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Non-invasive prenatal testing for aneuploidy: a systematic review of Internet advertising to potential users by commercial companies and private health providers

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The authors declare there are no conflicts of interest.

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Skirton, Goldsmith, Jackson, Lewis and contributed to the conceptualisation of the study. Goldsmith, Skirton and Jackson conducted the search and the analysis. Al authors contributed to the writing of the final manuscript.

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What is already known about this topic?

- Non-invasive prenatal testing (NIPT) can be used to screen the fetus for aneuploidy
- NIPT is regarded positively by consumers and health professionals
- Professional bodies have produced recommendations for use of NIPT for aneuploidy
- NIPT is advertised to potential consumers via the Internet.

What does this study add?

- Companies advertising NIPT via the Internet are not providing all the information recommended in professional guidelines
- Some companies provide balanced information, some use persuasive terms
- The authors recommend that all companies conform to guidance on information required by parents to make decisions about NIPT, including the information that no prenatal test can guarantee the health of a baby.

ABSTRACT

Background

The development of non-invasive prenatal testing has increased accessibility of fetal testing. Companies are now advertising prenatal testing for aneuploidy via the Internet.

Objectives

The aim of this systematic review of websites advertising non-invasive prenatal testing for aneuploidy was to explore the nature of the information being provided to potential users.

Methods

We systematically searched two Internet search engines for relevant websites using the following terms: ‘prenatal test’; ‘antenatal test’; ‘non-invasive test’; ‘noninvasive test’; ‘cell-free fetal DNA’; ‘cffDNA’; ‘Down syndrome test’ or ‘trisomy test’. We examined the first 200 websites identified through each search. Relevant web-based text was examined and key topics were identified, tabulated and counted. To analyse the text further, we used thematic analysis.

Main results

Forty websites were identified. While a number of sites provided balanced, accurate information, in the majority supporting evidence was not provided to underpin the information and there was inadequate information on the need for an invasive test to definitely diagnose aneuploidy.

Conclusions

The information provided on many websites does not comply with professional recommendations. Guidelines are needed to ensure that companies offering prenatal testing via the Internet provide accurate and comprehensible information.

Key words:

Systematic review; non-invasive prenatal testing; direct-to-consumer; websites; marketing; parents.

INTRODUCTION

Since the discovery that cell-free fetal DNA (cff-DNA) in maternal plasma could be used for prenatal testing,[1] there have been rapid advances in developing non-invasive methods to assess the genetic status, both for aneuploidy and monogenic disorders by analysis of cell free DNA in maternal blood.[2] Non-invasive prenatal testing (NIPT) can be used to identify fetuses at very high risk of Down Syndrome and other aneuploidies,[2] although in this situation invasive testing is recommended to confirm the diagnosis.[3] Non-invasive prenatal testing for Down syndrome is not available via the state-funded health systems in most countries however, it is actively marketed and offered privately by companies and private healthcare providers across Europe, the United States, Canada, Australia and China.[4] Some authors have reported that uptake has been high and has resulted in a decrease in invasive testing.[5]

For at least a decade, genetic and genomic tests have been available direct-to-consumer (DTC) for purchase over the Internet.[6] ~~Consumers who purchase a test are sent a test kit and return a sample (usually blood or saliva) to the company for analysis.~~ In the past, this could be done without the involvement of a health professional but that situation is changing, with more companies now providing counselling with the service or requesting a referral from a health professional.[7] ~~Concerns about the use of DTC testing have included the possibility of compromising informed consent for the test, the way in which consumers might interpret the results and the potential additional burden on health services by people who have purchased such tests.[8]~~ Direct to consumer access ~~tests for~~ to fetal testing was ~~genetic conditions or aneuploidy were~~ not available in the past because of the requirement for an invasive test performed by a skilled practitioner.

