## **ORIGINAL ARTICLE**



# Factors involved in the decision to decline prenatal screening with noninvasive prenatal testing (NIPT)

#### Correspondence

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### **Abstract**

**Objective:** To investigate factors involved in the decision to decline prenatal screening with noninvasive prenatal testing (NIPT).

**Method:** A questionnaire study was conducted among 219 pregnant women in the Netherlands who had declined prenatal screening with NIPT (TRIDENT-2 study). Respondents were selectively recruited from three hospitals and 19 midwifery practices, primarily located in or near socioeconomically disadvantaged neighborhoods. 44.3% of the respondents were of non-Western ethnic origin and 64.4% were religious.

**Results:** Most respondents (77.2%) found the decision to decline NIPT easy to make, and 59.8% had already made the decision before information about NIPT was offered. These respondents were more often religious, multigravida, and had adequate health literacy. The main reasons to decline NIPT were "I would never terminate my

Lisanne van Prooyen Schuurman and Karuna van der Meij contributed equally to this work.

A complete list of all members of the Dutch NIPT Consortium is provided in Appendix 1.

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pregnancy" (57.1%) and "every child is welcome" (56.2%). For 16.9% of respondents, the out-of-pocket costs (175 euros) played a role in the decision, and the women in this group were more often nonreligious, primigravida, and had inadequate health literacy. **Conclusion:** The primary factors involved in the decision to decline NIPT were related to personal values and beliefs, consistent with autonomous choice. Out-of-pocket costs of NIPT hinder equal access for some pregnant women.

## Key points

## What's already known about this topic?

- Women with low education levels and/or low income levels are less likely to opt for prenatal screening.
- Differences in screening uptake based on socioeconomic factors might indicate unequal access to prenatal screening.

### What does this study add?

- Personal beliefs and values play a prominent role in the decision to decline noninvasive prenatal testing (NIPT), which is in accordance with autonomous choice.
- The out-of-pocket costs play a role in the decision to decline NIPT in 16.9% of respondents.

## 1 | INTRODUCTION

In many developed countries, prenatal screening for fetal aneuploidy has become an integral part of prenatal care. <sup>1,2</sup> Its aim is to support expectant parents' reproductive autonomy by informing them early in pregnancy about the health of the fetus, and the possible course of actions thereafter.<sup>3</sup> There are different prenatal screening methods available, such as first-trimester combined testing (FCT), which involves a blood test and an ultrasound scan. One method that is increasingly being used is noninvasive prenatal testing (NIPT). NIPT is a recently established screening test that identifies chromosome abnormalities through the analysis of cell-free DNA in maternal blood circulation. <sup>4,5</sup> The popularity of NIPT is growing fast, mainly because of its accuracy in detecting trisomies 21, 18, and 13, <sup>6,7</sup> its timing, as it can be performed early in pregnancy, and the test's ease of use and safety.

The decision to participate in prenatal screening for fetal aneuploidy is a complex and personal one.<sup>8–10</sup> In the Netherlands, women are offered pretest counseling by obstetric health professionals to help them make an informed and autonomous choice that is consistent with their personal values and beliefs.<sup>11–14</sup> Another important aspect to support autonomous decision making in prenatal screening is assurance of equal access.<sup>11,15</sup> Factors, such as personal resources, that can restrict certain groups of women from having equal access to screening need to be carefully identified and eliminated to ensure this fundamental right.<sup>16,17</sup>

Previous studies have investigated the uptake of prenatal screening tests and various factors affecting the decision to have prenatal screening. Test acceptors' main reason for choosing screening was shown to be getting reassurance about the health of the fetus. <sup>18,19</sup> In addition, higher rates of screening uptake were associated with increased levels of income<sup>20–22</sup> and education,<sup>20,23</sup> knowledge of the condition(s) being screened for,<sup>24–26</sup> as well as higher maternal

age.<sup>20-22,24,27-29</sup> Test decliners' main reason for not opting for screening was a negative attitude toward termination of pregnancy.<sup>18,19,21,29-31</sup> Lower levels of income<sup>20-22</sup> and education,<sup>20,23</sup> religion,<sup>20,21,23-25,30</sup> and out-of-pocket costs of the screening test<sup>21,32</sup> were shown to be factors associated with the decision to decline prenatal screening. The disparities between test participants and nonparticipants might be explained in part by differences in individual values and beliefs; however, other factors, such as a lower socioeconomic status, may be restricting equal access or interfering with informed decision making.

Participation in fetal aneuploidy screening in the Netherlands has traditionally been lower than in surrounding countries.<sup>33</sup> After the introduction of NIPT as a first-tier screening test for all pregnant women (TRIDENT-2), the prenatal screening uptake (in 2020: 52%; 51% NIPT and 1% FCT)<sup>34</sup> remained much lower than in, for example, Belgium (in 2017-2019: 79% NIPT)<sup>35</sup> and England (in 2019: 84% FCT).<sup>36</sup> A possible explanation for the generally low uptake in the Netherlands may be the emphasis on women's 'right not to know' about the option of screening; before pretest counseling, expectant parents are first explicitly asked if they wish to be informed about prenatal screening. 33,37 This approach emphasizes that prenatal screening is not a routine medical procedure and that women are free to decline.<sup>38</sup> Other reported factors for the low uptake of prenatal screening in the Netherlands included a relatively positive attitude toward Down syndrome, a negative attitude toward termination of pregnancy, and out-of-pocket costs required for screening. 18,33

Recent research has shown that the uptake of NIPT in socioeconomically disadvantaged neighborhoods in the Netherlands is lower (20.3%) than in other neighborhoods (47.6%).<sup>16</sup> This raises questions about whether factors specific for these neighborhoods might hinder equal access and informed decision making, specifically in the case of NIPT. With this study, we therefore aim to investigate women's decision making and factors involved in the decision to decline prenatal screening with NIPT.

