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Non-invasive prenatal test uptake in socioeconomically disadvantaged neighborhoods

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Abstract

Objective: Non-Invasive Prenatal Testing (NIPT) is increasingly being implemented worldwide. In public health programs, equitable access to healthcare is a fundamental principle which also applies to fetal aneuploidy screening. However, the out-of-pocket costs of NIPT may lead to sociodemographic disparities in uptake of screening. This study assessed whether there is a difference in the uptake of NIPT in socioeconomically disadvantaged neighborhoods compared to all other neighborhoods in the Netherlands, where NIPT is implemented in a national screening program (TRIDENT-2 study).

Method: NIPT uptake, postal code and age of 156,562 pregnant women who received pre-test counselling for prenatal screening in 2018 were retrieved from the national prenatal screening database. Postal codes were used as a proxy to categorize neighborhoods as being either socioeconomically disadvantaged or other. The out-of-pocket costs for NIPT were €175.

Results: NIPT uptake in socioeconomically disadvantaged neighborhoods was 20.3% whereas uptake in all other neighborhoods was 47.6% ($p < 0.001$). The difference in NIPT uptake between socioeconomic disadvantaged neighborhoods and other areas was smaller for the youngest maternal age-group (≤25 years) compared to other age-groups.

Conclusion: The variation in uptake suggest underlying disparities in NIPT uptake, which undermines the goals of a national fetal aneuploidy screening program of providing reproductive autonomy and equitable access. This has ethical and policy implications for ensuring fair and responsible implementation of fetal aneuploidy screening.

Key points

What's already known about this topic?

- Equitable access and reproductive autonomy are fundamental principles of fetal aneuploidy screening, especially in the context of a public health screening program
- Financial barriers limit access to prenatal screening

What does this study add?

- NIPT uptake in socioeconomically disadvantaged neighborhoods was over two times lower than NIPT uptake in all other neighborhoods, suggesting underlying disparities
- The differences in NIPT uptake between neighborhoods were less for women younger than 25 years

1 | INTRODUCTION

Non-Invasive Prenatal Testing (NIPT) uses cell-free DNA, derived from maternal plasma, to screen for fetal aneuploidies. The test was first introduced in 2011 as a safe and reliable screening test to rule out common fetal aneuploidies in high-risk pregnant women, thereby reducing the number of invasive diagnostic test.[1] NIPT has many advantages compared to conventional screening methods: it can be done earlier in pregnancy, has fewer false-positives and exhibits higher sensitivity.[2] As a result, many countries have started to implement NIPT either in their public healthcare systems or commercially, and offer it as a first-tier test for all pregnant women or as a second-tier test for women at increased risk for fetal aneuploidy.[3] Recently, the American College for Obstetricians and Gynecologists (ACOG) recommended that NIPT be offered to all pregnant women, regardless of their age or prior risk.[2]

Fetal aneuploidy screening policies, reimbursement strategies and uptake vary greatly between countries.[3,4] The cost of NIPT generally ranges between €164 and €654 (or $200–800 USD) in most countries.[4] Concerns have been raised about inequitable access to NIPT due to high out-of-pocket costs, disproportionally affecting those of lower socioeconomic status.[4,5] In order to responsibly implement NIPT, especially in the context of public health programs, equitable access for all pregnant women should be a fundamental goal.[6]

In the Netherlands, all pregnant women are offered first-tier NIPT as part of the TRIDENT-2 study since April 2017 (TRIal by Dutch laboratories for the Evaluation of Non-invasive prenatal Testing).[7] Due to a law (the Dutch Population Screening Act) prohibiting the offer of screening for untreatable disorders without a governmental license, there are no commercial screening offers in the Netherlands.[4] After the introduction of NIPT as first-tier screening test in the Netherlands, uptake of fetal aneuploidy screening increased from 34% in 2016 to 46% in 2018.[8] Compared to other European countries the uptake of fetal aneuploidy screening in the Netherlands is low.[3] This may be explained by a combination of several factors such as the framing of the screening offer focusing on the 'right not to know', positive attitudes toward Down syndrome and negative attitudes toward termination of pregnancy.[9] Previous studies in the Netherlands, as well as in other countries, have shown that women of non-Western descent,[10-13] and women with lower education and lower income levels,[10,12-14] were less likely to have fetal aneuploidy screening due to language barriers, logistical barriers, provider-related determinants, insufficient knowledge and value inconsistency.

Enabling pregnant couples to make an informed and autonomous decision is the primary aim of fetal aneuploidy screening.[15] For ethical and responsible implementation of NIPT, equitable access is considered a fundamental prerequisite of a national prenatal screening program.[6] This study aimed to determine whether there is a difference in uptake of NIPT in socioeconomically disadvantaged neighborhoods compared to other neighborhoods in the Netherlands.

2 | MATERIALS AND METHODS

We conducted a retrospective cross-sectional cohort study to compare NIPT uptake in neighborhoods with different socioeconomic status. Pregnant women in the Netherlands during the year 2018 were included in the study.

