Trial by Dutch Laboratories for Evaluation of Non-Invasive Prenatal Testing.

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Trial by Dutch laboratories for evaluation of non-invasive prenatal testing. Part II—women’s perspectives†

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ABSTRACT

Objective To evaluate preferences and decision-making among high-risk pregnant women offered a choice between Non-Invasive Prenatal Testing (NIPT), invasive testing or no further testing.

Methods Nationwide implementation study (TRIDENT) offering NIPT as contingent screening test for women at increased risk for fetal aneuploidy based on first-trimester combined testing (>1:200) or medical history. A questionnaire was completed after counseling assessing knowledge, attitudes and participation following the Multidimensional Measure of Informed Choice.

Results A total of 1091/1253 (87%) women completed the questionnaire. Of these, 1053 (96.5%) underwent NIPT, 37 (3.4%) invasive testing and 1 (0.1%) declined testing. 91.7% preferred NIPT because of test safety. Overall, 77.9% made an informed choice, 89.8% had sufficient knowledge and 90.5% had positive attitudes towards NIPT. Women with intermediate (odds ratio (OR) = 3.51[1.70–7.22], p < 0.001) or high educational level (OR = 4.36[2.22–8.54], p < 0.001) and women with adequate health literacy (OR = 2.60[1.36–4.95], p = 0.004) were more likely to make an informed choice. Informed choice was associated with less decisional conflict and less anxiety (p < 0.001). Intention to terminate the pregnancy for Down syndrome was higher among women undergoing invasive testing (86.5%) compared to those undergoing NIPT (58.4%) (p < 0.001).

Conclusions The majority of women had sufficient knowledge and made an informed choice. Continuous attention for counseling is required, especially for low-educated and less health-literate women. © 2016 The Authors. Prenatal Diagnosis published by John Wiley & Sons, Ltd.

INTRODUCTION

Non-Invasive Prenatal Testing (NIPT) for fetal aneuploidy has changed the landscape of prenatal screening worldwide.1 NIPT uses sequencing of cell-free DNA (cfDNA) in maternal plasma to screen for trisomy 21, 18 and 13 with a high accuracy in both high- and low-risk populations.2,3 For women with an elevated
risk based on first-trimester or sequential screening, NIPT is considered a good follow-up test that prevents the need for invasive testing for most of them, thereby avoiding the risk of iatrogenic loss of pregnancy. invasive test confirmation is, however, still necessary because of potential false-positive NIPT results.

Although the advantages offered by NIPT have created a strong demand to implement this test, concerns have been raised regarding the potential impact on informed decision-making. Both pregnant women and health professionals have expressed fears that NIPT might become routinized or that women might feel pressured to accept it. This could potentially undermine the aim of prenatal screening, which is to enable pregnant women to make an autonomous reproductive choice.

Informed choice is most commonly defined as a decision made with sufficient knowledge, consistent with the decision-maker’s values and behaviorally implemented. The ability to make an informed choice has been shown to be associated with better psychological outcomes such as less decisional conflict regarding the choice. To safeguard the process of informed decision-making, the need for comprehensive counseling on NIPT has been emphasized.

On 1 April 2014, the Netherlands incorporated NIPT into their governmentally supported and healthcare-funded Fetal Trisomy Screening Program. This has been realized through a nationwide implementation study: the TRIDENT study (Trial by Dutch laboratories for Evaluation of Non-Invasive Prenatal Testing). NIPT is being offered as an additional choice to women with an elevated risk for fetal trisomy 21, 18 or 13 based on first-trimester combined testing (FCT) or on medical history. In the Netherlands, around 27% of pregnant women decide to have FCT.

The TRIDENT study had two main objectives. First, to evaluate the clinical impact (uptake, test performance, turnaround-time, pregnancy outcome), the results of which have been reported separately (Oepkes et al. Paper Part I). In this second part, we report on women’s preferences and decision-making (informed choice), decisional conflict and anxiety.

