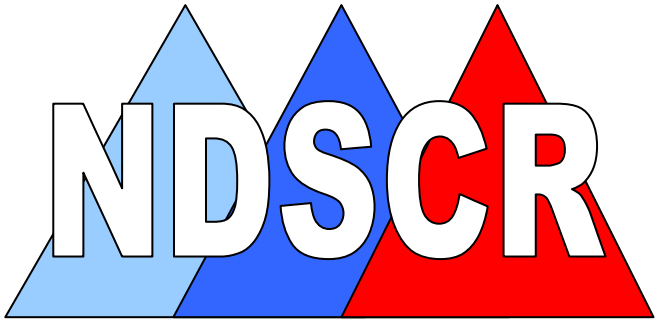

The National Down Syndrome Cytogenetic Register for England and Wales: 2008/9 Annual Report

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Foreword

This 2008/9 annual report contains information about the NDSCR as well as detailed data on all reported cytogenetically diagnosed cases of Down syndrome (trisomy 21) from 1989/90 to 2008/9, and Edwards syndrome (trisomy 18) and Patau syndrome (trisomy 13) from 2004/5 to 2008/9.

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

- This report is once again based on financial years, due to a request by the National Fetal Anomaly Screening Programme.
- In 2008/9 there were 1844 diagnoses of Down syndrome, 64% of which were made prenatally.
- In 2008/9 there were an estimated 687 Down syndrome live births, a live birth rate of 1.0 per 1000.
- In 2008/9 there were 172 diagnoses of Patau and 495 diagnoses of Edwards syndrome, of which an estimated 18 and 37 respectively were live births.
- The percentage of missing outcomes for the whole register is 5%, with only 2008/9 above 10% (13%).
- The type of screening that a woman received in 2008/9 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 2008/9.
- The NDSCR is approved to use Section 251 of the NHS Act 2006 and has ethics approval from Trent MREC.
- Data collection by the NDSCR was funded by the National Fetal Anomaly Screening Programme until March 2009. HQIP is funding the NDSCR until March 2010.

Suggested citation of this report:

Morris JK, De Souza E. The National Down Syndrome Cytogenetic Register for England and Wales 2008/9 Annual Report. Queen Mary University of London, Barts and The London School of Medicine and Dentistry 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 was funded by the National Fetal Anomaly Screening Programme until March 2009. HQIP (Healthcare Quality Improvement Partnership) is funding the NDSCR until March 2010. 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 2009 is shown in Appendix B). The form is self-copying and has 4 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 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 2005/6 combined, and separately for 2006/7, 2007/8 and 2008/9. This is always lowest in the most recent data where not all the clinicians have been contacted yet. 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 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.

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 2009 this approval was successfully renewed.

How the data are used

Audit of Down Syndrome Screening

- The NDSCR reports the annual numbers of pre- and postnatal diagnoses of Down, Patau and Edwards syndrome cases to the National Fetal Anomaly Screening Programme. These are acknowledged to be more complete than the figures on births and termination published by the National Congenital Anomaly Service (NCAS).

- 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.

- An NDSCR leaflet is provided to the Down Syndrome Association.

- An NDSCR leaflet is in preparation for 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.

Publications

A list of selected publications based on or using NDSCR data is provided 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 2008/9

Outcomes of Down syndrome cases

1844 Down syndrome diagnoses were made in 2008/9, 1189 (64%) prenatally and 655 (36%) postnatally (Table 1). The outcome of 226 of the prenatal diagnoses is unknown. Assuming that the proportion terminated remains as before 2008/9, the likely number of Down syndrome live births in England and Wales in 2008/9 would have been 687 (58 + 615 + 6% of 226), a prevalence of 1.0 per 1000 live births occurring in England and Wales in 2008/9.

Table 1: Down syndrome cases diagnosed in England and Wales in 2008/9* according to time of diagnosis and outcome

		Number	%
Prenatal	Termination of pregnancy	878	48
	Live Birth	58	3
	Still Birth / Miscarriage	27	1
	Unknown outcome†	226	12
		1189	64
Postnatal	Live Birth	615	34
	Still Birth / Fetal death	40	2
		655	36
Total		1844	100

* 2008/9 data are provisional. † About 6% of those with unknown outcomes are likely to result in a live birth.