2.1 | Setting

The Dutch prenatal screening program consists of: 1) first-trimester screening for fetal aneuploidies with a choice between NIPT (out-of-pocket costs €175 in 2018) as part of the TRIDENT-2 study or first-trimester combined testing (FCT out-of-pocket costs €170 in 2018), and 2) screening for fetal structural anomalies with the 20-week fetal anomaly ultrasound scan (free of charge). The offer of screening focuses on the 'right not to know' (i.e., women are first explicitly asked whether they want to receive information about the screening). Women who express an interest receive a 30-minute pre-test counselling session by a certified obstetric professional (mostly primary care midwives). Counselling sessions for fetal aneuploidy screening and NIPT uptake are registered in the Dutch prenatal screening registration database Peridos by counsellors to ensure quality of the Dutch prenatal screening program.

2.2 | Data collection

Anonymized pre-test counselling data (maternal age and postal codes) and NIPT uptake between January 1st 2018 and December 31th 2018 were retrieved from Peridos for analysis. FCT uptake (overall 2.6% in 2018)[8] was not included in this study. Approximately 10% of pregnant women in the Netherlands did not receive counselling for prenatal screening in 2018.

Neighborhoods were delineated by postal codes and categorized as being either socioeconomically disadvantaged or other as determined by the Dutch Healthcare Authority (NZa), an administrative authority under the auspices of the Dutch Ministry of Health in 2019. Postal codes are indexed by the NZa based on three criteria: 1) proportion of inhabitants with low income, 2) proportion of non-Western or Middle- or Eastern-European immigrants, and 3) proportion of inhabitants with entitlement to governmental benefits (excluding pensions). Low income was defined by NZa as a net monthly income of €1040 for a single person, and €1960 for a family with two children.[16]

2.3 | Data analysis

All statistical analysis was performed using IBM SPSS Statistics 26. Descriptive analysis and a comparison of means between groups was performed. Logistic regression analysis was calculated to test the association between disadvantaged and other neighborhoods and NIPT uptake. Age was tested as a possible confounder and effect modifier. The results from the logistic regression analysis were stratified by maternal age-groups.

2.4 | Ethical approval

Ethical approval for this database study was provided by the VU University Medical Center Ethical committee (VUMC No. 2017.165).

3 | RESULTS

In 2018, a total of 156,562 pregnant women were registered in the national database with complete records including counselling, NIPT uptake, postal codes and age. Approximately 10% of the women (n = 14,839) were living in socioeconomically disadvantaged areas. The average NIPT uptake in socioeconomically disadvantaged neighborhoods was 20.3% compared to 47.6% in all other neighborhoods ($p < 0.001$). Logistic regression analysis showed that pregnant women living in other areas were significantly more likely to elect for prenatal screening with NIPT compared to pregnant women living in socioeconomically disadvantaged areas (OR 3.56; 95% CI: 3.4–3.7).

Overall, the women who chose NIPT had a significantly higher mean age than women who did not have NIPT (31.5 vs. 29.4 years, respectively; $p < 0.001$). Age was not a confounding factor. However, age was shown to be an effect-modifier: the difference in NIPT uptake between socioeconomic disadvantaged neighborhoods and other areas was smaller in the youngest maternal age-group (≤25 years) compared to all other age-groups, due to fewer women in other neighborhoods choosing to participate (Table 1).

4 | DISCUSSION

The results from this nationwide database study demonstrate significant variation in the uptake of fetal aneuploidy screening in socioeconomically disadvantaged neighborhoods in the Netherlands compared to all other neighborhoods. This supports concerns regarding potential disparities in the uptake of NIPT, which conflicts with the primary goals of a government-supported national screening program of equitable access and reproductive autonomy. Our study corroborates findings from other high-income countries such as Australia,[17,18] the United Kingdom[12] and the United States,[19] where socioeconomic disparities in fetal aneuploidy screening uptake were also reported.

A possible explanation for the differences in the uptake of NIPT in the Netherlands might be the out-of-pocket costs of €175. On the one hand, it has been argued that a (small) financial barrier may encourage informed decision-making among pregnant women by promoting deliberation.[20] On the other hand, requiring a payment for NIPT could actively hinder equitable access to the test due to women being unable to pay for fetal aneuploidy screening, thus impeding on their freedom to choose.[5,19] A survey study among European healthcare providers indicated that the costs and a lack of reimbursement policy were considered to be the primary barrier to broader NIPT uptake.[21] Reimbursement of fetal aneuploidy screening might promote equitable access and informed decision-making.[5,22,23]

Studies have shown that when fetal aneuploidy screening is reimbursed, utilization increases significantly.[19,24] A Canadian survey study showed that a majority of pregnant women (66.4%) agreed that reimbursement of NIPT would greatly impact their decision to choose the test.[25] Furthermore, a vignette study among the Dutch general public showed that when NIPT was hypothetically fully reimbursed, significantly more respondents indicated they would consider NIPT, suggesting that reimbursement policies influence attitudes towards accepting or declining NIPT.[26]

In 2018, the uptake of fetal aneuploidy screening was 46% in the Netherlands,[8] whereas the uptake of the free-of-charge 20-week fetal anomaly scan was 83%.[27] Moreover, Posthumus et al.[10] showed that Dutch women of low socio-economic status were more likely to only have the 20-week anomaly scan without fetal aneuploidy screening compared to high/normal socio-economic status women (72% vs. 47%). Offering only one of the two screening programs free of charge may result in a misconstrued belief that the 20-week anomaly scan is more relevant than aneuploidy screening.