METHODS

In the TRIDENT study, women at increased risk for fetal trisomy were referred for in-depth counseling to one of the eight Dutch Regional Prenatal Diagnosis Centers or their satellite centers (n = 13). Pregnant women were offered the choice between NIPT, invasive testing (chorionic villus sampling (CVS) or amniocentesis (AC)) or no further testing. Details on the TRIDENT study can be found in our separate paper Part I (Oepkes et al. Paper Part I). In seven of the eight centers, women participating in the TRIDENT study during the first five months (1 April – 1 September 2014) were asked to fill out two questionnaires. Approval for the study was granted by the Dutch government through a Population Screening Act License (No. 350010-118701-PG) and local University Medical Ethics Committees.

PARTICIPANTS

Pregnant women with an increased risk for fetal trisomy 21, 18 or 13 based on the results of the first-trimester combined test (cut-off risk ≥1:200) or based on medical history (i.e. a prior pregnancy with a fetal trisomy 13, 18 or 21 or a parental balanced Robertsonian translocation with increased risk on T21 or T13) were considered eligible. Exclusion criteria were gestational age <10 + 0 weeks, <18 years old, inability to provide informed consent, multiple pregnancies, vanishing twin, nuchal translucency >3.5 mm or other structural fetal anomalies, maternal history of malignancy or a known maternal chromosomal abnormality. All participants received a unique TRIDENT study number.

INFORMATION AND COUNSELING

During the standard pre-test counseling, NIPT was discussed as an alternative option for invasive testing in the case of an FCT result indicating an elevated risk. All women were given oral counseling by obstetricians, maternal fetal medicine specialists or specially trained counselors. Women were also given written information on both NIPT and invasive diagnostic testing (CVS or AC). The following topics were addressed: test procedure (including risk of invasive testing); reporting time; test sensitivity for T21, 18 and 13; the meaning of an abnormal test result and the necessity to confirm abnormal NIPT results with invasive testing. Furthermore, a dedicated website (in Dutch) was launched (www.meerovernipt.nl) where women could find additional information or ask questions about NIPT and the TRIDENT study.

PROCEDURE

The two questionnaires were designed by a multidisciplinary team of social scientists, psychologists, obstetricians and a clinical geneticist. Women were asked to fill out the first questionnaire (Q1) directly after counseling. This was done either on paper (six centers) or online (one center). Some counselors in three centers, however, only asked women choosing NIPT, and not those choosing invasive testing, to fill out the questionnaire. Because the overall number of women electing invasive testing was low, this study mostly reflects the findings of women choosing NIPT. The second questionnaire (Q2) was completed after women had received their test results. Only responses from the first questionnaire (Q1) are presented here.

MEASURES

Q1 registered the indication for follow-up testing (abnormal FCT or medical history) and whether women would have had FCT if NIPT had not been available. Next, women were asked to indicate, from a list of options, the most important reason for preferring either NIPT, invasive testing or no further testing. Informed Choice was measured using a modified Multi-dimensional Measure of Informed Choice (MMIC) developed by Marteau et al.. This method comprises the dimensions of knowledge, attitude and uptake. The measure was adapted to reflect the test options in the current study. Women’s knowledge about NIPT was measured through a 5-item scale designed for this study (Supplementary Table S1). The questions covered information about NIPT’s characteristics and implications of testing discussed in the information leaflet and during counseling. Women’s knowledge of invasive testing...
was not assessed, except for one question that addressed the accuracy of NIPT compared to invasive testing. Women’s attitudes towards NIPT and invasive testing were each measured using a semantic differential 5-point scale with four bipolar adjective pairs based on van den Berg et al.\textsuperscript{12}: negative–positive, difficult–easy, frightening–not-frightening and reassuring–not-reassuring. In terms of reliability, the NIPT attitude scale and invasive testing attitude scale were internally consistent (Cronbach’s alpha = 0.79 and 0.85, respectively). The type of test women decided to have was anonymously assessed from the TRIDENT study laboratory database using the TRIDENT study number.