Acceptance of Screening

Table 2: Acceptance of prenatal screening tests among women with a Down syndrome diagnosis in 2008/9*

	Stage at diagnosis			
	Prenatal		Postnatal	
	Number	%	Number	%
Screened	1011	85	196	30
Declined screening	65	5	155	24
No information	113	10	304	46
Total	1189	100	655	100

* 2008/9 data are provisional.

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. 24% 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 46% of women with a postnatal diagnosis.

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 older women whereas 1st and 2nd trimester tests were equally likely in younger women. A greater percentage of younger than older women gave an ultrasound examination (usually the anomaly scan) as the indication, and 17% of prenatal diagnoses in younger women occurred at 21 weeks gestation or later, compared to only 6% of prenatal diagnoses in older women.

Table 3: Indication for prenatal diagnosis of Down Syndrome in 2008/9* according to maternal age

Indication for prenatal diagnosis	Maternal Age			
	< 35 years		≥ 35 years	
	Number	%	Number	%
1st Trimester screening	142	40	461	56
2nd Trimester screening	144	40	264	32
Ultrasound	56	16	45	5
Age	-	-	28	3
Other reasons	5	1	13	2
No information	11	3	14	2
Total	358	100	825	100

* 2008/9 data are provisional; 6 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 (57%) having a CVS than younger women (41%), and a smaller percentage of older women having an amniocentesis (37%) than younger women (53%). The tissue was either unspecified or not from an amniocentesis or CVS in 6% of women in both age groups.

For all women, the median time from CVS or amniocentesis to termination of pregnancy was 8 days. 90% of all terminations following CVS and 82% 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. 52% of terminations in older mothers took place before 15 weeks gestation, compared to only 34% in younger mothers. 7% of terminations in older mothers took place after 20 weeks gestation, compared to 19% in younger mothers.

Table 4: Gestation at termination following prenatal diagnosis of Down Syndrome in 2008/9* according to maternal age

Gestation at termination (following prenatal diagnosis)	Maternal Age			
	< 35 years		≥ 35 years	
	Number	%	Number	%
<15 weeks	89	34	320	52
15 to 20 weeks	122	47	252	41
≥21 weeks	51	19	40	7
Total	262	100	612	100

* 2008/9 data are provisional. Outcomes were assumed to occur one week after diagnostic sample if gestation was missing. 1 case had no maternal age. Gestation at outcome could not be estimated for 2 cases.

Maternal age at observed or expected date of delivery

The mean age of the mother 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 37.0 (95% CI: 36.6 , 37.3) compared to 34.0 (95% CI: 33.4 , 34.6) for those with a postnatal diagnosis. Overall 65% (1096/1694) of the women of known age were 35 or older (Table 5).

Table 5: Down syndrome cases diagnosed in 2008/9* according to maternal age at observed or expected date of delivery

Maternal age (years)	Number	%
<20	23	1
20-	99	5
25-	157	9
30-	319	17
35-	599	33
40-	447	24
45+	50	3
missing	150	8
Total	1844	100

* 2008/9 data are provisional.

Patau and Edwards syndrome cases diagnosed in 2008/9

Outcomes of Patau and Edwards syndrome cases

91% of Patau and 92% 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 30 Patau and 72 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, therefore the total number of live births is estimated to be 18 and 37 respectively.

Table 6a presents outcomes for Patau syndrome cases. The numbers were too small to present outcomes according to time at diagnosis. Table 6b presents outcomes for Edwards syndrome cases according to time at diagnosis.

Table 6a: Patau syndrome cases in 2008/9* according to outcome

	Number	%
Termination of pregnancy	111	65
Live Birth	17	10
Still Birth / Miscarriage/ Fetal death	14	8
Unknown outcome†	30	17
Total	172	100

Table 6b: Edwards syndrome cases in 2008/9* according to time of diagnosis and outcome

		Number	%
Prenatal	Termination of pregnancy	339	68
	Live Birth	11	2
	Still Birth / Miscarriage	35	7
	Unknown outcome†	72	15
Postnatal	Live Birth	24	5
	Still Birth / Fetal death	14	3
	Total	495	100

* 2008/9 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 25% of prenatal diagnoses of Patau syndrome in younger women were made at 21 weeks gestation or later, compared to 15% in older women. Approximately 22% of prenatal diagnoses of Edwards syndrome in younger women were made at 21 weeks gestation or later, compared to 13% in older women.