#### 2 | METHODS

A questionnaire study among pregnant women who declined NIPT was conducted between December 2020 and May 2021 as part of the TRIDENT-2 study, and was approved by the VU University Medical Center Amsterdam Ethical committee (VUMC No. 2020.09).

## 2.1 | Setting

Beginning in 2017, the TRIDENT-2 study investigated the implementation of NIPT as a first-tier screening test for all pregnant women within the national prenatal screening program for Down, Edwards, and Patau syndrome in the Netherlands. Maternity care providers (mostly primary care midwives) offer pregnant couples the option of screening with either FCT or NIPT in the first trimester of pregnancy. If interested, women are subsequently offered a 30-min pretest counseling consultation to support the decision-making process. Additionally, brochures (available in five different languages) and two websites are available with information regarding prenatal screening and the TRIDENT studies. NIPT is offered in addition to the second trimester structural anomaly ultrasound scan (uptake 2020: 86.4%<sup>34</sup>). Women need to pay 175 euros (175 dollars) for NIPT out of their pockets; there are no costs for the structural anomaly scan.

## 2.2 Respondents and procedure

Respondents were recruited from 19 midwifery practices and three hospitals across the Netherlands (n = 22). These practices and hospitals were selected and approached to participate in this study based on the ZIP Code List for Socioeconomically Disadvantaged Areas in the Netherlands, compiled by the Dutch Healthcare Authority (NZa).<sup>39</sup> Additionally, midwifery practices were recruited through an announcement on the websites and the newsletters of the eight Regional Centers for Prenatal Screening and through the Midwifery Science Department of Amsterdam UMC. Of the participating practices and/or hospitals, 4/22 (18.2%) were located in socioeconomically disadvantaged neighborhoods and 16/22 (72.7%) were located near these areas. In addition, 2/22 (9.1%) practices were located in so-called Bible belt. Five midwifery students were trained to administer the guestionnaires orally. Due to measures related to the COVID-19 pandemic, most questionnaires were administered by telephone or digitally instead of on location. All answers were processed in an online repository. At the request of participants, an online version of the questionnaire became available from January 2021, which women could complete themselves. Pregnant women who did not opt for prenatal screening with NIPT were asked to participate in this study by their maternity care provider after a favorable result of the second

trimester structural anomaly scan (no anomalies detected). Upon agreement, women were contacted by telephone and/or e-mail by the researchers to schedule an appointment for the interview, or they received an e-mail with a link to the online questionnaire, depending on individual preference. The exact percentage of nonresponse for this study is unknown, as the number of women approached by the maternity care providers is unknown. Respondents received a gift voucher of 10 euros. The midwifery practices and hospitals were offered a 25 euro gift voucher for their participation. The information

flyers and letters that were used in this study are given in Appendix 2.

## 2.3 | Questionnaire

The questionnaire used for this study was based on a previously developed questionnaire, with some modifications made by a multi-disciplinary group consisting of midwives, a clinical geneticist, a patient representative, and health scientists. The questionnaire was adapted to language level B1 by the Dutch Center of Expertise on Health Disparities (Pharos). Additionally, the questionnaire was piloted by Pharos using a think-aloud method with four women to assess comprehensibility and adjusted based on their feedback. Finally, it was translated into English for women with a non-native Dutch background. The questionnaire covered the following themes: sociodemographic characteristics, experience with information provision, the timing and ease of making the decision, (self-reported) knowledge of Down, Edwards, and Patau syndrome and NIPT, the role of costs in the decision, and reasons to decline NIPT. For a description of the variables used in this study, see the Supplementary Methods.

## 2.4 | Data analyses

The data of the online questionnaires and the questionnaires that were administered orally were analyzed together, as outcomes of these groups did not differ significantly. Descriptive statistics were used to describe the sociodemographic characteristics of the study population. Open-ended questions regarding self-reported knowledge of the syndromes and NIPT were labeled as being correct or incorrect by two independent researchers (LPS and KM). Differences in responses to the questions by sociodemographic characteristics were assessed using the Fisher Exact test, with p < 0.05 considered significant. Statistical analyses were carried out in R version 3.3.1 (R Project for Statistical Computing).

