Midwifery 56 (2018) 1–8

Contents lists available at ScienceDirect

Midwifery

journal homepage: www.elsevier.com/locate/midw

Introduction of non-invasive prenatal testing as a first-tier aneuploidy screening test: A survey among Dutch midwives about their role as counsellors

Linda Martin, PhD postdoc researcher[a,*], Janneke T. Gitsels-van der Wal, PhD postdoc researcher / midwife[a], Marjon A. de Boer, MD, PhD gynecologist perinatologist / researcher[b], Meredith Vanstone, PhD Assistant Professor[c], Lidewij Henneman, PhD Associate Professor[d]

[a] *Midwifery Science, AVAG, Amsterdam Public Health research institute, VU University Medical Center, Van der Boechorststraat 7, room: A-511, 1081 BT Amsterdam, The Netherlands*
[b] *Department of Obstetrics & Gynecology, VU University Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands*
[c] *Department of Family Medicine, McMaster University, Hamilton, Ontario, Canada*
[d] *Department of Clinical Genetics, Section Community Genetics, Amsterdam Public Health Research Institute, VU University Medical Center, Van der Boechorststraat 7, Room: A-515, 1081 BT Amsterdam, The Netherlands*

A B S T R A C T

In 2014, non-invasive prenatal testing (NIPT) for trisomies 21, 18 and 13 was added to the Dutch prenatal screening program as part of the TRIDENT study. Most (85%) pregnant Dutch women are counselled for prenatal aneuploidy screening by primary care midwives. This will remain when NIPT is implemented as a first-tier screening test. We therefore investigated midwife counsellors': 1) Knowledge about NIPT; 2) Attitudes towards NIPT as first-tier screening test; and 3) Experiences with informing clients about NIPT. Between April-June 2015, an online questionnaire to assess knowledge about NIPT, attitudes towards NIPT, and experiences with NIPT was completed by 436 Dutch primary care midwives. We found that 59% midwives answered ≥7 of 8 knowledge questions correctly. Continuing professional education attendance and more positive attitudes towards prenatal screening for Down syndrome were positively associated with the total knowledge score (β = 0.261; p = 0.007 and β = 0.204; p = 0.015, respectively). The majority (67%) were in favor of replacing First trimester Combined Test with NIPT, although 41% preferred to maintain a nuchal translucency measurement alongside NIPT. We conclude that midwives demonstrated solid knowledge about NIPT that may still be improved in some areas. Dutch midwives overwhelmingly support the integration of NIPT as a first-tier screening test.

Introduction

In the Netherlands, as in many other countries, there is an ongoing debate on the place and costs of non-invasive prenatal testing (NIPT) in the prenatal screening program (Dondorp et al., 2015; Henneman et al., 2015; Oepkes et al., 2016a). NIPT involves the analysis of cell-free DNA (cfDNA) in a maternal blood sample, which can be done from 9 or 10 weeks of gestation (Benn et al., 2015). Fetal DNA in maternal plasma originates from the placenta. NIPT can be used to screen for trisomy 21, 13 or 18 with a high accuracy, both in high risk and low risk populations (Gil et al., 2015; Taylor-Philips et al., 2016). In addition, NIPT can also be used to screen for sex chromosome anomalies (Benn, 2016), although currently not used for this purpose in the Netherlands (Oepkes et al., 2016b). Despite the favorable test characteristics of NIPT, false positive results do occur, signifying that a NIPT result indicating a trisomy still has to be confirmed by invasive testing for diagnostic certainty (Bianchi et al., 2014). Nevertheless, the introduction of NIPT has re-shaped the use of prenatal testing in many countries; the use of invasive tests and procedure-related iatrogenic miscarriages has decreased significantly (Oepkes et al., 2016b; Warsof et al., 2015).

In 2015, the International Society for Prenatal Diagnosis (ISPD) and Royal College of Obsetricians and Gynaecologists (2014) supported the use of NIPT as a first-tier screening test for all pregnant women

* Corresponding author.
E-mail addresses: linda.martin@INHOLLAND.nl (L. Martin), janneke@hllp.nl (J.T. Gitsels-van der Wal), m.deboer2@vumc.nl (M.A. de Boer), vanstomg@mcmaster.ca (M. Vanstone), l.henneman@vumc.nl (L. Henneman).

http://dx.doi.org/10.1016/j.midw.2017.09.008
Received 11 May 2017; Received in revised form 12 September 2017; Accepted 12 September 2017

(Benn et al., 2015; RCOG, 2014). NIPT has a higher detection rate and lower false positive rate than the first trimester combined test (FCT) (Benn et al., 2015), which involves measurement of nuchal translucency (NT) and maternal serum markers. However, opinions about the availability of NIPT in publicly funded healthcare systems are mixed, mainly reflecting concerns about the relatively high costs of NIPT compared to the FCT (Benn et al., 2015; Oepkes et al., 2016a). As NIPT use increases simultaneous to the evolution of policy, science, and evidence about the test, front line clinicians are challenged to keep abreast of the latest developments. For instance, clinical providers have reported difficulty maintaining up-to-date knowledge about the scope of NIPT, about the differences between tests characteristics offered by different laboratories, and reasons for false-positive NIPT results (Benn and Chapman, 2016). Recognizing these challenges, the American College of Medical Genetics and Genomics (ACMG) has stated that the introduction of NIPT should be accompanied by thorough education of counsellors, decisions about handling costs and healthcare policy decisions around NIPT (Gregg et al., 2013).

In the Netherlands, prenatal screening for fetal aneuploidy requires a governmental license according to the Dutch Population Screening Act. The aim of the Act is to protect the public from potential harm of screening (van El et al., 2012). A license proposal was submitted to the Ministry by the Dutch NIPT Consortium (represented by all institutions, organisations and stakeholders involved with NIPT). After obtaining a license in April 2014, NIPT for trisomy 21, 18 and 13 was added to the Dutch prenatal screening program as part of the TRIDENT study (Trial by Dutch laboratories for Evaluation of Non-Invasive Prenatal Testing) (Oepkes et al., 2016b). Within this context, NIPT is offered by Dutch university clinical genetic laboratories using an in-house validated test. If pregnant women waive their right not to know anything about prenatal screening, they are counselled for aneuploidy screening by a certified counsellor. These counsellors have to participate in continuing professional education about developments regarding counselling for prenatal anomaly screening in general and, as part of the TRIDENT study, on relevant aspects of NIPT (Oepkes et al., 2016b). At the time of this study, NIPT was only available for women at high-risk (≥ 1:200) for fetal aneuploidy based on the FCT or medical history such as a previous child with Down syndrome (Health Council of the Netherlands, 2013). Given this situation, many pregnant women who were not eligible for NIPT within the TRIDENT study, chose to pay for commercially offered NIPT in other countries, often supported – counselling and taking blood- by local midwives/hospitals who sent their samples abroad (Health Council of the Netherlands, 2016a).