Table 7: Indication for prenatal diagnosis of Patau and Edwards syndrome cases in 2008/9*

Indication for prenatal diagnosis	Patau syndrome		Edwards syndrome	
	Number	%	Number	%
1st Trimester screening	81	52	248	55
2nd Trimester screening	23	15	74	16
Ultrasound	40	25	92	20
Age and other reasons	4	2	10	2
No information	9	6	33	7
Total	157	100	457	100

* 2008/9 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 35.1 years for Patau syndrome and 36.6 years for Edwards syndrome, compared to 36.1 years for Down syndrome. For Patau syndrome 59% of women with known maternal age were aged 35 or over, and for Edwards syndrome 69% of women with known maternal age were aged 35 or over (Table 8).

Table 8: Patau and Edwards syndrome cases diagnosed in 2008/9* according to maternal age at observed or expected date of delivery

	Patau syndrome		Edwards syndrome	
Maternal age (years)	Number	%	Number	%
<25	14	8	36	7
25-	22	13	41	8
30-	32	19	72	15
35-	57	33	182	37
40+	42	24	154	31
missing	5	3	10	2
Total	172	100	495	100

* 2008/9 data are provisional.

Regional differences in cases diagnosed in 2008/9

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 births and all Down syndrome diagnoses according to region of maternal residence in 2008/09*

Government Office Region (GOR)	All Births †		Down syndrome diagnoses	
	Number (1000)	Percentage of mothers ≥35 (%)	Number	Percentage prenatally diagnosed (%)
North East	30	15	75	51
North West	88	17	197	54
Yorkshire & Humberside	66	16	144	53
East Midlands	54	18	109	61
West Midlands	72	17	157	64
East England	72	21	184	68
London	128	25	407	72
South East	104	24	315	72
South West	59	22	173	63
Wales	36	17	75	53
Total	709	20	1836	64

* 2008/9 data are provisional. 8 records have unknown GOR

† National data are for calendar year 2008

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 North West 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. (2 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 West and East Midlands are the least likely.

Table 10: Indication for prenatal diagnosis of Down syndrome according to region of maternal residence in 2008/09*

Government Office Region	Number of prenatal diagnoses	Indication for prenatal diagnosis (%)				
		1st trimester screen	2nd trimester screen	Ultrasound	Other/ Missing/ Age	Total
North East	38	24	55	16	5	100
North West	106	21	51	22	6	100
Yorkshire & Humberside	77	29	53	12	6	100
East Midlands	67	33	40	8	19	100
West Midlands	101	37	45	8	10	100
East England	125	46	41	9	4	100
London	294	66	22	8	4	100
South East	227	73	21	3	3	100
South West	109	57	29	7	7	100
Wales	40	23	60	7	10	100
Total	1184	51	34	9	6	100

* 2008/9 data are provisional. 5 cases have no GOR data.

Table 11: Gestation at termination after prenatal diagnosis of Down syndrome according to region of maternal residence in 2008/09*

Government Office Region	Number of terminations	Gestation at termination (%)			
		<15 weeks	15 to 20 weeks	21+ weeks	Total
North East	31	32	45	23	100
North West	65	17	69	14	100
Yorkshire & Humberside	61	36	51	13	100
East Midlands	48	19	67	14	100
West Midlands	84	37	50	13	100
East England	92	46	42	12	100
London	193	59	32	9	100
South East	175	64	30	6	100
South West	91	52	44	4	100
Wales	32	31	53	16	100
Total	876	47	43	10	100

* 2008/9 data are provisional. 2 cases had no gestation at outcome, 3 cases had no GOR data.

Patau and Edwards syndrome diagnoses according to maternal region of residence

Table 12 reports the numbers of Patau and Edwards syndrome diagnoses and the number that are prenatally diagnosed.

Table 12: Number of Patau and Edwards syndrome diagnoses according to region of maternal residence in 2008/09*

Government Office Region	Patau Syndrome (number)		Edwards Syndrome (number)	
	Total	Prenatal	Total	Prenatal
North East and North West†	13	11	46	39
Yorkshire & Humberside	19	19	36	34
East Midlands	8	8	36	33
West Midlands	8	5	40	33
East England	22	18	60	59
London	44	41	130	123
South East	32	32	73	69
South West	16	15	50	45
Wales	9	7	22	20
Total	171	156	493	455

*2008/9 data are provisional. 1 case of Patau syndrome and 2 of Edwards syndrome do not have GOR data.