However, the advent of non-invasive testing using a maternal blood sample has made prenatal testing potentially more accessible via the Internet. Non-invasive prenatal testing (NIPT) for determination of fetal sex, paternity, and aneuploidy is now advertised freely on the Internet, although providers indicate that testing for aneuploidy will only be offered through a health professional referral. At present, NIPT is not available without the involvement of a health professional, however, it is likely that potential users of NIPT for chromosome anomalies such as Down syndrome will use the Internet to gain information about such tests and to determine how and where to access them. Guidelines on the information that should be available to parents considering using NIPT have been developed by numerous professional organisations [3,8-10], however, adherence to the guidelines is not mandatory. For this reason, we consider it important to investigate the way commercial companies and private health providers are currently marketing non-invasive prenatal tests to patients. We have therefore conducted a systematic review of the information published on the websites of these companies.

METHODS

Design

A systematic review involves using a rigorous process to search, retrieve and analyse material on a specific topic. We followed the system described by the Centre for Reviews and Dissemination,[12] which involves using clear search terms and parameters and setting inclusion and exclusion criteria. We designed the study using the quality criteria mentioned by Eysenbach et al[13] in their review of studies of web-based health information, which includes being transparent about the search tools used, search terms, number of raters, and setting a priori criteria.

Data collection

We conducted systematic searches using two Internet search engines – Google UK and Bing to avoid bias associated with one specific engine. A search was carried out using each of the following terms:

'prenatal test'; 'antenatal test'; 'non-invasive test'; 'noninvasive test'; 'cell-free fetal DNA'; 'cffDNA'; 'Down syndrome test'; 'trisomy test'.

We deliberately used searches that were as close as possible to those that might be used by prospective parents. For this reason, we used single search terms (rather than Boolean operators) and deliberately used some phrases that were not directly related to NIPT but might be used by parents searching for a range of prenatal testing options.

We conducted the searches in both search engines, using the same computer on the same day, deleting cookies between each search to avoid any contamination of results. Due to the changing nature of the Internet, we printed out the search findings as it would have been unlikely that these would have been replicated if repeated, and by printing out the first twenty pages of each search (200 websites) we consider that we reached saturation.

Two researchers then independently read through the lists of findings and applied the following inclusion criteria to identify companies and providers relevant to the aim of this study:

- Companies offering prenatal tests using cffDNA or cffRNA*
- Private health providers from any country offering prenatal tests using cffDNA or cffRNA*

- Purpose of test to identify fetal abnormality or genetic condition
- Available for payment by consumer
- Websites or webpages in English.

Any webpages offering tests directly accessible by consumer, even if via health professionals, were included. Websites that contained information for both health professionals and patients were included, but not those directed only at health professionals. The search also yielded publications on NIPT or prenatal testing or screening, websites focused on maternal serum screening, ultrasound screening, invasive testing or paternity testing, and news reports: all of these were excluded.

To ensure rigour, the researchers then compared their findings and discussed any problematic areas. For example, it was sometimes difficult to establish whether websites were simply providing information about NIPT rather than offering it. ~~The results of the searches and number of relevant hits are presented in Table 1~~.There were more relevant sites identified through Google: all relevant websites identified by Bing were also identified using Google. The results of the searches and number of relevant hits are presented in Table 1

Place Table 1 about here....

All websites that were potentially for inclusion were then accessed to ensure that they fitted the inclusion criteria. A small number were excluded; reasons included links to websites that contained information about NIPT for aneuploidy but were targeted at health professionals, or those that contained detailed information about NIPT but no guidance about how to access such tests. We also made the decision to exclude any laboratories that were offering information on NIPT; detailed and informative information was often available, but was mainly aimed at health

professionals and any consumers accessing the site were advised to ask their health professional to order the test. In addition, we excluded one company website that was published in German, but included a 'translate' option. We considered that it would be unreasonable to analyse information on this website due to the quality of the translation, despite the fact that potential parents accessing this site would have to rely on the information. In order to analyse the text from webpages, we constructed tables that included the relevant text from the websites that could be directly accessed by potential consumers without opening other sites or downloading additional material. The text was then analysed qualitatively. We have not reproduced these tables in this paper due to the amount of text that was analysed, but include selected examples of text in the tables below.