The extent to which women accepted the fact that NIPT does not give 100% certainty and the fact that invasive testing has a miscarriage risk were both measured on a 5-point scale (compressed to a 3-point scale (not acceptable; neutral; reassuring)) in analysis. Women’s attitude towards termination of pregnancy in the case of Down syndrome or trisomy 13 or 18 were both measured with a single item on a 5-point scale (compressed into a 3-point scale: probably not, maybe/maybe not and probably).

Difficulties in decision-making or decisional conflict was assessed by the Dutch version of the 16-item Decisional Conflict Scale (DCS) developed by O’Connor\textsuperscript{16} and translated and validated by Koedoot et al.\textsuperscript{17} Cronbach’s alpha for the DCS was 0.97.

State anxiety was measured by a Dutch version of the six-item short form of the Spielberger State-Trait Anxiety Inventory (STAI).\textsuperscript{18,19} Cronbach’s alpha was 0.87.

Health literacy was measured by a Dutch version of Chew’s set of brief screening questions,\textsuperscript{20} translated and adapted by Fransen et al.\textsuperscript{21} Cronbach’s alpha was 0.68.

The following sociodemographic variables were assessed: age, parity, level of education, ethnicity, religion and level of religiousness (active/somewhat active; not active/not religious). Women were asked to indicate their gestational age and whether they had conceived naturally or via assisted reproductive technology (ART).

DATA ANALYSIS

Descriptive analyses were used to describe women’s characteristics. For the MMIC analysis, knowledge sumscores were dichotomized into sufficient or insufficient knowledge. Because no standard criteria for ‘sufficient’ or ‘insufficient’ knowledge are available, we decided that a cut-off of >2/5 questions would constitute sufficient knowledge. Questionnaires of women who left more than two knowledge questions blank were excluded from analyses. If a woman only left one or two questions blank or checked the box ‘I don’t know’ these were treated as incorrect answers. Attitude scores were categorized into positive, neutral or negative. Because responses to a neutral attitude cannot be classified as either having a positive or a negative attitude towards NIPT, they were excluded from the analysis, as was proposed by van den Berg et al.\textsuperscript{12} This is considered a better approach than the original application (dichotomization) of the MMIC attitude scale.\textsuperscript{21} Attitude was then combined with NIPT uptake to assess value-consistency; women who chose NIPT and have a positive attitude or who declined NIPT and have a negative attitude were classified as value-consistent. NIPT acceptors with a negative attitude or NIPT decliners with a positive attitude were classified as value-inconsistent. Based on their knowledge and value-consistency, it was assessed whether women had made an informed choice; if a woman had sufficient knowledge and was classified as value-consistent, an informed choice had been made.\textsuperscript{10,11} If women’s knowledge was insufficient and/or they were classified as value-inconsistent, their choice was considered to be uninformed.

Differences between women who chose NIPT and women who chose invasive testing were evaluated using the Fisher’s Exact Test. To evaluate variables associated with making an informed choice, univariate and multiple logistic regression was used with statistical significance set at p < 0.1 and p < 0.05, respectively. A Mann–Whitney test was used (because of non-normality of the items) to determine differences in decisional conflict and anxiety between women making an informed or uninformed choice. All analyses were performed using SPSS version 20 for Windows (IBM Statistics for Windows, IBM, NY, USA).

RESULTS

Women’s characteristics

In total, 1091/1253 pregnant women filled out Q1 (87% response). Women’s characteristics are presented in Table 1; 61.5% of women were highly educated and 74.9% were of Dutch origin. The mean age was 35.9 years (range 21–45) and the mean gestational age was 14.0 weeks (range 9–34). The majority of women (86%) had been offered NIPT because of a high risk (≥1:200) after FCT and 14% because of a medical history.

For the informed choice analysis using the MMIC, 52 questionnaires had to be excluded because of missing data on the attitude questions. Women with a neutral attitude (n=367) were excluded from analysis for the reasons mentioned above. Seven women left more than two knowledge questions blank, and these were excluded from analysis, resulting in a total sample of 665 participants used in the informed choice analysis.

