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The Journal of Obstetrics and Gynaecology

Journal of Obstetrics and Gynaecology

ISSN: 0144-3615 (Print) 1364-6893 (Online) Journal homepage: http://www.tandfonline.com/loi/ijog20

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To cite this article: J Dixon, M Pillai, D Mahendran & M Brooks (2004) An assessment of the Down syndrome antenatal screening policies of East and West Gloucestershire between 1993 and 1999, Journal of Obstetrics and Gynaecology, 24:7, 760-764, DOI: 10.1080/01443610410009444

To link to this article: https://doi.org/10.1080/01443610410009444

Published online: 02 Jul 2009.

Journal of Obstetrics and Gynaecology (October 2004) Vol. 24, No. 7, 760–764

Taylor & Francis
healthsciences

OBSTETRICS

An assessment of the Down syndrome antenatal screening policies of East and West Gloucestershire between 1993 and 1999

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Summary

This retrospective observational study of registered pregnancies in Gloucestershire between 1 April 1993 and 31 March 1999 compares the impact of different Down syndrome antenatal screening policies on detection and amniocentesis rates. The screening policies in East and West Gloucestershire are based on early second-trimester maternal serum and maternal age screening, respectively. Maternal serum screening can identify a greater proportion of pregnancies affected by Down syndrome than a programme founded on age-based amniocentesis and 20 weeks' ultrasound. In addition, maternal serum screening of women older than 34 approximately halves the number of amniocenteses performed to detect one affected fetus. However, the proportion of pregnant women who have amniocentesis is nearly doubled by offering serum screening to women aged over 24 years. These findings of the impact of established second-trimester screening policies in low-risk populations provides an useful benchmark to compare the performance of screening procedures that will be introduced in the United Kingdom over the next 3 years.

Introduction

Although the Royal College of Obstetricians and Gynaecologists (RCOG) reviewed antenatal Down syndrome screening in 1993 (RCOG, 1993), its recommendation of offering women serum screening to identify those pregnancies at significant risk of being affected was implemented inconsistently across the country, owing principally to the absence of authorities' national standards and financial support for implementation (National Screening Committee, 1998). Therefore, in the late 1990s, where screening was offered, it could be based on serum biochemical screening, nuchal translucency or invasive diagnostic testing offered on the basis of maternal age.

The United Kingdom government's announcement of the NHS Plan (July 2000) set a target of a nationwide Down syndrome screening programme by 2004. In April 2001, the Minister for Public Health announced initiatives to establish a Down syndrome screening programme open to all women irrespective of age, based as a minimum on the double test.

In April 2003, the Serum, Urine and Ultrasound Screening Study (SURUSS) report on first- and second-trimester screening for Down syndrome was published (Wald *et al*., 2003), followed by national guidelines from the Antenatal Subcommittee of the National Screening Committee (National Screening Committee, 2003) and the RCOG/National Institute for Clinical Excellence (National Collaborating Centre for Women's and Children's Health, 2003) later in the year. National best practice guidelines set a standard of 60% detection rate (DR) with 5% false positive rate (FPR) for Down syndrome screening by April 2004, with a target of 75% DR and 3% FPR to be achieved by April 2007 (Department of Health website, 2003). The SURUSS report recommended the adoption of the integrated test, serum-integrated combined test and quadruple test, as they should achieve a DR of 85% with FPRs of 1.3, 2.7, 6.1 and 6.2%, respectively (Wald *et al*., 2003), and meet the targets set for April 2007. In the same report, maternal serum screening based on the double test (α-fetoprotein and β-human chorionic gonadotrophin) was not supported because of its reported low detection rate (66%) and variable FPR.

Until April 2005, it is likely that the double test (used by 107 of 207 screening programmes in June 2003) will continue to be offered by many hospital trusts in England while they modernise their facilities to meet the new national standards. Therefore the performance of the double test and other screening regimens will continue to be relevant to an assessment of the quality of antenatal screening in the United Kingdom.