## 3 | RESULTS

In total, 219 pregnant women participated in the study. Questionnaires were administered through structured interviews (n=127, 58.0%) or completed online by the women themselves (n=92, 42.0%). Respondents' sociodemographic characteristics are given in Table 1. Respondents were on average 27.6 weeks pregnant at the

TABLE 1 Sociodemographic characteristics of respondents (n = 219) in comparison to the general Dutch (obstetric) population

**Total** 

**General Dutch** 

	N (%)	population <sup>a</sup> (%)		
Maternal age (years)				
<25	24 (11.0)	(7.8)		
25-29	64 (29.2)	(28.7)		
30-34	93 (42.5)	(40.7)		
≥35	38 (17.4)	(22.7)		
Education level <sup>b</sup>				
Low	21 (9.6)	(9.7)		
Intermediate	110 (50.2)***	(32.3)		
High	88 (40.2)***	(55.9)		
Ethnic origin <sup>c</sup>				
Dutch	113 (51.6)***	(68.8)		
Other Western	9 (4.1)***	(12.2)		
Non-Western	97 (44.3)***	(18.8)		
Moroccan	32 (14.6)***	(3.5)		
Turkish	20 (9.1)***	(3.5)		
Surinamese	14 (6.4)**	(2.3)		
Antillean	4 (1.8)	(1.1)		
Other	27 (12.3)*	(8.4)		
Religious affiliation				
None	78 (35.6)***	(64.5)		
Religion	141 (64.4)***	(35.5)		
Catholic	8 (3.7)**	(11.1)		
Protestant Christian	62 (28.3)***	(11.3)		
Islamic	61 (27.9)***	(7.7)		
Other	10 (4.6)	(5.4)		
Living in a socioeconomically disadvantaged neighborhood <sup>d</sup>				
Yes	68 (31.1)			
No	151 (68.9)			
Gestational age at the time of completing the questionnaire (weeks)				
≤20	28 (12.8)			
>20	191 (87.2)			
Gravidity				
Primi	64 (29.2)			
Multi	155 (70.8)			

TABLE 1 (Continued)

	Total N (%)	General Dutch population <sup>a</sup> (%)
Health literacy <sup>e</sup>		
Adequate	193 (88.1)	
Inadequate	26 (11.9)	

Note: N/% may deviate due to missing values.

<sup>a</sup>Maternal age of pregnant women in 2020 (Dutch National Obstetric Outcome Registration Perined<sup>52</sup>; n=165,272). Education level and ethnic origin for women in the age category 25–45 (Statistics Netherlands Q2 2021; n=2,131,000). Religious affiliation in 2019 in the age category 25–35 (Statistics Netherlands). Percentages may not add up to 100% due to missing values.

<sup>b</sup>Education levels were categorized as low: elementary school, low level secondary school, or lower vocational training; intermediate: high-level secondary school or intermediate vocational training; and high: high vocational training or university (Statistics Netherlands).

<sup>c</sup>Ethnic origin was categorized as Dutch: both parents were born in the Netherlands; other Western: one or both parents were born in Europe (excluding Turkey), North America, Oceania, Indonesia, or Japan; non-Western: one or both parents were born in Africa, Latin-America, Asia (excluding Indonesia or Japan), or Turkey. Maternal country of birth was leading if both parents were born abroad (Statistics Netherlands).

 $^{
m d}$ To determine whether the respondent lives in a socioeconomically disadvantaged neighborhood, the Dutch Healthcare Authority (NZa) Zip Code List was used.  $^{
m 39}$ 

<sup>e</sup>Health literacy measured by the question: 'You are sometimes asked to complete medical forms. Do you think that you complete them properly or do you have doubts?' Health literacy was classified as 'Inadequate' when respondents answered 'Sometimes I think I complete forms properly, sometimes I have doubts', or 'I often doubt whether I have completed forms properly' or 'I always doubt whether I have completed forms properly'.  $^*p < 0.05$ ;  $^{**p} < 0.01$ :  $^{***p} < 0.001$ .

time of the questionnaire assessment and had a mean age of 30.4 years (SD 4.6; range 21–43). Compared to the general Dutch (obstetric) population, respondents were less often highly educated (40.2% vs. 55.9%), more often of non-Western ethnic origin (44.3% vs. 18.8%), and more often religious (64.4% vs. 35.5%). Of those reporting to be religious, most identified as Protestant Christian (28.3% vs. 11.3%) or Islamic (27.9% vs. 7.7%). About one third of the respondents (31.1%) lived in socioeconomically disadvantaged neighborhoods.

## 3.1 | Experiences with information provision

In total, 202 (92.2%) respondents indicated that they had been offered and accepted information about NIPT, 10 (4.6%) indicated that the information had been offered but that they declined this

information, four (1.8%) stated that they were never informed about screening with NIPT, and three (1.4%) did not remember. Most women who had received information said it was via a leaflet (162/202, 80.2%) and/or via a 'short introductory conversation' with a healthcare provider (142/202, 70.3%) and/or a 'counseling consultation' (26/202, 12.9%). In addition, 22 (10.9%) respondents consulted a website for more information. Nonreligious respondents reported significantly more often that they had received a counseling consultation than religious respondents (Supplementary Table S1). Experience with the information provided is shown in Figure 1.

## 3.2 | The timing and ease of making the decision

The majority of respondents (169, 77.2%) had no difficulty deciding to decline prenatal screening with NIPT. These women were significantly more often multigravida and had adequate health literacy (Supplementary Table S1). In contrast, 15.5% (n=34) found it difficult to make the decision for screening and a small group (9, 4.1%) did not feel like they were making a decision. Respondents in the latter group were all religious. The remaining 3.2% (n=7) did not remember or considered it neither a difficult nor an easy decision. A majority of respondents (131, 59.8%) had already made the decision not to have NIPT before receiving information from the maternity care provider. Others (68, 31.1%) did not know their choice in advance or had not heard about NIPT before (19, 8.7%). One respondent (0.5%) did not remember this. Religious respondents.

multigravida respondents, and respondents with adequate health literacy significantly more often made the decision not to participate in prenatal screening with NIPT before information about prenatal screening was offered by the maternity care provider (Supplementary Table S1).

