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Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? An experimental study of health care professionals

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Abstract

Objective. Informed choice is a fundamental concept within prenatal care. The present study assessed the extent to which the introduction of non-invasive prenatal diagnosis (NIPD) of Down's syndrome may undermine the process of making informed choices to undergo prenatal testing or screening for Down's syndrome by altering the quality and quantity of pre-test counselling.

Methods. 231 obstetricians and midwives were randomly allocated one of three vignettes, each describing a different type of test: (a) invasive prenatal diagnosis (IPD), (b) non-invasive prenatal diagnosis (NIPD) or (c) Down's syndrome screening (DSS). Participants were then asked to complete a questionnaire assessing (1) the information considered important to communicate to women, (2) whether test offer and uptake should take place on different days, and (3) whether signed consent forms should be obtained prior to testing.

Results. Across the three test types, five out of the seven presented topics were considered equally important to communicate, including the information that testing is the woman's choice. Compared with participants receiving the IPD vignette, those receiving the NIPD and DSS vignettes were less likely to report that counselling and testing should occur on different days (IPD 94.7% versus 74.1% and 73.9% for NIPD and DSS respectively, $p = .001$) and that written consent was a necessity (IPD 96.1% versus 68.3% and 75.4% for NIPD and DSS respectively, $p < .001$).

Conclusion. This study provides the first empirical evidence to demonstrate that practitioners may view the consent process for NIPD differently to IPD. There is potential for the introduction of NIPD to undermine women making informed choices in the context of prenatal diagnostic testing for conditions like DS.

Practice implications. Given the importance of informed choice in reproductive decision-making, implementation of any programme based on NIPD should be designed to facilitate this.

Keywords: Informed choice; Prenatal; Down's syndrome; Non-invasive testing

Introduction

Recent reports have described the non-invasive diagnosis of Down's syndrome (DS—a genetic disorder characterised by an extra copy of chromosome 21) by analysis of foetal nucleic acids in the maternal plasma [1] and [2]. Whilst research is still in its infancy, and it is as yet unclear whether this test will replace DS screening as well as diagnostic testing, these advances have the potential to transform antenatal practice by superseding current diagnostic tests with non-invasive alternatives that do not entail a risk of miscarriage and which might be conducted at an earlier stage in pregnancy [1] and [2]. Despite the obvious benefits of such developments, there are concerns that non-invasive tests may compromise informed decision-making [3].

The importance of facilitating informed choice in the context of prenatal testing services is universally endorsed by policy makers. This is evident in the published guidelines that govern service delivery [4], [5], [6] and [7] as well as in the ethics literature [8]. Such guidelines stress the importance of communicating three sets of information: (1) a description of the condition for which testing is being offered, (2) an outline of test characteristics, and (3) the implications of possible test results. Written consent may serve as one means of ensuring that an understanding of the testing procedure has been achieved [9].

A major concern of women currently undergoing prenatal diagnostic testing is the risk of miscarriage associated with the invasive procedure [10]. As NIPD removes the need to discuss procedure related risks, the decision-maker may fail to adequately consider the remaining implications of test outcomes. These include discussion of the option of pregnancy termination if test results indicate an affected foetus. The widespread introduction of non-invasive procedures may also lead to a 'routinisation' of prenatal testing. Previous studies in the context of prenatal screening have shown that rates of informed choice are higher if screening is perceived as optional as opposed to routine [11] and [12]. Given that service providers' attitudes towards the conduct of prenatal screening have the potential to affect their practice [13], the likelihood of any prenatal test becoming 'routinised' may, in part, depend on health professionals' attitudes towards its delivery. If perceptions of the counselling needed for NIPD are more akin to those for screening, the introduction of these tests may have the potential to erode informed choice.

