknown outcomes | Termi-nations | Miscarriages /still births | Live births |
| | | | Reported | Estimated† | | | | |
| 1989/90 | 1,075 | 329 | 752 | 752 | 6 | 93.2 | 2.5 | 4.3 |
| 1990/91 | 1,106 | 386 | 741 | 742 | 14 | 88.4 | 4.3 | 7.3 |
| 1991/92 | 1,168 | 445 | 744 | 745 | 11 | 88.5 | 4.4 | 7.1 |
| 1992/93 | 1,128 | 514 | 625 | 626 | 18 | 92.1 | 3.2 | 4.6 |
| 1993/94 | 1,218 | 595 | 645 | 646 | 11 | 93.2 | 2.1 | 4.8 |
| 1994/95 | 1,234 | 622 | 628 | 629 | 24 | 91.6 | 3.2 | 5.2 |
| 1995/96 | 1,214 | 655 | 582 | 583 | 19 | 91.2 | 2.8 | 6.0 |
| 1996/97 | 1,352 | 758 | 607 | 608 | 17 | 92.7 | 2.8 | 4.5 |
| 1997/98 | 1,395 | 733 | 680 | 682 | 32 | 91.7 | 2.6 | 5.7 |
| 1998/99 | 1,266 | 684 | 610 | 612 | 30 | 91.6 | 2.0 | 6.4 |
| 1999/00 | 1,348 | 765 | 608 | 610 | 38 | 91.9 | 1.9 | 6.2 |
| 2000/01 | 1,387 | 822 | 591 | 595 | 70 | 92.4 | 1.3 | 6.3 |
| 2001/02 | 1,394 | 833 | 588 | 594 | 102 | 91.1 | 2.7 | 6.2 |
| 2002/03 | 1,481 | 908 | 603 | 609 | 106 | 92.4 | 2.1 | 5.5 |
| 2003/04 | 1,476 | 877 | 638 | 643 | 79 | 89.6 | 2.8 | 7.6 |
| 2004/05 | 1,735 | 1,039 | 716 | 725 | 143 | 89.8 | 3.8 | 6.4 |
| 2005/06 | 1,843 | 1,108 | 746 | 757 | 175 | 91.6 | 2.8 | 5.6 |
| 2006/07 | 1,825 | 1,108 | 729 | 740 | 176 | 91.3 | 3.2 | 5.5 |
| 2007/08 | 1,843 | 1,112 | 730 | 743 | 214 | 92.8 | 2.5 | 4.8 |
| Total | 26,488 | 14,293 | 12,563 | 12,641 | 1,285 | 91.4 | 2.8 | 5.8 |

+ Miscarriages before 20 weeks gestation that have not been diagnosed prenatally are excluded.

* 2007/8 data are provisional. † Estimated live births includes 6% of unknown outcomes. ‡ Calculated as a proportion of all known outcomes.

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




* 2007/8 data are provisional.

Table 12 shows that the proportions of prenatal diagnoses have increased over time, however, Figure 2 shows that the increases have occurred amongst women under 35 years of age, with the proportions of prenatal diagnoses remaining relatively constant for women 35 years and older.

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


* 2007/8 data are provisional.

**Indication for prenatal diagnosis 1989-2008**

Figure 3 and Table 13 show the changes in the indications for a prenatal diagnosis of Down syndrome. Cases which just specified that a screening test had been done were re-apportioned amongst the categories “Serum alone” and “Ultrasound < 16 weeks +/- serum” according to the relative proportions of these two types of test in each year. For older women there has been a clear shift from having a karyotype due to advanced maternal age to having a screening test. 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 are now detected due to screening.