# 3.3 | Self-reported knowledge

Most respondents (209, 95.4%) reported that they knew about Down syndrome and most respondents (190, 86.8%) reported understanding NIPT. This percentage was considerably lower (71, 32.4%) for knowledge on Edwards and Patau syndrome. Respondents with a low education level and non-Western respondents had significantly less knowledge regarding the common trisomies or about NIPT (Supplementary Table S2). Self-reported knowledge about Edwards and Patau syndrome and NIPT was significantly lower among women with a religious affiliation, women living in socioeconomically disadvantaged neighborhoods, and women with inadequate health literacy. Multigravida women had significantly lower self-reported knowledge about NIPT compared to primigravida. Participants who answered this question affirmatively: 'Do you know what non-invasive prenatal testing, also referred to as NIPT, is?' (190, 86.8%), were asked to give a description of this test in their own words. This open question showed that 14 (7.4%) respondents incorrectly thought that NIPT was an invasive test in which amniotic fluid or material was obtained directly from the fetus.

# What did you think about the information concerning NIPT?

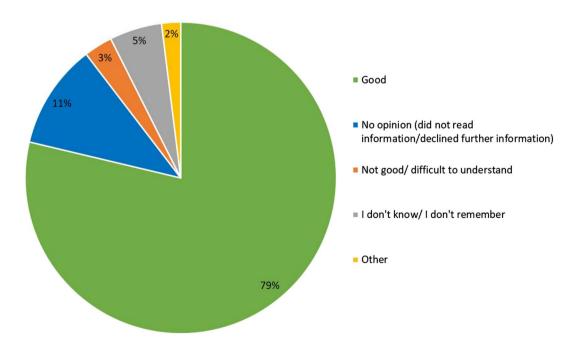


FIGURE 1 Experience with the received information about prenatal screening with noninvasive prenatal testing (NIPT). Question answered by 202/219 (92.2%) respondents who indicated that they had received information about NIPT.

# 3.4 | Reasons to decline NIPT

Three main reasons were given for declining NIPT: 'I would never terminate my pregnancy/because of my religion (which, as a matter of principle, forbids abortion)' (125, 57.1%), 'Every child is welcome; a child with Down, Edwards, or Patau syndrome as well' (123, 56.2%), and 'I do not want to unnecessarily worry' (91, 41.6%) (Table 2). Religious women mentioned the first two reasons significantly more often (Supplementary Table S3). None of the women mentioned that her obstetrician or doctor advised not to choose NIPT.

# 3.5 | Role of the out-of-pocket costs

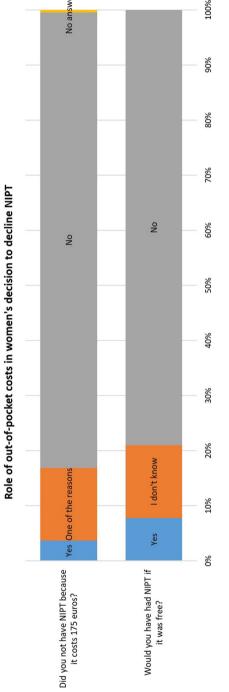
Of the respondents, 29 (13.2%) indicated that the costs were not the most important reason, but it was one of the reasons for not having NIPT, and eight (3.7%) respondents wanted NIPT but thought it was too expensive (Figure 2). Seventeen respondents (7.8%) would have opted for NIPT if it was free. Nonreligious women, primigravida women, and women with inadequate health literacy significantly more often did not have NIPT because of the costs (Supplementary

TABLE 2 Reasons to decline noninvasive prenatal testing

Reasons for declining prenatal screening with noninvasive prenatal testing	Responses N (%)
I would never terminate my pregnancy/ because of my religion (which, as a matter of principle, forbids abortion)	125 (57.1)
Every child is welcome; a child with down, Edwards, or Patau syndrome as well	123 (56.2)
I do not want to unnecessarily worry	91 (41.6)
Other <sup>a</sup>	52 (23.7)
I think I have a low risk of having a child with down, Edwards, or Patau syndrome	44 (20.1)
I think the test is too expensive	33 (15.1)
I am afraid I will regret testing when faced with an abortion decision	29 (13.2)
I am not worried about my child's health	18 (8.2)
I do not want to know if my child has a disorder	13 (5.9)
My partner, family or someone else advised not to do it	9 (4.1)
My obstetrician or doctor advised not to do it	0 (0.0)

Note: Respondents (n = 219) could give multiple reasons.

<sup>a</sup>Other reasons included 'the test does not provide 100% certainty about the health of my child (n=4)', 'the test is not 100% reliable (n=4)', 'I would never opt for invasive follow-up testing because of the risk of a miscarriage (n=10)', 'I prefer the second-trimester anomaly scan (n=3)', and '(major) anomalies can also be detected on the second-trimester anomaly scan (n=5)'.



Role of out-of-pocket costs in women's decision to decline noninvasive prenatal testing (NIPT) FIGURE 2

Table S4). Women with insufficient health literacy would have chosen to have NIPT significantly more often if the test was offered for free (Supplementary Table S4).

