








A cross-country comparison of pregnant women's decision-making and perspectives when opting for non-invasive prenatal testing in the Netherlands and Belgium

Lore Lannoo^{1,2}  | Karuna R. M. van der Meij^{3,4}  | Mireille N. Bekker⁵ |
 Luc De Catte¹ | Sarah Deckers¹ | Koenraad Devriendt⁶ | Nele Roggen⁷ |
 Robert-Jan H. Galjaard⁸ | Janneke Gitsels-van der Wal^{9,10} |
 Merryn V. E. Macville¹¹  | Linda Martin^{9,12} | Erik A. Sistermans^{3,4}  |
 Kristel Van Calsteren^{1,2}  | Joachim Van Keirsbilck¹³ | Neeltje Crombag^{2,5}  |
 Lidewij Henneman^{3,4} 

Correspondence

Lidewij Henneman, Department of Human Genetics, Amsterdam UMC, PO Box 22660, 1100 DD Amsterdam, The Netherlands.
 Email: l.henneman@amsterdamumc.nl

Funding information

ZonMw, Grant/Award Number: 543002001; University Hospital Leuven

Abstract

Background: The Netherlands and Belgium have been among the first countries to offer non-invasive prenatal testing (NIPT) as a first-tier screening test. Despite similarities, differences exist in counseling modalities and test uptake. This study explored decision-making and perspectives of pregnant women who opted for NIPT in both countries.

Methods: A questionnaire study was performed among pregnant women in the Netherlands (NL) ($n = 587$) and Belgium (BE) ($n = 444$) opting for NIPT, including measures on informed choice, personal and societal perspectives on trisomy 21, 18 and 13 and pregnancy termination.

Results: Differences between Dutch and Belgian women were shown in the level of informed choice (NL: 83% vs. BE: 59%, $p < 0.001$), intention to terminate the pregnancy in case of confirmed trisomy 21 (NL: 51% vs. BE: 62%, $p = 0.003$) and trisomy 13/18 (NL: 80% vs. BE: 73%, $p = 0.020$). More Belgian women considered trisomy 21 a severe condition (NL: 64% vs. BE: 81%, $p < 0.001$). Belgian women more frequently indicated that they believed parents are judged for having a child with trisomy 21 (BE: 42% vs. NL: 16%, $p < 0.001$) and were less positive about quality of care and support for children with trisomy 21 (BE: 23% vs. NL: 62%, $p < 0.001$).

Conclusion: Differences in women's decision-making regarding NIPT and the conditions screened for may be influenced by counseling aspects and country-specific societal and cultural contexts.

Lore Lannoo and Karuna R. M. van der Meij are shared first authors; Neeltje Crombag and Lidewij Henneman are shared last authors.

ESHG 2022: 12/06/2022 Lore Lannoo. BeSHG-NVHG 2022: annual meeting: 21/04/2022 Karuna van der Meij.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2023 The Authors. Prenatal Diagnosis published by John Wiley & Sons Ltd.

Key points**What is already known?**

- Informed choice is considered important when deciding whether or not to participate in prenatal screening to ensure reproductive autonomy.
- Non-invasive prenatal testing (NIPT) implementation in various countries reveals striking similarities and differences

What does this study add?

- Level of informed choice for screening with NIPT differs between Dutch (83%) and Belgian women (59%).
- Societal, cultural and counseling aspects may impact pregnant women's perspectives and decision-making on prenatal screening with NIPT.

1 | INTRODUCTION

In 2011, the non-invasive prenatal test (NIPT) was introduced as a new screening test for the detection of the most common fetal aneuploidies: trisomy 21 (Down syndrome), 18 (Edwards syndrome) and 13 (Patau syndrome). This highly accurate test is based on the analysis of cell-free DNA derived from the placenta in maternal blood.¹⁻³

The clinical implementation of NIPT differs widely between countries.⁴ In many countries, NIPT is provided by commercial organizations, medical professional associations and private insurers only (e.g. the United States), while in other countries, NIPT is embedded in public health (e.g. Canada).^{4,5} Important differences exist regarding the costs of NIPT, which can be either fully, partly or not reimbursed within (national) prenatal screening programs. These costs of NIPT may constitute a barrier for pregnant women to consider NIPT, raising concerns about justice and inequitable access.^{4,6} NIPT can be offered to high-risk populations with an increased risk of fetal aneuploidy following first-trimester combined screening (FTCS) or as a first-tier screening test offered to all pregnant women.⁴ NIPT can be implemented using screening methods specifically targeting at trisomy 21, 18 and 13,^{7,8} single-nucleotide polymorphism-based with also detection of fetal microdeletion syndromes,⁹ or as a genome-wide approach.¹⁰ Some countries report on fetal sex and additional findings (findings other than trisomy 21, 18 and 13), while others choose not to.

Belgium and the Netherlands are among the few countries worldwide to offer NIPT as a first-tier screening test to all pregnant women as part of a national prenatal screening program. Because of the potential clinical and moral dilemmas in case of an abnormal or inconclusive test result, an informed and autonomous decision, as proposed by national advisory boards in both countries, should precede participation in prenatal screening for fetal aneuploidy.¹¹⁻¹⁴

The explicit emphasis on providing non-directive counseling and neutral information should prevent routinized or unconsidered use of prenatal screening tests.

Despite similarities, both countries differ in their NIPT implementation strategies, counseling modalities, reporting strategies, costs, prenatal care systems, societal and cultural aspects and legal conditions for the termination of pregnancy. Also, the uptake of NIPT

between both countries differs: in 2019, NIPT uptake in Belgium was 79%¹⁵ compared with 46% in the Netherlands.¹⁶

It remains unclear how these differences impact women's perspectives and subsequent decision-making regarding NIPT. Therefore, this study aims to explore and compare informed decision making, perspectives on trisomy 21, 18 and 13 and pregnancy termination among pregnant women who opted for NIPT in Belgium and the Netherlands.