Data analysis

There are numerous tools that can be used to assess website quality, however these tools are not necessarily useful for assessing quality of health information content.[14] In particular, we were looking for accuracy of information, potential biased perspectives and evidence of persuasive approaches.[15] We therefore took an approach based on thematic analysis, [16] which is consistent with searching for particular features within qualitative data. All relevant web-based text was read by two authors independently. A table was prepared to identify the type of topic covered in each website. Basic codes were extracted from the data and these were then grouped into categories and themes, using thematic analysis.[16] These themes were then discussed by three authors until consensus was reached.

In our analysis, we used the term 'balanced' to describe information that was presented in a neutral way, providing both positive and negative aspects (where

appropriate) and without emotive language. Material was described as 'persuasive' if it included statements that appeared to be designed to convince the reader to use the test. 'Inaccurate' information was that which was not consistent with published evidence (for example, a good result would ensure a healthy baby). 'Unsubstantiated' information was not supported by evidence in the text and 'conflicting' statements were those where the text included statements that could seem to be opposed, for example where different levels of accuracy were cited on the same website. In some cases, statements were allocated more than one code, for example a statement could be both inaccurate and persuasive.

In addition a table (Table 3) was prepared using the professional guidelines on information that should be provided for parents considering using NIPT, and the content of each website was assessed against those recommendations.

RESULTS

We identified 40 websites (listed in Table 2) that satisfied the inclusion criteria. These were websites of companies or organisations based in eight different countries. The majority (n=21) were based in the UK, seven in Australia, four in the United States (US), three in Canada and one each in Belgium, Dubai and Ireland (Table 2).

Place Table 2 about here.

Initially the topics covered in each website were identified: these are presented in Table 3. The topic was counted if it was mentioned, regardless of the depth or accuracy of the information. Examples of relevant text are included in Table 5.

Place Table 3 about here

Following in-depth analysis of the web-based text, four main themes relating to the text emerged (Table 4).

Place Table 4 about here

The themes are discussed below, and relevant examples of each type of text are presented in Table 5.

The first theme included information that was of good quality and provided accurate and balanced information to the consumer: this type of information was identified on 14 of the 40 websites included in the review. However, the information that the test was not able to detect all abnormalities was mentioned by only 6/40 companies and only just over half (21/40) mentioned that an invasive test would still be required to make the diagnosis. Several sites included statements confirming that the decision was a personal one and that the mother's consent was necessary. Other sites suggested that the mother should discuss her decision with her personal doctor, and three websites referred to counselling for the mother provided by their own genetic counsellors.

The second theme mainly related to statements about test accuracy and included statements that are unsubstantiated or required evidence in the form of reference to a published paper or document. Many webpages included claims about the 'accuracy' of NIPT, some relating to specific products and some making general claims. Some make non-specific claims, whilst others cited specific accuracy figures that were not supported by evidence presented to the potential user. Others still provided specific information relating to clinical studies but omitted any reference to those studies.

The third theme includes statements that use persuasive or emotive language. To an extent this is to be expected as the websites identified were commercial enterprises, and as such, are marketing a product. Although language used on the websites varied in its tone, some statements could be described as persuasive or designed to appeal to the emotional vulnerability of expectant mothers who may consider themselves at risk, for example using the phrase '*NIFTY can save many women from the agonising decision of whether to risk amnio or CVS*.' *(Nurture Antenatal Clinic)*. One company emphasised that their objective in marketing the test was to reduce the number of avoidable miscarriages. This seemed designed to reassure potential customers of the goodwill and altruism of the company.

The fourth category included statements that were misleading, incomplete or conflicted with other information on the same website. This category included claims that appear to be overstating the range of the tests. Others gave contradictory information, for example claiming results were definitive and then quoting sensitivities less than 100%. Some statements appeared confusing in the way that they were presented to consumers: *'A good test result gives a risk of a chromosomal problem of less than 1:10000. A bad result gives a risk of 1:2.'* Finally, some websites contained outdated information and provided previous versions of information sheets from the company undertaking the test.

DISCUSSION

Main findings

The use of Internet marketing of health related products has been well-documented for over a decade,[13] but the development of fetal testing that is non-invasive in nature has introduced new players into the field. To make informed decisions about

use of such tests, consumers need to not only think about their own beliefs and circumstances, but the level of trust they can invest in the marketing website of the product they are considering using. This requires a level of evaluation, and consumer assessment of website information has been the subject of much research over the past 15 years. Multiple instruments have been produced to support consumers in assessing the veracity and usefulness of website information.[17] However in a study of such tools, Bernstam et al[17] found that they were of limited practical use to patients using the Internet for health related information.