TABLE 1 Differences in NIPT uptake between socioeconomically disadvantaged neighborhoods and all other areas stratified by maternal age

Age-group (years)	NIPT (%)	No NIPT (%)	OR (95% CI)
≤25 years			
Socioeconomic disadvantaged area (ref)	401 (10.7)	3346 (89.3)	
All other areas	4628 (23.5)	15,096 (76.5)	2.6 (2.3–2.9)*
26–30 years			
Socioeconomic disadvantaged area (ref)	975 (19.4)	4048 (80.6)	
All other areas	23,399 (44.8)	28,846 (55.2)	3.4 (3.1–3.6)*
31–35 years			
Socioeconomic disadvantaged area (ref)	1072 (26.7)	2935 (73.3)	
All other areas	27,907 (55.9)	21,991 (44.1)	3.5 (3.2–3.7)*
≥36 years			
Socioeconomic disadvantaged area (ref)	570 (27.7)	1491 (72.3)	
All other areas	11,544 (58.1)	8313 (41.9)	3.6 (3.3–4.0)*

Abbreviations: CI, Confidence Interval; NIPT, Non-Invasive Prenatal Test; OR, Odds Ratio; Ref, reference category.
Note: *$p < 0.001$.

Other factors besides costs might also influence the variation in NIPT uptake. Healthcare professionals might also play a role; for example, by overestimating a woman's knowledge or understanding of prenatal screening, or allowing insufficient time for pre-test counselling because of other pressing concerns.[28] Literacy, or religious or cultural factors might also influence uptake.[11,29-32] Differences in uptake of screening might create disparities in other (health) outcomes, such as the live birth prevalence of Down syndrome.[33] In addition, when invasive testing is reimbursed and NIPT is not, there may be an increased exposure to iatrogenic risk from the invasive testing for high-risk women.[17]

The differences in uptake of NIPT between socioeconomically disadvantaged neighborhoods and other areas was smaller in the age-group of ≤25 years. Advanced maternal age is an established risk-factor for trisomy 21.[34] Previous research has shown that aneuploidy screening uptake is lower among women younger than 25,[8] likely due to a perceived lower risk of having a child with Down syndrome.[35] Because of this, the differences in uptake between socio-economic disadvantaged and other areas may be less among younger women. Another explanation may be that the socio-economic differences may be larger in other age-groups resulting in bigger differences in uptake between socioeconomically disadvantaged neighborhoods and other neighborhoods compared to the youngest age-group. According to Statistics Netherlands (CBS), the average household income for the age-group below 25 years is over two times lower than the average income in the age-group between 25 and 35 years.[36]

Strengths of this study include the use of a large national database, allowing us to accurately report on the differences in NIPT uptake between socioeconomically disadvantaged neighborhoods and all other neighborhoods. This study also has limitations. Only cases with complete registrations of counselling, NIPT uptake, postal code and age were included in our study, excluding an estimated 10% of women in the Netherlands who did not receive counselling in 2018. It is unclear how this number is distributed between socioeconomically disadvantaged areas and other neighborhoods. It is possible that more women living in socioeconomically disadvantaged neighborhoods did not receive counselling for prenatal screening, which could have caused underrepresentation of socioeconomically disadvantaged areas in our study. However, the reasons why 10% of Dutch women did not receive counselling are not clear. In order to preserve their 'right not to know' women may refuse counselling, which likely explains part of the proportion of women that did not receive counselling. Furthermore, FCT uptake was excluded from this study. It is possible that women who did not choose NIPT elected for FCT instead. However, FCT uptake in 2018 was only 2.6% and is therefore not likely to have influenced our results much.

In conclusion, NIPT uptake was more than two times lower in socioeconomically disadvantaged neighborhoods compared to other neighborhoods. The variation in NIPT uptake between neighborhoods supports concerns regarding underlying disparities in the uptake of fetal aneuploidy screening. Within the context of national prenatal screening programs, equitable access and reproductive autonomy are principal goals.[15] These aims cannot be achieved when disparities in uptake to screening persist.[22] Though our results indicate unequal uptake of fetal aneuploidy screening, the reasons behind this result remain unclear. It is imperative that potential barriers to uptake are identified and addressed. Research is needed to determine whether the out-of-pocket payment (€175) is a barrier for prenatal screening uptake, especially for women living in socioeconomically disadvantaged areas. Our findings have

both ethical and policy implications, and can assist policy makers in promoting the equitable implementation of NIPT within public healthcare systems.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Peridos the national digital registration system for prenatal screening in the Netherlands. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors only with permission of Peridos.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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