2 | MATERIALS AND METHODS

A cross-country comparative study on pregnant women's decision-making and perspectives on trisomy 21, 18 and 13 was conducted between the Netherlands and Belgium using a questionnaire. The questionnaire study was approved by the VU University Medical Center Amsterdam Ethical Committee (the Netherlands: VUMC No 2017.165) and by the Ethical Committee of UZ Leuven (Belgium: No S63445).

2.1 | Context: Prenatal care and screening in the Netherlands and Belgium

Box 1 presents a comparison between prenatal screening policies in both countries.¹⁷⁻²¹ While in the Netherlands NIPT counseling is standardized (30 min at the time of study by a trained and certified obstetric health care professional), and only for women that acknowledge their wish to receive information about prenatal screening, in Belgium, the counseling is performed during the pregnancy intake consultation by a midwife, a family doctor or an obstetrician without additional training. The cost of NIPT for women in Belgium is €8.68 compared to €175 in the Netherlands. While in the Netherlands genome-wide NIPT is performed, with or without additional findings, in Belgium, the offer differs between commercial and academic centers in terms of targeted versus genome-wide NIPT. In the Netherlands, NIPT is centralized in three laboratories, whereas in Belgium, besides the academic genetic centers also, many smaller local laboratories perform the test.

Box 1. Differences and similarities in the organization of prenatal screening in the Netherlands and Belgium

	Netherlands	Belgium
Implementation of NIPT	Since 2017, NIPT is offered as part of a national prenatal screening program within the TRIDENT-2-study. ¹⁷ The offer of prenatal screening is standardized and coordinated by the National Institute for Public Health and the Environment (RIVM).NIPT is subsidized by the Ministry of Health	Since 2017 NIPT is reimbursed by the National Institute for Health and Disability Insurance (NIHDI) and offered as first-tier prenatal screening test
Initial obstetric care provider	Community midwife (90%) ¹⁸ Obstetrician (10%)	Obstetrician (44%) Obstetrician + midwife + family doctor (55%) Midwife (0.3%) ^{19,20}
Pre-test information and counseling NIPT	Uniform: all women should be offered a 30-min counseling session by a certified obstetric care provider. ²¹ Information leaflet is available in five languages. Two websites offer information about prenatal screening and the TRIDENT-2 study	Diverse: offered information (tools) and counseling differs between centers and obstetric care providers. Women are informed on disorders which can be detected by NIPT, cost and reporting policy. Women's questions were answered
NIPT offer	Uniform: genome-wide NIPT screening for trisomies 21, 18 and 13. Women may opt to be informed on additional findings (findings other than trisomies 21, 18 and 13). Sex chromosomes are not analyzed and fetal sex is not reported. Blood draw from 11 + 0 weeks	Diverse: differences exist between genetic and regional centers, most (70%) centers offer only genome-wide NIPT, while some offer only targeted NIPT (only trisomies 21, 18 and 13). Sex chromosomal aneuploidies are not reported, fetal sex is reported on women's request. Blood draw from 11 + 1 weeks
Out-of-pocket costs NIPT	€175	€8.68
NIPT uptake in 2019 ^a	46%	79%
Prenatal screening for structural anomalies	Second-trimester anomaly scan (18–21 weeks) ^b	First-trimester anomaly scan (11 + 0–13 + 6 weeks), second-trimester anomaly scan (18–20 weeks)
Termination of pregnancy limit	Allowed until 24 weeks gestation, both for social and medical reasons	Allowed until 14 weeks for social reasons, no restrictions based on gestational age for severe medical reasons (also trisomy 21) with ethical approval

^aAt the time of the study pregnant women in the Netherlands could choose between NIPT and First trimester combined screening (FTCS). In 2019, the uptake of FTCS was 2%.

^bSince September 2021 the first-trimester anomaly scan is offered at 12w3–14w3.

2.2 | Study procedure

In both countries, pregnant women were asked to participate in a questionnaire study prior to their decision on whether to opt for NIPT. Pregnant women were provided with a patient information sheet, a questionnaire and information on how to return the questionnaire. Pregnant women who declined NIPT were excluded from analyses in addition to those who were not eligible for NIPT as a first-tier screening test based on TRIDENT-2 exclusion criteria (e.g. high-risk women based on medical history), women under the age of 18 years and those who were not able to communicate in the language of the available questionnaires.

In the Netherlands, between September 2017 and October 2018, written questionnaires were handed out by prenatal counselors in five hospitals and 28 midwifery practices across the Netherlands to pregnant women who had received counseling for prenatal screening. The questionnaire was only available in Dutch. The results of this study have been published earlier¹⁷ and the data are used for a comparison with Belgium.

In Belgium, the questionnaires were distributed between September 2020 and May 2021. Women were recruited in three

large hospitals and one private practice in the Flemish part of Belgium offering genome-wide NIPT only. Respondents were recruited by the healthcare providers (obstetrician and midwives) that conducted the NIPT counseling as part of the pregnancy intake consultation. The questionnaire was available in both English and Dutch.

2.3 | Measures

The questionnaire was developed as part of the TRIDENT-2 study in the Netherlands by a multidisciplinary group of stakeholders.²² This TRIDENT-2 questionnaire was adapted for Belgian women with contextual adjustments for language (Dutch/English) and country-related policies. The average time to complete the questionnaires was around 15 min.

