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Non-invasive prenatal testing for trisomy 21: a cross-sectional survey of service users' views and likely uptake

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Objective To assess the views and likely uptake of non-invasive prenatal testing (NIPT) for trisomy 21 among potential service users in the UK.

Design Cross-sectional survey.

Setting Four antenatal clinics in England and two websites.

Sample A total of 1131 women and partners.

Methods Questionnaire conducted with women (and partners) recruited through antenatal clinics, a random sample of members of the website Mumsnet, and viewers of the website and Facebook page of the support group Antenatal Results and Choices (ARC).

Main outcome measures Factors impacting decision-making towards prenatal testing; views on NIPT, including service delivery and likely uptake; hypothetical scenarios, focused on current screening, invasive testing, and NIPT offered to women with a high-risk screening result.

Results The vast majority (95.7%; 1071/1119; 95% CI 94.4–96.8%) thought NIPT was a positive development in prenatal care, with 88.2% (972/1103; 95% CI 86.1–90%) indicating that they would use the test, including respondents who would currently decline trisomy 21 screening ($P < 0.001$). Of the respondents who would have NIPT, 30.7% (299/973; 95% CI = 27.8–33.7%) said that they were 'likely' to terminate an affected pregnancy (including those who would currently decline screening or invasive testing), and 36.5% (355/973; 95% CI 33.5–39.6%) were 'not likely' to terminate an affected pregnancy. Respondents overwhelmingly indicated that safety for the baby was the most important attribute of NIPT (70.1%; 712/1015; 95% CI 67.2–73%).

Conclusion Respondents were overwhelmingly positive towards the introduction of NIPT. Uptake is likely to be high, and includes women who currently decline screening as well as those who will use the test for information only. Pre-test counselling to ensure that women understand the implications of the test result is essential.

Keywords Aneuploidy, cell-free fetal DNA, non-invasive prenatal testing, trisomy 21.

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Introduction

Formal programmes that offer prenatal screening and diagnosis for trisomy 21 to pregnant women are well established in the UK, Europe, and the USA.[1,2] These tests, frequently delivered in the first trimester by a combination of fetal ultrasound and maternal serum biomarkers,[3] provide an individualised risk estimate of the fetus being affected. Women identified as high risk (≥1:150, in the UK) are then offered invasive testing, either by chorionic villus sampling (CVS) from 11 weeks of gestation or by amniocentesis from 15 weeks of gestation, for a definitive diagnosis.[4] These tests carry a small but significant risk of miscarriage (0.5–1.0%).[5]

Rapid advances in non-invasive prenatal testing (NIPT) based on cell-free fetal DNA in maternal plasma have now made it possible to identify pregnancies affected by trisomy 21 from 10 weeks of gestation, with high accuracy (>99%) and a low false-positive rate (0.1%), via a blood test.[6–10] Detection rates are also high for trisomy 18 (>99%) and trisomy 13 (up to 90%).[11–14] NIPT has two key clinical advantages over invasive testing: it carries no risk of

miscarriage, and can be conducted early in pregnancy. The test, however, is not currently considered fully diagnostic, and therefore requires invasive testing to confirm a positive result.[15,16]

Implementation of NIPT for trisomy 21 into state-funded healthcare systems has not yet been initiated (although testing is now available through the private sector), and there is widespread discussion about how best to bring NIPT into routine clinical practice within the UK's National Health Service (NHS).[17,18] This includes how to offer NIPT within the current prenatal testing pathway in the NHS: as a screening test offered to all pregnant women; as a contingent screening test offered to women with a high-risk screening result; or as a replacement for invasive testing. There are important economic implications attached to each of these possibilities. For example, if NIPT were offered to all women, more trisomy 21 cases would be detected but costs would increase.[17] At present, it seems likely that NIPT will initially be offered as a contingent test. This approach would allow for the preservation of the benefits of the current trisomy 21 screening tests, which includes the identification of common aneuploidies and other pregnancy complications,[3] and could be cost-effective.[17,19] To guide implementation, a small number of qualitative studies have been conducted.[20,21] These have highlighted that NIPT for trisomy 21 is perceived as a positive advancement in prenatal care, and that uptake is likely to be high.[21] Currently, however, no large-scale quantitative research has been carried out with women (and partners) in the UK. This research is important in order to quantify the expected uptake and generalise findings to a larger population of interest. A quantitative survey is therefore timely.

Methods

Ethics approval

Approval for this study was obtained from an NHS Research Ethics Committee (10/H0724/41) in June 2010.

Participants and setting

A cross-sectional survey using a questionnaire was conducted (Appendix S1). Survey respondents were recruited in one of three ways.

1 Pregnant women (and their partners) over 18 years of age, and who had an adequate understanding of written English, were purposively sampled through one of four antenatal clinics located across England (London, West Midlands, Yorkshire, and North West England). Potential participants were invited to complete a paper survey whilst waiting for their antenatal appointment.
2 A random sample of members of the website Mumsnet, a site providing parenting tips and advice for parents and soon-to-be parents, were invited to complete the survey online via an email alert.
3 A notice placed on the Antenatal Results and Choices (ARC) website and Facebook page invited viewers to follow a link to complete the survey online (opportunistic sampling). ARC is a charity providing non-directive support and information to people throughout and after the antenatal screening and testing process.

The rationale behind recruiting from different sources was to enable the comparison of participants from different backgrounds and with different experiences of prenatal testing. For example, participants recruited through ARC would be expected to have had difficult or traumatic experiences in previous pregnancies, and thus may have different views towards NIPT than those recruited through antenatal clinics. At the time of completing the survey, participants were given a participant information sheet explaining the study. This included the phone number of one of the research team in case of any questions, and a helpline number for ARC in case any concerns around prenatal testing arose as a result of taking part in the study. The surveys were completed anonymously; however, respondents were given the option of giving their email address so that they could be entered into a prize draw to win a £100 gift voucher. The email address was kept separately from the survey responses, and was not used for any other purpose. The online survey was hosted by the secure website SurveyMonkey (Survey Monkey Inc., Palo Alto, California, USA).

Questionnaire design

This was a descriptive survey to inform clinical practice. As such, we did not include validated measures. Many of the questions, including the closed-question response options, were informed by our previous qualitative work in this area.[21] To refine the questions, a modified Delphi technique of two consultation rounds was conducted with the RAPID (Reliable, Accurate Prenatal, non-Invasive Diagnosis) psychosocial research group, which includes health professionals from a variety of backgrounds, including fetal medicine, midwifery, genetic counselling, psychology, and the director of the ARC. At each stage questions were added or eliminated and then categorised into domains.