When individuals are using web-based health information to make decisions about their health and the future of a pregnancy, then accuracy is obviously a concern. However, in a study of health information related to breast cancer,[14] the findings indicated that there were inaccurate statements on 5.2% of the 343 websites studied. In our study we found few instances of actual inaccuracy, those that existed were mainly in the form of overly reassuring statements about normal results. However, there were some companies that appeared to overstate the capability of the tests, for example by claiming the tests could ensure normality of the fetal chromosomes. Even if a full karyotype is performed, the normality of the fetal chromosomes cannot be assured, and the health and wellbeing of the fetus cannot be ascertained using NIPT, or any other prenatal test. In addition to these statements, we found few examples of persuasive advertising.

Websites were more likely to discuss test benefits than test limitations or the potential psychological implications such as increased anxiety whilst waiting for test results. This is a concern, given that informed decision making requires potential service users to have sufficient knowledge and understanding of test limitations, as well as benefits. A similar issue was identified in a recent study assessing how the

UK press media are reporting advances in NIPT.[18] Journalists discussed concerns and limitations less frequently than test attributes. Only a third of the articles analysed in that study were considered to be balanced articles, giving equal weight to benefits and limitations or the inclusion of multiple viewpoints. Several studies have reported on the significant value women place on the relative safety of NIPT. Indeed one recent study conducted in the UK found that women were predominantly concerned with test safety, whereas health professionals valued test accuracy,[19] As test safety is at the forefront of women's minds when making decisions around NIPT, it is possible that if test providers aggressively promote NIPT on this basis, women may focus on the issue of safety and agree to testing without considering all the potential implications that may be important to them.

In this review the majority of websites we assessed included material that was not substantiated on the site by reference to other sources, which is one of the key criteria proposed by when considering quality of website information. [20] It is difficult therefore for us to check the veracity of the claims, as it would be for potential test users. In some cases, the papers from which figures were taken were cited in the health professional sections of the website, so technically potential consumers could find them if they searched further, however should this be necessary? One argument against including scientific sources is that consumers do not need or do not wish to check for accuracy of claims, however where there are conflicting statements within even the same website, this is surely essential. Another issue relates to the current status of the information. In our review, we found that different websites using the same testing company referred readers to different versions of the test company literature, some of which were outdated. Where companies and health professionals are offering tests, it would appear to be important that they

regularly update and maintain their websites ensuring that all information is as accurate and current as possible. While there is no legal requirement to do this, it would be considered responsible business practice.

Strengths and limitations

In any web-based study, one of the limitations lies in the transient nature of the material.[14]. Because web sites and the order in which search results appear changes, replication of this study, even the day after the searches were performed, would not be possible. We addressed this by ensuring that all the searches were done on the same day and that we printed the results to ensure we had a concrete record. In addition, two experienced researchers conducted the analysis independently before discussing the results. As Eysenbach and Kohler[13] state that most users of the Internet do not utilise results beyond the first page, we consider that by reviewing the first 20 pages of the searches we accessed all sites that would have been accessed by potential consumers. Our search used UK versions of Google and Bing and thus identified relatively more UK websites. We were only able to analyse those websites written in English, therefore the findings do not reflect the content of websites in other languages.

Interpretation

Recommendations on the information that should be available to potential users of NIPT for aneuploidy have been published by a number of national and international bodies , including the RCOG,[3] The American Congress of Obstetricians and Gynecologists,[8] the National Society of Genetic Counselors,[21] the American College of Medical Genetics and Genomics,[10] the Italian College of Fetal Maternal Medicine [9] and the Society of Obstetricians and Gynaecologists of Canada.[22] These