Data were collected on:

- Sociodemographic variables: maternal age (years), gestational age (weeks), educational level (high, intermediate, low), background (Dutch/Belgian, other-Western, non-Western), religious affiliation

(religious, not religious), health literacy²³ (adequate, not adequate), parity (primiparous, multiparous), and method of conception (natural, assisted).

- Reasons for choosing prenatal screening were measured using a predetermined list of reasons. An open space field was provided to list any other reasons not mentioned on the list. Perceived societal pressure to accept prenatal screening with NIPT was measured using a 1-item question “I feel pressured by society to opt for screening for trisomy 21” on a 5-point Likert-scale.
- Informed choice was assessed according to the adapted Multidimensional Measure of Informed Choice.²² A choice is considered informed if the decision is made based on sufficient knowledge, if it is value-consistent and adequately deliberated.
 - o Knowledge on prenatal screening was questioned using five true-false statements regarding prenatal screening in general with three options: true, false or do not know. Good knowledge was considered with $\geq 3/5$ correctly answered questions. Questions that were left unanswered or answered as “do not know” were interpreted as incorrect.
 - o Value consistency was assessed by combining attitude toward prenatal screening (positive or negative) with test-uptake (intention). Attitude was measured by inviting the respondents to score five bipolar adjective pairs (bad-good; unimportant-important; frightening-not frightening; not reassuring-reassuring; not desirable-desirable).²⁴ Respondents were categorized as having a negative, neutral or positive attitude based on the sum of the scores. Women with a neutral attitude were excluded from the analysis of informed choice.²⁵
 - o Deliberation was assessed using a 6-item Likert-scale; the mid-point of the scale was used to discriminate a deliberated choice ($>18/30$ points).^{25,26}
- Attitude toward termination of pregnancy in case of trisomy 21, 18 and 13 was assessed by the likelihood; respondents were to terminate their pregnancy in case of a confirmed trisomy 21 and in case of a confirmed trisomy 13 and 18 on a 5-point Likert scale.
- Societal and personal perspectives on trisomy 21 were addressed using five statements on a 5-point Likert-scale.
- Willingness to pay was evaluated with the question: “What is the maximum amount you would be willing to pay to have NIPT?”. Respondents could indicate their maximum amount from a pre-defined list ranging from zero to €550 with €50 increments. The price of €175 was added as this is the current out-of-pocket payment for NIPT in the Netherlands. A text box was provided for respondents to write another amount not included in the answer options.

2.4 | Data analysis

Chi-square tests for categorical and *t*-tests for continuous variables were used for the comparison between the two countries for different variables. A *p*-value <0.05 was considered statistically significant. IBM SPSS Statistics 28.0 was used for statistical analyses.

3 | RESULTS

3.1 | Respondents

The response rate was 48% (752/1561) in the Netherlands and 64% (448/697) in Belgium. After excluding respondents who did not opt for NIPT, a total of 587 pregnant women in the Netherlands and 444 women in Belgium were included in the study. Table 1 presents the characteristics of respondents for both countries.²³ Compared to the Dutch study group, the Belgian group had a lower mean maternal age (32.0 vs. 30.6 years, respectively), a higher mean gestational age (10.8 vs. 11.4 weeks), a higher proportion of highly educated respondents (69% vs. 80%), a higher proportion of inadequate health literacy (13% vs. 18%) and a higher proportion of religious affiliated respondents (29% vs. 43%). Other characteristics were not significantly different.

3.2 | Reasons for choosing prenatal screening

Table 2 shows pregnant women's reasons for accepting prenatal screening for fetal aneuploidies. The main reasons to choose prenatal screening were similar in both countries and included “I want to be reassured that my child does not have Down, Edwards or Patau syndrome” and “I want to have as much information as possible about the health of my baby” being the most frequently selected reason. More Dutch respondents compared to Belgian respondents chose the option of prenatal screening to be able to prepare for the birth of a child with trisomy 21, 18 or 13 (24% vs. 12%, respectively). More Dutch respondents reported not to feel societal pressure to accept screening compared to the Belgian respondents (88% vs. 77%).

3.3 | Informed choice

More Dutch than Belgian respondents made an informed choice for screening with NIPT (83% vs. 59%, $p < 0.001$) (Figure 1). More Dutch than Belgian respondents had sufficient knowledge (94% vs. 82%, $p < 0.001$) (Table S1). Fewer Dutch than Belgian respondents held a positive attitude toward prenatal screening in general (81% vs. 89%, $p < 0.001$). Of the Dutch respondents, 87% had adequately deliberated their choice compared to 70% of Belgian respondents ($p < 0.001$). All Dutch respondents (100%) made a value-consistent choice compared to 98% of Belgian respondents ($p = 0.002$).

3.4 | Attitude toward termination of pregnancy

More Belgian than Dutch respondents said that they would probably opt for termination of pregnancy in case of trisomy 21 (62% vs. 51%, $p = 0.003$). In case of trisomy 18 or trisomy 13, fewer Belgian than Dutch respondents said that they would probably opt for termination of pregnancy (73% vs. 80%, $p = 0.020$).

TABLE 1 Respondents' characteristics in the Netherlands and Belgium.