The questionnaire comprised four sections: (1) factors impacting decision-making towards prenatal testing; (2) views on NIPT, including service delivery and likely uptake; (3) scenarios asking people to place themselves in hypothetical antenatal situations that were designed to gather views of various screening and diagnosis pathways, including current screening, invasive testing offered to women with a high-risk screening result, NIPT offered to women with a high-risk screening result, and NIPT offered direct to consumer (DTC) over the internet; and (4) demographic questions. Each question focused on a single construct. Factors impacting decision-making were measured using a

five-point Likert scale (1, extremely important; 5, not at all important). To ascertain agreement with statements, we used the options 'Definitely yes', 'Probably yes', 'Probably not', 'Definitely not', and 'Not sure'. Single-response questions and multiple-response questions were also included. All questions were closed-question responses.

In the survey, we described NIPT as a blood test from the mother's arm, with no risk of miscarriage, and which is over 99% accurate (in comparison with invasive testing, which was described as giving a definitive yes or no answer), and that it is likely to be offered from around 11 weeks of gestation. In line with the National Screening Committee's focus on trisomy 21 in the existing screening programme, the survey only describes the screening and diagnosis of trisomy 21, and does not include the detection of trisomy 18 and trisomy 13.

A pilot survey was conducted with 25 people recruited through one antenatal clinic. Participants were asked to complete the survey whilst waiting for their appointment and then take part in a short face-to-face interview to discuss the survey length, layout, and answerability, and to check whether all the relevant response categories were included. Minor changes to the wording were made at this stage. On average, it took participants 13.5 minutes to complete the survey. Given that women usually wait 10–15 minutes for their antenatal appointment, we considered that the vast majority of women would be able to complete the survey prior to their appointment. We did, however, provide freepost envelopes at reception for those women who wanted to return the survey by post. Based on a confidence level of 95%, a confidence interval of 4% (based on responses to pilot study questions), and a population size of 723 000 (the number of births in England in 2011), and using a power calculation tool (www.surveysystem.com/sscalc.htm), we calculated that we would need a sample size of 600.

Analysis

Data were analysed using SPSS 18 (IBM, Chicago, IL, USA). Analysis included descriptive statistics on single items; on the agreement scale, 'Definitely yes' and 'Probably yes' (and 'Definitely no' and 'Probably no') were collapsed together to yield a dichotomous index of agreement. The relationship between variables was examined using the chi-square test for categorical variables, and using the Student's *t*–test or analysis of variance (ANOVA) for continuous variables. Data from the five-point Likert scale were treated as ordinal and analysed using the Mann–Whitney *U*–test (as data were not normally distributed). McNemar's test was used to compare paired proportions. For all tests, $P < 0.05$ was considered to be statistically significant. As there were a small number of missing cases on each variable relative to the total sample size, cases that had missing values were omitted from the analysis using pairwise deletion. With this method, all available observations for each particular variable are used to calculate means and variances, whereas all available pairs of values are used to calculate covariances.[22]

Results

Sample characteristics

Data collection took place between September 2012 and March 2013. In total, 1138 people completed the survey: 623 were recruited through Mumsnet (623/6495, a 25% response rate; this relates to completed surveys only, as we are unable to detect how many people started but did not complete and submit the survey); 459 were recruited through antenatal clinics (459/481, a 95% response rate; this only relates to those who agreed or declined to complete the survey when approached, as we do not know how many agreed but did not return the survey); and 59 were recruited through the ARC (we are unable to calculate a response rate, as we cannot identify how many people viewed the survey invitation). We are unable to comment on reasons for nonparticipation. Seven respondents were omitted from the analysis because they were younger than 18 years of age. Therefore, a total of 1131 were included in the analysis. Overall, the sample consisted of a highly educated population who were predominantly white, with a mean age of 34.3 years (SD 6.7 years; range 18–58 years), the vast majority of whom were women (98.4%; Table 1). Seventy-two percent had screening in this or a previous pregnancy, 11.1% had been identified as high risk, and 9.1% had previously undergone invasive testing. Of those, 13.7% had a diagnosis of trisomy 21, and 13.7% had a diagnosis of another condition (Table 1). There were also significant differences between the antenatal clinics, Mumsnet, and ARC respondents in terms of participant demographics and prior experience. These are described in Table S1.

Psychosocial factors associated with decision-making

Table 2 lists the importance that respondents placed on a list of psychosocial factors (personal, social, and ethical) associated with decision-making about prenatal testing for trisomy 21, which had been identified as being significant in our prior research.[21] 'Not wanting to risk the safety of my baby' was considered the most important factor, followed by 'my wish to have as much information as possible about the baby' and 'the quality of life of a child with Down syndrome'. The least important factor was 'my family's religious beliefs' followed by 'the impact less people being born with Down syndrome would have on the disabled community' and 'my religious beliefs'. Most