Dutch midwives provide initial prenatal care for 85% of Dutch pregnant women, and offer counselling for fetal anomaly screening (FCT and Fetal Anomaly Scan) to all clients (www.perinnet.nl 2013). Since the introduction of NIPT as a second-tier test in 2014, midwives have been informing their clients about NIPT as possible follow-up test. If pregnant women opt for FCT they pay ~€165 (Oepkes et al., 2016b). Clients with elevated risk based on FCT are referred to a Center for Prenatal Diagnosis, to be counselled for NIPT by a prenatal screening specialist (i.e. obstetrician, maternal fetal medicine specialist). If clients choose to opt for follow-up testing, including NIPT, testing is reimbursed by the compulsory health insurance after subtraction of a deductible of ~360 euros (Oepkes et al., 2016b).

If NIPT becomes available for all pregnant women as a first-tier screening test, it will necessitate major changes in the field of prenatal screening and counselling. One significant change is the type of healthcare provider who will provide counselling for NIPT. In the TRIDENT study aimed at high-risk women, prenatal screening specialists offered pretest counselling. If NIPT becomes more widely available as first-tier screening, midwives will assume the burden of pretest counselling because they provide early prenatal care to most pregnant Dutch women (http://www.perinatreg.nl/ 2013). Therefore, it is important to know more about factors that may or may not require additional attention prior to and during implementation of counselling for NIPT as a first-tier screening test by midwives. When it comes to healthcare implementations, Grave et al. (2006) and Légaré et al. (2008) suggest focusing on three main factors: professionals' knowledge, attitudes, and behavior.

Little is known about the knowledge of NIPT among counsellors for prenatal screening, although some studies suggest this knowledge is insufficient (Allyse et al., 2015; Farrell et al., 2016). Global evidence indicates that providers' attitudes towards the availability of NIPT for all pregnant women as a first trimester screening test is positive (Benn et al., 2014; Hill et al., 2012, 2014; Musci et al., 2013; Tamminga et al., 2015; Yotsumotu et al., 2012). Most frequently mentioned concerns about implementing NIPT as first-tier screening are the potential for less informed decision-making by pregnant women based on concerns that offering NIPT could become routinized, or merged into the barrage of blood draws that accompany pregnancy visits (Allyse et al., 2015; Verweij et al., 2015). Less research has been done about the provision of pre-test counselling for NIPT, including the content and quality of this service. Research from the US shows that clinicians have adopted NIPT more quickly than anticipated in their clinical practice, also because of strong public demand, and, as a consequence, without sufficient training (Allyse et al., 2015). This might be problematic since it is known that genetic counselling in general needs optimization especially with regards to providing decision-making support (Martin et al., 2015; Roter et al., 2006). In this study we investigated midwives': 1) knowledge about NIPT; 2) perceived competence with counseling women about NIPT; 3) attitudes towards NIPT as first-tier prenatal aneuploidy screening; and 4) behavior and experience with NIPT.

Methods

Design

We used an online cross-sectional survey of primary care midwives.

Participants and procedure

In 2015, 1984 midwives were active in Dutch primary care practice (Van Hassel, 2016). The majority, 98% of Dutch midwives are members of the Royal Dutch Organization of Midwives (KNOV). In April 2015, we circulated an invitation letter containing a link to the questionnaire to all primary care midwifery practices known by the KNOV (N = 529 practices). All midwives at each practice were asked to complete the questionnaire as an individual. To increase response rates, a call to complete the questionnaire was placed in an online newsletter of KNOV, and emails were sent by some coordinators of regional Perinatal Networks to individual midwives within their region. After three weeks, a reminder was sent to all midwifery practices. Data were collected till June 2015. Vouchers worth 25 euros were raffled among the participants.

Survey instrument

A questionnaire was constructed based on questionnaires used in previous Dutch studies (Verweij, 2014; Tamminga et al., 2015; van Schendel et al. 2015, 2016) and a review of the literature by a multidisciplinary team including representatives of midwifery, gynecology, psychology, clinical genetics and health sciences. The research team deliberated about the validity of the questions and the need for additional questions. The resulting questionnaire assessed background characteristics (gender, age, religiosity, work field (Primary midwifery-led care or midwife and sonographer), years since graduation, postal code (first two numbers), and whether participants had attended Continuing Professional Education (CPE) about NIPT). It also included items to assess knowledge about NIPT, perceived counseling competence, attitudes towards NIPT as first-tier screening test and behavior and experience with NIPT.

Table 1
Background characteristics of study participants (N = 436) compared to the Dutch midwives or Dutch population.

	Study population N (%)	Dutch midwives* / population† (%)
Gender		
Male	2 (0.5)	(1.3)*
Female	434 (99.5)	(98.7)*
Age (years)		
< 35	246 (56.4)	(48.2)*
35–49	123 (28.2)	(35.2)*
> 49	67 (15.4)	(16.6)*
Religiosity		
Religious	139 (31.9)	(51)†
Non-religious	297 (68.1)	(49)†
Work field		
Primary midwifery-led care	373 (85.6)	–
Midwife and sonographer	63 (14.4)	–
Years since graduation		
0–5	104 (23.9)	–
6-10	120 (27.5)	–
11–15	86 (19.7)	–
6-20	50 (11.5)	–
> 20	76 (17.4)	–
Attitude towards providing prenatal screening for Down syndrome		
Very negative or negative	17 (3.9)	–
Neutral	253 (58.0)	–
Positive or very positive	166 (38.1)	–

* Van Hassel et al., 2016.
† StatLine database 2014.

1) Knowledge about NIPT was measured using 8-items to be answered as: true, false, I do not know (based on Van Schendel et al., 2016). Knowledge items are listed in Table 2. These items addressed topics such as test-characteristics (accuracy), eligibility for NIPT in the Netherlands, origin of cfDNA used for NIPT. Self-perceived knowledge about NIPT was assed using 4-items, to be answered as insufficient or sufficient. These items are listed in the first part of Table 3.
2) Perceived competence to counsel woman about NIPT was measured using 4-items, to be answered as insufficient or sufficient (see second part of Table 3, based on Tamminga et al., 2015). *S*elf-efficacy to counsel for NIPT (2 items, 4-point scale (very) insufficient- (very) sufficient) and perceived difficulties / opportunities for counselling (4 items, 4-point scale: (totally) disagree – (totally) agree) were assessed (last two parts of Table 3).
3) Attitudes towards NIPT as first-tier screening test were measured by assessing agreement with 10 statements, to be answered on a 4-point scale: (totally) disagree-(totally) agree (Table 5). In addition, midwives were asked about the preferred position of NIPT in the prenatal screening program (based on Tamminga et al., 2015) (Table 4). Furthermore, we included a general question on counsellor's attitude towards providing prenatal screening for Down syndrome to be answered on a 5-point scale: (very) negative, neutral, (very) positive (based on Verweij, 2014). Finally, participants were asked what, in their opinion, would be an affordable price for clients to pay for NIPT (to be answered as: 530, 250, 165 euros (same as FCT) or other) (based on van Schendel et al., 2015). At the time of this study, the estimated costs for NIPT were 530 euro.
4) Behavior and experiences with NIPT were measured by 5-items, to be answered on a 4 point scale: Yes, always/sometimes, - No, only if the women asks for it / never (see Table 6).

