Original

Sixteen years of screening for Down syndrome in England and Wales: 1989-2004

JK Morris
Director National Down Syndrome Cytogenetic Register Centre for Environmental and Preventive Medicine, Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry

Correspondence:
JK Morris
Charterhouse Square, London EC1M 6BQ, UK
E-mail: j.k.morris@qmul.ac.uk
Web del NDSCR: www.wolfson.qmul.ac.uk/ndscr

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Introduction

The National Down Syndrome Cytogenetic Register (NDSCR, hereafter called the Down syndrome register)[1,2] has been collecting data on all cytogenetic or DNA reports of trisomy 21 and its cytogenetic variants occurring in England and Wales since 1989. One aim of the Down syndrome register is to monitor the effectiveness and availability of the relevant prenatal diagnostic genetic services. In this article we use data from the Down syndrome register to examine the changes in screening for Down syndrome that occurred between 1989 and 2004.

Methods

The Down syndrome register currently holds anonymous data on over 20,000 cases of prenatally or postnatally Down syndrome diagnosed in England and Wales from 1 January 1989 to 31 December 2004. The information held is derived from all clinical cytogenetic laboratories in England and Wales, who are requested to send a completed form for each diagnosis of trisomy 21 and its variants. The form contains details of the date, place of and indications for referral, maternal age, and family history. Most laboratories send a copy of this form to the referring physician for confirmation and completion. The outcome of the pregnancy is requested for all cases diagnosed prenatally, but may not be known for several months. By comparing the Down syndrome register data with that from the Office for National Statistics (ONS) it is estimated that the ascertainment of the Down syndrome register is at least 93%, although this may be an underestimate because the matching of anonymous cases sometimes fails due to lack of sufficient information. There is also evidence that some of the 'cases' notified to ONS were not cytogenetically confirmed.

Results

The total number of Down syndrome diagnoses

The number of diagnoses of Down syndrome (figure 1 and table 1) has increased dramatically since 1989, from 1067 to over 1659 in 2004 (a 55% increase). The number of prenatally diagnosed cases has increased by over 300% from 321 in 1989 to 1021 in 2004, with the number of live births only falling slightly from 750 down to 638. These changes reflect both the increasing maternal age in England and Wales and also the increasing number of pregnancies that are being screened for Down syndrome. Since the rate of natural fetal loss in Down syndrome is very high, the potential losses in those diagnosed and subsequently terminated early must be considered when looking at trends. In figure 1 the numbers of prenatal diagnoses outlined in bold are the numbers of fetal losses that would have been expected to occur in the prenatally diagnosed pregnancies that were terminated. These numbers represent the increases in Down syndrome diagnoses that are directly attributable to more screening being performed. After adjusting for these fetal losses the remaining increases are directly

attributable to increases in maternal age since the maternal age-related risk of a Down syndrome pregnancy has not changed.[3]

From 1989 to 2004 the proportion of women deciding to have a termination on receiving a prenatal diagnosis of Down syndrome has remained constant at around 92%. Of all prenatal diagnoses only 6% result in a live birth with the remaining 2% being miscarried or still born.

Reasons for Karyotyping amongst prenatal diagnoses of Down syndrome

In 1989 the most common reason for having a prenatal karyotype was advanced maternal age (77%). Serum screening was just starting to be performed (6%) with the remainder of prenatal karyotypes due to late ultrasound scans detecting various fetal anomalies. This picture has changed since then (figure 2 and table 2), with serum screening becoming increasingly common up until 1996 and an increasing number of women receiving a routine fetal anomaly scan. In 1996 36% of the karyotypes were due to serum screening, and 25% due to late ultrasounds. Since 1994, measuring nuchal translucency (NT) has become more frequent and now accounts for 39% of all prenatal karyotypes, with serum screening decreasing to 13% and ultrasound anomaly scans rising to 29%. Recently developed screening tests combining serum screening with NT measurements are increasingly common, accounting for 8% of diagnoses in 2004. The use of maternal age alone as an indication for karyotyping has decreased steadily, and in 2004 it was given as a sole indication in only 8% of prenatal diagnoses.

Tissue used for Karyotyping

In 1989, 77% of karyotyped tissue was from amniocentesis and 18% from chorionic villus sampling (CVS). In 2004, 51% were from amniocentesis and 47% from CVS. The number of amniocenteses compared to the number of CVSs reflects how early a diagnostic test is requested, which in turn reflects how early screening for Down syndrome occurs. In 1993, when serum screening (performed in the 2nd trimester) was at its most common, the median gestation at which the sample for karyotyping was obtained was 17 weeks. With the rise in NT screening, which occurs around 10-13 weeks, the median gestation has fallen to 15 weeks and there has been a corresponding increase in the number of samples obtained by CVS.