Table 1. Sample characteristics

Characteristic	Total (%) *n* = 1131	Antenatal clinic *n* = 449	Mumsnet *n* = 623	ARC *n* = 59
Sex				
Female	1087 (98.4)	434 (96.7)	595 (98.2)	58 (100)
Male	18 (1.6)	7 (1.6)	11 (1.8)	0
Age				
18–34 years	582 (53.9)	311 (74.9)	244 (40.3)	27 (46.6)
35 + years	497 (46.1)	104 (25.1)	362 (59.7)	31 (53.4)
Education				
No qualification	12 (1.1)	10 (2.4)	2 (0.3)	0 (0)
GCSE or O level	78 (7.2)	49 (11.6)	26 (4.3)	3 (5.3)
GCE, A level, or similar	90 (8.3)	38 (9.0)	43 (7.1)	9 (15.8)
Vocational (BTEC/NVQ/Diploma)	191 (17.6)	112 (26.4)	75 (12.4)	4 (7)
Degree level or above	714 (65.8)	215 (50.7)	458 (75.8)	41 (71.9)
Ethnicity				
White or white British	980 (89.0)	360 (82.4)	565 (93.2)	55 (94.8)
Asian or Asian British	45 (4.1)	40 (9.2)	5 (0.8)	0 (0)
Black or black British	18 (1.6)	13 (3.0)	4 (0.7)	1 (1.7)
Mixed	27 (2.5)	9 (2.1)	16 (2.6)	2 (3.4)
Other ethnic group	31 (2.8)	15 (3.4)	16 (2.6)	0 (0)
Do you have a religious faith?				
Yes	444 (41.1)	189 (43.1)	234 (39.9)	21 (38.2)
No	636 (58.9)	250 (56.9)	352 (60.1)	34 (61.8)
If yes, which religion?				
Christian	357 (83.8)	130 (76.0)	207 (88.5)	20 (95.2)
Jewish	13 (3.1)	6 (3.5)	7 (3)	0 (0)
Muslim	17 (4.0)	15 (8.8)	2 (0.9)	0 (0)
Sikh	3 (0.7)	3 (1.8)	0 (0)	0 (0)
Hindu	20 (4.7)	17 (9.9)	3 (1.3)	0 (0)
Buddhist	1 (0.2)	0 (0)	1 (0.4)	0 (0)
Other	15 (3.5)	3 (1.8)	11 (4.7)	1 (1.7)
Relationship status				
Single	61 (5.5)	20 (4.6)	39 (6.4)	2 (3.4)
In a relationship	1039 (94.5)	417 (95.4)	566 (93.6)	56 (96.6)
Do you have children?				
Yes	848 (77.1)	231 (52.9)	582 (96.2)	35 (60.3)
No	252 (22.9)	206 (47.1)	23 (3.8)	23 (39.7)
Are you or your partner currently pregnant?				
Yes	507 (48.0)	439 (99.3)	58 (10)	10 (28.6)
No	549 (52.0)	0 (0.0)	524 (90)	25 (71.4)
If yes, how many weeks?				
0–12 weeks	30 (7.4)	10 (2.9)	17 (29.3)	3 (30)
13–27 weeks	185 (45.5)	157 (46.3)	23 (39.7)	5 (50)
28+ weeks	192 (47.2)	172 (50.7)	18 (31)	2 (20)
Have you or your partner had a screening test for Down syndrome in this or any previous pregnancy?				
Yes	760 (72.1)	341 (78.0)	387 (66.5)	32 (91.4)
No	277 (26.3)	95 (21.7)	180 (30.9)	2 (5.7)
Not sure	17 (1.6)	1 (0.2)	15 (2.6)	1 (2.9)
If yes, what was the outcome?				
High risk	85 (11.1)	27 (7.9)	42 (10.8)	16 (50)
Low risk	668 (87.4)	311 (90.9)	342 (87.7)	15 (46.9)
Not sure	11 (1.4)	4 (1.2)	6 (1.5)	1 (3.1)
Have you or your partner had an invasive test in this or any previous pregnancy?				
Yes	96 (9.1)	27 (6.2)	45 (7.7)	24 (68.6)
No	932 (88.8)	386 (89.1)	536 (92.1)	10 (28.6)
Not sure	22 (2.1)	20 (4.6)	1 (0.2)	1 (2.9)

Table 1. (Continued)

Characteristic	Total (%) *n* = 1131	Antenatal clinic *n* = 449	Mumsnet *n* = 623	ARC *n* = 59
If yes, what was the outcome?				
Diagnosis or Downsyndrome	14 (13.7)	4 (12.1)	0 (0)	10 (41.7)
Diagnosis of another condition	14 (13.7)	2 (6.1)	4 (8.9)	8 (33.3)
Normal result	68 (66.7)	23 (69.7)	41 (91.1)	4 (16.7)
Not sure	6 (5.9)	4 (12.1)	0 (0)	2 (8.3)
Do you have a child with Down syndrome?				
Yes	7 (0.7)	3 (0.7)	4 (0.7)	0 (0)
No	1047 (99.3)	434 (99.3)	578 (99.3)	35 (100)
Does anyone you know have a child with Down syndrome?				
Yes	491 (44.6)	151 (34.5)	315 (52.1)	25 (43.1)
N	610 (55.4)	287 (65.5)	290 (47.9)	33 (56.9)

In some cases numbers may not add up to total number because of missing data. Percentages may not add up to 100 as a result of rounding.

Table 2. Importance of factors associated with decision-making about prenantal testing for trisomy 21

When making a decision about antenatal testing for Down syndrome, factors that would influence my decision include…	Extremely important					
	1 (%)	2 (%)	3 (%)	4 (%)	Not at all important 5 (%)	Mean score
…not wanting to risk the safety of my baby	55.3	22.9	13.4	2.4	6.0	1.81
…my wish to have as much information as possible about the baby	50.9	22.2	13.9	6.6	6.4	1.97
…the quality of life of a child with Down syndrome	47.1	27.4	14	3.6	7.9	1.98
…whether I felt I could cope raising a child with Down syndrome	51.9	16.8	12.9	6.9	11.6	2.10
…my personal values and beliefs about termination of pregnancy	47.5	20.1	13.8	6.3	12.3	2.16
…my partner's attitude to having a baby with Down syndrome	44.5	22.1	13.3	7.5	12.6	2.22
…the impact of a child with Down syndrome on my family	39.0	23.9	17.8	7.6	11.7	2.29
…the support available in society for people with Down syndrome	32.5	27.5	18.5	10.1	11.5	2.41
… the advice of my midwife and other maternity care staff	20.7	28.7	30.0	11.1	9.8	2.61
…feeling that we should use all the medical tests available to us	24.5	20.8	25.7	12.3	16.7	2.76
…my personal experience of knowing people with a disability	18.2	21.6	30.0	13.5	16.7	2.89
…my wider family's attitude to having a baby with Down syndrome	12.6	17.6	23.3	18.8	27.7	3.31
…my family's values and beliefs about termination of pregnancy	13.9	13.1	20.9	17.8	34.3	3.46
…not wanting to interfere with nature	11.8	12.6	18.0	15.6	41.9	3.63
…preferring not to know too much about the baby till it's born	9.1	8.6	21.1	18.5	42.8	3.77
…my religious beliefs	13.9	6.9	11.2	9.4	58.7	3.92
…the impact less people being born with Down syndrome would have on the disabled community	6.3	5.6	17.4	15.4	55.4	4.08
…my family's religious beliefs	9.4	5.3	9.9	12.2	63.2	4.15

The lower the mean score, the more important the factor was. Percentages may not add up to 100% as a result of rounding.

respondents (63.8%) thought the final decision about antenatal testing should be a joint decision between the woman and her partner, and 35.0% thought it should be the woman's decision only.

Non-invasive prenatal testing

Views towards NIPT are shown in Table 3. The vast majority of respondents (95.7%) thought NIPT would be a positive development in antenatal care, and a similarly high number (95.7%) thought it should be offered to women. When asked whether they would have NIPT for trisomy 21, 88.2% of respondents said that they would. Of those, 1.5% said they would, but would prefer invasive testing.