## 4 DISCUSSION

This study assessed women's decision making and factors involved in the decision to decline prenatal screening with NIPT. The strategy used for recruitment of the participants was aimed at the inclusion of pregnant women living in socioeconomically disadvantaged neighborhoods. One third of the respondents lived in these neighborhoods. Additionally, the study population comprised of a relatively high number of non-Western (44.3% vs. 18.8%) and religious respondents (64.4% vs. 35.5%), compared to the average Dutch women in the reproductive age group. Our results show that most respondents (77.2%) found the decision to decline NIPT easy to make and that 59.8% had already made the decision before information about NIPT was offered. The main reasons to decline NIPT were: 'I would never terminate my pregnancy' and 'every child is welcome'. These reasons were also reported in a previous Dutch study (TRIDENT-2), which included mostly highly educated and non-religious respondents, as the main reasons to decline fetal aneuploidy screening. 18 Our study shows that personal (religious) beliefs and values are important factors in the decision to decline screening.

Self-reported knowledge of Edwards and Patau syndromes was low among respondents; only about one third of respondents indicated that they knew about these syndromes. Additionally, knowledge levels were lower among religious, non-Western respondents and respondents with lower educational levels and health literacy. It has previously been shown that (lack of) knowledge of the disorders that are being screened for is an important factor in the decision to participate in prenatal screening,<sup>25</sup> and that women who decline prenatal screening are less likely to make an informed decision, in part due to a lack of knowledge. 18 The question of how much and which knowledge is required for women to make an informed decision has been often posed in the past decades.<sup>40</sup> Especially when declining prenatal screening based on (religious) values and beliefs, it could be argued that less technical and procedural knowledge may be required to make a decision.<sup>14</sup> While giving consideration to women's right not to know about the option of screening, decisions should not be made on the basis of incorrect knowledge. A way to mitigate this could be to improve genetic education among the general population, and more specifically about Down syndrome and prenatal screening. Moreover, differences in sociodemographic characteristics of respondents associated with differences in knowledge levels show a need to address deficiencies in the communication between counselors and couples. This is in line with the result of a recent interview study, which showed that prenatal counselors experience difficulties in communicating with women of non-Western migrant background, which contributes to suboptimal counseling.41 Therefore, counselors need to receive continuing education based on the latest insights to support their clients in making informed and value-consistent decisions.<sup>42</sup> The ability to tailor counseling regarding these aspects can support women in making an informed and autonomous decision.

Concerns have been raised that the positive test characteristics of NIPT (e.g., the test can be done early in pregnancy with high sensitivity and specificity) might lead to increased societal or provider pressure on pregnant women to accept prenatal screening with NIPT.<sup>38</sup> The results of this study, however, showed that women felt free to decline NIPT based on reasons in line with their personal beliefs and values, and we found no evidence of provider pressure.

For 16.9% of the respondents, the out-of-pocket costs played a role in the decision to decline NIPT. This percentage was about two times higher than the percentage found in earlier Dutch studies among the general obstetric population (6%-10%). 18,43 The difference may indicate that a disadvantaged economic status is a factor in prenatal screening decisions and that the requirement to pay for screening inhibits the freedom to choose. This is alarming, especially for countries with health services circumstances that require women to fully pay for NIPT or where reimbursement is more limited than in the Netherlands. Australia, for example, has no formal screening program and no federal funding for NIPT.<sup>2</sup> Also, the test is not reimbursable through private health insurance. Previous studies in this country show that women who opt for NIPT tend to live in metropolitan areas and areas of greater socioeconomic advantage, 44,45 justifying concerns of inequity by sociodemographic background. In Canada, variability exists in NIPT funding models within the country.<sup>2</sup> In a qualitative Canadian study, healthcare professionals expressed concerns about cost barriers promoting access inequalities for NIPT.46 Additionally, both women in Canada<sup>32</sup> and in the United States<sup>47</sup> indicated that any out-of-pocket costs would be a highly determining factor in the decision to test. Countries in which the offer of NIPT is not highly regulated and where there is no public funding for NIPT should therefore carefully reevaluate their current prenatal screening policy to prevent the test from being available only to the privileged.

Recently, the Dutch health authorities have announced that starting in 2023, NIPT will be offered to all pregnant women in the Netherlands free of charge.<sup>48</sup> Previously, concerns have been raised that the reimbursement of NIPT might lead to a sharp increase in uptake, with pregnant women accepting screening without proper counseling or consideration.<sup>49</sup> These concerns were fueled by studies from other countries, which showed that costs are an important factor influencing NIPT utilization. 45,50,51 In our study, 79% of the women who declined NIPT reported that they would not opt for NIPT if the test was free of charge, suggesting that a change in reimbursement policy is unlikely to have a large effect. Additionally, of the 16.9% of women who mentioned that the costs of NIPT played a role in the decision to decline NIPT, only 3.7% of the respondents said that the costs were the main reason to decline NIPT. This suggests that in most cases, the costs were not the decisive factor to decline screening, but rather an additional factor supporting the decision to decline. This is in line with the findings of a previous Dutch qualitative study among women who were offered FCT.<sup>19</sup> However, future research must show what the actual impact will be

of eliminating the out-of-pocket costs for NIPT on the test uptake in the Netherlands

#### 5 | STRENGTHS AND LIMITATIONS

A strength of our study was that participants were mainly recruited from midwifery practices primarily located in or near socioeconomically disadvantaged neighborhoods. This group included significantly more migrant and religious women and allowed us to investigate factors that may hinder equal access and informed decisions that may explain the lower-than-average uptake of NIPT in these regions. A consequence is that our results cannot be generalized for the general obstetric population. This questionnaire contained several questions of a sensitive nature, for example, regarding the costs of NIPT. This may have resulted in some respondents giving socially desirable answers due to shame or embarrassment, and therefore, this may have caused an underestimation of the percentage of women for which the costs of NIPT are a barrier to participate. In addition, only women with a favorable result of the second trimester structural anomaly scan were asked to participate in this study. This excluded women with an abnormal scan and the group that declines all options of prenatal screening from this study. This is an important group that should also be researched. Lastly, due to national COVID-19 restrictions, the questionnaires were predominantly administered digitally instead of in person. This made the planning of appointments and reaching low-literacy groups more challenging and may have resulted in a selective drop-out of participants. Additionally, certain subpopulations are less likely to have Internet access and computer skills and therefore are less likely to respond to an online questionnaire. This may has contributed to a selection bias.