Test preference

In our sample of 1091 women, 1053 (96.5%) had NIPT, 37 women (3.4%) had invasive testing and one woman (0.1%) declined further testing. The main reason for preferring NIPT was its safety (91.7%) (Table 2). Almost half of the women who preferred invasive testing did so because of test accuracy (47.1%) and 35.3% did so because of faster test results. The only woman who refrained from testing did so to avoid anxiety.

Women who had invasive testing significantly more often had a very high a priori risk (≥1:10), compared to women who had NIPT (p < 0.001). There was no significant difference in age, level of education, parity, having a medical history and conception via ART between women who chose invasive testing and women who chose NIPT.
The majority of women (77%) undergoing NIPT found it acceptable (p < 0.001). In contrast, the fact that invasive testing was associated with an increased risk of miscarriage was acceptable to 73% of women undergoing invasive testing and to only 15.9% of women having NIPT (p < 0.001) (Table S2).

**Intention in the case of an abnormal result**

Intention to terminate the pregnancy for Down syndrome was higher among women who had invasive testing (86.5%) compared to those who had NIPT (58.4%) (p < 0.001). This was also the case for trisomy 13 and 18, although less pronounced (94.6% vs 77.6%, respectively, p = 0.013) (Table S2).

**Informed choice**

As shown in Table 3, 89.8% of all women had sufficient knowledge on NIPT, 90.5% had a positive attitude towards NIPT and 86.3% made a decision that was value-consistent.

Women with intermediate or higher education were more likely to have sufficient knowledge about NIPT than those with a lower level of education (p < 0.001). There was no significant difference in knowledge between women who had NIPT and women who had invasive testing. Answers to separate knowledge questions are presented in Supplementary Table S2.

Informed choice analysis showed that 77.9% of all women had made an informed choice for NIPT. Those who made an uninformed choice (22.1%) did so because of insufficient knowledge (8.4%), value-inconsistency (11.7%) or because they had both insufficient knowledge and a value-inconsistent decision (2%) (Table 4). All women who had invasive testing had a positive attitude towards NIPT and therefore, based on the criteria of the MMIC, were scored as having made a value-inconsistent choice. However, data showed that 78.6% of these women also had a positive attitude towards invasive testing, so their choice for invasive testing was value-consistent and thus probably not uninformed (this could not be calculated because women’s knowledge about invasive testing was not measured). When women who had invasive testing were excluded from the analysis, the percentage of informed choice was 81%. There was no significant difference in informed choice between women who were offered testing because of high-risk FCT results and those who had a high risk based on their medical history. There was also no difference in rates of informed choice between the seven participating centers.

As shown in Table 5, univariate analysis revealed that women making an informed choice were significantly more likely to be ≥36 years old, have intermediate or higher education, have a low level of religiousness, have adequate health literacy and had heard of NIPT before participating in the study. Women of non-Western ethnicity were significantly less likely to make an informed choice. Multivariate analysis showed that women with an intermediate- (odds ratio (OR) = 3.51 [95% confidence interval (CI), 1.70–7.22], p < 0.001) and high level of education (OR = 4.36 [95%CI, 2.22–8.54], p < 0.001) and those having adequate health literacy (OR = 2.60 [95%CI, 1.36–4.95], p = 0.004) were significantly more likely to make an informed decision.
Decisional conflict and anxiety

Women who made an uninformed choice experienced more decisional conflict (Median (Mdn) = 21.88) than women who made an informed choice (Mdn = 6.25), $U = 26,942, p < 0.001, r = 0.22$. Moreover, women who made an uninformed choice (Mdn = 50.00) experienced more anxiety than those who made an informed choice (Mdn = 36.67), $U = 18,737, p < 0.001, r = 0.34$.

DISCUSSION

The majority of high-risk pregnant women preferred NIPT because it is safe for the child. Higher test accuracy and faster results were the most frequently mentioned reasons to prefer invasive testing. Most women had sufficient knowledge, a positive attitude towards NIPT and were able to make an informed choice. Women with an intermediate or high level of education and adequate health literacy were more likely to make an informed choice. Informed choice was associated with experiencing less decisional conflict and less anxiety.