Data analysis

We recoded postal codes into four regions (North, East, South and West). Knowledge items were recoded into 'correct' or 'incorrect' scoring the answer 'I don't know' as 'incorrect'. A 'total knowledge' score was computed by adding up correct answers.

Descriptive statistics (N/%) were used to provide basic information about counsellors' knowledge, attitudes and behavior regarding NIPT and counselling for NIPT. Regression analyses were performed to assess associations between knowledge and participants' age, Continuing Professional Education (CPE) about NIPT, work field, attitudes towards prenatal screening for Down Syndrome and offering NIPT testing abroad. The analyses were performed using SPSS 22.0.

Findings

Participants

In total 436 primary care midwives completed the questionnaire (response rate 22%, 436/1984). Participants' characteristics are presented in Table 1. Most (N = 373; 85.6%) participants worked in primary midwifery-led care; 63 (14.4%) participants combined midwifery-led care with their work as sonographer. Compared to the Dutch general population fewer participants were religious, respectively 51) and 32%; around one-third of the participants (N = 131; 30.0%) came from the North-West of the Netherlands while about 17% of the Dutch midwives practice in this area (Van Hassel et al., 2016). The majority of participants (N = 274; 62.8%) had participated in CPE about NIPT.

Knowledge

Overall, 257 (59.0%) of participants answered ≥7 of 8 knowledge questions correctly (range: 4–8; Mean knowledge sum score = 6.7; SD = 0.9). Table 2 shows the correct knowledge scores per item. The three

Table 2
Midwives' knowledge scores about NIPT and Dutch NIPT policy (N = 436).

Item	Knowledge questions	N (%) correct
1	(In the Netherlands) pregnant women who have an increased risk based on the first-trimester combined test result are eligible for NIPT*. (True)	435 (99.8)
2	(In the Netherlands) pregnant women ≥ 36 years of age are directly eligible for NIPT. (False)	433 (99.3)
3	A positive (condition indicated) NIPT result means that the fetus definitely has a trisomy 21, 18 or 13. (False)	427 (97.9)
4	If the NIPT result is positive (condition indicated), follow-up diagnostic testing (CVS / amniocentesis) is advised in case parents want to terminate the pregnancy. (True)	422 (96.8)
5	In case of a negative (no condition indicated) NIPT result there is still a very small chance that the child has a trisomy 21, 18 or 13. (True)	422 (96.8)
6	(In the Netherlands) an increased nuchal translucency measurement is no indication for NIPT. (True)	290 (66.5)
7	(In the Netherlands) pregnant women who previously carried a child with Down syndrome are only eligible for NIPT after an increased risk based on the first-trimester combined test. (False)	280 (64.2)
8	Cell-free DNA in the maternal plasma that is used for NIPT originates from the placenta. (True)	206 (47.2)

Items ranged from high to low. **Valid percentages are shown. CVS = Chorionic Villus Sampling.**
* In the Netherlands, NIPT is only eligible within the TRIDENT-study.

Table 3
Midwives' perceptions of their knowledge and counseling skills (N = 436).

Perceived knowledge about NIPT		
To what extent do you think your knowledge about NIPT is sufficient regarding:	**Insufficient N (%)**	**Sufficient N(%)**
Eventual confirmative follow-up tests after abnormal NIPT	29 (6.7)	406 (93.3)
Reliability of NIPT	60 (13.8)	375 (86.2)
What NIPT can(not) detect	128 (29.4)	307 (70.6)
The (added) value of NT measurement if NIPT is available as first-tier screening test	192 (44.1)	243 (55.9)
Perceived competence to counsel for NIPT		
To what extent do you feel sufficiently competent to counsel about NIPT?	**Insufficient N (%)**	**Sufficient N(%)**
To counsel the client in a non-directive way, not influenced by my own opinion	11 (2.5)	424 (97.5)
To have a triadic conversation with the pregnant woman and her partner	9 (2.1)	426 (97.9)
To support the client in making her decision	20 (4.6)	415 (95.4)
Help client recognize influence of their own religious or moral values regarding pregnancy termination	28 (6.4)	407 (93.6)
Self-efficacy to counseling for NIPT	**Very insufficient / Insufficient N (%)**	**Sufficient / Very sufficient N (%)**
To what extent do you feel sufficiently trained to counsel for NIPT in the event of an increased risk after the first trimester combined test?	86 (19.7)	349 (80.2)
To what extent do you feel sufficiently trained to counsel for NIPT in cases where there is NO increased risk?	57 (13.1)	378 (86.9)
Perceived difficulties / opportunities for counseling	**Fully disagree / Disagree N (%)**	**Agree / Totally agree N(%)**
I find it hard to explain the differences between NIPT and first trimester combined test	413 (94.9)	22 (5.1)
I think it is complicated to explain why NIPT costs 530 euros and the combined test 165 euros	261 (60.0)	174 (40.0)
I find it difficult to inform clients about medical (test) information regarding NIPT	351 (80.7)	84 (19.3)
I believe / expect counseling about NIPT as first-tier screening to be easier than counseling for the combined test	176 (40.5)	259 (59.5)

Valid percentages are shown; NT = Nuchal Translucency.

Table 4
Midwives' opinion about NIPT in the current prenatal screening program (N = 436).

In your opinion, where should NIPT be placed in the current prenatal screening program?	**N(%)**	**N(%)**
a.) As first follow-up test after an increased risk of > 1:200 based on the combined test	74 (17.0)	80 (18.4)
b.) As first follow-up test after an increased risk of > 1:1000 based on the combined test	6 (1.4)	
c.) As replacement of the first trimester combined test, while maintaining NT measurement	177 (40.6)	292 (67.0)
d.) As (full) replacement of the first trimester combined test, without maintaining NT measurement	115 (26.4)	
e.) Not (NIPT should not be offered)	9 (2.1)	
f.) I do not know	33 (7.6)	54 (12.4)
g.) Other*	21 (4.8)	

Valid percentages are shown. CVS = Chorionic Villus Sampling. NT = Nuchal Translucency.
* e.g.: NIPT and a 12–16 weeks ultrasound; It depends on the balance of costs and benefits. If NIPT remains very expensive in comparison to the first trimester combined test, the FCT is in favor as first screening test.

Table 5
Midwives' agreement on statements regarding NIPT versus FCT (N = 436).