† North East and North West GORs have been combined due to small numbers.

Summary of regional differences

There are clear regional differences in screening for Down syndrome in England and Wales in 2008/09. 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 1989-2009

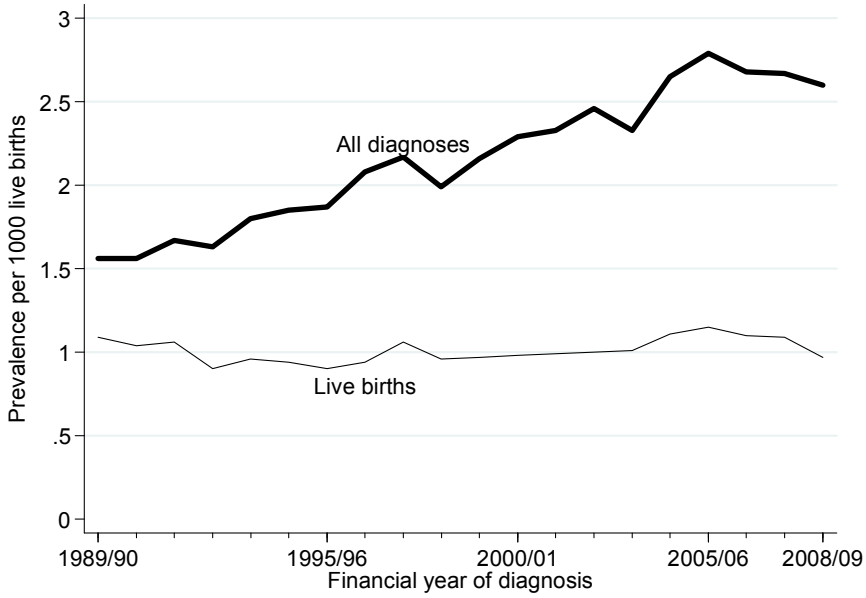
Since the register started collecting data on 1st January 1989 the annual number and prevalence of Down syndrome diagnoses has increased (Table 13 and Figure 1), firstly due to the considerable increases in maternal age, the major known risk factor, and secondly due to the increase in the numbers of 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 92% 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 2008/9*

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				
1989/90	1,070	328	748	748	6	93.2	2.5	4.3
1990/91	1,101	386	736	737	14	88.4	4.3	7.3
1991/92	1,165	443	743	744	11	88.4	4.4	7.2
1992/93	1,124	512	623	624	18	92.1	3.2	4.7
1993/94	1,215	594	643	644	11	93.1	2.1	4.8
1994/95	1,232	622	626	627	24	91.6	3.2	5.2
1995/96	1,211	654	580	581	19	91.2	2.8	6.0
1996/97	1,351	757	607	608	16	92.7	2.8	4.5
1997/98	1,394	733	679	681	28	91.8	2.5	5.7
1998/99	1,263	683	608	609	24	91.6	2.0	6.4
1999/00	1,343	764	604	606	34	91.9	1.9	6.2
2000/01	1,382	821	588	592	68	92.3	1.3	6.4
2001/02	1,384	826	583	589	98	91.2	2.9	5.9
2002/03	1,464	900	593	599	97	92.5	2.1	5.4
2003/04	1,446	857	627	631	60	89.8	3.0	7.2
2004/05	1,698	1,020	701	708	123	89.9	3.6	6.5
2005/06	1,800	1,081	731	740	143	91.3	3.1	5.6
2006/07	1,792	1,082	729	737	140	90.8	3.4	5.8
2007/08	1,845	1,116	747	755	130	91.2	2.7	6.1
2008/09*	1,844	1,189	673	687	226	91.2	2.8	6.0
Total	28,124	15,368	13,169	13,247	1,290	91.3	2.8	5.9

* 2008/9 data are provisional. † Estimated live births includes 6% of unknown outcomes. ‡ Calculated as a percentage of all known outcomes.