Women choosing NIPT, as compared to those undergoing invasive testing, were less likely to accept the miscarriage risk of invasive testing and less often considered pregnancy termination for Down syndrome. This might imply that women opting for NIPT have different motives than women opting for invasive testing in that they want to prepare themselves for a child with Down syndrome and therefore prefer a risk-free test. Results from two questionnaire studies also showed that NIPT will probably be used more readily in women who just want to prepare themselves.24,25 In a UK study, where women were offered NIPT as a second screening test through the National Health Service (NHS), 31% (13/42) of women with a confirmed diagnosis of Down syndrome after NIPT continued the pregnancy, compared to 7% (2/29) after direct invasive testing.26 It needs to be established if this remains true once NIPT is fully incorporated in prenatal care.

Women who had invasive testing significantly more often had a very high a priori risk ($\geq 1:10$). In that case, it is understandable that they would prefer a test that is more accurate and delivers faster results, as was also concluded from a previous study in the US.27

<table>
<thead>
<tr>
<th>Measure</th>
<th>Description</th>
<th>Items</th>
<th>Reliability</th>
<th>Range</th>
<th>Mean (SD)</th>
<th>Cut-off</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge score</td>
<td>Knowledge about characteristics of NIPT and meaning of test results</td>
<td>Five correct/incorrect items</td>
<td>—</td>
<td>0–5</td>
<td>4.0 (1.1)</td>
<td>&gt;2</td>
<td>Sufficient knowledge: 89.8%</td>
</tr>
<tr>
<td>Attitude scale</td>
<td>Attitude towards having NIPT</td>
<td>Four 5-point items</td>
<td>0.79</td>
<td>4–20</td>
<td>16.7 (3.5)</td>
<td>&gt;14 = positivea</td>
<td>Positive attitude: 90.5%</td>
</tr>
<tr>
<td>Test uptake</td>
<td>Whether the woman had NIPT or not</td>
<td>Based on laboratory records</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Test uptake: 96.5%</td>
</tr>
<tr>
<td>Value-consistency</td>
<td>Consistency between value (attitude) and behavior (test uptake)</td>
<td>Calculatedb</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Value-consistent: 86.3%</td>
</tr>
<tr>
<td>Informed choice</td>
<td>A knowledgeable and value-consistent decision</td>
<td>Calculatedc</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Informed choice: 77.9%</td>
</tr>
</tbody>
</table>

SD, standard deviation.
aAttitudes were divided into three equal categories. Neutral attitudes (the middle category) (n = 367) were excluded from the analysis.12

bWomen who had a positive attitude towards NIPT and chose to have NIPT or women who had a negative attitude and chose not to have NIPT were classified as value-consistent.

cAn informed choice was made if a woman had sufficient knowledge and made a value-consistent decision. In all other cases, the decision was labeled as uninformed.
In our study, the rate of informed choice among women who chose NIPT (81%) is somewhat lower to that shown in the recent UK NHS study (94% informed choice).22 In our study, we also showed that most women choosing invasive testing made a value-consistent decision.

In line with previous studies,11,12 the results of the present study underscore the importance of making an informed choice in connection with beneficial psychological outcomes such as experiencing less decisional conflict. In contrast to other studies,12,13 we also found that the anxiety level was less high in women making an informed choice as compared to those making an uninformed choice.

Table 4: Types of informed and uninformed choice (n = 665)∗

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Attitude</th>
<th>Uptake</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed choice</td>
<td>Good Positive Yes</td>
<td>518</td>
<td>77.9</td>
<td></td>
</tr>
<tr>
<td>Good Negative No</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninformed choice</td>
<td>Good Positive No</td>
<td>22</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Good Negative Yes</td>
<td>56</td>
<td>8.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Positive Yes</td>
<td>56</td>
<td>8.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Negative No</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Positive No</td>
<td>6</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor Negative Yes</td>
<td>7</td>
<td>1.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

∗Typology based on Marteau et al.10 Women with ‘neutral attitudes’ [n = 367] were excluded from the analysis, based on van den Berg et al.12.