It was suggested that the performance of maternal serum screening programmes were overstated when compared with programmes that relied on maternal age-based amniocentesis and ultrasound anomaly scanning. Howe *et al*. reported a 68% Down syndrome antenatal detection rate in a tertiary referral hospital in Southampton, UK, using a screening method based on maternal age and mid-gestation scan (Howe *et al*., 2000). They concluded that the detection rate was considerably higher than assumed in maternal serum screening demonstration projects and proposed that the benefits of serum screening were exaggerated. Wellesley *et al*. (2002) reported similar Down syndrome detection rates (52 – 57%) in adjacent district hospitals that used either (i)

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ISSN 0144-3615 print/ISSN 1364-6893 online/04/070760-05
DOI: 10.1080/01443610410009444

maternal serum screening for all ages or (ii) maternal age with serum screening or nuchal translucency available to limited groups or (iii) maternal age > 35 years and anomaly scans.

The adoption of serum screening by one district general hospital in Gloucestershire, while the other adopted a policy similar to that described by Howe *et al*. (2000), permitted an assessment of the benefits and consequences of serum screening. This is the first direct comparison of offering vs. not offering serum screening with a dating scan in two adjacent obstetric units, who both offer a mid-gestation anomaly scan to all women and amniocentesis to women older than 34 years.

In May 1993, East Gloucestershire NHS Hospital Trust ('East Gloucestershire') started an 'opt-in' Down syndrome maternal serum screening service to women older than 24 years. Nuchal translucency screening for Down syndrome was not available as part of the National Health Service in Gloucestershire. There was a limited private service in the area and the number of women who used it was not known, but it was assumed to be a small minority during 1993–99. Women with a positive serum test, a history of a pregnancy affected by aneuploidy or older than 34 years were offered amniocentesis or chorionic villous sampling (CVS).

By contrast, West Gloucestershire NHS Trust did not offer serum screening for Down syndrome unless requested by a woman or her doctor. Serum samples from East and West Gloucestershire were tested in the same laboratory. The indications for amniocentesis and chorionic villous sampling before 17 weeks' gestation to women were the same in both districts.

Both districts offered amniocentesis if anomalies associated with Down syndrome were found by a mid-gestation fetal anomaly scan.

Methods

Confirmation of gestational age by ultrasound was offered in East Gloucestershire at about 15 weeks' gestation. If maternal serum screening was accepted, a blood sample was collected between 15 and 19 weeks' gestation and α-fetoprotein and free β-human chorionic gonadotrophin concentrations were determined (the double test). Serum assays, gestational age, maternal age and weight were used by Swiftlab Biochemistry Pregnancy Screening Software (EDS Healthcare, Bristol, UK) to calculate the risk of Down syndrome. The 'high-risk' threshold for Down syndrome was increased from 1 : 250 to 1 : 200 in January 1994.

Pregnancies affected by Down syndrome between May 1993 and April 1999 were identified from the regional cytogenetic laboratory records and the Gloucestershire Community Paediatric Service register. Details of maternal age, screening tests offered and results, diagnostic tests offered and indications, pregnancy outcome and ultrasound findings were retrieved from the medical notes of women with an affected pregnancy. Computer records were checked to establish if a double test had been performed. Maternity services computer records supplied data on annual pregnancy bookings, deliveries and maternal age distribution.

Categorical data were analysed by the χ^2 test or Fisher's exact test. Parametric data were tested for normality and equal variance before statistical comparison using *t*-test. Statistical data analysis was performed using Sigmastat version 2.0 (Jandel Corporation).

Results

Study population (Table I)

Women booking their pregnancies in West Gloucestershire were significantly younger than in East Gloucestershire (χ^2 test $p < 0.001$).

Down syndrome cases (Table I)

East Gloucestershire. Down syndrome affected 31 pregnancies. Twenty-one cases were identified antenatally by amniocentesis at 15–17 weeks' gestation because of maternal age ($n = 5$) and positive serum test ($n = 16$). Three other cases were identified after intrauterine death before 18 weeks' gestation. Twenty affected pregnancies were terminated. A 33-year-old woman with a true positive serum screening test accepted amniocentesis only after a cardiac anomaly was diagnosed. Her baby was live-born, but later died. There were seven other live births of babies with Down syndrome, three of whose mothers had false negative serum screening results. Of the remainder, three declined serum screening and one, younger than 25 years, was not offered serum screening.

West Gloucestershire. Down syndrome affected 35 pregnancies. Sixteen cases were identified antenatally by anomalous 20-week ultrasound ($n = 6$), maternal age ($n = 6$), maternal serum test ($n = 2$) and first-trimester nuchal translucency measurement ($n = 2$). One 38-year-old woman had a negative serum test (1 : 250 in 1997), but later had a positive invasive test after a fetal cardiac defect was detected at 22 weeks' gestation. Her baby was born at term.