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

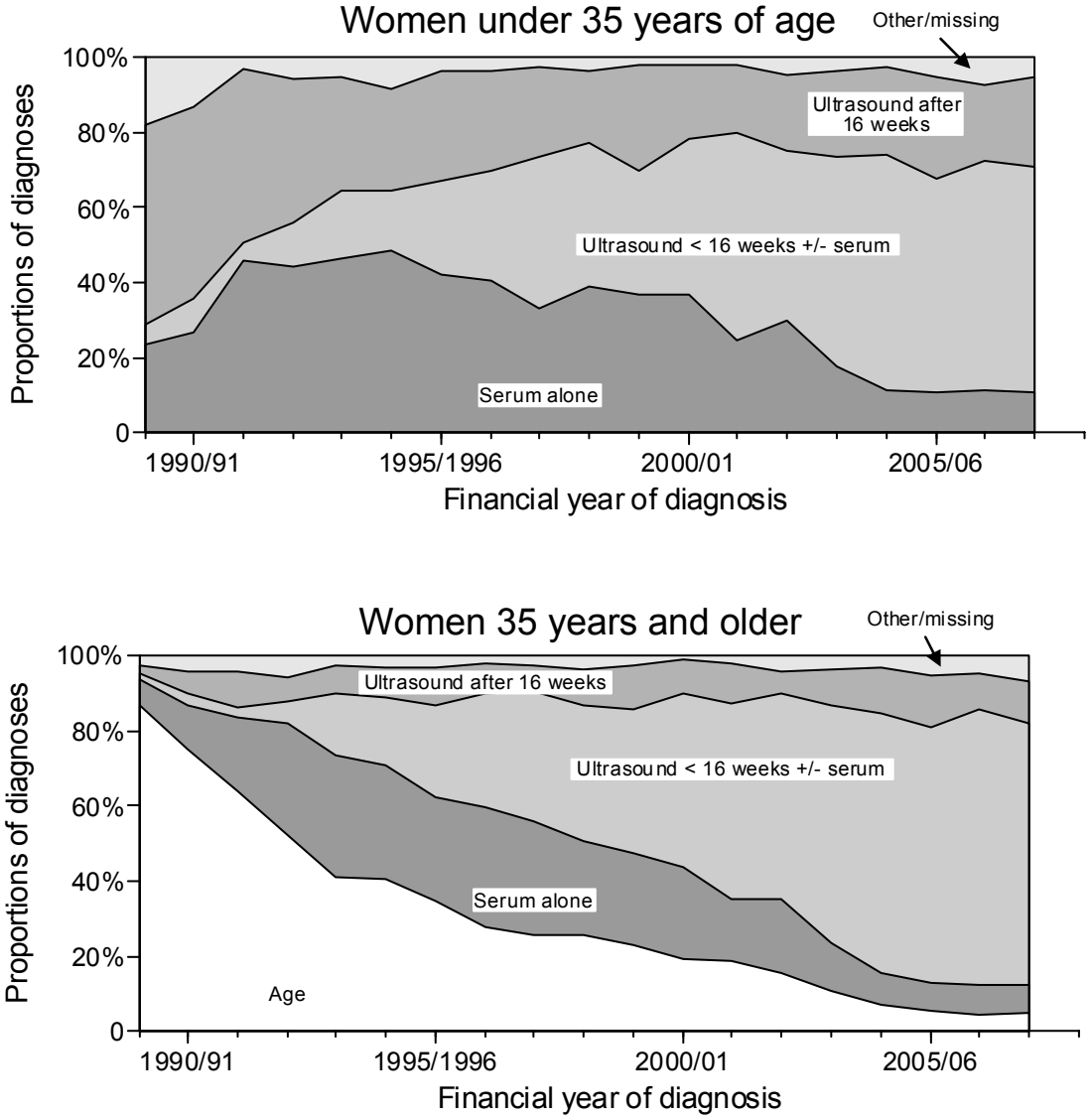


Table 13: Indication for Down syndrome prenatal diagnosis according to maternal age from 1989 to 2007/8*