Statements	**Fully disagree /Disagree N(%)**	**Totally agree / Agree N(%)**
NIPT is a reliable test to detect Down-, Patau- and Edwards syndromes	22 (5.1)	413 (95.0)
NIPT is a better follow-up test than CVS / amniocentesis	53 (12.2)	382 (87.8)
NIPT is a better first-tier screening test than the combined test	107 (24.6)	228 (75.4)
It is unacceptable that NIPT as first-tier screening is not offered to everyone in the Netherlands	194 (44.6)	241 (55.4)
I am afraid to be sued if I offer NIPT as first-tier screening right now	306 (70.3)	129 (29.6)
NIPT is relatively expensive for women who want to take this test only to prepare for a child with Down syndrome. I think it is unacceptable if women only use NIPT for this reason.	377 (86.6)	51 (11.7)
I would still offer NT measurement when pregnant women choose NIPT	210 (48.2)	225 (51.7)
I think that most clients in my practice *cannot* pay 530 euros for NIPT	152 (34.9)	283 (65.0)
I think that most clients in my practice do *not want* to pay 530 euros for NIPT	114 (26.2)	321 (73.8)

Valid percentages are shown. CVS = Chorionic Villus Sampling. NT = Nuchal Translucency.

questions that were most frequently answered incorrectly reflect a lack of knowledge about: the origin of the cell-free DNA in the maternal plasma used for NIPT (N = 230;52.8%), eligibility for NIPT in the Netherlands regarding women who previously carried a child with Down syndrome (N = 156;35.8%), and in the eligibility for NIPT in case of a NT $\geq$ 3.5 mm (N = 146; 33.5%). Regression analyses only showed that continuing professional education attendance (β = 0.261; p = 0.007) and more positive attitudes towards prenatal screening for Down syndrome (β = 0.204; p = 0.015) were positively associated with the total knowledge score. Participant's age, work field and offering NIPT testing abroad were not associated with the knowledge score. Of the participants who had participated in CPE about NIPT (N = 274; 62.8%), 171 (62.5%) answered ≥7 of 8 knowledge questions correctly. Of the participants (N = 162; 37.2%) who had never participated in CPE about NIPT, 85 (52.5%) answered ≥7 of 8 knowledge questions correctly.

Table 6
Midwives' experiences informing clients about NIPT (N = 436).

Item	**Yes,** always /sometimes **N (%)**	**No,** only if the women asks for it / never **N(%)**
During standard pre-test counseling on prenatal screening for Down syndrome, do you also inform your clients about the availability of NIPT as a possible follow-up test (besides CVS or amniocentesis)	418 (95.9)	18 (4.2)
If there is an increased risk based on the combined test, do you provide clients information about NIPT as a possible follow-up test?	397 (91.0)	22 (5.1)
Do you inform your clients about the availability of NIPT as first-tier screening test abroad?	101 (23.2)	334 (76.7)

Valid percentages are shown. CVS = Chorionic Villus Sampling.

The first part of Table 3 shows participants' *perceived* knowledge about NIPT. Almost half of participants 192 (44.1%) felt they had insufficient knowledge about the use of NT measurement in conjunction with NIPT if the latter becomes available as first-tier screening test; 128 (29.4%) participants were unsure about 'what NIPT can detect and what cannot be detected using NIPT'.

Perceived competence

The second part of Table 3 shows participants' *perceived* competence to counsel for NIPT. Almost all participants perceived themselves to be competent to counsel about NIPT if it became available as first-tier screening. These perceptions were measured across four items, with perceived competence ranging from 93.6%-97.9% (Table 3). Slightly more than half of the participants (N = 259; 59.5%) expected counselling for NIPT as first-tier screening test to be easier than counselling for the first trimester combined test.

Attitudes

Most participants had a neutral (N = 258; 58%) or positive (N = 132; 38.1%) attitude towards providing prenatal screening for Down syndrome.Regarding the implementation of NIPT in the prenatal screening program 381 (87.5% = 18.4% + 67.0% + 2.1%) of the participants showed positive attitudes to one of the prescribed answer options regarding where NIPT should be placed in the prenatal screening program or provided an alternative option. Two third of the participants (N = 292; 67.0%) were in favor of replacing the FCT by NIPT (Table 4); but 177 (40.6%) preferred maintaining the NT measurement alongside NIPT. From the 177 participants who preferred to maintain the NT measurement 149 (84.2%) were primary care midwives and 28 (15.8%) were midwives who also worked as a sonographer. A minority (N = 80;18.4%) was in favor of offering NIPT as first follow-up test after an increased risk of > 1:200 (N = 74; 17.0%) or 1:1000 (N = 6; 1.4%) based on the combined test; 33 (7.6%) of the participants did not know where NIPT should be placed in the Dutch prenatal screening program. Few participants 21 (4.8%) added alternative options, for instance, offering NIPT as first-tier screening together with an ultrasound scan between 12–16 weeks of pregnancy. The remaining 9 (2.1%) participants were of the opinion that NIPT should not be offered at all.

Table 5 shows that 241 (55.4%) participants held the opinion that it is unacceptable that NIPT as first-tier screening is not offered to everyone in the Netherlands. Most midwives (N = 382; 87.8%) agreed that 'NIPT is a better follow-up test after FCT than CVS / amniocentesis'. A minority of midwives (N = 51; 11.7%) agreed that 'it is unacceptable if women use NIPT only to prepare for a child with Down syndrome, because NIPT is relatively expensive'.

On the topic of cost, 174 (40.0%) were of the opinion that 'it is complicated to explain why NIPT costs a client around 530 euros (estimated cost at time of questionnaire) and the combined test around 165 euros'; 173 (40.0%) participants thought a maximum of 250 euros would be an acceptable fee for NIPT, with 128 (29.3%) participants indicating 165 euros would be acceptable and 38 (8.8%) indicating that 530 euros would be acceptable.

Behavior and experiences

Participants estimated that their counselling for prenatal aneuploidy screening with FCT lasts on average 12 minutes (SD = 4.3; range = 3–30 minutes). A large number of the participants (N = 307; 70.0%) of the participants thought they would need the same amount of time to counsel for NIPT as first-tier screening test, 91 (20.9%) thought less time and 37 (8.5%) more time (range = 2–30 minutes). Table 6 shows that during prenatal counselling for the FCT, the majority of midwives (N = 374; 88.8%) say they inform their clients about the availability of NIPT as a possible follow-up test (beside the CVS or amniocentesis). Most midwives (N = 302; 69.4%) reported that they inform clients about NIPT availability abroad only when the woman asks about it; while 79 (18.1%) midwives sometimes inform their clients about NIPT abroad. The rest either 'always' (N = 22; 5.1%) or 'never' (N = 32; 7.3%) informed their clients about NIPT abroad. Furthermore, since NIPT was only available within the TRIDENT-study context for women at increased risk, 37 (8.5%) participants reported that they offered to send blood for NIPT-testing abroad outside the legal framework, while 11 (2.5%) participants did not want to say if they did or not.