recommendations include the need for women to be aware of false positive and false negative rates, the fact that a negative result does not necessarily mean the fetus is unaffected, that an invasive test is required to confirm a positive result and that the woman should discuss her decisions after NIPT with her personal health professional. The analysis of topics included in the website materials indicated that these requirements were not met by all websites. Only nine of the forty websites stated that a negative NIPT did not mean that the fetus was definitely unaffected or may have a chromosomal rearrangement not detectable by NIPT. Just over half (52%) stated that an invasive test was required to confirm a positive NIPT result. Only 25% of websites stated that pre-test counselling with a health professional was important, even though the vast majority of professional guidelines emphasise the importance of this.[8-10] Even where the topics were mentioned, there was an issue was about the way in which companies presented, or did not present, their data on false positive and false negative results. A quarter (25 %) presented the detection rate (e.g. detects more than 99% of trisomy 21) but did not mention false positives or false negatives. Others (25%) used the term 'false negative' but did not explain what this means in understandable terms.

Trust in the website is one of the components that could lead potential users to request a test. Research has indicated that those seeking information on the Internet are more likely to trust information from sources they see as credible, for example those linked to pharmaceutical or medical organisations.[15, 23] This could mean that sites with organisational names that include terms such as health, clinic or hospital in the title might be more credible to users than sites operated by other companies. However, such a strategy could mislead consumers. In a study of 20 companies offering health screening tests online (of which 11 had health in the title),

Lovett et al[24] found that only 15% of the tests offered were recommended for use in the target group, while 30% were offered against the specific recommendations for the use of the test. As there is a potential for women to base their prenatal decisions on misleading marketing information, it is important that health professionals who are involved in prenatal care are familiar with the relevant aspects of NIPT use and can advise and guide women who may be considering such tests.

CONCLUSIONS

Although parents considering NIPT may seek information from other sources, with widespread access to the internet this will increasingly become a primary source. Companies and organisations who market online should have a duty to provide sufficient relevant and balanced information to help facilitate informed decision making. As a result of this review, we would recommend that companies offering prenatal testing services via the Internet should be required to review and maintain their information for prospective parents to ensure it is comprehensive, accurate and easily accessible and includes information recommended by national and international bodies. In addition, clear statements of false positive and false negative rates should be made in a way that is understandable to lay readers. Finally, it should be mandatory for companies to clarify that no prenatal test can guarantee the health and wellbeing of a baby.

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Table 1 Findings from two search engines using eight different search terms related to NIPT

	Google			Bing		
	Relevant findings	Total	% relevant	Relevant findings	Total	% relevant
‘prenatal test’	30	200	15.0%	1	200	0.5%
‘antenatal test’	3	200	1.5%	1	200	0.5%
‘non-invasive test’	24	200	12.0%	27	200	13.5%
‘noninvasive test’	6	200	3.0%	4	200	2.0%
‘cell-free fetal DNA’	4	200	2.0%	2	200	1.0%
‘cffDNA’	4	200	2.0%	0	200	-
‘Down syndrome test’	7	200	3.5%	4	200	2.0%
‘trisomy test’	20	200	10.0%	5	200	2.5%

Table 2. Test providers and country in which based.

Provider/ testing company used	**Country in which based**
3fivetwo Healthcare/Harmony	United Kingdom (UK)
92 Harley Street/Harmony	UK
Baby Scan Studio/Harmony	UK
BabyCenter/Not stated	Canada
Beard Mill Clinic/Harmony	UK
Birmingham Women's NHS Foundation Trust/Harmony	UK
Bristol Spire Hospital/Harmony	UK
Dr Gary Sykes/Harmony & verifi	Australia
Fetal Imaging Center/Not stated	United States (US)
GENDIA/Harmony	Belgium
Genesis Perinatal Care Clinic/Harmony & MaterniT21	Dubai
Glasgow Centre for Reproductive Medicine/Harmony	UK
Innermost Healthcare/NIFTY & Harmony	UK
Liverpool Women's Hospital/Not stated	UK
London Ultrasound Centre/Harmony	UK
Manchester Fertility/Harmony	UK
Mark E Richey O & G/Not stated	US
Medcan Clinic/not clear	Canada
Melbourne IVF/Panorama	Australia