| | Women under 35 (%) | | | | Women 35 + (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Year of diagnosis | Serum only | US < 16 wks +/- serum | US > 16 wks | Other | Age alone | Serum only | US < 16 wks +/- serum | US > 16 wks | Other |
| 1989/90 | 24 | 5 | 53 | 18 | 87 | 7 | 2 | 3 | 2 |
| 1990/91 | 27 | 9 | 51 | 13 | 75 | 12 | 3 | 6 | 4 |
| 1991/92 | 46 | 5 | 46 | 3 | 64 | 20 | 2 | 10 | 4 |
| 1992/93 | 45 | 11 | 39 | 5 | 52 | 30 | 6 | 6 | 5 |
| 1993/94 | 47 | 18 | 30 | 5 | 41 | 32 | 17 | 8 | 2 |
| 1994/95 | 49 | 16 | 27 | 8 | 40 | 30 | 18 | 8 | 3 |
| 1995/96 | 42 | 25 | 29 | 3 | 35 | 28 | 25 | 10 | 3 |
| 1996/97 | 41 | 29 | 26 | 3 | 28 | 32 | 30 | 8 | 2 |
| 1997/98 | 33 | 41 | 24 | 2 | 26 | 30 | 34 | 7 | 3 |
| 1998/99 | 39 | 38 | 19 | 3 | 26 | 25 | 36 | 10 | 4 |
| 1999/00 | 37 | 33 | 28 | 2 | 23 | 24 | 39 | 12 | 3 |
| 2000/01 | 37 | 42 | 20 | 1 | 19 | 24 | 47 | 9 | 1 |
| 2001/02 | 24 | 55 | 18 | 2 | 19 | 17 | 52 | 10 | 2 |
| 2002/03 | 30 | 46 | 20 | 2 | 16 | 20 | 54 | 6 | 2 |
| 2003/04 | 18 | 56 | 23 | 2 | 11 | 13 | 63 | 10 | 2 |
| 2004/05 | 11 | 63 | 24 | 1 | 7 | 8 | 69 | 12 | 1 |
| 2005/06 | 11 | 57 | 27 | 1 | 5 | 8 | 68 | 14 | 1 |
| 2006/07 | 11 | 61 | 20 | 3 | 4 | 8 | 73 | 10 | 2 |
| 2007/08 | 11 | 60 | 24 | 1 | 5 | 7 | 70 | 11 | 2 |

* 2007/8 data are provisional.

**Gestational age at prenatal diagnosis 1989-2008**

The move to earlier screening tests is reflected in the decreases in gestational age at diagnosis (Table 14).

**Maternal age at diagnosis 1989-2008**

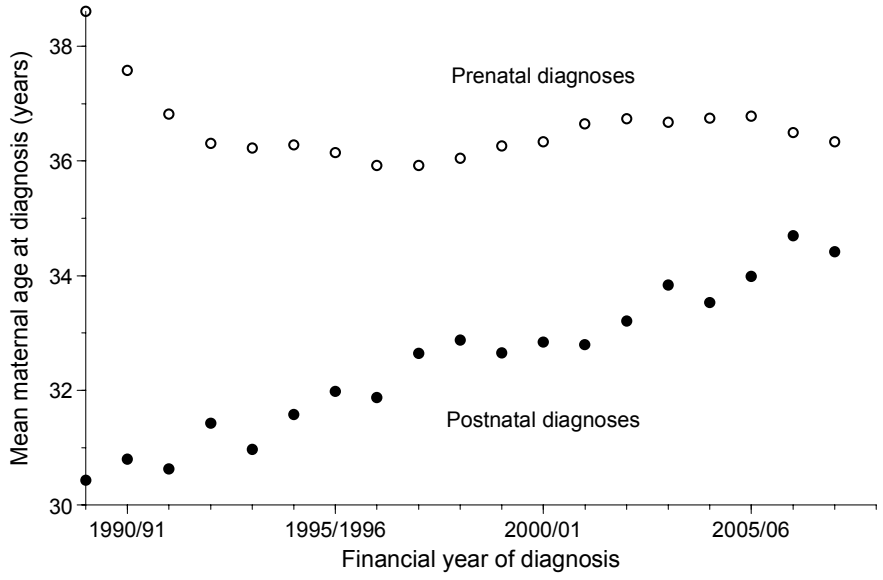
At the start of the register, the main prenatal screening test available was a mother's age and so the majority of prenatal diagnoses occurred in older women. As screening became more available and detection rates for younger women improved, more younger women received prenatal diagnoses. This is reflected in the average maternal age at diagnosis (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 14: Gestational age at prenatal diagnosis according to year of diagnosis

| Year of diagnosis | Gestational age at diagnosis (%) | | | |
|---|---|---|---|---|
| | < 15 weeks | 15-20 weeks | 21 + weeks | All |
| 1989/90 | 16 | 80 | 5 | 100 |
| 1990/91 | 17 | 73 | 10 | 100 |
| 1991/92 | 13 | 76 | 11 | 100 |
| 1992/93 | 13 | 82 | 5 | 100 |
| 1993/94 | 19 | 75 | 6 | 100 |
| 1994/95 | 24 | 70 | 6 | 100 |
| 1995/96 | 24 | 70 | 6 | 100 |
| 1996/97 | 28 | 64 | 7 | 100 |
| 1997/98 | 32 | 62 | 6 | 100 |
| 1998/99 | 36 | 57 | 7 | 100 |
| 1999/00 | 34 | 56 | 10 | 100 |
| 2000/01 | 39 | 54 | 7 | 100 |
| 2001/02 | 45 | 47 | 8 | 100 |
| 2002/03 | 45 | 47 | 8 | 100 |
| 2003/04 | 47 | 45 | 7 | 100 |
| 2004/05 | 45 | 48 | 8 | 100 |
| 2005/06 | 48 | 42 | 10 | 100 |
| 2006/07 | 50 | 41 | 8 | 100 |
| 2007/08* | 51 | 40 | 9 | 100 |

* 2007/8 data are provisional.