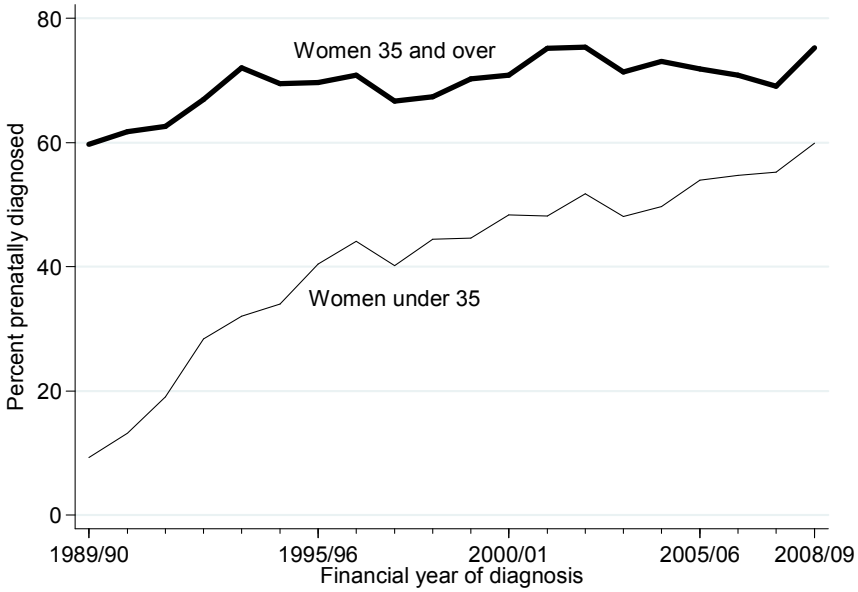
Figure 1: Prevalence of Down syndrome diagnoses and live births per thousand livebirths in England and Wales according to year of diagnosis*