Merrion Fetal Health/Harmony	Ireland
Nurture Antenatal Clinic/NIFTY	UK
Olive Fertility/verifi	Canada
Omni Ultrasound and Gynae Care	Australia
Pacific Centre for Reproductive Medicine/Harmony	Canada
Peninsula Diagnostic Imaging/verifi, MaterniT21 & Panorama	US
Private Birth Surrey/Harmony & Panorama	UK
Procrea Swiss Fertility Centre/Harmony	Switzerland
Queensland Fertility Group	Australia
Sheffield Private Pregnancy Care/Harmony	UK
The Birth Company/Harmony & Panorama	UK
The Harley Street Centre for Women/Harmony	UK
The Portland Hospital	UK
The Private Pregnancy Website/Harmony & Panorama	UK
The Women's Wellness Centre/Harmony	UK
Ultrasound Care/Not stated	Australia
Ultrasound Diagnostic Services/NIFTY & Harmony	UK
Victoria Clinical Genetics Services/Panorama	Australia
Wayne Young O & G/MaterniT21*	US
Women's Scan Clinic/Harmony	UK
Women's Ultrasound Melbourne/Harmony	Australia

Table 3. Table of topics covered in NIPT DTC websites

Topic	**Number of websites where mentioned** (n= 40)
Used to detect chromosomal disorders	33 (82%)
Detection rates for relevant disorders	31 (77%) Of these, 27 (67%) provided actual figures
Test is based on maternal blood sample	31 (77%)
Who the test is suitable for	26 (65%)
Invasive prenatal testing may still be advised for diagnosis	21 (52%)
False positive or negative rates	21 (52%)
Gestation when test can be performed	20 (50%)
New or novel test	17 (42%)
Low risk to fetus	16 (40%)
Advised to discuss with personal doctor or discussion with personal doctor mentioned	10 (25%)
NIPT more accurate than other forms of screening	9 (22%)
Test does not rule out all abnormalities	6 (15%)
Time between sample taking and results	6 (15%)
Test can provide reassurance to parents	5 (12%)
Signed consent form required	4 (10%)
Discussion offered with company health professional	3 (7%)
Inconclusive results possible	1 (2%)

Table 4 Themes identified from the webpage text

Theme	**Number of webpages including text coded under this theme**
Balanced, accurate information	14/40
Unsubstantiated or needing evidence	33/40
Persuasive or emotive language	15/40
Conflicting, misleading or incomplete	6/40

Table 5. Topics covered in NIPT DTC websites with examples of text

Topic	Number of websites where mentioned (n= 40)	Examples of text
Test is used to detect chromosomal disorders	33 (82%)	*'NIPT can detect pregnancies affected by two chromosome problems, Down syndrome and trisomy 18. While they are each caused by the presence of an extra chromosome, they have distinct features. Down syndrome causes mild to moderate problems in development; trisomy 18 tends to be more severe.'(Pacific Centre for Reproductive Medicine)* *'Non-invasive prenatal testing (NIPT) analyses cell-free DNA circulating in the pregnant mother's blood. It is a new option in prenatal screening for Down syndrome (Trisomy 21) and other fetal chromosomal conditions (Trisomies 18 and 13), X and Y chromosome conditions. ' (Merrion Fetal Health)* *'The laboratory is now able to extract free fetal DNA from the pregnant woman's blood, to test for extra fragments of chromosome 21.If extra fragments of chromosome 21 are detected it can signify the presence of Trisomy 21 (Down syndrome) in the fetus. This test also detects extra fragments of chromosome 18 and 13 and can also detect some sex chromosome abnormalities. It will tell you the sex of the baby.' (Ultrasound Care)*
Detection rates for relevant disorders	31 (77%) Only 27 gave explicit figures	*'Panorama NIPT detects >99% of the chromosome conditions for Trisomy 13 (Patau Syndrome), 18 (Edwards Syndrome) and 21 (Down syndrome), making it the most accurate NIPT test available.' (Queensland Fertility Group)* *'Clinical studies have shown that the Ariosa Harmony™ Prenatal Test has exceptional accuracy for assessing fetal trisomy risk.' (Merrion Fetal Health)*
Test is based on maternal	31 (77%)	'*The test needs a sample of the mother's blood rather than cells from the placenta, as in a chorionic villous sample (CVS), or fluid from around the baby as in an amniocentesis.'*