Participant characteristics that were associated with being more likely to use NIPT included: having or knowing someone who has a child with trisomy 21 ($\chi^2 = 10.4$, $P = 0.001$); not having children ($\chi^2 = 9.04$, $P = 0.003$); and being of non-white ethnicity ($\chi^2 = 5.10$, $P = 0.024$). Having had screening in this or a previous pregnancy (χ^2 =214,

Table 3. Views of responders towards NIPT

	Total (%) *n* = 1131	Antenatal clinic *n* = 449	Mumsnet *n* = 623	ARC *n* = 59
Would you have NIPT?				
Yes	956 (86.7)	381 (87.6)	520 (85.2)	55 (87.9)
Yes, but I'd prefer invasive testing	16 (1.5)	12 (2.8)	4 (0.7)	0 (0.0)
No	91 (8.3)	27 (6.2)	63 (10.3)	1 (1.7)
Not sure	40 (3.6)	15 (3.4)	23 (3.8)	2 (3.4)
Single most important factor in decision about NIPT				
The safety of the baby	712 (70.1)	307 (75.2)	368 (67.0)	37 (63.8)
Accurate results	171 (16.8)	55 (13.5)	71 (12.9)	11 (19.0)
Results being available early	123 (12.1)	42 (10.3)	105 (19.1)	10 (17.2)
Convenience of the test	6 (0.6)	4 (1.0)	2 (0.4)	0 (0.0)
Test being freely available	3 (0.3)	0 (0.0)	3 (0.5)	0 (0.0)
Would NIPT be a positive development in antenatal care?				
Yes	1071 (95.7)	426 (95.3)	586 (95.6)	59 (100)
No	25 (2.2)	10 (2.2)	15 (2.4)	0 (0)
Not sure	23 (2.1)	11 (2.5)	12 (2.0)	0 (0)
Would you like to see NIPT being offered in antenatal care?				
Yes	1071 (95.7)	426 (95.3)	586 (95.6)	59 (100)
No	22 (2.0)	10 (2.2)	12 (2.0)	0 (0)
Not sure	26 (2.3)	11 (2.5)	15 (2.4)	0 (0)
Ideally, how do you think NIPT should be offered?				
Routinely to all pregnant women	560 (50.7)	213 (47.8)	310 (51.7)	37 (62.7)
To women identified as high risk through screening and women who ask for it, e.g. women at low risk who are still anxious	289 (26.2)	114 (25.6)	163 (27.2)	12 (20.3)
Only to women who have been identified as high risk through screening	232 (21.0)	106 (23.8)	117 (19.5)	9 (15.3)
Other	13 (1.2)	4 (0.9)	8 (1.3)	1 (1.7)
I don't think it should be offered	11 (1.0)	9 (2.0)	2 (0.3)	0 (0.0)
How much time would you want to make a decision about NIPT?				
I would make a decision during the appointment	742 (67.0)	306 (69.7)	388 (63.6)	48 (82.8)
I would want a few days to think about it	354 (32.0)	127 (28.9)	217 (35.6)	10 (17.2)
Not sure	11 (1.0)	6 (1.4)	5 (0.8)	0 (0.0)
Where would you want the test conducted?				
Don't mind	461 (47.8)	173 (44.0)	275 (53.2)	13 (23.6)
Antenatal clinic	384 (39.8)	186 (47.3)	161 (31.1)	37 (67.3)
GP surgery	99 (10.3)	25 (6.4)	72 (13.9)	2 (3.6)
Other	12 (1.2)	0 (0)	9 (1.7)	3 (5.5)
Not sure	9 (0.9)	9 (2.3)	0 (0)	0 (0.0)
Who should give you information about the test, including the test results?				
Midwife	415 (42.9)	159 (40.6)	234 (44.9)	22 (40.0)
Don't mind	250 (25.8)	117 (29.8)		1 (1.8)
Obstetrician	202 (20.9)	96 (24.5)	82 (15.7)	24 (43.6)
General practitioner	59 (6.1)	16 (4.1)	41 (7.9)	2 (3.6)
Other	25 (2.6)	0 (0)	25 (4.8)	0 (0.0)
Not sure	4 (0.4)	9 (2.3)	13 (2.5)	0 (0.0)
How would you want to receive the test results?				
In person	514 (52.9)	229 (58.0)	267 (51.2)	18 (32.7)
Depends on result	249 (25.6)	40 (10.1)	189 (36.3)	20 (36.4)
Don't mind	78 (8.0)	55 (13.9)	22 (4.2)	1 (1.8)
Phone	60 (6.2)	29 (7.3)	17 (3.3)	14 (25.5)
Letter	38 (3.9)	26 (6.6)	12 (2.3)	0 (0.0)
Email	16 (1.6)	10 (2.5)	5 (1.0)	1 (1.8)
Other	10 (1.0)	0 (0)	9 (1.7)	1 (1.8)
Not sure	6 (0.6)	6 (1.5)	0 (0.0)	0 (0.0)

In some cases numbers may not add up to the total number because of missing data. Percentages may not add up to 100 as a result of rounding.

$P < 0.001$), and being likely to have screening ($\chi^2 = 390$, $P < 0.001$), having had invasive testing ($\chi^2 = 10.4$, $P = 0.001$), and being likely to have invasive testing ($\chi^2 = 183$, $P < 0.001$), and being likely to terminate an affected pregnancy ($P = 0.002$) were also associated with the uptake of NIPT. ARC respondents were also significantly more likely to use NIPT compared with antenatal clinic or Mumsnet respondents ($\chi^2 = 9.92$, $P = 0.007$). Only one ARC respondent said that they would decline NIPT (Table S2).

There were also significant differences in the importance participants who would use NIPT placed on certain psychosocial factors, compared with those who would decline NIPT. NIPT 'accepters' were more likely to score 'feeling we should use all the medical tests available to us' ($P < 0.001$, $r = 0.28$), followed by 'my wish to have as much information as possible about the baby' ($P < 0.001$, $r = 0.27$), and 'the impact of a child with Down's syndrome on my family' ($P < 0.001$, $r = 0.20$) as most important. NIPT 'decliners' were more likely to score 'preferring not to know too much about the baby till it's born' ($P < 0.001$, $r = 0.22$), followed by 'not wanting to interfere with nature' ($P < 0.001$, $r = 0.16$), and 'not wanting to risk the safety of my baby' ($P < 0.001$, $r = 0.11$) as most important (Table S3).

When asked to identify the single most important factor in making a decision about NIPT, respondents overwhelmingly indicated that the safety of the baby (no risk of miscarriage) was most important (70.1%), followed by test accuracy (16.8%).

Service delivery

Half (50.7%) of respondents thought that NIPT should be offered routinely to all pregnant women; however, 26.2% thought that it should be offered to women identified as high risk through screening and to women who ask for it. The majority of respondents didn't mind where the test was conducted (47.8%), or preferred the test to be done at the antenatal clinic (39.8%). They wanted information about the test, including test results, to be provided by their midwife (42.9%), and preferred to receive the test results in person (52.9%), or said that it depended on the results (25.6%).

Regarding the time needed to make a decision about testing, 67.0% of respondents would make a decision about NIPT at the same appointment as pre-test counselling, and 32.0% would want a few days to think about it ($\chi^2 = 137.358$, $P < 0.001$). When asked the same question in relation to screening, 59.0% of respondents would make a decision about screening at the same appointment, and 38.4% would want a few days to think about it ($\chi^2 = 48.821$, $P < 0.001$). Concerning invasive testing, 25.9% would make a decision about invasive testing at the same appointment and 70.8% would want a few days to think about it ($\chi^2 = 223.819$, $P < 0.001$).