Two other affected fetuses were identified after intrauterine death at 18 and 28 weeks' gestation in women aged 27 and 36, respectively. Fifteen pregnancies affected by Down syndrome were terminated. Of the pregnant population in West Gloucestershire, 1.6% had a double test, of whom two women aged 30 and 34 years had true positive results and one woman had a false negative result. There were 17 unexpected live births of babies with Down syndrome.

The distribution of Down syndrome cases by maternal age (Fisher's exact test $P = 0.14$) and antenatal and postnatal detection rates of Down syndrome (Fisher's exact test, $P = 0.12$) in East and West Gloucestershire were not significantly different.

Antenatal invasive testing for Down syndrome (Tables II and III)

The invasive test rate in West Gloucestershire (4.4%: 95% confidence interval 3–5.9%) was significantly less than in East Gloucestershire (7.6%: 95% confidence interval 6.6–8.6%; *t*-test $P < 0.001$). The invasive test rates in women older than 34 in West Gloucestershire and in the 25–34 age group in East Gloucestershire were significantly higher (χ^2 test, $P < 0.001$ and $P < 0.001$, respectively) than in the opposite side of the county.

Table I. New cases of Down syndrome in Gloucestershire 1993–99

	Age group (years)					
	East Gloucestershire			*West Gloucestershire*		
	< 25	*25–34*	*> 34*	*< 25*	*25–34*	*> 34*
Number of registered pregnancies (%) (χ^2 test $P < 0.001$)	3806 (25%)	8713 (59%)	2344 (16%)	6875 (29%)	14305 (61%)	2432 (10%)
Number of cases	1	11	19	1	18	16
Cases diagnosed in the antenatal period (excluding IUD)	0	6	15	0	6	10
Primary method of screening						
Serum test		6	10		2	0
1st-trimester scan	0	0	0	0	0	2
18–20-week scan	0	0	0	0	4	2
Maternal age > 34			5			6
Cases diagnosed after live birth	1	4	2	1	11	5
Cases diagnosed after intrauterine death	0	1	2	0	1	1

Table II. Antenatal invasive test (amniocentesis and chorion villus sampling) rates for Down syndrome in Gloucestershire 1993–98

		1993	*1994*	*1995*	*1996*	*1997*	*1998*	*1993–98*
East Gloucestershire	Tests	201	186	163	179	192	207	1128
	Bookings	2370	2448	2322	2484	2623	2616	14863
	%	8.5	7.6	7	7.2	7.3	7.9	7.6
West Gloucestershire	Tests	136	161	153	206	199	187	1042
	Bookings	4175	4064	3851	3877	3869	3776	23612
	%	3.3	4	4	5.3	5.1	5	4.4

Table III. Antenatal invasive testing for Down syndrome in Gloucestershire 1993–99

	Age group (years)					
	East Gloucestershire			*West Gloucestershire*		
	< 25	*25–34*	*> 34*	*< 25*	*25–34*	*> 34*
Indication for test						
Positive serum test	20	370	320	3	33	41
Maternal age or request	1	26	320	0	0	868
Ultrasound anomaly	7	12	10	18	30	9
Previous history of aneuploidy	4	17	21	3	24	13
Total	32	425	671	24	87	931
Rate (total/population)	0.8%	4.8%	29%	0.3%	0.61%	38%
Invasive tests to detect an affected fetus		71	45		15	93
Invasive test acceptance rate after positive serum test	87%	93%	86%			

Maternal serum test statistics in East Gloucestershire (Table IV)

Fetal losses after invasive testing in East Gloucestershire (Table V). The causes of death in two cases were proven to be unrelated to the procedure. A cause was not found in the other three cases. Six of 1128 miscarriages might have been procedure related. The equivalent miscarriage rate in the untested population is unknown.