Discussion

This study aimed to explore **midwives**' *knowledge* about NIPT, their *attitudes* towards implementation of NIPT as first-tier prenatal screening and *experiences* with informing clients about NIPT. Most participants showed sufficient *knowledge* about NIPT. Knowledge was positively associated with CPE participation and more positive attitudes towards prenatal screening for Down Syndrome. Generally, counsellors' attitudes towards NIPT as first-tier screening test were positive, however, a significant proportion preferred to maintain NT measurement alongside NIPT. About half of the participants found it unacceptable that, at the time of the study, NIPT was not yet offered to every pregnant woman as first-tier screening in the Netherlands. Almost all participants reported that they already have *experience* in informing clients about NIPT as second-tier screening test. A small minority of the participants reported that they offer to draw blood from their clients so the clients are able to access NIPT testing abroad.

Knowledge

Counsellors' knowledge about NIPT was generally strong. Incorrect answers were mostly made on knowledge items concerning the origin of cfDNA used for NIPT and the exclusion of women for NIPT in case of an increased NT measure. It is of importance that counsellors understand that the cfDNA used for NIPT originates from placenta (the cytotrophoblast of chorionic villi), which explains discrepancies between false positive and sometimes even false negative NIPT results and the actual fetal karyotype (Opstal and van et al., 2016). Furthermore, in case of ultrasound abnormalities, including NT ≥ 3.5mm, counsellors should understand that NIPT is not indicated, because in these cases NIPT is inferior to conventional karyotyping and microarray analysis (Beulen et al., 2017).

Thirty percent of midwives acknowledged that they felt they had

insufficient knowledge about what NIPT can and what cannot be detected with NIPT. One way to improve their knowledge is offering training (Oxenford et al., 2017). In line with other research (Allyse et al., 2015; Brewer et al., 2016), we found that knowledge about NIPT was indeed associated with participation in a CPE. In order to guarantee high quality of NIPT counselling, more effective education of all counsellors is needed, and not just for early adopters of NIPT. This argument is supported by others, who suggest using a wide variety of educational tools including summaries of key information that should be known by professionals (Allyse et al., 2015; Brewer et al., 2016; Farrell et al., 2016; Gregg et al., 2016; Sachs et al., 2015). In our study, two-thirds of the participants reported attending a CPE and only 6% of the participants intended to participate in the future. This means that a quarter of the participants have not attended a CPE about NIPT and do not intend to do so. More insight into how to stimulate this group of counsellors to attend is needed. The Dutch policy to motivate counsellors to participate in CPE is to make participation obligatory for those who engage in counselling (http://www.rivm.nl/dsresource?objectid=ad3d3f25-3103-4087-9452-df219e06f95e&type=pdf&disposition=inline).

Perceived competence

At the time of this study, midwives were required to inform their clients briefly about NIPT as a follow-up test. The counselling provided for those who indicated interest in NIPT - e.g. providing health education as well as decision-making support (Martin et al., 2013), was provided by specialized counsellors within a Center for Prenatal Diagnosis. If NIPT is offered more broadly in the Netherlands, the majority of counselling will shift from these specialized counsellors to all midwives. Considering that midwives may become the designated counsellors, we surveyed participants about their perceived competence, finding that almost all midwives perceived themselves to be competent to counsel clients about NIPT. Furthermore, like Tamminga et al. (2015) we found that most participants expected counselling for NIPT to be easier than counselling for the FCT. This expectation might be based on the fact that they struggle to explain the reporting format of FCT (i.e. risk estimation) compared to the reporting format of NIPT (i.e. condition indicated / not indicated). Nevertheless, although NIPT is a better test than the FCT in terms of the higher prenatal detection rate of Down syndrome and the lower false positive rate, it is important that to facilitate informed autonomous decision making, counsellors also address other aspects –such as reporting formats and a review of clinical features and variability of conditions (Sachs et al., 2015). Moreover, it should be emphasized that testing is optional and should not be seen as routine care nor as a diagnostic test (Sachs et al., 2015; Schendel et al., 2015; Tamminga et al., 2015). Especially the need to ensure voluntary participation in NIPT on the basis of autonomous informed decision-making seems repeatedly a source of concern (Dondorp et al., 2015; Jong de et al., 2011; Schendel et al., 2015). Furthermore, our findings may suggest an overestimation of counselling competency, since in general counselling skills have been found to be suboptimal especially regarding the provision of decision-making support (Gitsels-van der Wal et al., 2014; Martin et al., 2015; Roter et al., 2006).

Attitudes

Almost all participants had a neutral or positive attitude towards prenatal screening for Down Syndrome in general. As in other studies, the overall attitudes towards implementation of NIPT as first-tier screening test were positive; half of the participants held the opinion that it is unacceptable that NIPT was not offered, or even available, to all pregnant women in the Netherlands at the time of this study (Benn et al., 2014; Hill et al., 2012, 2014; Musci et al., 2013; Tamminga et al., 2015). Two thirds thought NIPT should replace the FCT, as they consider it a better screening test than the FCT. Most of the other third of participants wanted to keep the FCT as primary screening test for Down-, Edwards- or Patau syndrome with NIPT as optional secondary screening test. This is a departure from policy decisions made in other jurisdictions, with most of our participants opposing the proposed model in many North American jurisdictions and the United Kingdom (Chitty et al., 2016; Vanstone et al., 2015). In the United Kingdom Chitty et al. (2016) investigated implementation of NIPT as optional secondary test to be used in conjunction with a lower risk threshold from FCT (e.g. ≥1: 1000). Theoretically, this scenario provides a good balance between costs, detection rate and the number of invasive tests. However, our results show that only 1,4% of our participants support this model of implementation. The effect of lowering the risk threshold is that a much larger group of women (estimated at 28% by Henneman et al., 2015) will face an intermediate/increased risk and as a consequence more (potentially unnecessary) stress and anxiety (Kleinveld et al., 2006) and referral to a Centre for Prenatal Diagnosis. Further research should provide insight into the rationale behind midwives' preferences for either putting NIPT as first-tier screening test or as optional secondary screening test, because of the potential impact of these attitudes on the behavior of the midwife counsellors and the prenatal counselling they provide.