Comparison of screening pathways

When considering the current screening pathway (whereby women at high risk are offered invasive testing for definitive diagnosis), 77.7% of respondents indicated that they would have screening, and of those, 60.1% would have invasive testing. When considering a screening pathway in which NIPT was offered to women at high risk, however, 84.1% of respondents said that they would have screening. McNemar's test demonstrated that there was a significant increase in the number of people who would have screening if NIPT were available ($\chi^2 = 38.549$, $df = 1$, $P < 0.001$). Of the respondents who would currently decline screening, those aged 18–34 years were significantly more likely than those over 35 years to have screening if NIPT were available to women at high risk (50.4 versus 32.1%, $df = 1$, $\chi^2 = 6.516$, $P = 0.011$).

The most commonly cited reason to accept all three tests, particularly when considering invasive testing, was 'to help me make a decision about whether or not to continue with the pregnancy' (54.1% [screening], 72.3% [invasive testing], and 52.7% [NIPT]), followed by 'to plan and prepare for the birth of a baby with Down syndrome' (52.7, 42.7, and 52.6%, respectively). The most commonly cited reason for declining screening and NIPT was 'I would never terminate an affected pregnancy so there is no point taking the test' (69.9 and 85.3%, respectively); however, in the case of invasive testing, the most commonly cited reason for declining was 'I would never choose to have an invasive test and put my pregnancy at risk' (Table S4).

Using NIPT for information only

Of the respondents who would have NIPT ($n = 973$), 30.7% said that they were 'likely' to have a termination of pregnancy if the baby had trisomy 21, 36.5% said that they were 'not likely' to terminate their pregnancy, and 32.8% said that they were 'unsure'. Those respondents who would use NIPT for information only (i.e. would not have a termination) were significantly more likely to: have a religious affiliation ($\chi^2 = 13.9$, $P < 0.001$); have or know someone who has a child with trisomy 21 ($\chi^2 = 9.81$, $P = 0.002$); be under 35 years of age ($\chi^2 = 8.83$, $P = 0.003$); have existing children ($\chi^2 = 7.91$, $P = 0.005$); and have an education level of A level/vocational or lower ($\chi^2 = 7.45$, $P = 0.006$). They were also more likely to not have had screening in this or a previous pregnancy ($\chi^2 = 34.9$, $P < 0.001$), and would not be likely to have screening ($\chi^2 = 84.8$, $P < 0.001$), had undergone screening but were found to be low risk ($\chi^2 = 7.49$, $P = 0.006$), had not had invasive testing ($\chi^2 = 38.0$, $P < 0.001$), and would not be likely to have invasive testing ($\chi^2 = 253$, $P < 0.001$). Respondents recruited through

Mumsnet or antenatal clinics were significantly more likely to have NIPT for information only than people recruited through ARC ($\chi^2 = 34.8$, $P < 0.001$; Table S5).

Significant differences relating to the importance participants placed on psychosocial factors were also found between those who would be likely to terminate an affected pregnancy and those who would use NIPT for information only. For those who would be likely to terminate their pregnancy, 'whether I felt I could cope raising a child with Down syndrome' ($P < 0.001$, $r = 0.41$) was the most important factor, followed by 'the impact of a child with Down syndrome on my family' ($P < 0.001$, $r = 0.32$). For those who would use NIPT for information only, the most important factor was 'not wanting to interfere with nature' ($P < 0.001$, $r = 0.30$), followed by 'preferring not to know too much about the baby till it's born' ($P < 0.001$, $r = 0.21$; Table S6).

Termination of pregnancy

Of the respondents who would currently decline screening ($n = 225$), two (1.7%) said that they would be 'likely' to terminate an affected pregnancy and 16 (13.7%) were not sure. Of those who would currently decline invasive testing ($n = 320$), two (0.9%) said that they would be 'likely' to terminate an affected pregnancy and 32 (14.8%) were not sure. This suggests a slight increase in the number of terminations for trisomy 21 if NIPT was introduced.

Direct-to-consumer testing

If NIPT was available through the NHS, only 10.1% of respondents would order a test over the internet, 83.5% would not do so, and 9.7% weren't sure. The main reasons why respondents would not order a test online were because 'I would rather have one through my antenatal department or GP surgery' (69.0%) and 'I don't trust tests over the internet' (49.3%) (note: respondents were allowed to select up to two responses). The main reasons why respondents would order a test over the internet were because 'it is convenient' (69.8%) and 'I do most things over the internet these days' (33.7%); however, if the test was not available through the NHS, over a quarter (26.6%) of respondents would order a test over the internet. The most that the majority of respondents (35.7%) would be prepared to pay for the test was £100 (options ranged from £50 to £1000).

Discussion

Main findings

The results of this study indicate that NIPT for trisomy 21 is seen as a positive development in prenatal care, and that uptake is likely to be high and may include a proportion of women who would currently decline screening. The number of terminations of pregnancy for trisomy 21 may also increase, although a significant number are likely to use NIPT to prepare for the birth of a child with trisomy 21. Although these results must be interpreted with some degree of caution, as what women say and do in practice may differ,[23] they do give some indication as to the likely impact of offering a risk-free and early test for trisomy 21. Regarding test attributes, potential service users placed the greatest value on the safety of the test and expressed a preference for testing to occur on the same day as pre-test counselling provided by a midwife. Most respondents thought that NIPT should be offered routinely to all women; however, until the cost of the test is reduced, NIPT as a first-line test is unlikely to be attractive to commissioners.[17,19] These results provide valuable evidence to guide clinical practice and the development of appropriate care pathways.

Strengths and limitations

A key strength of this work is that questions (and answer options) were grounded in previous qualitative research, ensuring that they reflected 'real-life' views and experiences. Moreover, the survey was developed through an iterative process conducted with experts and piloted to ensure clarity and answerability. The survey is not a validated instrument that can be used outside the context of this research; however, the purpose of this research was to inform clinical practice rather than explain a phenomenon. For this reason, a descriptive survey was considered adequate. The survey included a series of hypothetical scenarios. As such, the findings may not reflect the choices that patients actually make in practice.[23] Moreover, it is not yet clear how NIPT will be introduced into current prenatal testing pathways, and women's attitudes to NIPT may change according to the way the testing is offered: for example, it may be more acceptable to some women if it is offered earlier than the current first-trimester screening. Further research as and when NIPT becomes available clinically through the NHS is therefore vital.