* 2008/9 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*

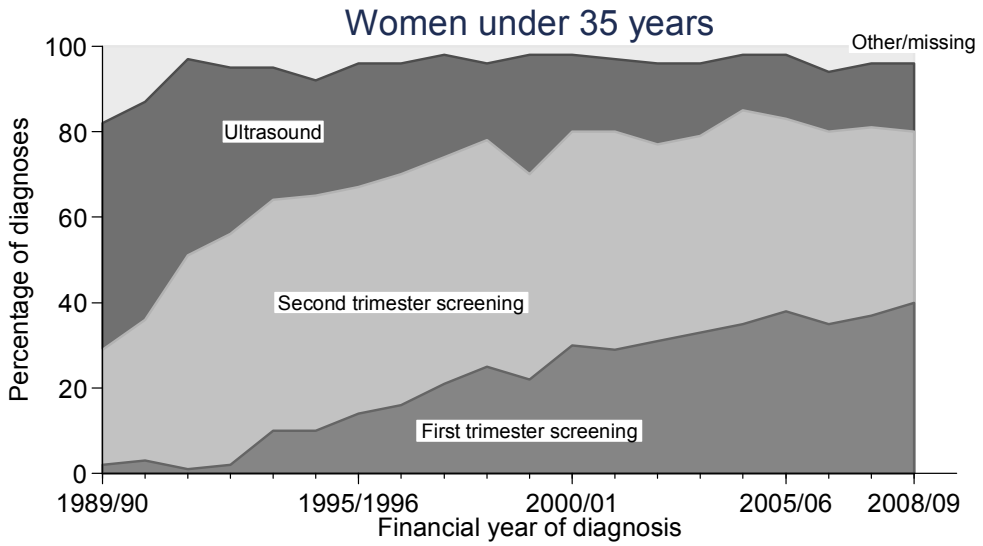


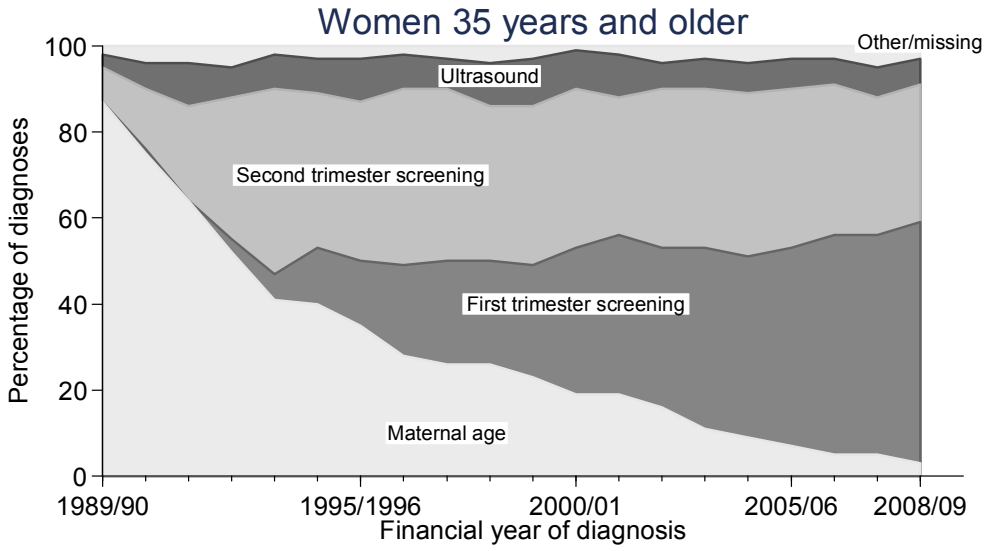
* 2008/9 data are provisional.

Indication for prenatal diagnosis 1989-2009

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 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.

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





* 2008/9 data are provisional

Table 14: Indication for Down syndrome prenatal diagnosis according to maternal age from 1989 to 2008/9*

	Women under 35 (%)				Women 35+ (%)				
Year of diagnosis	1st Trimester	2nd Trimester	Ultra-sound	Other/ Missing	Age alone	1st Trimester	2nd Trimester	Ultra-sound	Other/ Missing
1989/90	2	27	53	18	87	0	8	3	2
1990/91	3	33	51	13	75	1	14	6	4
1991/92	1	50	46	3	64	0	22	10	4
1992/93	2	53	39	6	52	2	34	7	5
1993/94	10	55	30	5	41	6	43	8	2
1994/95	10	55	27	8	41	12	36	8	3
1995/96	14	53	29	4	35	15	37	10	3
1996/97	16	53	27	4	28	21	41	8	2
1997/98	21	53	24	2	26	24	40	7	3
1998/99	25	53	18	4	26	25	36	10	3
1999/00	22	48	28	2	23	26	37	12	2
2000/01	30	49	19	2	19	33	38	9	1
2001/02	29	51	17	3	18	37	33	10	2
2002/03	31	46	19	4	16	37	37	6	4
2003/04	33	46	17	4	11	41	38	7	3
2004/05	35	50	13	2	9	42	38	7	4
2005/06	38	45	15	2	7	46	37	7	3
2006/07	35	45	14	6	5	52	35	5	3
2007/08	37	44	15	4	5	52	32	6	5
2008/09*	40	40	16	4	3	56	32	5	4

* 2008/9 data are provisional.

Gestational age at termination following prenatal diagnosis

The shift towards earlier screening has increased the percentage of prenatal diagnoses with terminations before 15 weeks gestation, for younger and older women (Table 16). The percentage of terminations taking place at 21 weeks gestation or later has decreased for younger and older women but the percentage remains higher for younger women.

Maternal age at observed or expected date of delivery 1989-2009

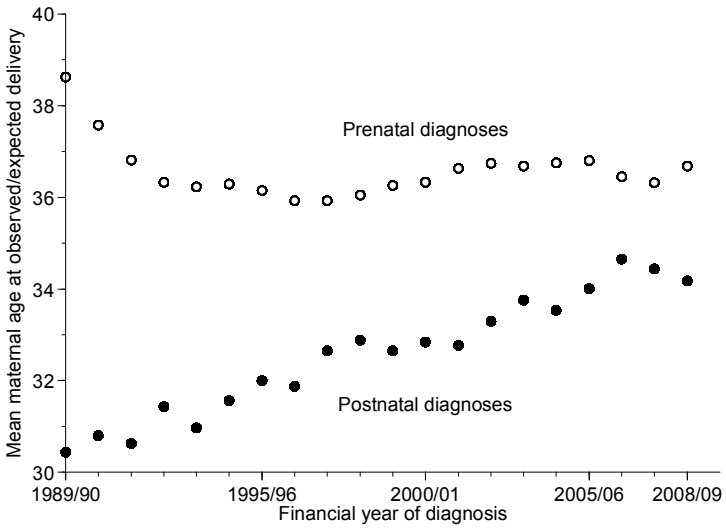
At the start of the register, the main prenatal screening test available was a mother's age and so the majority of prenatal diagnoses occurred in older women. As screening became more available and detection rates for younger women improved, more younger women received prenatal diagnoses. This is reflected in the average maternal age (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 16: Gestation at termination after prenatal diagnosis of Down syndrome according to maternal age from 1989 to 2008/9*