## 6 | CONCLUSION

Our results show that personal (religious) beliefs and values play a large role in the decision to decline NIPT. A majority of women had already made the decision not to have NIPT before being offered information or pretest counseling. Costs were not a major factor for the decision not to have NIPT but were a significant barrier for some women, indicating unequal access. Pretest counseling could be improved to ensure that the decision-making process is not based on incorrect knowledge. Counseling should take into account cultural, religious, and other sociodemographic factors that can possibly influence the decision regarding participation in prenatal screening.

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#### **CONFLICT OF INTEREST**

The authors declare no competing interests.

#### **DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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#### **REFERENCES**

- Gadsboll K, Petersen OB, Gatinois V, et al. Current use of noninvasive prenatal testing in Europe, Australia and the USA: a graphical presentation. Acta Obstet Gynecol Scand. 2020;99(6):722-730. https:// doi.org/10.1111/aogs.13841
- Ravitsky V, Roy MC, Haidar H, et al. The emergence and global spread of noninvasive prenatal testing. Annu Rev Genomics Hum Genet. 2021;22(1):309-338. https://doi.org/10.1146/annurev-genom-083 118-015053
- 3. Dondorp W, de Wert G, Bombard Y, et al. Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening. *Eur J Hum Genet*. 2015;23(11): 1438-1450. https://doi.org/10.1038/ejhg.2015.57
- Chandrasekharan S, Minear MA, Hung A, Allyse M. Noninvasive prenatal testing goes global. Sci Transl Med. 2014;6(231):231fs215. https://doi.org/10.1126/scitranslmed.3008704
- Lo YM, Corbetta N, Chamberlain PF, et al. Presence of fetal DNA in maternal plasma and serum. *Lancet*. 1997;350(9076):485-487. https://doi.org/10.1016/s0140-6736(97)02174-0
- Taylor-Phillips S, Freeman K, Geppert J, et al. Accuracy of noninvasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and metaanalysis. BMJ Open. 2016;6(1):e010002. https://doi.org/10.1136/ bmjopen-2015-010002
- Gil MM, Accurti V, Santacruz B, Plana MN, Nicolaides KH. Analysis of cell-free DNA in maternal blood in screening for aneuploidies: updated meta-analysis. *Ultrasound Obstet Gynecol*. 2017;50(3): 302-314. https://doi.org/10.1002/uog.17484
- Di Mattei V, Ferrari F, Perego G, Tobia V, Mauro F, Candiani M. Decision-making factors in prenatal testing: a systematic review. Health Psychol Open. 2021;8(1):2055102920987455. https://doi.org/ 10.1177/2055102920987455
- van Bruggen MJ, Henneman L, Timmermans DRM. Women's decision making regarding prenatal screening for fetal aneuploidy: a qualitative comparison between 2003 and 2016. *Midwifery*. 2018;64: 93-100. https://doi.org/10.1016/j.midw.2018.06.010
- Gottfredsdóttir H, Björnsdóttir K, Sandall J. How do prospective parents who decline prenatal screening account for their decision? A qualitative study. Soc Sci Med. 2009;69(2):274-277. https://doi.org/ 10.1016/j.socscimed.2009.05.004