Study participants were predominantly white, older, and well-educated females, demographic factors that are associated with higher levels of interest in NIPT, and not necessarily representative of the UK population.[24] A number of other potential biases related to previous prenatal testing experience also exist when comparing our sample with the 'normal' obstetric population. In our sample, 11.1% of respondents had been identified as being at high risk through screening, compared with 3.1% in the general population,[25] 9.1% of our sample had undegone invasive testing, compared with 2.9% of the general population,[26] and 29.2% had received a diagnosis of trisomy 21 or another condition, which is again much higher than the 9% identified in the general population.[26] As such, our

sample may have been biased towards viewing NIPT favourably, given that these participants had experienced adverse outcomes in previous pregnancies. Another bias may have arisen as a result of our recruitment strategy. Half the participants were recruited through the website Mumsnet. This website was found to represent a particular demographic group (white, older, and well-educated women), who by virtue of being an active member of the website may represent a particular viewpoint. Moreover, only 25% of the users contacted responded to the survey. Those that chose to respond may have had particularly strong views about the subject matter. These factors may have biased the responses, and therefore the results must be interpreted with some degree of caution. For these reasons, further studies with women from populations under-represented in this study (i.e. younger, less well-educated, non-white women), as well as those specifically targeted at recruiting more men, would be worthwhile. Nevertheless, these results are useful as they show that numerically NIPT is appealing, and help us to gauge the likely uptake and provide useful information to guide implementation. They also add weight to the existing qualitative evidence supporting women's desire to use NIPT for trisomy 21 as well as other single-gene disorders.[21,27,28]

Interpretation

The reported high likely uptake of NIPT for trisomy 21 concurs with other hypothetical studies in this area, where likely uptake ranged between 70 and 97%.[21,24,29] Nevertheless, some of the first papers to be published from the US reporting actual uptake have shown lower numbers than might be expected, of between 28 and 40%.[30–32] Authors suggest that an important factor in NIPT uptake was cost, as insurance coverage varied, and some people had out-of-pocket expenses for NIPT but not for invasive testing; this is not likely to be an issue within the NHS, as the cost will be covered, and hence uptake rates are likely to be higher. Other factors reported to contribute to low uptake included having certainty and additional information from invasive testing,[19] later gestational age at the time of being offered the test, ethnic background, and desire for screening that includes ultrasound (if NIPT is offered as an alternative to screening).[31] Differences in reported hypothetical uptake and actual uptake highlight the importance of conducting research once the test becomes available.

The results suggest that there will be an increase in the number of women who accept screening if NIPT is available for high-risk pregnancies, and that termination rates may also increase, a prediction made by other commentators.[33,34] Given that a key reason women decline screening is the miscarriage risk associated with invasive testing, the likely increase in screening uptake if NIPT were available is not surprising.[35,36] According to recently published data, most women (around 92%) who receive a prenatal diagnosis of trisomy 21 in England and Wales request a termination of pregnancy.[37] Although the number of terminations might increase overall with the introduction of NIPT, our findings indicate that some women may continue their pregnancy following a positive result, and that these women are likely to be younger, have a lower education level, or have a religious affiliation, demographic factors that have been associated with lower rates of termination for trisomy 21 elsewhere.[24,38–41] As there may be more women continuing with their pregnancy following a diagnosis of trisomy 21 rather than finding out at birth, research into the type of information and support that these women need during the remainder of their pregnancy will be essential to help parents prepare and minimise prenatal anxiety. If women do decide to undergo testing, it will be vital to ensure that they do so fully informed of the potential implications of the test results, and on the basis that the results will be of benefit to them. Interestingly, ARC respondents were significantly more likely to terminate an affected pregnancy than respondents recruited through Mumsnet or antenatal clinics. This may reflect their experience of adverse results in a previous pregnancy.

The finding that safety was the most important attribute of NIPT supports other research in this area.[24,42] As safety is a priority when women are making decisions about NIPT, care must be taken to ensure that other aspects of the test, including potential disadvantages, are presented so that all test attributes are taken into consideration when choosing testing pathways. For example, women's preferences may alter depending on the time it takes to receive NIPT results. If waiting 7 days for an NIPT result pushes back the time when invasive testing could be performed, those with a higher risk may prefer a faster route to the most accurate diagnosis.[31] Other psychosocial factors, such as the quality of life of a child with trisomy 21 and whether people felt that they could cope raising a child with the condition, were also important determinants in decision-making. Given the importance of these factors healthcare providers should ensure that they are discussed with patients, including the provision of accurate information about trisomy 21, in a non-directive manner, so that women and partners make prenatal testing choices in line with their personal beliefs and values. Our results also suggest that women may take less time to think about NIPT than for screening or invasive testing, a finding that has been reported elsewhere (Silcock et al.).[21,43,44] This may reflect that it is easier to make a decision about NIPT than for screening, as results are more certain, and invasive testing carries the risk of miscarriage; however, it could also indicate that women may not consider the implications of NIPT as carefully as they would for invasive testing, even

though both are highly accurate. Safeguards to ensure that NIPT is offered in a way that promotes informed consent are therefore essential. Moreover, given that the psychosocial factor with the largest effect size for NIPT 'accepters' was 'feeling that we should use all the medical tests available', care needs to be taken to ensure that the test does not become routine or accepted without sufficient knowledge about the purpose for which it is being performed, an issue that has been identified with regards to trisomy 21 screening.[45]

Finally, our results highlight that at present the offer of DTC NIPT is of interest to a small proportion of people, as most would rather access tests through a health professional. A similar finding was reported in a recent systematic review on genomic testing.[46] Nevertheless, our study found that interest in DTC tests increased if NIPT was not available through the NHS. If DTC NIPT testing does become available, one concern is that women who are not offered this test through the NHS (for example, if it is only offered to women found to be at high risk through screening) may choose this option. This raises concerns about misinterpretation of test results or patients not fully comprehending the limitations and implications of testing.[47,48] Clear and accessible information to support such tests and guidelines for consumers is therefore vital.

Conclusion

The successful introduction of NIPT for trisomy 21 into the NHS requires incorporating the views and preferences of a diverse set of stakeholders. Our research shows that NIPT for trisomy 21 is viewed as a positive advancement in prenatal care by potential service users, and that uptake is likely to be high. These findings are likely to be relevant to other countries with similar profiles to the UK who may also begin offering NIPT routinely through their national health service providers. Nevertheless, future research at the time of clinical implementation is vital, as what is predicted to happen may not reflect what actually happens in practice. Strategies to ensure that pre-test counselling allows women time to reflect on the benefits and potential limitations of different testing options, as well as providing the opportunity to reflect on their own beliefs and values, are critical so that informed, considered decisions are made.

Disclosure of interests

The authors declare that they have no conflicts of interest.

Contribution to authorship

CL, MH, and LSC conceived of the study. All authors contributed equally to the planning of the study. MH and RD oversaw data collection. CL, MH, and CS analysed the data. CL wrote the first draft of the article and then circulated it to the other authors for comments.