Table 5: Univariate and multiple logistic regression: factors associated with making an informed choice

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate logistic regression</th>
<th>Multiple logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Informed choice (n = 665)</td>
<td>Informed choice (n = 581)∗</td>
</tr>
<tr>
<td></td>
<td>Odds ratio (95%CI)</td>
<td>Odds ratio (95%CI)</td>
</tr>
<tr>
<td></td>
<td>p-Value (∗)</td>
<td>p-Value (∗)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤25</td>
<td>2.85 (0.80–10.16)</td>
<td>1.50 (0.35–6.41)</td>
</tr>
<tr>
<td>26–35</td>
<td>4.29 (1.21–15.21)</td>
<td>2.25 (0.33–9.58)</td>
</tr>
<tr>
<td>≥36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>4.10 (2.11–7.98)</td>
<td>3.51 (1.70–7.22)</td>
</tr>
<tr>
<td>High</td>
<td>4.56 (2.46–8.44)</td>
<td>4.36 (2.22–8.54)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutch</td>
<td>0.75 (0.45–1.26)</td>
<td>0.77 (0.43–1.38)</td>
</tr>
<tr>
<td>Other Western</td>
<td>0.42 (0.25–0.71)</td>
<td>0.58 (0.32–1.06)</td>
</tr>
<tr>
<td>Non-Western</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low level of religiousness</td>
<td>1.60 (1.02–2.52)</td>
<td>1.23 (0.73–2.04)</td>
</tr>
<tr>
<td>Adequate health literacy</td>
<td>3.14 (1.77–5.57)</td>
<td>2.60 (1.36–4.95)</td>
</tr>
<tr>
<td>parity ≥1</td>
<td>0.96 (0.66–1.40)</td>
<td>0.838 (0.38–1.38)</td>
</tr>
<tr>
<td>Already heard of NIPT</td>
<td>2.28 (1.26–4.10)</td>
<td>1.90 (0.98–3.67)</td>
</tr>
</tbody>
</table>

Cl, confidence interval.

∗Multiple logistic regression excluded 84 women who had missing values on one of the variables.

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Because no information was available on the survey decliners, potential selection bias cannot be excluded. Moreover, although the MMIC is often used as a measure of informed choice for screening, it does have some limitations. It requires a knowledge measure that is specific to the condition being tested, but because there is no gold standard for good knowledge this is subjective. In our study, only knowledge on NIPT was assessed. To fully comprehend whether women made an informed choice, also knowledge of invasive testing should have been assessed. Another limitation of using the MMIC is that, because it is developed to measure informed choice between women either accepting or declining a test, it is unable to account for variations that exist when measuring informed choice between women choosing between different tests, as seen in our study with women who had both a positive attitude towards NIPT and invasive testing. Recently, the MMIC has been adapted and validated for women considering NIPT as a second screening test, also including women’s deliberation. Our sample predominantly comprised older, highly educated women. However, Dutch women are shown to be more likely to have prenatal screening if they are older and have above-average income. Moreover, highly educated women often delay childbearing and are thus more likely to have a high risk result on the FCT. Finally, in the Netherlands, prenatal testing is offered in a nationally organized prenatal screening system, the uptake of which is relatively low (~27%), and thus caution is needed when generalizing the results to other contexts, for example, to other countries.

In conclusion, implementation of NIPT within the setting of the TRIDENT study was successful as the knowledge of the vast majority of pregnant women on NIPT was sufficient and most were able to make an informed decision. Most women choose NIPT because they want a safe test. Compared to women having invasive testing, women who choose NIPT less frequently intend to terminate their pregnancy in the case of Down syndrome, Edwards syndrome or Patau syndrome, possibly indicating that they more often undergo NIPT just to prepare themselves. To safeguard informed decision-making on NIPT outside the context of a controlled study, emphasis has to be placed on maintaining information and counseling skills among obstetric caregivers and exploring innovative strategies and counseling aids especially, but not exclusively, for women with low educational levels and/or inadequate health literacy.

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REFERENCES


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