- Cernat A, De Freitas C, Majid U, Trivedi F, Higgins C, Vanstone M. Facilitating informed choice about non-invasive prenatal testing (NIPT): a systematic review and qualitative meta-synthesis of women's experiences. *BMC Pregnancy Childbirth*. 2019;19(1):27. https://doi.org/10.1186/s12884-018-2168-4
- Skirton H, Barr O. Antenatal screening and informed choice: a crosssectional survey of parents and professionals. *Midwifery*. 2010;26(6): 596-602. https://doi.org/10.1016/j.midw.2009.01.002
- Prinds C, der Wal JG.-v, Crombag N, Martin L. Counselling for prenatal anomaly screening—a plea for integration of existential life questions. *Patient Educ Counsel*. 2020;103(8):1657-1661. https://doi. org/10.1016/j.pec.2020.03.025
- Kater-Kuipers A, de Beaufort ID, Galjaard RH, Bunnik EM. Rethinking counselling in prenatal screening: an ethical analysis of informed consent in the context of non-invasive prenatal testing (NIPT). Bioethics. 2020;34(7):671-678. https://doi.org/10.1111/bioe.12760
- Gezondheidsraad. Prenatale Screening; 2016. Publication nr 2016/
   Accessed April 4, 2022. https://www.gezondheidsraad.nl/documenten/adviezen/2016/12/22/prenatale-screening
- van der Meij KRM, Kooij C, Bekker MN, Galjaard R.-JH, Henneman L, Dutch NC. Non-invasive prenatal test uptake in socioeconomically disadvantaged neighborhoods. *Prenat Diagn*. 2021;41(11): 1395-1400. https://doi.org/10.1002/pd.6043
- Rolfes V, Schmitz D. Unfair discrimination in prenatal aneuploidy screening using cell-free DNA? Eur J Obstet Gynecol Reprod Biol. 2016;198:27-29. https://doi.org/10.1016/j.ejogrb.2015.12.023
- van der Meij KRM, Njio A, Martin L, et al. Routinization of prenatal screening with the non-invasive prenatal test: pregnant women's perspectives. Eur J Hum Genet. 2022;30(6):661-668. https://doi.org/ 10.1038/s41431-021-00940-8
- Crombag NM, Boeije H, Iedema-Kuiper R, Schielen PC, Visser GH, Bensing JM. Reasons for accepting or declining Down syndrome screening in Dutch prospective mothers within the context of national policy and healthcare system characteristics: a qualitative study. BMC Pregnancy Childbirth. 2016;16(1):121. https://doi.org/10. 1186/s12884-016-0910-3
- Gitsels-van der Wal JT, Verhoeven PS, Mannien J, et al. Factors affecting the uptake of prenatal screening tests for congenital anomalies; a multicentre prospective cohort study. BMC Pregnancy Childbirth. 2014;14(1):264. https://doi.org/10.1186/1471-2393-14-264
- Bakker M, Birnie E, Pajkrt E, Bilardo CM, Snijders RJ. Low uptake of the combined test in The Netherlands-which factors contribute? *Prenat Diagn*. 2012;32(13):1305-1312. https://doi.org/10.1002/pd. 4001
- Hayeems RZ, Campitelli M, Ma X, Huang T, Walker M, Guttmann A. Rates of prenatal screening across health care regions in Ontario, Canada: a retrospective cohort study. CMAJ Open. 2015;3(2): E236-E243. https://doi.org/10.9778/cmajo.20140110
- Wolf HT, Wulff CB, Ekelund C, Sundberg K, Tabor A. Characteristics of first-trimester screening of non-responders in a high-uptake population. *Dan Med J.* 2016;63(4):A5219.
- Schoonen M, Wildschut H, Essink-Bot ML, Peters I, Steegers E, de Koning H. The provision of information and informed decision-making on prenatal screening for Down syndrome: a questionnaire- and register-based survey in a non-selected population. *Patient Educ Couns*. 2012;87(3):351-359. https://doi.org/10.1016/j.pec.2011.10.001
- Chilaka VN, Konje JC, Stewart CR, Narayan H, Taylor DJ. Knowledge of Down syndrome in pregnant women from different ethnic groups. *Prenat Diagn*. 2001;21(3):159-164. https://doi.org/10.1002/1097-0223(200103)21:3<159::aid-pd20>3.0.co;2-v
- Dahl K, Hvidman L, Jorgensen FS, et al. First-trimester Down syndrome screening: pregnant women's knowledge. *Ultrasound Obstet Gynecol.* 2011;38(2):145-151. https://doi.org/10.1002/uog.8839

- Posthumus AG, Peters IA, Borsboom GJ, Knapen M, Bonsel GJ. Inequalities in uptake of prenatal screening according to ethnicity and socio-economic status in the four largest cities of The Netherlands (2011-2013). Prenat Diagn. 2017;37(10):959-967. https://doi.org/10.1002/pd.5089
- Maxwell S, Brameld K, Bower C, et al. Socio-demographic disparities in the uptake of prenatal screening and diagnosis in Western Australia. Aust N Z J Obstet Gynaecol. 2011;51(1):9-16. https://doi. org/10.1111/j.1479-828x.2010.01250.x
- Verweij EJ, Oepkes D, de Vries M, van den Akker ME, van den Akker ES, de Boer MA. Non-invasive prenatal screening for trisomy 21: what women want and are willing to pay. *Patient Educ Couns*. 2013;93(3):641-645. https://doi.org/10.1016/j.pec.2013.08.006
- Gitsels-van der Wal JT, Mannien J, Ghaly MM, Verhoeven PS, Hutton EK, Reinders HS. The role of religion in decision-making on antenatal screening of congenital anomalies: a qualitative study amongst Muslim Turkish origin immigrants. *Midwifery*. 2014;30(3): 297-302. https://doi.org/10.1016/j.midw.2013.04.001
- Seven M, Akyuz A, Eroglu K, Daack-Hirsch S, Skirton H. Women's knowledge and use of prenatal screening tests. J Clin Nurs. 2017; 26(13-14):1869-1877. https://doi.org/10.1111/jocn.13494
- Birko S, Ravitsky V, Dupras C, et al. The value of non-invasive prenatal testing: preferences of Canadian pregnant women, their partners, and health professionals regarding NIPT use and access. BMC Pregnancy Childbirth. 2019;19(1):22. https://doi.org/10.1186/s12884-018-2153-y
- Crombag NM, Vellinga YE, Kluijfhout SA, et al. Explaining variation in Down's syndrome screening uptake: comparing The Netherlands with England and Denmark using documentary analysis and expert stakeholder interviews. BMC Health Serv Res. 2014;14(1):437. https://doi.org/10.1186/1472-6963-14-437
- Scientific Center for Quality of Healthcare (IQ Healthcare).
   Professionals monitor 2020 Prenatale screening op down-, edwardsen patausyndroom en het Structureel Echoscopisch Onderzoek. Accessed April 4, 2022. https://www.pns.nl/documenten/
  professionalsmonitor-2020-screeningsprogramma-down-edwards-enpatausyndroom-en-seo
- Van Den Bogaert K, Lannoo L, Brison N, et al. Outcome of publicly funded nationwide first-tier noninvasive prenatal screening. *Genet Med.* 2021;23(6):1137-1142. https://doi.org/10.1038/s41436-021-01101-4
- National Health Service. Antenatal Screening Standards: Data Report 1 April 2019 to 31 March 2020. Accessed May 16, 2022. https:// www.gov.uk/government/statistics/antenatal-screening-standardsdata-report-2019-to-2020
- Lou S, Petersen OB, Jorgensen FS, Lund IC, Kjaergaard S, Vogel I. National screening guidelines and developments in prenatal diagnoses and live births of Down syndrome in 1973-2016 in Denmark. Acta Obstet Gynecol Scand. 2018;97(2):195-203. https://doi.org/10.1111/apgs 13273
- Kater-Kuipers A, Bunnik EM, de Beaufort ID, Galjaard RJH. Limits to the scope of non-invasive prenatal testing (NIPT): an analysis of the international ethical framework for prenatal screening and an interview study with Dutch professionals. BMC Pregnancy Childbirth. 2018;18(1):409. https://doi.org/10.1186/s12884-018-2050-4
- De Nederlandse Zorgautoriteit. Prestatie- en tariefbeschikking huisartsenzorg en multidisciplinaire zorg 2021 TB/REG-21627-02;
   2021. Accessed April, 4 2022. https://puc.overheid.nl/nza/doc/PUC\_315836\_22/1/
- Schoonen HM, van Agt HM, Essink-Bot ML, Wildschut HI, Steegers EA, de Koning HJ. Informed decision-making in prenatal screening for Down's syndrome: what knowledge is relevant? *Patient Educ Couns*. 2011;84(2):265-270. https://doi.org/10.1016/j.pec.2010. 07.037