In line with a previous questionnaire study performed among health professionals in two regions of the Netherlands, about 40% of the participants would still want to offer their clients an NT measurement when the woman chooses NIPT (Tamminga et al., 2015). From our data it remains unclear why. It may be that participants in our study in practice experience that many women value the (NT) ultrasound as a chance to see the baby, 'confirm' that everything is all right before sharing news with family and friends (Vanstone et al., 2015). Participants might also have concerns that important information about fetal conditions, such as structural anomalies, currently sometimes detected during NT measurement, will be overlooked (Dondorp et al., 2015; Tamminga et al., 2015; Norton et al., 2015). Ultrasound examination is useful to confirm gestation and viability ahead of NIPT. The value of NT measurement to detect chromosomal anomalies, however, seems to be limited (Lichtenbelt et al., 2015). Recently, the Society for Maternal-Fetal Medicine (SMFM) stated that for women who have already received a negative cfDNA screening, an ultrasound at 11–14 weeks of gestation solely for the purpose of NT measurement is not recommended (Norton et al., 2017). In the Netherlands, there is currently no license to offer a 13-week fetal anomaly scan, although this policy is under discussion. Recently, the Health Council of the Netherlands has advised the Minister of Health, Welfare and Sport to add a 13-week scan to the prenatal screening program - within a study context - to evaluate the benefits and possible harms of an early ultrasound, as well as the way women experience it (Health Council, 2017).

Most counsellors (40%) thought a maximum of 250 euros would be an acceptable fee for NIPT while previous studies have shown that most Dutch women do not want to pay more than ~150 euros (Verweij et al., 2013; van Schendel et al., 2015). A small minority of midwives stated that it is unacceptable for women to use NIPT only to prepare for a child with Down syndrome, because NIPT is relatively expensive. These midwives may be assuming that the state will pay for testing. The ethics literature bases the ethical permissibility of NIPT on the right of an individual to make autonomous decisions about her reproductive choices. It would then follow that the availability of NIPT is predicated on the potential that some women may wish to use this information for purposes other than to terminate an affected pregnancy (Health Council of the Netherlands, 2016b). So, if counsellors are of the opinion that it is unacceptable if women use NIPT only to prepare for a child with Down syndrome, they are only allowing "choice" to be defined as terminate or not terminate. This limits the reproductive choices based on prenatal screening, which is both in contrast with the aim of the prenatal screening program as well as unfortunately limiting quality care. For instance, a woman may wish to know about the chromosomal status

of her pregnancy so she could make decisions including intrapartum choices and potentially choices about career / parental leave, childcare, parental education about caring for a child with Down syndrome (Helm et al., 1998; www.niptconsortium.nl, 2017).

Behavior and experiences

In the Netherlands midwife counsellors receive a fee for each counseling they provide; this fee is based on a planned counselling duration of 30 minutes in which both first-trimester anomaly screening as well as second trimester screening should be discussed (RIVM, 2016, 2017). At the time of the study participants estimated prenatal counselling duration for the FCT was on average 12 minutes (range 3–30 minutes). Most participants thought that they could offer counselling for NIPT as a first-tier screening test in about the same amount of time; about one fifth of the participants thought they will need less time to counsel for NIPT. Several studies found an average duration of prenatal counselling for anomaly screening of 9 minutes (Martin et al., 2015; Peters et al., 2017; Spelten et al., 2015). It seems an underestimation of the time needed to provide tailored information about NIPT that comprises more than rudimentary information (van den Heuvel et al., 2010; Sachs et al., 2015).

Almost all counsellors declared they inform their clients about the availability of NIPT as a possible follow-up test beside CVS or amniocentesis. So, midwife counsellors have experience informing clients about NIPT, even though most detailed counselling was provided in the Centers for Prenatal Diagnosis. This is an important finding given the Dutch context, in which, from April 2017 on, a license was given to implement NIPT as first-tier aneuploidy screening test next to the FCT as part of the TRIDENT 2-study (Health Council of the Netherlands, 2016a). As a result, midwives role in counselling for NIPT will become more important.

Limitations

The survey was sent to all Dutch midwifery practices known by the KNOV. One fifth of all Dutch midwives participated in our study. This response rate is relatively low compared to response rates found in other comparable studies (on average 50%) (Baruch and Holtom, 2008). The invitation letter, including the link to the survey, was to midwifery practices instead of individual midwives. Although we tried to make clear that we wanted all individual midwives of a practice to complete the questionnaire, this request might have been overlooked. However, compared to the Dutch midwifery population the response group corresponds with regards to age, gender and offering prenatal counselling. Relatively few participants described themselves as religious (van Hassel et al., 2016). The study sample could have been a biased selection of participants who had more interest in and knowledge about NIPT compared to the non-responders. As a consequence, our study results might be an overestimation of counsellors' knowledge, attitudes and experience regarding NIPT. Furthermore, although we constructed the questionnaire used in this study in a multidisciplinary team, based on the literature and questionnaires used in other studies, we did not extensively validate the questionnaire. Therefore, further research might focus on assessing counsellors' knowledge by using an extensive knowledge questionnaire and monitor attitudes towards a screening program including NIPT and behavior regarding prenatal counselling for aneuploidy screening once NIPT is added to the prenatal screening program.

Key conclusion

Our results suggest that midwife-counsellors' knowledge about NIPT seems good, but needs to be improved especially regarding the origin of cfDNA used for NIPT and the exclusion of women for NIPT in case of an increased NT measurement. Counsellors' attitudes towards NIPT as first- tier screening test are positive, although many prefer to maintain NT measurement in addition to NIPT as first-tier screening test. Furthermore, participating midwives already have been informing clients about NIPT, and expect counselling for NIPT as first screening test to be easier compared to counselling for the FCT.

Acknowledgements

We gratefully acknowledge the contribution of midwives who completed the questionnaire for this study. We further acknowledge Liselore van der Waal and Eva van Rooij, who collected the data and run the first analyses on a subsample during their Midwifery Bachelor thesis.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors contributions

We declare that all authors have made substantial contributions to (1) the conception and design of the study, (2) drafting the article or revising it critically for important intellectual content, (3) and approve the final version of the paper to be submitted.Conflict of interest statement

The authors declare that they have no competing interests.Ethical approval

Ethical approval from a Medical Ethics Committee was not considered necessary according to the Dutch legislation as this study does not impair medical integrity, it is not stressful for participants and no interventions are performed.