Whilst concerns about the impending introduction of non-invasive prenatal diagnosis upon informed decision-making have been expressed [3], we are unaware of any empirical data to confirm or refute such concerns. In anticipation of its implementation in clinical practice we present here the first study providing evidence concerning the potential for non-invasive prenatal tests to erode informed choice. The aim of the current study is to describe and compare the attitudes of health care professionals already involved in the delivery of prenatal services towards those characteristics of counselling that are likely to facilitate informed decision-making in the contexts of (a) invasive prenatal diagnosis (IPD—amniocentesis or chorionic villus sampling), (b) non-invasive prenatal diagnosis (NIPD) and (c) Down's syndrome screening (DSS—a blood test which gives a risk ratio for the disorder).

Methods

A vignette study, with a between-subjects design, was used to assess the impact of three types of prenatal tests on the delivery of prenatal counselling: (a) invasive prenatal diagnostic tests (IPD), (b) non-invasive prenatal diagnosis (NIPD) and (c) Down's syndrome screening (DSS).

Participants

Participants were health care professionals currently involved in the provision of prenatal testing attending at three conferences. Only participants practicing in the UK were included in the final sample. Four hundred and seven health professionals were approached to take part in the study, of

whom 248 (158 recruited at a conference, 90 recruited from three UK maternity units) agreed to participate. 17 (6.9%) individuals attending the conferences did not practice in the UK and hence were subsequently excluded from the analyses, leaving a total of 231 study participants (141 from the conference, 90 from maternity units). The demographic composition of this sample is provided in Table 1.

Table 1. Participants' demographic characteristics and responses to the outcome measures.

	Total	IPD	NIPD	DSS	p-Value
Number of subjects (n)	231	76	82	73	
Mean age (years, SD)	39.7 (10.1)	38.6 (9.7)	37.8 (9.8)	37.3 (9.3)	.724
Gender (%)					.262
Male	20.3	22.4	14.6	24.7	
Female	79.7	77.6	85.4	75.3	
Profession (%)					.226
Obstetrician	59.3	57.9	57.3	63.0	
Midwife	29.9	36.8	28.2	24.2	
Other	10.8	5.3	14.6	12.3	
Topics important to communicate (% of respondents who identified topic)					
Description of Down's syndrome	85.7	84.2	90.2	82.2	.324
Her personal risk	92.2	94.7	92.7	89.0	.423
The procedure itself	64.1	86.8	40.2	67.1	<.001
Likelihood of miscarriage	63.2	90.8	39.0	61.6	<.001
Likelihood of test not giving result	70.6	71.1	76.8	63	.168
Testing/screening is a choice	96.5	94.7	98.8	95.9	.357
Options available if test positive	90.9	86.8	93.9	91.8	.290
Timing presentation and uptake test (%)					.001
Same day	19	5.3	25.9	26.1	
Different days	81	94.7	74.1	73.9	
Perceived need for written consent (%)					<.001
Definitely yes	47.2	63.2	36.6	42.5	
Probably yes	32.5	32.9	31.7	32.9	
Probably not	17.3	3.9	28.2	19.2	
Definitely not	3.0	0	3.7	5.5	

Materials

Three vignettes were developed and pre-piloted in small sub-sample of 31 health professionals and ethicists to gauge the appropriateness and clarity of the information contained therein. Any information considered problematic by the majority of these respondents was altered according to the recommendations given. Each vignette required participants to imagine working in an antenatal clinic at a point in time when all pregnant women are routinely offered prenatal testing for DS. Vignettes varied in terms of test type (IPD, NIPD, DSS) and accordingly, their respective specifications, i.e. the predictive power of the test (99%, 80%) and the presence or absence of a procedure related risk of miscarriage (Box 1) [5].

Box 1. Vignettes

Invasive prenatal diagnosis (IPD)

Imagine yourself in 5 years' time. You are working in an antenatal clinic at a time when all pregnant women are routinely offered a diagnostic test for Down's syndrome, for example amniocentesis or CVS. Sarah Jones is 10 weeks pregnant and visits the clinic to be seen by you. You are discussing this test with Sarah.