- 41. Koopmanschap I, Martin L, Gitsels-van der Wal JT, Suurmond J. Counselling for prenatal anomaly screening to migrant women in The Netherlands: an interview study of primary care midwives' perceived barriers with client-midwife communication. *Eur J Midwifery*. 2022; 6(May):29-9. https://doi.org/10.18332/ejm/147911
- Martin L, Gitsels-van der Wal JT, Bax CJ, et al. Nationwide implementation of the non-invasive prenatal test: evaluation of a blended learning program for counselors. PLoS One. 2022;17(5):e0267865. https://doi.org/10.1371/journal.pone.0267865
- Crombag NM, van Schendel RV, Schielen PC, Bensing JM, Henneman L. Present to future: what the reasons for declining first-trimester combined testing tell us about accepting or declining cell-free DNA testing. *Prenat Diagn*. 2016;36(6):587-590. https://doi.org/10.1002/pd.4824
- Abdalla O, Woods C, de Costa C. A clinical audit of combined first trimester screening and non-invasive prenatal testing offered to pregnant women in a regional Australian hospital. Aust N Z J Obstet Gynaecol. 2019;59(1):157-160. https://doi.org/10.1111/ajo.12842
- Hui L, Barclay J, Poulton A, Hutchinson B, Halliday JL. Prenatal diagnosis and socioeconomic status in the non-invasive prenatal testing era: a population-based study. Aust N Z J Obstet Gynaecol. 2018;58(4):404-410. https://doi.org/10.1111/ajo.12778
- Haidar H, Vanstone M, Laberge AM, Bibeau G, Ghulmiyyah L, Ravitsky V. Implementation challenges for an ethical introduction of noninvasive prenatal testing: a qualitative study of healthcare professionals' views from Lebanon and Quebec. *BMC Med Ethics*. 2020;21(1):15. https://doi.org/10.1186/s12910-020-0455-x
- Farrell RM, Pierce M, Collart C, et al. Making the most of the first prenatal visit: the challenge of expanding prenatal genetic testing options and limited clinical encounter time. *Prenat Diagn*. 2020; 40(10):1265-1271. https://doi.org/10.1002/pd.5752
- Dutch Government letter. Structurele implementatie NIPT;
   2022. Accessed May 16, 2022. https://www.rijksoverheid.nl/documen

- ten/kamerstukken/2022/04/14/kamerbrief-over-structurele-imple mentatie-nipt
- Vanstone M, Cernat A, Majid U, Trivedi F, De Freitas C. Perspectives of pregnant people and clinicians on noninvasive prenatal testing: a systematic review and qualitative meta-synthesis. Ont Health Technol Assess Ser. 2019;19(5):1-38.
- Quinlan TAG, Schroeder B, Kwon S, et al. Economic impact of coverage expansion for non-invasive prenatal testing through a performance-based risk-sharing agreement. *Pharmacoecon Open*. 2021;5(3):449-458. https://doi.org/10.1007/s41669-021-00261-y
- Bellai-Dussault K, Meng L, Huang T, et al. A 2-year review of publicly funded cell-free DNA screening in Ontario: utilization and adherence to funding criteria. *Prenat Diagn*. 2020;40(2):164-172. https:// doi.org/10.1002/pd.5563
- Dutch National Obstetric Outcome Registration Perined. Accessed April 4, 2022. https://www.peristat.nl/

#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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