	Netherlands n = 587	Belgium n = 444	p-Value
Maternal age, mean (SD), missing 3/4	32.0 (4.1)	30.6 (3.6)	0.024
Gestational age, mean (SD), missing 4/0	10.8 (1.7)	11.4 (3.2)	<0.001
Education level ^a , n (%), missing 1/4			
Low	20 (3)	13 (3)	
Intermediate	164 (28)	75 (17)	
High	402 (69)	352 (80)	<0.001
Background ^b , n (%), missing 2/1			
Dutch/Belgian	497 (85)	366 (83)	
Other Western	52 (9)	49 (11)	
Non-Western	36 (6)	28 (6)	0.5
Religious affiliation ^c , n (%), missing 9/2			
Religious	170 (29)	192 (43)	
Not religious	408 (71)	250 (57)	<0.001
Health literacy ^d , n (%), missing 4/4			
Adequate	509 (87)	359 (82)	
Not adequate	74 (13)	81 (18)	0.012
Parity, n (%), (missing 1/0)			
Nulliparous	298 (51)	223 (50)	
Multiparous	288 (50)	221 (50)	0.842
Method of conception ^e , n (%), missing 4/1			
Natural	529 (91)	394 (89)	
Assisted	54 (9)	49 (11)	0.342

Abbreviation: SD, standard deviation; missing (Netherlands/Belgium).

^aEducation levels categorized as low: elementary school, low-level secondary school of low vocational training; intermediate: high-level secondary school or intermediate vocational training; high: high vocational training or university.

^bBackground categorized as Dutch/Belgian: both parents were born in the Netherlands/Belgium; 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.

^cReligious affiliation was measured by the question "which denomination or ideology do you consider yourself as?" Answers were dichotomized: having no religious affiliation if answered "none" or having a religious affiliation if an affiliation was selected.

^dHealth literacy was measured according to Chew et al. with the set of three brief screening questions.²³ Health literacy classified as inadequate if answered anything other than "never" or "occasionally" on one or more questions.

^eMethods of conception considered assisted: intrauterine insemination, ovulation-induction, in vitro fertilization, intracytoplasmic sperm injection or preimplantation genetic diagnosis.

3.5 | Societal and personal perspectives on trisomy 21

Table 3 presents the respondents' societal and personal perspectives on trisomy 21. Only 16% of the Dutch respondents compared to 42% of the Belgian respondents agreed that parents are judged by society for having a child with trisomy 21 ($p < 0.001$). The majority of Dutch women (62%) agreed that the organization of care and support for children with trisomy 21 is well organized in the Netherlands, while only a minority of Belgian women (23%) thought that this was the case in Belgium ($p < 0.001$). Belgian respondents more often disagreed with the statement that trisomy 21 is not a serious disorder compared to Dutch respondents (81% vs. 64%, $p < 0.001$).

3.6 | Willingness to pay

Most Dutch respondents (43%) were willing to pay €175, which is the current out-of-pocket cost for the parents of NIPT in the Netherlands. Most Belgian respondents (40%) indicated a willingness to pay between €50 and €150 for NIPT (Figure 2). The majority of both Dutch and Belgian respondents did not experience the costs of NIPT as a barrier to access screening (NL: 92%, BE: 96%).

4 | DISCUSSION

The two adjoining countries, Belgium and the Netherlands, were the first to implement NIPT as a first-tier screening test. Worldwide, both countries were pioneers to do so. However, in these countries, different strategies were used for implementation with regard to counseling modalities, cost, reporting on fetal sex and additional findings. The main results of this study show lower rates of informed choice in Belgian respondents and also differences between perspectives on trisomy 21, 18 and 13 in both countries.

Belgium and the Netherlands differ significantly in counseling modalities. Despite this, knowledge scores differed, but were generally high. This may indicate that, despite less extensive counseling, current available information provision in Belgium and required informed consent may be sufficient to a certain extent. The mainly high level of education of the Belgian study respondents could be an alternative explanation. A study in England that assessed informed choice in high-risk pregnant women also indicated a positive association between higher education of the pregnant women and a higher knowledge score for NIPT, whereas education was not associated with attitude toward NIPT or deliberation scores.²⁷ In our study, the finding that fewer Belgian respondents would opt for a termination of pregnancy in case of confirmed trisomy 18 and 13 as compared to their Dutch counterparts is unexpected. The more severe phenotype of trisomy 18 and

TABLE 2 Reasons for choosing prenatal screening from $n = 587$ Dutch and $n = 444$ Belgian respondents.

	Netherlands, $n = 1466$ responses, n (% of cases)	Belgium, $n = 1165$ responses, n (% of cases)
I want to be reassured that my child does not have Down, Edwards or Patau syndrome	369 (64)	318 (72)
I want to have as much information as possible about the health of my baby	330 (57)	305 (69)
I do not want to have a child with Edwards or Patau syndrome	254 (44)	181 (41)
I do not want to have a child with Down syndrome	183 (32)	164 (37)
I want to be able to prepare myself for the birth of a child with Down, Edwards or Patau syndrome	139 (24)	51 (12)
I am afraid that I will regret not getting tested later on	80 (14)	57 (13)
My partner, family or someone around me wants to have the test	65 (11)	45 (10)
My midwife or doctor thinks it is a good idea	3 (0.5)	20 (5)
I think I have a high risk of having a child with Down syndrome	15 (3)	1 (0.2)
Other ^a	16 (3)	9 (2)
Because of my (maternal) age ^b	7 (1)	3 (0.7)
I want to know the sex of the child ^b	0 (0)	6 (1)
Because of personal experience with (a child with) a cognitive or physical disability ^b	5 (0.9)	5 (1)

Note: Respondents could give multiple responses.

^aExamples of other responses include: "I want to learn information about my own health" (NL), "Third child so this will impact the entire family" (NL), "Because the possibility to test is there" (BE) and "It is safe" (BE).

^bAdded reason based on other responses in free text.