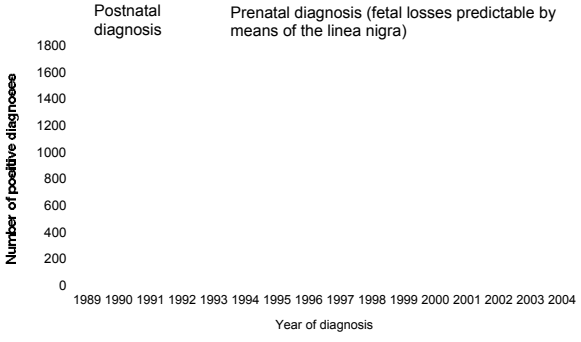

Figure 1 : The number of prenatal and postnatal diagnoses of Down syndrome in England and Wales according to year of diagnosis.

Table 1
Down syndrome diagnoses and outcomes in England and Wales from 1989 to 2004*

Year	No. Diag-noses	% of prenatal diagnoses	No. Live bom	No. TOP	No. misc/+ Still	No. Unknown outcome
1989	1.067	30	750	293	16	8
1990	1.095	34	738	328	17	12
1991	1.144	38	735	369	31	9
1992	1.146	44	662	442	24	18
1993	1.155	48	622	507	18	8
1994	1.234	50	638	542	29	25
1995	1.214	54	579	578	32	25
1996	1.304	55	606	651	31	16
1997	1.390	53	667	658	40	25
1998	1.297	54	632	609	21	35
1999	1.315	55	606	642	31	36
2000	1.365	59	591	686	23	65
2001	1.365	60	571	666	30	98
2002	1.448	61	590	686	41	131
2003	1.444	59	625	635	31	153
2004	1.659	62	638	640	58	323
Total	20.642	52	10.250	8.932	473	987

+ Only miscarriages after prenatal diagnosis are included.
* 2004 data are provisional.

Conclusion

Since 1989 there have been rapid and dramatic changes in screening for Down syndrome in England and Wales. The total numbers of Down syndrome diagnoses have increased by 55% and the number that are detected prenatally has increased by over 300%, with these diagnoses occurring earlier in pregnancy, mainly due to the increase in nuchal translucency screening.

Figure 2 : Indication for karyotyping according to year of diagnosis.

Table 2
Down syndrome prenatal diagnoses in England and Wales : 1989 to 2004*

Year	No. prenatal diagnoses	% of Indication for Karyotyping						
		Serum	Serum <15 weeks	Serum + serum <15 weeks	serum ⩾15 weeks	Ange only reason	Other reasons	Total
1989	321	6	0	0	13	77	4	100
1990	374	16	0	0	16	63	4	100
1991	430	23	1	0	22	50	5	100
1992	500	34	2	0	24	36	4	100
1993	558	38	5	0	23	30	4	100
1994	613	38	7	0	24	27	4	100
1995	660	34	14	0	26	22	4	100
1996	721	36	16	0	25	20	3	100
1997	739	34	21	0	28	15	2	100
1998	704	29	22	0	29	18	3	100
1999	729	31	21	1	29	15	3	100
2000	811	30	27	1	28	12	1	100
2001	819	21	24	4	36	14	2	100
2002	888	24	29	5	29	11	1	100
2003	850	19	37	5	25	12	2	100
2004*	1.021	13	39	8	29	8	4	100
Total	10.738	27	20	1	26	22	3	100

* 2004 data are provisional.

Table 3
Tissue sample for karyotyping of prenatal diagnoses in England and Wales : 1989 to 2004*

Year of diagnosis	Proportion of tissue karyotyped			
	CVS	Amnio	Others	Total
1989	18	77	5	100
1990	16	76	8	100
1991	15	73	11	100
1992	11	79	11	100
1993	17	77	6	100
1994	23	69	8	100
1995	25	69	6	100
1996	30	65	5	100
1997	35	61	4	100
1998	36	61	3	100
1999	33	61	6	100
2000	38	60	3	100
2001	45	52	3	100
2002	43	55	2	100
2003	47	52	1	100
2004*	47	51	2	100
Total	33	62	5	100

* 2004 data are provisional.

References

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Acknowledgements

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