Discussion

Principal findings

In East Gloucestershire, the Down syndrome antenatal detection rates (excluding intrauterine deaths) in the 25–34

Table IV. East Gloucestershire maternal serum test statistics 1993–98

	Maternal age group (years)				
	< 25	*25–34*	*> 34*	*> 24*	*All ages*
Bookings	3806	8713	2344	11057	14863
Tested	610	5753	1236	6989	7599
% uptake	16%	66%	53%	63%	51%
Positive test	23	398	370	768	791
% positive	3.8%	6.9%	29.9%	11%	10.4%
True positive	0	6	10	16	16
False positive	23	392	360	752	775
True negative	587	5353	865	6218	6808
False negative	0	2	1	3	3
Sensitivity	–	75%	91%	84%	84%
Specificity	96%	93%	70.6%	89%	89.7%
False Positive rate	3.8%	6.8%	29.4%	10.8%	10.2%
Positive Predictive value	0%	1.5%	2.7%	2%	2%
Effectiveness*	0	11	3.1	7.8	8.3

*The effectiveness of the test is a measure of how well a test distinguishes between affected and unaffected individuals, and is expressed as sensitivity divided by false positive Rate (Grudzinskas and Ward. 1997).

Table V. Fetal losses after amniocentesis or CVS (excluding terminations for abnormal results or other problems) in East Gloucestershire 1993–99

Year	*Amnio/CVS*	*Miscarriages*	*IUD at 20-week scan*
1993–94	201	0	1
1994–95	186	1*	0
1995–96	163	0	1
1996–97	179	1**	0
1997–98	192	0	1
1998–99	207	1	2***
Total	1128	3	5

*24 hours after procedure; **3 weeks after procedure; *** unrelated.

and > 34 age groups were 60% and 83%, respectively, and 35% and 67% in West Gloucestershire. The 77% overall antenatal detection rate in East Gloucestershire was considerably better than several maternal serum and age based Down syndrome screening demonstration projects (RCOG 1993). The sensitivity of the double test in East Gloucestershire was 84% at best, and the false positive rate was 10.2%, which is similar to the 85% DR and 13% FPR described in the SURUSS report (Wald *et al*., 2003). Both the DR and FPR would be adversely affected if undetected false negatives were taken into account.

Amniocentesis rates

Maternal age > 34 was the principle indication for invasive testing in West Gloucestershire, whereas a positive maternal serum result in women aged 25–34 was the main indication and cause of the significantly higher amniocentesis rate in East Gloucestershire.

Serum screening in the > 34-year age group in East Gloucester was associated with a substantial reduction in the number of amniocenteses required to detect an affected fetus compared to age-based amniocentesis in West Gloucestershire. Conversely, although biochemical screening in East Gloucestershire ensured that the antenatal detection rate in the 25–34-year age group was better than West Gloucestershire, 71 amniocenteses were necessary to detect an affected fetus, compared to only 15 in West Gloucestershire. Despite this, miscarriages of normal fetuses were fewer than detected Down syndrome cases because the pregnancy loss rate after invasive testing was less than 1 : 180 in East Gloucestershire between 1993–99 (Table V), equivalent to 53 procedure related losses per 100 000 women screened, which is lower than the 65–94/100 000 reported in SURUSS. Nevertheless, this rate is considerably higher than 9 and 19 /100 000 predicted for the integrated and serum integrated tests (Wald *et al*., 2003).

The invasive testing uptake rate after a positive double test of 86–93% was appreciably higher than the 43–77% reported for the United Kingdom (National Collaborating Centre for Women's and Children's Health, 2003), but similar to the 90% amniocentesis/CVS uptake rate assumed in the SURUSS safety calculations.

East Gloucestershire's screening policy

The acceptance rate of the double test suffered a steady decline from 67% in 1993–94 to 47% in 1998–99 in East Gloucestershire. The highest acceptance rate was 66% in the 25–34-year age group.

The effectiveness of the double test (sensitivity divided by false positive rate) was best in the 25–34-year age group. The overall false positive rate was considerably higher than 5% and may reflect the skewed age distribution towards older mothers. A threshold nearer 1 : 100 may be necessary to reduce the false positive rate to 5%; however this would adversely affect the detection rate.

West Gloucestershire

The West Gloucestershire screening policy achieved a 48% detection rate, which may fall to 36% without the contribution of serum and nuchal translucency screening. As the proportion of cases detected by routine anomaly

ultrasound and age-based amniocentesis are equal, the 15% detection rate assumed for age-based amniocentesis programmes by the RCOG (1993) appears justified in this population, where 10% of the population were > 34 years.