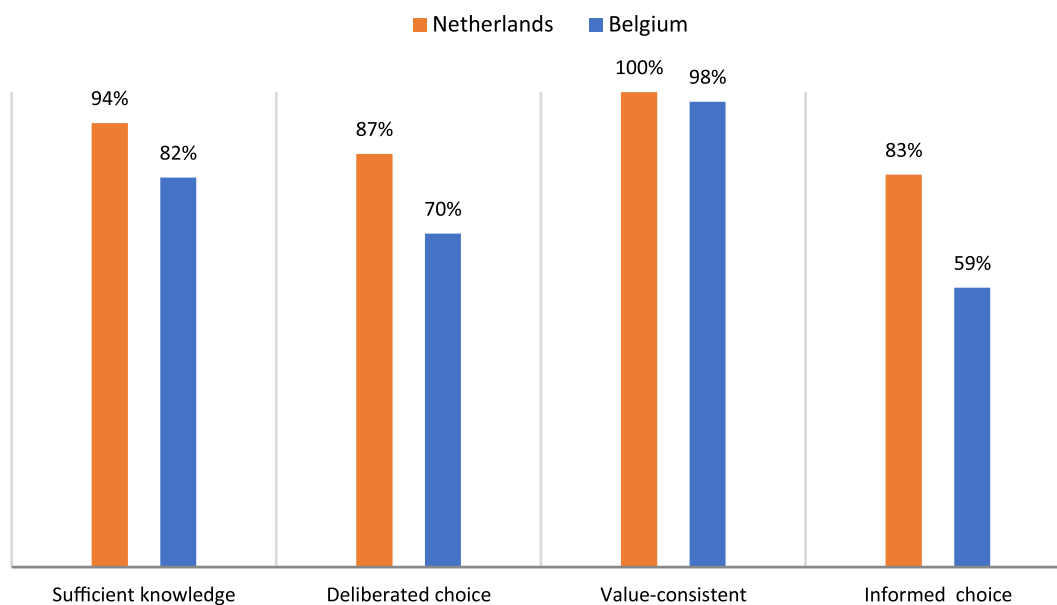


FIGURE 1 Comparison of informed choice and its components (knowledge [NL: $n = 582$; BE: $n = 444$], deliberated choice [NL: $n = 578$; BE: $n = 433$] and value-consistency [NL: $n = 465$; BE: $n = 403$] between Dutch and Belgian respondents). Respondents with a neutral attitude were not included in the calculation of informed choice. [Colour figure can be viewed at wileyonlinelibrary.com]

13 compared to trisomy 21 would presume an increased likelihood for the intention to terminate. This also may indicate a certain lack of knowledge in the Belgian study population and a potential effect of (lack of) counseling. Unfortunately, national data on termination rates for trisomy 21, 18 and 13 is non-existent to further investigate this finding.

Despite general relatively high levels of knowledge in both groups, more Dutch respondents made an informed choice as compared to Belgian respondents. This may partly be explained by differences in knowledge, but may also be related to the significant difference in deliberation of choice this study found. Deliberation of choice requires weighing pros and cons of all options and potential

TABLE 3 Respondents' agreements on societal and personal perspectives on trisomy 21.

	Netherlands (N = 587), n (%)	Belgium (N = 444), n (%)	p-Value
I think children with Down syndrome are less accepted in society (missing 6/4)			
(Very much) agree	325 (56)	274 (63)	
Neither agree nor disagree	125 (22)	90 (21)	
(Very much) Disagree	131 (23)	76 (17)	0.124
I think care and support for children with Down syndrome are well arranged in our country (missing 3/7)			
(Very much) agree	362 (62)	98 (23)	
Neither agree nor disagree	178 (31)	202 (46)	
(Very much) Disagree	44 (8)	137 (31)	<0.001
I think parents are judged for having a child with Down syndrome (missing 4/5)			
(Very much) agree	95 (16)	186 (42)	
Neither agree nor disagree	134 (23)	125 (29)	
(Very much) Disagree	354 (61)	128 (29)	<0.001
I think Down syndrome is not a serious condition (missing 4/5)			
(Very much) agree	51 (9)	15 (3)	
Neither agree nor disagree	157 (27)	69 (16)	
(Very much) Disagree	375 (64)	355 (81)	<0.001
I would experience it as a great burden to raise a child with Down syndrome (missing 6/5)			
(Very much) agree	412 (71)	328 (75)	
Neither agree nor disagree	127 (22)	74 (17)	
(Very much) Disagree	42 (7)	37 (8)	0.216

Note: Percentages may not add up to 100% because of rounding.

implications and is an important aspect of informed choice. By providing neutral and comprehensive information as well as non-directive support in decision-making, Dutch counseling modalities ideally focus on deliberation to help increase the levels of informed choice.^{28–31} Dedicated counseling time and educated counselors may be another explanation for the higher levels of informed choice in the Dutch group.^{27,32}

To maintain high levels of informed choice, in pregnant women with lower levels of education, dedicated counseling is important. However, differences in allocated time and financial resources for prenatal counseling between different healthcare systems do not always allow for an equal approach.⁴ Additional written information and/or e-learning tools may in certain circumstances further improve informed decision-making.³³ Larger studies are needed to explore

the ideal setting and mode of counseling to enable optimal informed choice, also considering the unique financial and organizational contexts of countries.

This study also found that the majority of respondents in both countries did not feel societal pressure to accept NIPT. This finding was in line with earlier research in Canada and the Netherlands, indicating that most women do not feel pressured to test.^{34,35} In our study, a comparable number of pregnant women in both countries considered raising a child with trisomy 21 as a burden, but more Dutch than Belgian women (24% vs. 12%) mentioned the reason “Wanting to be able to prepare myself for the birth of a child with trisomy 21, 18 and 13” as an important reason to opt for NIPT. This difference is remarkable and can be a result of the emphasis that is given to “reproductive autonomy” in Dutch counseling as compared to Belgium.¹⁴ However, this may as well indicate a difference in perspectives toward having a child with a disability between countries due to different societal, cultural and health care systems. For example, more Belgian respondents felt that parents would be judged by society for having a child with trisomy 21.