blood sample		*(Bristol Spire Hospital)*
Who the test is suitable for	26 (65%)	*'The Harmony™ Prenatal Test is only available at a few private clinics in the UK, but any parents can choose to have the test and can contact Beard Mill Clinic directly. A referral from your GP is not required. It can be performed in all single and twin pregnancies, including those conceived by IVF.' (Beard Mill Clinic)* *'The test is suitable for any woman who has had an ultrasound scan to confirm that her pregnancy is singleton, that the fetus is alive, and that the fetal length is equivalent to a gestation of 10 weeks or more.' (Women's Scan Clinic)*
Invasive prenatal testing may still be advised for diagnosis	21 (52%)	*'However the Harmony prenatal test is not 100% accurate nor diagnostic so we always recommend that you consider a diagnostic DNA test like a CVS or amniocentesis rather than having another screening test.'(London Ultrasound Centre)*
False positive or negative rates	21 (52%)	*The Medcan-offered NIPT provides a high sensitivity rate (>99%) and low false-positive rate (<0.1%) making it highly accurate.' (Medcan Clinic)* *'NIPT with Verifi is:* *Extremely Accurate* • *99.9% detection rate for Down syndrome* • *Low false positive rate of <0.2%* • *Low test failure rate of 0.07%' (Olive Fertility)* *'It has been found to have a detection rate of greater than 99% for Down's Syndrome, in comparison to the tests previously available, which have a detection rate of only 84%. It also has a much lower false positive rate than other tests which means if the result is negative it is highly unlikely that the baby has one of the chromosome abnormalities' (Liverpool Womens Hospital)* *'NIPT is a screening test and therefore in rare circumstances positive and negative results*

		can be inaccurate. The test will detect up to 99% of babies affected by Down, Edwards or Patau syndrome. A false positive result occurs in less than 0.3% of cases (1:300). This is significantly better than traditional screening tests which have a detection rate of 75-95% for a false positive rate of 3-5%.' (Harley Street Centre for Women)
Gestation when test can be performed	20 (50%)	'*NIFTY TEST – A safe, simple, accurate, affordable test for Down Syndrome from 10 weeks of pregnancy. Also 99% accurate for fetal sex (gender).' (Innermost Healthcare)* *'Non-invasive Prenatal Testing(NIPT) is a single blood test that uses cutting-edge technology to screen pregnant women for chromosome problems, as early as 10-weeks in pregnancy.' (Medcan Clinic)*
New or novel test	17 (42%)	*'NIPT is an exciting new development in prenatal diagnosis.' (Genesis Perinatal Care Clinic)* *'At Sheffield Private Pregnancy Care, we are pleased to announce that we are working in conjunction with TDL Genetics in London to offer a brand new and revolutionary service to our clients – Non-Invasive Prenatal Testing (NIPT). This simple blood test represents the future of screening for chromosomal abnormalities and we are one of the first to offer this service to the women of Sheffield.' (Sheffield Private Pregnancy Care)*
Low risk to fetus	16 (40%)	*'The testing is non-invasive: it involves taking a blood sample from the mother. The pregnancy is not put at risk of miscarriage, or from other adverse outcomes that are associated with invasive testing procedures such as amniocentesis.' (Baby Scan Studio)* *'In contrast to invasive diagnostic testing (CVS and amniocentesis), NIPT does not pose a risk of miscarriage to the pregnancy since it involves only a maternal blood sample.' (Peninsula Diagnostic Imaging)*
Advised to discuss with personal doctor or discussion with personal	10 (25%)	*'You certainly have already discussed the risk of foetal chromosomal abnormalities with your doctor. In addition to the other possibilities, the non-invasive screening for chromosomal aneuploidy (the wrong number of chromosomes in a cell), it offers the chance to screen for the presence of trisomies 21, 18 or 13 during pregnancy in a non-invasive way and at no risk to your child.* *ProCrea would like to provide helpful information about this test, which can be useful*