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



# Appendix A

**Data Completeness**

The following table shows the completeness of the different data items for the years 1989 to 2004/5, 2005/6, 2006/7 and 2007/8. We are still following up the missing data from 2005 onwards. The data from 1989 to 2005 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 2007/8*

| | Percentage complete | | | |
|---|---|---|---|---|
| Data Item | 1989-2005 | 2005/6 | 2006/7 | 2007/8* |
| Reason for referral for diagnosis | 100 | 98 | 97 | 95 |
| Type of tissue karyotyped | 100 | 98 | 99 | 98 |
| Sex of fetus (some DNA based diagnoses such as FISH and q-PCR do not include sex chromosome analysis) | 100 | 98 | 99 | 97 |
| Maternal age | 96 | 90 | 91 | 90 |
| Gestational age at sample for prenatal diagnosis | 100 | 100 | 100 | 100 |
| Outcome of pregnancy† | 96 | 94 | 90 | 88 |
| Number of previous pregnancies | 66 | 64 | 64 | 50 |
| Post Codes (some information) | 93 | 91 | 91 | 92 |
| (complete postcodes) | 83 | 87 | 88 | 86 |
| Maternal NHS number (requested from 2005) | NA | 52 | 57 | 47 |

* 2007/8 data are provisional.

## Appendix B

**Form in 2007/8**

Reference No. 16438 NDSCR |__|__|__|__|__|

# NATIONAL DOWN SYNDROME CYTOGENETIC REGISTER

**NOW INCLUDING TRISOMIES 13 AND 18** *(In collaboration with the National Screening Committee)*

**PLEASE RETURN THIS FORM TO:**
Joan Morris, Wolfson Institute of Preventive Medicine, Barts and the London, Charterhouse Square, London, EC1M 6BQ
Telephone: 020 7882 6220 Fax: 020 7882 6221 Website: http://www.wolfson.qmul.ac.uk/ndscr/
**AND FORWARD BLUE AND GREEN COPIES TO THE REFERRING CLINICIAN. THANK YOU FOR YOUR HELP.**

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

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

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

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

Karyotype .....

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

## SCREENING TESTS

(please complete at least one of the following three sections)

|__| **Yes (NHS)** Screen: +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 .....

|__| **Yes (Private)** Screen: +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 .....

|__| **No screening because:**
Too late |__| Not offered |__| Declined |__|
Other .....

## TIMING OF DIAGNOSIS AND INDICATIONS

**Prenatal** Screen result |__| Mat Age |__| Family history |__|
|__| U/S findings (please specify) |__| .....
Other .....

**Postnatal** No indication |__| Indication but test declined |__|
|__| Diagnosed after miscarriage |__| Other .....

## FOR AUDIT PURPOSES ONLY— please complete

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 |__|

Other chromosomal anomaly, including parents' if known:
.....

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

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** A
Reference No. 16438 NDSCR |__|__|__|__|__|
Laboratory |__|__| Trisomy 21 13 18 pren/ postn/ misc
Specimen ID |__|__|__|__|__|__|__|__|

## Appendix C : NDSCR Publications


1. 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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15. 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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17. 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, 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.
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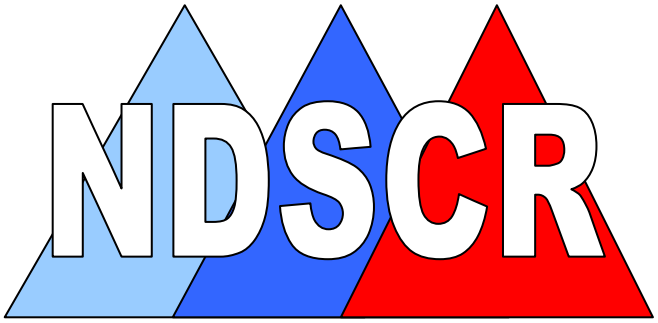


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