Dutch respondents less often intended to terminate the pregnancy in case of trisomy 21. Research showed only a minimal effect of the introduction of NIPT in the Netherlands on the trend in the live birth prevalence of trisomy 21.³⁶ In Belgium, a small decline in live births with trisomy 21 was observed since the introduction of NIPT, but this could also be explained by a decline in false-negative results compared to FTCS.¹⁵ Sociocultural values, attitudes toward disability and termination of pregnancy as well as the legal aspects toward termination of pregnancy may partly explain the use of NIPT, which varies widely between countries.⁴ To better understand some of the reasons behind these differences in perspectives, more studies are needed.

Women also differed in their perceptions on the care and support for children with special needs in their country. In Belgium, only a minority of respondents thought that the care and support for children with a trisomy are well organized, while in the Dutch group, the majority agreed on this. This finding is difficult to explain as it is unclear on what this perception of Belgian women is based. In Flanders, the part of Belgium where this survey was conducted, four well organized clinics for children and adults with trisomy 21 exist. Also, the “Down syndrome Flanders” foundation, founded by parents of children with trisomy 21, is very active and plays an important role in improving care provision and societal inclusion. But this does not necessarily mean that women are aware of this or considered it as well-organized care. A potential reason may be the ongoing media attention regarding the lack of financial governmental support for children with disabilities in general.

Most Dutch respondents indicated that they would be willing to pay the current €175 for the NIPT, while Belgian respondents indicated that they would be willing to pay between €50 and €150. This is a remarkable finding as currently in Belgium, NIPT is almost fully reimbursed. This finding should, however, be interpreted carefully, as the study population mainly consisted of highly educated women, most likely without financial constraints. In countries that do not

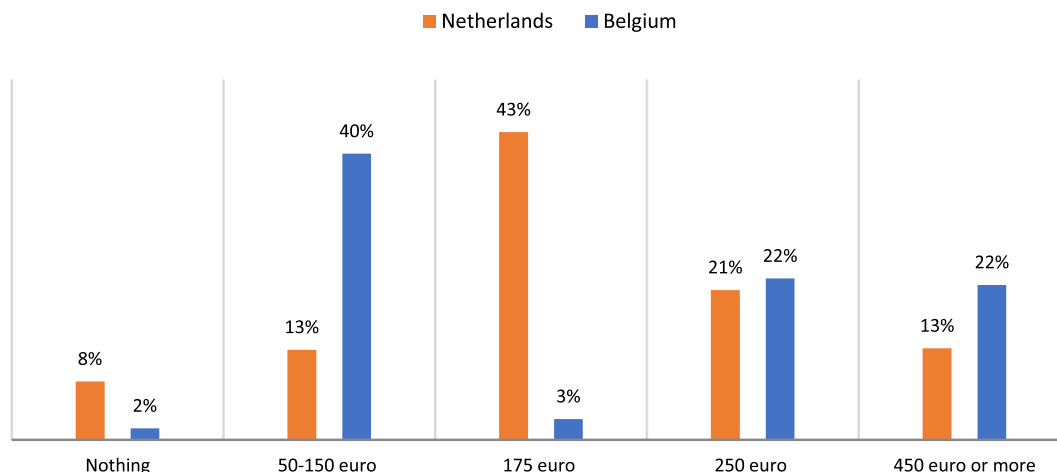


FIGURE 2 The maximum amount (in euro) Dutch and Belgian respondents are willing to pay for NIPT. [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/pd.6329)]

offer public funding, costs are considered a barrier, thereby raising concerns about equitable access.⁴ However, this finding could also reflect the extent to which Belgian respondents want to be reassured that the child does not have trisomy 21, 18, 13.

4.1 | Strengths and limitations

An important strength of this study is the large group of respondents in two countries in which NIPT is offered as a first-tier screening test within a publicly funded nationwide program. It therefore provides valuable information on women's perspectives for other countries who are offering or considering offering NIPT as a first-tier test. This study offers some valuable suggestions for counseling not only for trisomy 21, but also for trisomy 13 and 18. This study also has limitations. Most respondents were highly educated. In Belgium, only women having a genome-wide NIPT were included, while also targeted NIPT is offered in some hospitals, which may limit its representability of Belgium, even though we know from recent research that 81.5% of Belgian pregnant women are offered genome-wide NIPT.¹⁵ In the Netherlands, the questionnaire was only available in Dutch, potentially excluding non-Dutch speaking participants. Another limitation is the measure of informed choice that was used, as up till now, there is no standard, uniform, validated way to measure this, especially what knowledge is needed to make an informed choice, which makes it difficult to compare results between different studies.³⁷

5 | CONCLUSION

Differences in pregnant women's perspectives and decision-making regarding prenatal aneuploidy screening with NIPT between the Netherlands and Belgium were found, which may be explained by societal, cultural and counseling aspects, although a causal relationship cannot be inferred with current data. As the aim of prenatal

screening is to provide autonomous reproductive choices for prospective parents, the potential impact of context-related aspects should be further studied and potentially considered in future implementation strategies. More so, as the scope of NIPT is expanding, professionals will be challenged further to offer adequate counseling that will enable prospective parents' informed decision-making.