References

⟨http://niptconsortium.nl/over-nipt/nipt-consortium/⟩ (In Dutch).
⟨Http://www.perinatreg.nl/uploads/150/153/PRN_jaarboek_2013_09122014.pdf⟩ [homepage on the Internet]. 2013.
Allyse, M., Minear, M.A., Berson, E., Sridhar, S., Rote, M., Hung, A., Chandrasekharan, S., 2015. Non-invasive prenatal testing: a review of international implementation and challenges. International Journal of Womens Health 7, 113–126.
Baruch, Y., Holtom, B.C., 2008. Survey response rate levels and trends in organizational research. Human Relations 61, 1139–1160.
Benn, P., 2016. Expanding non-invasive prenatal testing beyond chromosomes 21, 18, 13, X and Y. Clinical Genetics 90 (6), 477–485.
Benn, P., Chapman, A.R., 2016. Ethical and practical challenges in providing noninvasive prenatal testing for chromosome abnormalities: an update. Current Opinion in Obstetrics and Gynecology 28, 119–124.
Benn, P., Chapman, A.R., Erickson, K., Defrancesco, M.S., Wilkins-Haug, L., Egan, J.F., et al., 2014. Obstetricians and gynecologists' practice and opinions of expanded carrier testing and noninvasive prenatal testing. Prenatal Diagnosis 34, 145–152.
Benn, P., Borrell, A., Chiu, R.W., Cuckle, H., Dugoff, L., Faas, B., et al., 2015. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenatal Diagnosis 35, 725–734.
Beulen, L., Faas, B.H.W., Feenstra, I., van Vugt, J.M.G., Bekker, M.N., 2017. Clinical utility of non-invasive prenatal testing in pregnancies with ultrasound anomalies.. Ultrasound Obstetrics Gynecology 49, 721–728.
Bianchi, D.W., Lamar Parker, R., Wentworth, J., Madankumar, R., Saffer, C., Das, A.F., et al., 2014. DNA Sequencing versus Standard Prenatal Aneuploidy Screening. New England journal of medicine 370, 799–808.
Brewer, J., Demers, L., Musci, T., 2016. Survey of US obstetrician opinions regarding NIPT use in general practice: implementation and barriers. Journal of Maternal-Fetal Neonatal Medicine 2, 1–4.
Chitty, L.S., Wright, D., Hill, M., Verhoef, T.I., Daley, R., Lewis, C., et al., 2016. Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units. British Medical Journal 354, i3426.
Dondorp, W., de Wert, G., Bombard, Y., Bianchi, D.W., Bergmann, C., Borry, P., et al., 2015. Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening. European Journal of Human Genetics 23, 1438–1450.
El, van C., Pieters, T., Cornel, M., 2012. Genetic screening and democracy: lessons from debating genetic screening criteria in the Netherlands. Journal of Community Genetics 3, 79–89.
Farrell, R.M., Agatisa, P.K., Mercer, M.B., Mitchum, A.G., Coleridge, M.B., 2016. The use of noninvasive prenatal testing in obstetric care: educational resources, practice patterns, and barriers reported by a national sample of clinicians. Prenatal Diagnosis 36, 499–506.