You know that invasive tests, which will detect more than 99% of pregnancies affected by Down's syndrome, carry a small procedure related risk of miscarriage.

As this is Sarah's first pregnancy she is not likely to be familiar with the diagnostic test.

Non-invasive prenatal diagnosis (NIPD)

Imagine yourself in 5 years' time. You are working in an antenatal clinic at a time when all pregnant women are routinely offered a diagnostic test for Down's syndrome. Sarah Jones is 10 weeks pregnant and visits the clinic to be seen by you. You are discussing this test with Sarah.

Imagine that at this point in time Down's syndrome can be diagnosed non-invasively using a sample of maternal blood. This blood test will detect more than 99% of pregnancies affected by Down's syndrome and does not carry a procedure related risk of miscarriage like amniocentesis.

As this is Sarah's first pregnancy she is not likely to be familiar with the diagnostic test.

Down's syndrome screening (DSS)

Imagine yourself working in an antenatal clinic at a time when all pregnant women are routinely offered prenatal screening for Down's syndrome. The screening test is a blood test, which will detect 80% of pregnancies affected with Down's syndrome and has a false positive rate of 3%. Sarah Jones is 10 weeks pregnant and visits the clinic to be seen by you. You are discussing this test with Sarah.

There is no direct procedure related risk involved with the blood test, but if the test is positive, amniocentesis or CVS is required for a definitive diagnosis.

As this is Sarah's first pregnancy she is not likely to be familiar with either the screening or diagnostic test.

Following the presentation of these vignettes, participants were given two tasks:

Task 1: Participants were asked to imagine counselling a pregnant woman at her first visit to the antenatal clinic.

Task 2: Participants were asked to advise a clinic manager on service organisation for the test presented in the vignette.

Measures

Attitudes towards aspects of pre-test counselling likely to facilitate informed choice were assessed using a questionnaire. These were (1) the information considered important to communicate during counselling, (2) the timing of the test and (3) the perceived need to sign a consent form.

1) Type of information considered important to communicate:

This was assessed in response to Task 1 (advising a pregnant woman) by asking participants to select the topics, from a list of seven possibilities (see Table 1) that they believed should be incorporated into a counselling session.

2) Timing of the test:

Attitudes towards the timing of the test were assessed in response to Task 2 (advising a clinic manager). Participants were informed that the test can either be performed on the same day as it is offered or on a return visit, thereby providing women with some time for reflection. Participants were asked to imagine advising a manager either way.

3) Perceived need to sign a consent form:

This was assessed in response to Task 2 with the question: 'Do you think it is important for women undergoing this test to sign a consent form?' Responses were measured on a 4-point scale ranging from 1, definitely yes to 4, definitely not. This response format was used to allow those with varying degrees of uncertainty to indicate either a general sense of favourableness or unfavourableness. In order to generate a binary outcome for multivariate analyses, this variable was dichotomised into 'Yes' and 'No' by collapsing 'definitely' and 'probably'. See Table 1 for non-dichotomised data.

Demographic details (age, gender, and profession) were recorded by participants in the questionnaire.

Procedure

The study was approved by a research ethics committee in the UK (King's College London Research Ethics Committee 05/06-141). Recruitment of participants was opportunistic and took place at three professional educational meetings convened in the UK that were predominantly attended by obstetricians and midwives (n = 141). The recruitment procedure at the conferences involved inserting questionnaires in conference packs. At the beginning of each meeting conference organisers brought attention to their presence and asked that individuals either posted responses in the pre-paid envelopes provided or left them at a designated place in the auditorium. An additional sample of 150 obstetricians and midwives from three UK maternity units were also invited to take part in the study. These individuals were sent one of the three vignettes and the associated questionnaire via internal post. Non-responders were sent one reminder. An online random number generator was used to randomise the order in which vignettes were presented. Participants were provided with a pre-paid envelope to return their completed questionnaires.