AFFILIATIONS

¹Department of Obstetrics and Gynaecology, Fetomaternal Medicine, University Hospitals Leuven, Leuven, Belgium

²Department of Development and Regeneration, Cluster Woman and Child, Biomedical Sciences, KU Leuven, Leuven, Belgium

³Department of Human Genetics, Amsterdam UMC, location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

⁴Amsterdam Reproduction and Development Research Institute, Amsterdam UMC, Amsterdam, The Netherlands

⁵Department of Obstetrics and Gynaecology, Utrecht University Medical Center, Utrecht, The Netherlands

⁶Department of Human Genetics, University Hospitals Leuven, Leuven, Belgium

⁷Department of Obstetrics and Gynaecology, AZ Imelda, Bonheiden, Belgium

⁸Department of Clinical Genetics, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

⁹Department of Midwifery Science, Amsterdam UMC, location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

¹⁰Amsterdam Public Health Research Institute, Quality of Care, Amsterdam, The Netherlands

¹¹Department of Clinical Genetics, GROW School for Oncology and Reproduction, Maastricht University Medical Center+, Maastricht, The Netherlands

¹²Midwifery Academy Amsterdam Groningen, InHolland, Amsterdam, The Netherlands

¹³Department of Obstetrics and Gynaecology, AZ Sint Jan, Bruges, Belgium

ACKNOWLEDGMENTS

The authors would like to acknowledge all pregnant women for completing the questionnaires and to thank all prenatal counselors who made this study possible. Members of the Belgian and Dutch

NIPT Consortium are thanked for fruitful discussions. This work was supported by Clinical Research Funding (KOOR-Funding University Hospital Leuven for Lore Lannoo/Kristel Van Calsteren). Grant from the Netherlands Organisation for Health Research and Development (ZonMw) grant no 543002001 for the Dutch TRIDENT-2 study.

CONFLICT OF INTEREST STATEMENT

No conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Lore Lannoo  <https://orcid.org/0000-0002-6271-221X>

Karuna R. M. van der Meij  <https://orcid.org/0000-0002-1801-588X>

Merryn V. E. Macville  <https://orcid.org/0000-0003-1675-2234>

Erik A. Sistermans  <https://orcid.org/0000-0001-7187-4563>

Kristel Van Calsteren  <https://orcid.org/0000-0002-2438-6783>

Neeltje Crombag  <https://orcid.org/0000-0002-6808-0874>

Lidewij Henneman  <https://orcid.org/0000-0003-3531-0597>

REFERENCES

- 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](https://doi.org/10.1016/s0140-6736(97)02174-0)
- 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>
- Chiu RW, Akolekar R, Zheng YW, et al. Non-invasive prenatal assessment of trisomy 21 by multiplexed maternal plasma DNA sequencing: large scale validity study. *BMJ*. 2011;342(jan11 1):c7401. <https://doi.org/10.1136/bmj.c7401>
- Ravitsky V, Roy MC, Haidar H, et al. The emergence and global spread of noninvasive prenatal testing. *Annu Rev Genom Hum Genet*. 2021;22(1):309-338. <https://doi.org/10.1146/annurev-genom-0831-18-015053>
- Gadsbøll 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>
- Bunnik EM, Kater-Kuipers A, Galjaard RH, de Beaufort ID. Should pregnant women be charged for non-invasive prenatal screening? Implications for reproductive autonomy and equal access. *J Med Ethics*. 2020;46(3):194-198. <https://doi.org/10.1136/medethics-2019-105675>
- Sparks AB, Wang ET, Struble CA, et al. Selective analysis of cell-free DNA in maternal blood for evaluation of fetal trisomy. *Prenat Diagn*. 2012;32(1):3-9. <https://doi.org/10.1002/pd.2922>
- Liao GJ, Chan KC, Jiang P, et al. Noninvasive prenatal diagnosis of fetal trisomy 21 by allelic ratio analysis using targeted massively parallel sequencing of maternal plasma DNA. *PLoS One*. 2012;7(5):e38154. <https://doi.org/10.1371/journal.pone.0038154>
- Wapner RJ, Babiarsz JE, Levy B, et al. Expanding the scope of noninvasive prenatal testing: detection of fetal microdeletion syndromes. *Am J Obstet Gynecol*. 2015;212(3):332.e1-332.e3329. <https://doi.org/10.1016/j.ajog.2014.11.041>
- Fiorentino F, Bono S, Pizzuti F, et al. The clinical utility of genome-wide non invasive prenatal screening. *Prenat Diagn*. 2017;37(6):593-601. <https://doi.org/10.1002/pd.5053>
- Belgian Advisory Committee on Bioethics. Opinion no. 66 of 9 May 2016 on the ethical challenges posed by non-invasive prenatal testing (NIPT) for trisomies 21, 13 and 18. Accessed September 1, 2022. <https://www.health.belgium.be/en/opinion-no-66-non-invasive-prenatal-testing-nipt>
- Belgian Advisory Committee on Bioethics. Advise nr 76 - advise on desirability of communicating numerical aberrations of the sex chromosomes detected by NIPT. Accessed September 1, 2022. <https://www.health.belgium.be/en/node/39210>
- Health Council of the Netherlands. Additional findings from NIPT; 2020. Publication no. 2020/12. Accessed September 1, 2022. <https://www.healthcouncil.nl/documents/advisory-reports/2016/12/22/prenatal-screening>
- Health Council of the Netherlands. Prenatal Screening; 2016. Publication no. 2018/19. Accessed September 1, 2022. <https://www.healthcouncil.nl/documents/advisory-reports/2016/12/22/prenatal-screening>
- 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>
- Atsma F, Liefers J. Professionalsmonitor 2020. Prenatale screening op down-, edwards- en patau'syndroom en het Structureel Echo-scopisch Onderzoek. Scientific Center for Quality of Healthcare, Radboudumc. 2021. Accessed September 1, 2022. Monitor | Prenatale en neonatale screenings (pns.nl)
- van der Meij KRM, Sistermans EA, Macville MVE, et al. TRIDENT-2: national implementation of genome-wide non-invasive prenatal testing as a first-tier screening test in the Netherlands. *Am J Hum Genet*. 2019;105(6):1091-1101. <https://doi.org/10.1016/j.ajhg.2019.10.005>
- Martin L, Gitsels-van der Wal JT, de Boer MA, Vanstone M, Henneman L. Introduction of non-invasive prenatal testing as a first-tier aneuploidy screening test: a survey among Dutch midwives about their role as counsellors. *Midwifery*. 2018;56:1-8. <https://doi.org/10.1016/j.midw.2017.09.008>
- Benahmed Nadia LM, Wendy C, Carl D, et al. Health Services Research (HSR). Brussels. Belgian Health Care Knowledge Centre (KCE). Towards integrated antenatal care for low-risk pregnancy. 2019. Accessed September 1, 2022. https://kce.fgov.be/sites/default/files/2021-11/KCE_326_Prenatal_care_Report.pdf
- KCE. Belgian Health Care Knowledge Centre. What are the recommended clinical assessment and screening tests during pregnancy? 2015. Accessed September 1, 2022. <https://kce.fgov.be/en/publications/all-reports/what-are-the-recommended-clinical-assessment-and-screening-tests-during-pregnancy>
- Perined. The Netherlands Perinatal Registry. Perinatal care in the Netherlands 2020. Accessed September 1, 2022. <https://www.perined.nl/onderwerpen/publicaties-perined/kerncijfers-2020https://www.perined.nl/onderwerpen/publicaties-perined/kerncijfers-2020>
- 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>
- Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *Fam Med*. 2004;36(8):588-594.
- Fransen MP, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers EAP, Wildschut HIJ. Ethnic differences in informed decision-making about prenatal screening for Down's syndrome. *J Epidemiol Community Health*. 2010;64(3):262-268. <https://doi.org/10.1136/jech.2009.088237>