Gil, M.M., Quezada, M.S., Revello, R., Akoleka, r R., Nicolaides, K.H., 2015. Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis. Ultrasound in Obstetrics and Gynecology 45, 249–266.
Gitsels-van der Wal, J.T., Manniën, J., Gitsels, L.A., Reinders, H.S., Verhoeven, P.S., Ghaly, M.M., et al., 2014. Prenatal screening for congenital anomalies: exploring midwives' perceptions of counseling clients with religious backgrounds. BMC Pregnancy Childbirth 19, 237–245.
Grave, l K., Légaré, F., Graham, I.D., 2006. Barriers and facilitators to implementing shared decision-making in clinical practice: a systematic review of health professionals' perceptions. Implement Science 1, 16–31.
Gregg, A.R., Gross, S.J., Best, R.G., Monaghan, K.G., Bajaj, K., Skotko, B.G., et al., 2013. ACMG statement on noninvasive prenatal screening for fetal aneuploidy. Genetics in Medicine 15, 395–398.
Gregg, A.R., Skotko, B.G., Benkendorf, J.L., Monaghan, K.G., Bajaj, K., Best, R.G., et al., 2016. Update: a position statement of the American College of Medical Genetics and Genomics. Genetics in medicine 18, 1056–1065.
Health Council of the Netherlands, 2013. [Population Act**:** non-invasive prenatal testing in case of an increased risk for trisomies.]. Health Council; publication number 2013/35 [In Dutch].
Health Council of the Netherlands, 2016a. [Population Act: NIPT as first-tier screening for Down-, Patau- and Edwards syndrome]. Health Council; publication number 2016/10 [In Dutch].
Health Council of the Netherlands. Prenatal screening. The Hague: Health Council of the Netherlands, 2016b; publication no. 2016/19 [in Dutch].
Helm, D.T., Miranda, S., Angoff Chedd, N., 1998. Prenatal Diagnosis of Down Syndrome: mothers' Reflections on Supports Needed From Diagnosis to Birth. Mental Retardation 36, 55–61.
Henneman, L., Page-Chrisiaens, G.C., Oepkes, D., 2015. [Non-invasive prenatal testing: challenges for future implementation]. Nederlands Tijdschrift voor Geneeskunde 159, A9479, (In Dutch).
Heuvel, van den A., Chitty, L., Dormandy, E., Newson, A., Deans, Z., Attwood, S., et al., 2010. Will the introduction of non-invasive prenatal diagnostic testing erode informed choices? An experimental study of health care professionals. Patient Education and Counseling 78, 24–28.
Hill, M., Fisher, J., Chitty, L.S., Morris, S., American College of Medical Genetics and Genomics. 2012. Women's and health professionals' preferences for prenatal tests for Down syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive testsGenetics in Medicine 14, 905–913.
Hill, M., Wright, D., Daley, R., Lewis, C., McKay, F., Mason, S., et al., 2014. Evaluation of non-invasive prenatal testing (NIPT) for aneuploidy in an NHS setting: a reliable accurate prenatal non-invasive diagnosis (RAPID) protocol. BMC Pregnancy and Childbirth 14, 229–237.
Jong de, A., Dondorp, W.J., Frints, S.G.M., de Die-Smulders, C.E.M., de Wert, G.M.W.R., 2011. Advances in prenatal screening: the ethical dimension. Science and Society 12, 657–663.
Kleinveld, J.H., Timmermans, D.R., de Smit, D.J., Adér, H.J., van der Wal, G., ten Kate, L.P., 2006. Does prenatal screening influence anxiety levels of pregnant women? A longitudinal randomised controlled trial. Prenatal Diagnosis 26, 354–361.
Légaré, F., Ratté, S., Gravel, K., Graham, I.D., 2008. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. Patient Education and Counseling 73, 526–535.
Lichtenbelt, K.D., Diemel, B.D., Koster, M.P., Manten, G.T., Siljee, J., Schuring-Blom, G.H., et al., 2015. Detection of fetal chromosomal anomalies: does Nuchal Translucency measurement have an added value in the era of Non-Invasive Prenatal Testing? Prenatal Diagnosis 31, 765–772.
Martin, L., Van Dulmen, S., Spelten, E., De Jonge, A., De Cock, P., Hutton, E., 2013. Prenatal counseling for congenital anomaly tests: parental preferences and perceptions of midwife performance. Prenatal Diagnosis 33, 341–353.
Martin, L., Hutton, E.K., Gitsels-van der Wal, J.T., Spelten, E.R., Kuiper, F., Pereboom, M.T.R., et al., 2015. Antenatal counselling for congenital anomaly tests: an exploratory video-observational study about client-midwife communication. Midwifery 31, 37–46.
Musci, T.J., Fairbrother, G., Batey, A., Bruursema, J., Struble, C., Song, K., 2013. Non-invasive prenatal testing with cell-free DNA: us physician attitudes toward implementation in clinical practice. Prenatal Diagnosis 33, 424–428.
Norton, M.E., Jacobsson, B., Swamy, G.K., Laurent, L.C., Ranzini, A.C., Bra, r H., et al., 2015. Cell-free DNA analysis for noninvasive examination of trisomy. New England Journal of Medicine 2372, 1589–1597.
Norton, M.E., Biggio, J.R., Kuller, J.A., Blackwell, S.C., 2017. The role of ultrasound in women who undergo cell-free DNA screening. American Journal Obstetrics Gynecology 216, B2–B7.
Oepkes, D., Bartha, J.L., Schmid, M., Yaron, Y., 2016a. Benefits of contingent screening vs primary screening by cell-free DNA testing: think again. Ultrasound in Obstetrics Gynecology 47, 542–545.
Oepkes, D., Page-Christiaens, L.G.C., Bax, C.J., Mireille, N., Bekker, M.N., Bilardo, C.M., et al., 2016b. Trial by Dutch laboratories for evaluation of non-invasive prenatal. Part I-clinical impact. Prenatal Diagnosis 36, 1083–1090.
Opstal, van, D., Srebniak, M.I., Polak, J., de Vries, de, F., Govaerts, L.C.P., Joosten, M., et al., 2016. False Negative NIPT Results: risk Figures for Chromosomes 13, 18 and 21 Based on Chorionic Villi Results in 5967 Cases and Literature Review. PLoS One 11, e0146794.
Oxenford, K., Daley, R., Lewis, C., Hill, M., Chitty, L.S., 2017. Development and evaluation of training resources to prepare health professionals for counselling pregnant women about non-invasive prenatal testing for Down syndrome: a mixed methods study. BMC Pregnancy Childbirth 17, 132–143.
Peters, I.A., Reijerink-Verheij, J.C.I.Y., Knapen, M.F.C.M., Ursem, N.T.C., 2017. [A new method to assess counseling for prenatal anomaly screening; the Rotterdam method]. Nieuwe toetsingsmethode counseling over prenatale screening; De Rotterdamse methode. Nederlands Tijdschrift voor Obstetrie Gynaecologie 130, (In Dutch).
RIVM, 2016. [Newsletter prenatal and neonatal screening.] 9 (6): ⟨http://www.rivm.nl/Nieuwsbrieven/nbr0-it-0012.nsf/NieuwsbriefSendWeb?OpenForm&Query=EE9A8218C94D506AC125803B002C0BDD⟩. (In Dutch).
RIVM, 2017. . Kwaliteitseisen counselors prenatale screening [Quality requirements counselors prenatal screening]. (Version 7, determined by the RIVM-CvB on the advice of the Program committee Prenatal Screening March 23th 2017). (In Dutch). ⟨http://www.rivm.nl/dsresource?Objectid=ad3d3f25-3103-4087-9452-df219e06f95e&type=pdf&disposition=inline⟩.
Roter, D.L., Ellington, L., HambyErby, L., Larson, S., Dudley, W., 2006. The genetic counseling video project(GCVP):models of practice. American Journal of Medical Genetics Part C 142C, 209–220.
Royal College of Obsetricians and Gynaecologists, 2014. Non-invasive prenatal testing for chromosomal abnormality using maternal plasma DNA (Scientific Impact Paper No. 15). ⟨https://www.rcog.org.uk/globalassets/documents/guidelines/sip_15_04032014.pdf⟩.
Sachs, A., Blanchard, L., Buchanan, A., Norwitz, E., Bianchi, D.W., 2015. Recommended pre-test counseling points for noninvasive prenatal testing using cell-free DNA: a 2015 perspective. Prenatal Diagnosis 35, 968–971.
Schendel, van, R.V., Dondorp, W.J., Timmermans, D.R., van Hugte, E.J., de Boer, A., Pajkrt, E., et al., 2015. NIPT-based screening for Down syndrome and beyond: what do pregnant women think? Prenatal Diagnosis 35, 598–604.
Spelten, E.R., Martin, L., Gitsels-van der Wal, J.T., Pereboom, M.T.R., Hutton, E.K., Van Dulmen, S., 2015. Introducing video recording in primary care midwifery for research purposes: procedure, dataset, and use. Midwifery 31, 95–102.
Tamminga, S., van Schendel, R.V., Rommers, W., Bilardo, C.M., Pajkrt, E., Dondorp, et al., 2015. Changing to NIPT as a first-tier screening test and future perspectives: opinions of health professionals. Prenatal Diagnosis 35, 1316–1323.
Taylor-Phillips, S., Freeman, K., Geppert, J., Agbebiyi, A., Uthman, O.A., Madan, J., Clarke, A., Quenby, S., Clarke, A., 2016. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. BMJ Open 6, e010002. http://dx.doi.org/10.1136/bmjopen-2015- 010002.
Van Hassel, D.T.P., Kasteleijn, A., Kenens, R.J., 2016. [Figures from the registration of midwives; year 2015]. NIVEL. [In Dutch].
Van Schendel, R.V., Page-Christiaens, G.C., Beulen, L., Bilardo, C.M., de Boer, M.A., Audrey B. C. Coumans, A.B.C., et al., 2016. Trial by Dutch laboratories for evaluation of non-invasive prenatal testing. Part II—women's perspectives. Prenatal Diagnosis 36, 1091–1098.
Vanstone, M., Yacoub, K., Giacomini, M., Hulan, D., McDonald, S., 2015. Women's experiences of publicly funded non-invasive prenatal testing in Ontario, Canada: considerations for health technology policy-makingQualitative Health Research 25, 1069–1084.
Verweij, E.J., 2014. NIPT: Non-Invasive Prenatal Testing: Towards Implementation in the Netherlands. Leiden University, (Thesis Chapter 7)⟨https://openaccess.leidenuniv.nl/handle/1887/25414⟩.
Verweij, E.J., Oepkes, D., Vries, M., de, Akker, M.E., van den, Akker, E.S., van den, Boer, M.A. de, 2013. Non-invasive prenatal screening for trisomy 21: what women want and are willing to pay. Patient Education and Counseling 93, 641–645.
Verweij, E.J., Romeijn, J.M., Koelewijn, K.M., Heetkamp, M.A., de Boer, D., Oepkes, D., 2015. Prenatale screening en de non-invasieve prenatale test: hoe denken eerstelijns verloskundigen erover? Tijdschrift voor Verloskundigen 1, 16–20, (In Dutch).
Warsof, S.L., Larion, S., Abuhamad, A.Z., 2015. Overview of the impact of noninvasive prenatal testing on diagnostic procedures. Prenatal Diagnosis 35, 972–979.
Yotsumotu, J., Sekizawa, A., Koide, K., Purwosunu, Y., Ichizuka, K., Matsuoka, R., et al., 2012. Attitudes toward non-invasive prenatal diagnosis among pregnant women and health professionals in Japan. Prenatal Diagnosis 32, 1–6.