Analysis

Distributions of responses for categorical variables and differences in means for continuous variables were examined descriptively across groups. A series of univariate analyses was conducted across test types to compare three characteristics of prenatal counselling: topics considered important to communicate, timing of the test, and the perceived need for written consent. These were conducted using $\chi 2$ for categorical variables and ANOVAs for continuous variables. Significant differences were examined further with post hoc analyses. Logistic regression analyses were conducted to identify

independent predictors of beliefs about the timing of the test and the perceived need to sign a consent form.

Results

The response rate was 61% (248/407 participants, of whom 17 were ineligible because they were not practicing in the UK). The majority of respondents were obstetricians (59.3%), female (79.7%) with a mean age of 39.7. Age, gender, profession and data source (i.e. the conference or maternity unit) were distributed evenly across intervention groups. An overview of the distribution of demographic background variables and responses to the three components of counselling across intervention groups is displayed in Table 1.

Topics important to communicate

Five of the seven topics presented were considered equally important to communicate across experimental conditions. These were 'a description of Down's syndrome', 'communication of her personal risk', 'likelihood of the test not giving a result', 'the fact that testing/screening is a choice' and 'options available if the test confirms Down's syndrome'. Respondents who received the IPD vignette considered two of the seven topics, 'the procedure itself' and 'the likelihood of miscarriage', more important to communicate compared with respondents who received the NIPD or the DSS vignettes ($\chi2 = 37$, df = 2, $p < .001$, $\chi2 = 45$, df = 2, $p < .001$).

Timing of the test

Test type affected beliefs about the timing of the test; 94% of respondents who received the IPD vignette indicated that the presentation and uptake of prenatal tests should occur on different days ($\chi2 = 14$, df = 2, $p = .001$) (Table 1), compared with 74% of respondents who received either the NIPD or the DSS vignettes. Post hoc analyses confirmed that timing preferences differed significantly between NIPD and IPD ($\chi2 = 12$, df = 1, $p < .001$) but not between NIPD and DSS.

Perceived need to sign a consent form

Perceived need to sign a consent form varied by test type ($\chi2 = 23$, df = 6, $p = .001$): 96% of respondents who received the IPD vignette believed that testing should definitely or probably be preceded by written consent, compared with 68% and 75% of respondents who received the NIPD or DSS vignettes respectively. Post hoc analyses confirmed that the distribution of responses in the NIPD condition differed significantly from the IPD condition ($\chi2 = 22$, df = 3, $p < .001$) but not from the DSS condition.

Two multiple logistic regression analyses were conducted to identify independent predictors of (a) preference (Table 2) for test offer and uptake to occur on different days and (b) the perceived need (Table 3) for written consent. Test type was identified as the only independent predictor of both preference for separated test offer and uptake and the need for written consent. Age, gender and profession each had no effect.

Table 2. Predictors of preference for test presentation and uptake to occur on different days.

Predictors	OR	95% CI	p-Value
Age	1.01	.97–1.06	.52
Gender			
Male	1.0		
Female	1.20	.49–2.90	.70

Profession			
Obstetrician	1.0		
Midwife	1.56	.59–4.11	.37
Other	1.06	.37–3.07	.91
Test type			
IPD	1.0		
NIPD	.16	.05–.51	.002
DSS	.17	.05–.52	.002

−2ll = 200, model χ2 = 19, HL χ2 = 3.13, p = .93.

Table 3. Predictors of perceived need for written consent.

Predictors	OR	95% CI	p-Value
Age	1.04	1.00–1.08	.08
Gender			
Male	1.0		
Female	.70	.28–1.72	.43
Profession			
Obstetrician	1.0		
Midwife	.823	.33–2.06	.68
Other	1.26	.43–3.72	
Test type			
IPD	1.0		
NIPD	12.03	3.40–42.65	<.001
DSS	7.57	2.07–27.69	.002

−2ll = 197, model χ2 = 28, HL χ2 = 7.84, p = .45.