Details of ethics approval

Approval for this study was obtained from NHS Research Ethics Committee (REC) North London REC 2 (10/H0724/41) in June 2010.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Antenatal testing for trisomy 21.

Table S1. Significant differences across recruitment groups.

Table S2. Significant differences in likelihood to use NIPT.

Table S3. Importance placed on psychosocial factors for NIPT by 'accepters' and 'decliners'.

Table S4. Reasons why respondents would accept or decline testing.

Table S5. Likelihood to use NIPT for information only.

Table S6. Importance that NIPT accepters placed on psychosocial factors: comparison between those who would be likely to terminate an affected pregnancy with those who would use NIPT for information only. ■

References

1 United Kingdom National Screening Committee. Antenatal screening–working standards for Down's syndrome screening. 2007.
2 American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 77: screening for fetal chromosomal abnormalities. *Obstet Gynecol* 2007;109:217–27.
3 Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. *Prenat Diagn* 2011;31:7–15.
4 Alfirevic Z, Gosden CM, Neilson JP. Chorion villus sampling versus amniocentesis for prenatal diagnosis. *Cochrane Database Syst Rev* 2000;2:CD000055.
5 Tabor A, Alfirevic Z. Update on procedure-related risks for prenatal diagnosis techniques. *Fetal Diagn Ther* 2010;27:1–7.
6 Chiu RW, Akolekar R, Zheng YW, Leung TY, Sun H, Chan KC, et al. Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study. *BMJ* 2011;342:c7401.
7 Sehnert AJ, Rhees B, Comstock D, de Feo E, Heilek G, Burke J, et al. Optimal detection of fetal chromosomal abnormalities by massively parallel DNA sequencing of cell-free fetal DNA from maternal blood. *Clin Chem* 2011;57:1042–9.
8 Palomaki GE, Kloza EM, Lambert-Messerlian GM, Haddow JE, Neveux LM, Ehrich M, et al. DNA sequencing of maternal plasma to detect Down syndrome: an international clinical validation study. *Genet Med* 2011;13:913–20.
9 Nicolaides KH, Syngelaki A, Ashoor G, Birdir C, Touzet G. Noninvasive prenatal testing for fetal trisomies in a routinely screened first-trimester population. *Am J Obstet Gynecol* 2012;207:374.e1–6.
10 Ehrich M, Deciu C, Zwiefelhofer T, Tynan JA, Cagasan L, Tim R, et al. Noninvasive detection of fetal trisomy 21 by sequencing of DNA in maternal blood: a study in a clinical setting. *Am J Obstet Gynecol* 2011;204:205.e1–11.
11 Bianchi DW, Platt LD, Goldberg JD, Abuhamad AZ, Sehnert AJ, Rava RP. Genome-wide fetal aneuploidy detection by maternal plasma DNA sequencing. *Obstet Gynecol* 2012;119:890–901.
12 Palomaki GE, Deciu C, Kloza EM, Lambert-Messerlian GM, Haddow JE, Neveux LM, et al. DNA sequencing of maternal plasma reliably identifies trisomy 18 and trisomy 13 as well as Down syndrome: an international collaborative study. *Genet Med* 2012;14:296–305.
13 Norton ME, Brar H, Weiss J, Karimi A, Laurent LC, Caughey AB, et al. Non-Invasive Chromosomal Evaluation (NICE) Study: results of a multicenter prospective cohort study for detection of fetal trisomy 21 and trisomy 18. *Am J Obstet Gynecol* 2012;207:137.e1–8.
14 Ashoor G, Syngelaki A, Wang E, Struble C, Oliphant A, Song K, et al. Trisomy 13 detection in the first trimester of pregnancy using a chromosome-selective cell-free DNA analysis method. *Ultrasound Obstet Gynecol* 2013;41:21–5.
15 The American College of Obstetricians and Gynecologists Committee on Genetics. Noninvasive prenatal testing for aneuploidy – Committee opinion. *Obstet Gynecol*. 2012;120:1532–4.
16 Gregg AR, Gross SJ, Best RG, Monaghan KG, Bajaj K, Skotko BG, et al. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. *Genet Med* 2013;15:395–8.
17 Chitty LS, Hill M, White H, Wright D, Morris S. Noninvasive prenatal testing for aneuploidy-ready for prime time? *Am J Obstet Gynecol* 2012;206:269–75.
18 Hall A, Bostanci A, Wright CF. Non-invasive prenatal diagnosis using cell-free fetal DNA technology: applications and implications. *Public Health Genomics* 2010;13:246–55.
19 Morris S, Karlsen S, Chung N, Hill M, Chitty L. Model-based analysis of costs and outcomes of non-invasive prenatal testing for Down's syndrome using cell free fetal DNA Submitted. 2013.
20 Kelly SE, Farrimond HR. Non-invasive prenatal genetic testing: a study of public attitudes. *Public health genomics.* 2012;15:73–81.
21 Lewis C, Silcock C, Chitty LS. Non-invasive prenatal testing for Down's syndrome – pregnant women's views and likely uptake. *Public Health Genomics* 2013;16:223–32.
22 Raymond MR, Roberts DM. A comparison of methods for treating incomplete data in selection research. *Educ Psychol Meas* 1987;47:13–26.
23 Kleinveld JH, van den Berg M, van Eijk JT, van Vugt JM, van der Wal G, Timmermans DR. Does offering prenatal screening influence pregnant women's attitudes regarding prenatal testing? *Community Genet* 2008;11:368–74.
24 Tischler R, Hudgins L, Blumenfeld YJ, Greely HT, Ormond KE. Noninvasive prenatal diagnosis: pregnant women's interest and expected uptake. *Prenat Diagn* 2011;26:1292–9.
25 UK National Screening Committee Screening in England 2010–11 Annual Report. Annual Report: UK National Screening Committee; 2011.
26 Morris JK, Waters JJ, de Souza E. The population impact of screening for Down syndrome: audit of 19 326 invasive diagnostic tests in England and Wales in 2008. *Prenat Diagn* 2012;32:596–601.
27 Lewis C, Hill M, Chitty L. Non-invasive prenatal diagnosis for single gene disorders: experience of patients. *Clin Genet* 2013; doi: 10.1111/cge12179.
28 Lewis C, Hill M, Skirton H, Chitty L. Non-invasive prenatal diagnosis for fetal sex determination – benefits and disadvantages from the service users' perspective. *Eur J Hum Genet* 2012;20:1127–33.
29 Zamerowski ST, Lumley MA, Arreola RA, Dukes K, Sullivan L. Favorable attitudes toward testing for chromosomal abnormalities via analysis of fetal cells in maternal blood. *Genet Med* 2001; 3:301–9.
30 Chetty S, Garabedian MJ, Norton ME. Uptake of noninvasive prenatal testing (NIPT) in women following positive aneuploidy screening. *Prenat Diagn* 2013;33:542–6.
31 Taylor JB, Chock VY, Hudgins L. NIPT in a Clinical Setting: an analysis of Uptake in the First Months of Clinical Availability. *J Genet Couns* 2013; [forthcoming].
32 Vahanian SA, Allaf MB, Yeh C, Chavez MR, Kinzler WL, Vintzileos AM. Patient acceptance of non-invasive testing for fetal aneuploidy via cell-free fetal DNA. *J Maternal Fetal Neonatal Med* 2013;27: 109–9.
33 Greely HT. Get ready for the flood of fetal gene screening. *Nature* 2011;469:289–91.
34 Verweij EJ, Oepkes D, de BM. Changing attitudes towards termination of pregnancy for trisomy 21 with non-invasive prenatal trisomy testing: a population-based study in Dutch pregnant women. *Prenat Diagn* 2013;33:397–9.
35 Markens S, Browner CH, Press N. 'Because of the risks': how US pregnant women account for refusing prenatal screening. *Soc Sci Med* 1999;49:359–69.
36 Gottfredsdottir H, Bjornsdottir K, Sandall J. How do prospective parents who decline prenatal screening account for their decision? A qualitative study *Soc Sci Med* 2009;69:274–7.
37 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.
38 Leung TN, Ching CM, Chang JJ, Leung TY, Fung TY, Lau TK. Attitudes towards termination of pregnancy among Hong Kong Chinese women attending prenatal diagnosis counselling clinic. *Prenat Diagn* 2004;24:546–51.
39 Bryant L, Hewison JD, Green JM. Attitudes towards prenatal diagnosis and termination in women who have a sibling with Down's syndrome. *J Reprod Infant Psychol* 2005;23:181–98.