doctor mentioned		*during discussion with your doctor, who might indicate whether or not this non-invasive test is appropriate for you.' (Procrea Swiss Fertility Centre)* *'All results should be interpreted by a clinician in the context of clinical and familial data: patients should continue with their usual scan appointments following testing.' (Baby Scan Studio)* *'At this stage, it is recommended that you consult with your doctor to address any emotional issues raised by the results of the test and take advantage of all the attention and support you need.' (Melbourne IVF)*
NIPT more accurate than other forms of screening	9 (22%)	*'When compared to standard nuchal testing options, the Harmony test is almost 10% more accurate in the diagnosis of Down's.' (Glasgow Centre for Reproductive Medicine)* *'So the NIPT:* *• is more accurate than NTS and serum in detecting the commonest chromosomal abnormalities (Trisomy 21, 13 and 18),' (Dr Gary Sykes)*
Test does not rule out all abnormalities	6 (15%)	*'Limits of the test* *Most pregnancies end with the birth of a healthy baby. This may be not true in a small percentage, unfortunately.* *Nowadays many diseases can be diagnosed during pregnancy. Despite that, all known disease cannot be excluded. No one can guarantee you will have a healthy baby.'* *(Procrea Swiss Fertility* Centre) *'Unfortunately this cannot guarantee that your baby won't have any medical issues. This is because the NIPT (Non-Invasive Prenatal Testing) is only designed to look for aneuploidies of chromosomes 21, 18 and 13 as well as sex chromosomes. Even if the test comes back negative for aneuploidy it does not completely rule out all of the potential problems with those specific chromosomes.' Omni Ultrasound and Gynae Care)*
Time between sample taking and results	6 (15%)	*'The result will be available in 10-14 business days.' (Women's Ultrasound Melbourne)*
Test can	5 (12%)	*'As a mum-to-be, you'll be no stranger to worries about the health of your unborn child.*

provide reassurance to parents		*While there are indeed some women who don't opt for prenatal screening, many couples consider it essential to have an awareness of any possible foetal abnormalities they may be facing, in order to best prepare for any trying times ahead.* *However the traditional screening method, the Nuchal Translucency or 12 Week Scan can leave some room for doubt (it has a predictive value of 92%). Some women will proceed to more accurate tests, such as chorion villous sampling (CVS) or amniocentesis, however these invasive procedures have a 1 in 100 risk of miscarriage.* *Now thanks to expert research conducted by doctors at Kings College London, a simple blood test is available that could save the lives of hundreds of babies every year. The Harmony test was developed by American firm Ariosa Diagnostics. It has been extensively screened and given the thumbs up by a leader in the field of foetal medicine, the specialist that developed nuchal fold testing, Dr Kypros Nicolaides.' (The Private Pregnancy Website)* *'3fivetwo Healthcare is delighted to be the first in Ireland to offer the Harmony Prenatal Test. This service is now available to every pregnant woman with a singleton pregnancy who wants a safe, reliable, early and accurate test to verify that their baby has normal chromosomes.' (3fivetwo Healthcare)* *'NIFTY blood test however, is highly accurate, simple, safe and risk-free, giving mums peace of mind that they have a healthy fetus.' (Nurture Antenatal Clinic)*
Signed consent form required	4 (10%)	'*Women electing to have the cffDNA test will be given an information sheet and required to sign a consent form. Additional information and counselling will be available from our Doctors.' (Women's Ultrasound Melbourne)*
Discussion offered with company health professional	3 (7%)	*'At Olive you will meet with Rachel Butler, our certified genetic counselor, where you can learn about your options and discuss any concerns you may have. After your information session you will have a single blood sample drawn. When the results are available Rachel will review them with you and provide you and your care provider with a detailed report. Dr. Taylor is also available to answer pregnancy related questions and perform an ultrasound if necessary.' (Olive Fertility)*
Inconclusive results	1 (2%)	*'There are 3 possible results from NIPT:* *1. Positive – predicted to be affected by Down, Edward's or Patau syndrome*

possible		*2. Negative – highly unlikely to be affected by Down, Edward's or Patau syndrome* *3. Inconclusive – inconclusive results happen in less than 4% of cases. This is usually because the proportion of DNA present in the sample is not high enough to give an accurate result. NIPT may be repeated (no additional fee) with the hope that cell free DNA levels will have increased due to the increased pregnancy gestation.' (The Harley Street Centre)*

Table 5