Discussion

This study provides the first empirical evidence to suggest that practitioners will view the consent process for prenatal diagnostic testing differently depending upon whether it is an invasive or non-invasive test. This has the potential to undermine women making informed choices about non-invasive testing based on the assumption that separating in time test offer and test procedure facilitates informed choices, as might the process of seeking written consent. Given the rapid development of NIPD [14], considering the implications of these findings for clinical practice becomes urgent.

Conclusion

Our ability to draw firm conclusions from the data presented here is limited by the extent to which the measures used can be considered valid indices of informed choice. Despite the fact that separating test offer and uptake provides time for reflection, there is no empirical evidence to support or indeed refute the implicit assumption that this period of reflection actually facilitates informed choice. Whilst conducting counselling and testing on the same day has been associated

with higher uptake rates, immediate choices to undergo screening are not necessarily less well informed [15]. One observational study found rates of informed choice to be higher in the context of same day counselling and testing [16], although when this was experimentally manipulated no difference was found [17]. Moreover, the removal of the procedure related risk in NIPD may conceivably facilitate rather than impede value-consistent choices by reducing the ambivalence associated with invasive testing, a situation in which parents are asked to pit the risk to the baby against gaining knowledge about potential foetal abnormalities [18].

Presently, there is an absence of evidence to substantiate the assumption that obtaining written consent in the context of clinical practice aids patient understanding and helps facilitate informed choice, nonetheless it is recommended practice [6]. Studies exploring written consent in the context of clinical research have generated mixed results with some showing no differences in comprehension between oral and written consent and others suggesting that written consent, in combination with an oral explanation, leads to better retention [19]. Whilst our results suggest that the information provided to individuals is likely to remain unaffected by whether testing is invasive or not, knowledge is only one component of an informed choice. The extent to which people act consistently with their values is also important in relation to testing decisions, and may be more affected by service organisation than aspects of pre-test counselling [20] and [21].

The strength of the current study is that it is, to our knowledge, the first to anticipate the implications for the quality of women's decision-making of the impending introduction of NIPD into clinical practice. The use of an experimental design strengthens the conclusion that health care professionals are likely to approach counselling and service provision of non-invasive diagnostic tests in a clinically significantly different way to invasive procedures. The extent to which this will erode women making informed choices and how best this can be prevented must await further study after implementation and will require comparing the actual content of counselling provided to women undergoing invasive, non-invasive and screening procedures.

Practice implications

If NIPD is allowed to develop along the lines suggested by this empirical study, there is a danger that current universal guidelines favouring informed choice might be undermined. For this reason, it is imperative that standards for the practice of NIPD need to be developed in order that present guidelines continue to be adhered to. If NIPD does transform Down's syndrome testing in such a way that current screening and diagnostic tests form part of the same procedure, this technology may also have wider economic and societal implications, affecting both health care resources and attitudes towards disability. Future research in this area would benefit from the use of validated measures of informed choice in the context of prenatal diagnosis, further investigation into the value of current informed consent procedures in facilitating informed choice, and assessment of women and health professionals' views of pre-test counselling once NIPD has been implemented.

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References

[1] Lo YMD, Tsu NBY, Chiu RWK, Lau TK, Leung TN, Heung MMS, Gerovassili A, Jin Y, Nicolaides KH, Cantor CR, Ding C. Plasma placental RNA allelic ratio permits noninvasive prenatal chromosomal aneuploidy detection. Nat Med 2007;13:218–23.

[2] Fan HC, Blumenfeld YJ, Chitkara U, Hudgins L, Quake SR. Noninvasive diagnosis of fetal aneuploidy by shotgun sequencing DNA from maternal blood. PNAS 2008 [epub 2008 October 6].