25. van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JMG, van der Wal G. Are pregnant women making informed choices about prenatal screening? *Genet Med*. 2005;7(5):332-338. <https://doi.org/10.1097/01.gim.0000162876.65555.ab>
26. van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. *Patient Educ Counsel*. 2006;63(1-2):110-117. <https://doi.org/10.1016/j.pec.2005.09.007>
27. Lewis C, Hill M, Chitty LS. Offering non-invasive prenatal testing as part of routine clinical service. Can high levels of informed choice be maintained? *Prenat Diagn*. 2017;37(11):1130-1137. <https://doi.org/10.1002/pd.5154>
28. Sachs A, Blanchard L, Buchanan A, Norwitz E, Bianchi DW. Recommended pre-test counseling points for noninvasive prenatal testing using cell-free DNA: a 2015 perspective. *Prenat Diagn*. 2015;35(10):968-971. <https://doi.org/10.1002/pd.4666>
29. Martin L, Van Dulmen S, Spelten E, De Jonge A, De Cock P, Hutton E. Prenatal counseling for congenital anomaly tests: parental preferences and perceptions of midwife performance. *Prenat Diagn*. 2013;33(4):341-353. <https://doi.org/10.1002/pd.4074>
30. Vanstone M, Yacoub K, Giacomini M, Hulan D, McDonald S. Women's experiences of publicly funded non-invasive prenatal testing in Ontario, Canada: considerations for health technology policy-making. *Qual Health Res*. 2015;25(8):1069-1084. <https://doi.org/10.1177/1049732315589745>
31. Kuppermann M, Pena S, Bishop JT, et al. Effect of enhanced information, values clarification, and removal of financial barriers on use of prenatal genetic testing: a randomized clinical trial. *JAMA*. 2014;312(12):1210-1217. <https://doi.org/10.1001/jama.2014.11479>
32. Liehr T. Non-invasive prenatal testing, what patients do not learn, may be due to lack of specialist genetic training by gynecologists and obstetricians? *Front Genet*. 2021;12:682980. <https://doi.org/10.3389/fgene.2021.682980>
33. Metcalfe SA. Genetic counselling, patient education, and informed decision-making in the genomic era. *Semin Fetal Neonatal Med*. 2018;23(2):142-149. <https://doi.org/10.1016/j.siny.2017.11.010>
34. Ravitsky V, Birko S, Le Clerc-Blain J, et al. Noninvasive prenatal testing: views of Canadian pregnant women and their partners regarding pressure and societal concerns. *AJOB Empir Bioeth*. 2021;12(1):53-62. <https://doi.org/10.1080/23294515.2020.1829173>
35. Bakkeren IM, Kater-Kuipers A, Bunnik EM, et al. Implementing non-invasive prenatal testing (NIPT) in the Netherlands: an interview study exploring opinions about and experiences with societal pressure, reimbursement, and an expanding scope. *J Genet Counsel*. 2020;29(1):112-121. <https://doi.org/10.1002/jgc4.1188>
36. de Groot-van der Mooren M, de Graaf G, Weijerman ME, et al. Does non-invasive prenatal testing affect the livebirth prevalence of Down syndrome in the Netherlands? A population-based register study. *Prenat Diagn*. 2021;41(10):1351-1359. <https://doi.org/10.1002/pd.6003>
37. Ames AG, Metcalfe SA, Dalton Archibald A, Duncan RE, Emery J. Measuring informed choice in population-based reproductive genetic screening: a systematic review. *Eur J Hum Genet*. 2015;23(1):8-21. <https://doi.org/10.1038/ejhg.2014.89>

SUPPORTING INFORMATION

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

How to cite this article: Lannoo L, van der Meij KRM, Bekker MN, et al. A cross-country comparison of pregnant women's decision-making and perspectives when opting for non-invasive prenatal testing in the Netherlands and Belgium. *Prenat Diagn*. 2023;43(3):294-303. <https://doi.org/10.1002/pd.6329>