Year of diagnosis	Women under 35 (%)			Women ≥35 (%)		
	<15 weeks	15 to 20 weeks	≥21 weeks	<15 weeks	15 to 20 weeks	≥21 weeks
1989/90	2	50	48	16	65	19
1990/91	8	48	44	13	64	23
1991/92	1	53	46	13	67	20
1992/93	4	61	35	9	70	21
1993/94	12	43	45	14	65	20
1994/95	10	57	33	20	63	17
1995/96	14	49	37	20	64	15
1996/97	16	53	31	27	59	14
1997/98	21	52	27	28	60	12
1998/99	25	52	24	27	59	13
1999/00	21	48	30	31	56	13
2000/01	29	48	23	36	53	11
2001/02	29	48	23	42	49	9
2002/03	31	48	20	41	51	8
2003/04	33	47	20	45	47	8
2004/05	29	51	20	43	48	9
2005/06	37	43	20	46	45	9
2006/07	33	49	18	46	46	8
2007/08	38	46	16	51	40	8
2008/09*	34	47	19	52	41	7

* 2008/9 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*



* 2008/9 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 2004/5 (Tables 17 and 18) due to increases in maternal age, the major known risk factor, and due to the increase in the numbers 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 2008/9 is lower than in 2007/8, the reason for which is unclear.

Table 17: Patau syndrome diagnoses and outcomes in England and Wales from 1989 to 2008/9*

Year of diagnosis	Patau syndrome: Numbers of Diagnoses				
	All	Prenatal	Live births		Unknown outcomes
			Reported	Estimated†	
2004/05	156	143	15	15	10
2005/06	177	147	27	28	15
2006/07	198	176	23	24	15
2007/08	210	185	29	30	14
2008/09*	172	157	17	18	30
Total	913	808	111	115	84

* 2008/9 data are provisional. † Estimated live births include 4% of unknown outcomes.

Table 18: Edwards syndrome diagnoses and outcomes in England and Wales from 1989 to 2008/9*

Year of diagnosis	Edwards syndrome: Numbers of Diagnoses				
	All	Prenatal	Live births		Unknown outcomes
			Reported	Estimated†	
2004/05	389	355	35	37	56
2005/06	434	385	47	49	57
2006/07	480	418	58	60	51
2007/08	489	437	61	63	54
2008/09*	495	457	35	37	72
Total	2,287	2,052	236	246	290

* 2008/9 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 2005/6, 2006/7, 2007/8 and 2008/9. We are still following up the missing data from 2005 onwards. The data from 1989 to 2006 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 2008/9*

Data Item	Percentage complete			
	1989-2006	2006/7	2007/8	2008/9*
Reason for referral for diagnosis	99	97	98	97
Type of tissue karyotyped	99	98	96	96
Sex of fetus (some DNA based diagnoses such as FISH and q-PCR do not include sex chromosome analysis)	99	97	97	96
Maternal age	96	94	95	93
Gestational age at sample for prenatal diagnosis	100	99	99	98
Outcome of pregnancy	96	92	92	87
Post Codes (some information)	93	92	95	94
Maternal NHS number (requested from 2005)	NA	61	68	57

* 2008/9 data are provisional.

Appendix B: Form in 2008/9

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: 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.
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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.
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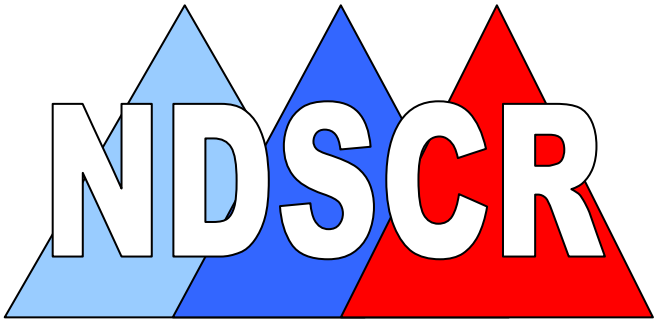

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