[3] Wright C. Cell-free fetal nucleic acids for non-invasive prenatal diagnosis. In: Report of the UK expert working group. PHG Foundation; 2009.

[4] World Health Organization. Statement of WHO expert advisory group on ethical issues in medical genetics [online]. Geneva: WHO; 1998. Available from: http://whqlibdoc.who.int/hq/1998/WHO_HGN_ETH_98.2.PDF .

[5] American College of Obstetricians and Gynecologists. Screening for fetal chromosomal abnormalities. Washington (DC): American College of Obstetricians and Gynecologists; 2007 January 11. ACOG practice bulletin; no. 77.

[6] Joint Working Party of the Royal College of Obstetricians and Gynaecologists and the Royal College of Paediatrics and Child Health. Fetal abnormalities— guidelines for screening, diagnosis and management: report of a joint working party of the Royal College of Obstetricians and Gynaecologists and the Royal College of Paediatrics and Child Health. London: RCOG Press; 1997.

[7] Royal College or Obstetricians and Gynaecologist. Amniocentesis and chorionic villus sampling, 3rd ed., London: Royal College of Obstetricians and Gynaecologists; 2005 [guideline No. 8 (revised)].

[8] Newson AJ. Ethical aspects arising from non-invasive fetal diagnosis. Semin Fetal Neonatal Med 2008;13:103–8.

[9] General Medical Council. Consent: patients and doctors making decisions together. London: General Medical Council; 2008.

[10] Bishop AJ, Marteau TM, Armstrong D, Chitty LS, Longworth L, Buxton MJ, Berlin C. Women and health care professionals' preferences for Down's syndrome screening tests: a conjoint analysis study. Br J Obstet Gynaecol 2004;111:775–9.

[11] Jaques AM, Sheffield LJ, Halliday JL. Informed choice in women attending private clinics to undergo first-trimester screening for Down syndrome. Prenat Diagn 2005;25:656–64.

[12] Van den Berg M, Timmermans DRM, Ten Kate LP, van Vugt JMG, van der Wal G. Are pregnant women making informed choices about prenatal screening? Genet Med 2005;7:332–8.

[13] Levy V. Protective steering: a grounded theory study of the processes by which midwives facilitate informed choices during pregnancy. J Adv Nurs 1999;29: 104–12.

[14] Hahn S, Chitty LS. Noninvasive prenatal diagnosis: current practice and future perspectives. Curr Opin Obstet Gynecol 2008;20:146–51.

[15] Lorenz RP, Botti JJ, Schmidt CM, Ladda RL. Encouraging patients to undergo prenatal genetic counseling before the day of amniocentesis. Its effect on the use of amniocentesis. J Reprod Med 1985;30(12):933–5.

[16] Dormandy E, Hooper R, Michie S, Marteau TM. Informed choice to undergo prenatal screening: a comparison of twohospitals conducting testing either as part of a routine visit or requiring a separate visit. J Med Screen 2002;9: 109–14.

[17] Dormandy E, Michie S, Hooper R, Marteau TM. Informed choice in antenatal Down syndrome screening: a cluster-randomised trial of combined versus separate visit testing. Patient Educ Couns 2006;61:56–64.

[18] Dormandy E, Hankins M, Marteau TM. Attitudes and uptake of a screening test: the moderating role of ambivalence. Psychol Health 2006;21:499–511.

[19] Raich PC, Plomer KD, Coyne CA. Literacy, comprehension, and informed consent in clinical research. Cancer Investig 2001;19:437–45.

[20] Dormandy E, Michie S, Weinman J, Marteau TM. Variation in uptake of serum screening: the role of service delivery. Prenat Diagn 2002;22:67–9.

[21] Kellar I, Sutton S, Griffin S, Prevost A, Kinmonth AL, Marteau TM. Evaluation of an informed choice invitation for type 2 diabetes screening. Patient Educ Couns 2008;72:232–8.