The detection rate of an age-based screening programme is determined by the proportion of affected pregnancies found in women older than the age threshold and the amniocentesis acceptance rate. In West Gloucestershire, 46% of pregnancies affected by Down syndrome occurred in the > 34-year age group, of whom 36% opted for amniocentesis. The difference between the actual 48% and predicted 16% detection rates may reflect the contribution of second-trimester ultrasound anomaly screening, and *ad-hoc* nuchal translucency measurement and the double test. The double test was more acceptable than age-based screening in the > 34-year age group where both policies achieved their highest detection rates.

Discussion of previous studies

The Down syndrome antenatal detection rate in West Gloucestershire (48%) is lower than the 68% (95% CI 56–80%) reported by Howe *et al*. using a similar screening programme during the same period. Although 10% of the population were older than 34 in West Gloucestershire and Southampton, there was considerable disparity between the proportion of cases detected by ultrasound (38% vs. 8%) and maternal age (38% vs. 61%) (Howe *et al*., 2000).

This study found the 63% acceptance rate of Down syndrome screening to be less than the 100% assumed when the RCOG considered economic aspects of serum screening and the 80% described by Wald *et al*. (1997). However, it is representative of the variable 7–90% uptake rate reported in England (Ward and Gray, 2002). The 38% acceptance rate of age-based amniocentesis in West Gloucestershire was also less than the 50% assumed when the RCOG considered the economic aspects of serum screening.

Conversely, the acceptance rate of invasive testing after a positive screening result was higher than the reported 80% (Wald *et al*., 1997). These discordant observations may, in part, explain and support Howe *et al*.'s (2000) contention that the actual Down syndrome detection rate of a serum screening programme is less than predicted in demonstration projects, possibly because of discrepancies in predicted and actual acceptance rates of the different screening programmes.

Our findings show that in Gloucestershire, between 1993 and 1999, the double test identified a greater proportion of pregnancies affected by Down syndrome than a programme founded on age-based amniocentesis and 20-week ultrasound.

This study demonstrates the contribution of the double test, amniocentesis based on maternal age and mid-trimester anomaly scan to Down syndrome screening in a clinical setting, and provides an useful standard to compare the performance of new screening procedures set to be introduced in the next 3 years.

References

Department of Health (2003) Model of best practice for providing Down's Syndrome screening services. Available at http://www.nelh.nhs.uk/screening/dssp/modelbestpractice.pdf

Grudzinskas J.G. and Ward R.H.T. (eds) (1997) *Screening for Down Syndrome in the First Trimester*. London, RCOG Press.

Howe D.T., Gornall R., Wellesley D., Boyle T. and Barber J. (2000) Six year survey of screening for Down's syndrome by maternal age and mid-trimester ultrasound scans. *British Medical Journal*, **320**, 606–610.

National Collaborating Centre for Women's Health and Children's Health (2003) Screening for Fetal Amonolies. In: *Antenatal Care: routine care for the healthy pregnant woman*, edited by Moody J., pp. 72–78. London: RCOG Press.

National Screening Committee (1998) *First Report of the UK National Screening Committee*. Available at http://www.nsc.nhs.uk/pdfs/nsc.firstreport.pdf

National Screening Committee (2003) *Antenatal Screening for Down's Syndrome—Policy and Quality Issues*. Available at http://www.nelh.nhs.co.uk/screening/dssp/dssp_policy.pdf

Royal College of Obstetricians and Gynaecologists (RCOG) (1993) *Report of the Working Party on Biochemical Markers and the Detection of Down's syndrome*. London, RCOG Press.

Wald N.J., Kennard A., Hackshaw A. and McGuire A. (1997) Antenatal screening for Down's syndrome. *Journal of Medical Screening*, **4**, 181–246.

Wald N.J., Rodeck C., Hackshaw A.K., Walters J., Chitty L. and Mackinson A.M. (2003) First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). *Health Technology Assessment*, **7**(11), 1–77.

Ward P. and Gray J. A. M. (2002) Antenatal Screening Service for Down Syndrome in England, 2001. Oxford, UK. National Screening Committee Programmes Directorate. Available at http://www.nelh.nhs.uk/screening/dssp/down-survey.pdf

Wellesley D., Boyle T., Barber J. and Howe D.T. (2002) Retrospective audit of different antenatal screening policies for Down's syndrome in eight district general hospitals in one health region. *British Medical Journal*, **325**, 15–20.