40 Britt DW, Risinger ST, Miller V, Mans MK, Krivchenia EL, Evans MI. Determinants of parental decisions after the prenatal diagnosis of down syndrome: bringing in context. *Am J Med Genet* 2000;5:410–16.
41 Dzurova D, Pikhart H. Down syndrome, paternal age and education: comparison of California and the Czech Republic. *BMC Public Health* 2005;17:69.
42 Hill M, Fisher J, Chitty LS, Morris S. Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests. *Genet Med* 2012;14:905–13.
43 Silcock C, Liao L-M, Hill M, Chitty L. Will the introduction of noninvasive prenatal testing for Down's syndrome undermine informed choice: a questionnaire study. 2013; [forthcoming].
44 van den Heuvel A, Chitty L, Dormandy E, Newson A, Deans Z, Attwood S, et al. Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? An experimental study of health care professionals. *Patient Educ Couns* 2009;78:24–8.
45 Garcia J, Bricker L, Henderson J, Martin MA, Mugford M, Nielson J, et al. Women's views of pregnancy ultrasound: a systematic review. *Birth* 2002;29:225–50.
46 Goldsmith L, Jackson L, O'Connor A, Skirton H. Direct-to-consumer genomic testing: systematic review of the literature on user perspectives. *Eur J Hum Genet* 2012;20:811–16.
47 Skirton H, Goldsmith L, Jackson L, O'Connor A. Direct to consumer genetic testing: a systematic review of position statements, policies and recommendations. *Clin Genet* 2012;82:210–18.
48 Hill M, Karunaratna M, Lewis C, Forya F, Chitty L. Views and preferences for the implementation of non-invasive prenatal diagnosis for single gene disorders from health professionals in the united kingdom. *Am J Med Genet A* 2013;161A:1612–8.

Commentary on 'Non-invasive prenatal testing for trisomy 21: a cross-sectional survey of service users' views and likely uptake'

Lewis and colleagues assess the views and likely uptake of non-invasive prenatal testing (NIPT) for trisomy 21 among women from the UK. Having analysed questionnaires from over 1000 women and their partners, they conclude that respondents were overwhelmingly positive towards the introduction of NIPT and that uptake is likely to be high. This is an important survey of end-user views conducted by an experienced group of researchers, and will no doubt have an important influence on healthcare service providers.

The author's conclusions are somewhat coloured by the skewed demographic characteristics of the populations sampled: 89% were white and 66% had a higher university degree. The fact that no pre-test information on NIPT was provided (apart from what was contained within the individual queries) makes these population characteristics important. In the UK, NIPT is still relatively new and is only available privately to those who are knowledgeable about the test and able to afford it. Interestingly, the populations sampled had previously undergone routine trisomy 21 screening in the majority of cases (72%), and only a fraction more would consider having NIPT if available (86%). Even within Europe, the uptake of trisomy 21 screening varies from as low as 30% in some countries to 61% in the UK and 90% in Denmark. This variation is surprising given the similar cultural and social values: it appears that the population's beliefs about termination of pregnancy, quality of life for individuals with trisomy 21, and the guidance of the healthcare professional were strong influences on the parent's decision-making (Crombag NM *et al.*, *J Matern Fetal Neonatal Med* 2013;26:1676–81).

As expected, 'safety of NIPT' was a major attraction for 55% of the respondents, but wishing to 'have as much information as possible about the baby' is also a strong motivation in the same proportion of women. This may explain the unexpectedly lower commercial uptake of NIPT in the USA and in some European countries, where many doctors continue to recommend 'diagnostic' invasive testing as having significant advantages over NIPT 'screening'. Such bias from doctors is unlikely to be a significant problem in the UK, where an established and effective National Health Service screening programme for trisomy 21 has resulted in a significant decline in invasive testing over the last decade (Morgan S *et al.*, *Ultrasound Obstet Gynecol* 2013;41:526–9).

Despite the apparent appetite of expectant parents for NIPT, there is a natural conservatism of professional bodies such as the American Congress of Obstetricians and Gynecologists (ACOG) to advocate NIPT (ACOG, *Obstet Gynecol* 2012;120:1532–4). In contrast, doctors involved in the field of prenatal diagnosis have little doubt that NIPT technology represents a much needed sea change in screening efficiency for trisomy 21 (Hui L. *Ultrasound Obstet Gynecol* 2013;41:2–6). Importantly, only 50% of this well-informed and well-educated population of respondents thought that NIPT should be offered routinely to all women, with the remainder favouring contingent NIPT for women found to be at high risk through screening. It would seem that for women and institutions alike, cost, convenience, and timing of screening test were, and will continue to be, important considerations when it comes to the inevitability of implementing NIPT into healthcare systems.

Disclosure of interests

B.T. is a partner at *Ultrasound Diagnostic Services*, a private women's ultrasound service in London that currently provides both Harmony™ and NIFTY™ NIPT at a non-profit cost to clients. ■

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