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

Content of the opinion

The question put to the Committee

On 21 October 2013, Mrs Onkelinx, then Deputy Prime Minister and Minister for Social Affairs and Public Health, asked the Advisory Committee on Bioethics for an opinion.
The issue related to Non-Invasive Prenatal Testing (NIPT) for genetic and chromosomal abnormalities (i.e.Non Invasive Fetal Trisomy Testing) and read as follows:

> *"The aforementioned tests have been made possible thanks to the technological innovation in the field of human genome research. They are extremely promising and are billed by the promoters of this research as an essential means to detect certain chromosomal abnormalities that have a significant impact at an early stage.*
> *However, these tests raise a number of urgent medical and ethical issues because both gynaecologists and a number of (foreign) laboratories are currently prescribing or offering them outside of the regulatory reimbursement framework, without any guarantees as to their quality or to a genetic counselling support system.*
> *Moreover, several commercial players have emerged who introduce patients to these tests directly and go as far as recruiting them via the Internet.*
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> *For these reasons, we urgently ask the Superior Health Council (SHC), the Belgian Health Care Knowledge Centre (KCE) and the Advisory Committee on Bioethics (CCB) for an opinion. It goes without saying that we would also welcome a contribution from the Centre for Human Genetics of the FPS.*
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> *- We ask the SHC and the KCE for an opinion on the indication and positioning of these tests and to formulate a number of viable health recommendations in terms of covering and organising these tests should they prove to be a useful prenatal screening tool.*
> *- We ask the CCB to give its opinion on the ethical issues these tests raise, notably in matters of informed consent, the counselling required and the notification procedure with regard to the possible termination of a pregnancy on the basis of the interpretation of the test result.*
> *Kindly provide me with your opinion by 31 May 2014 at the latest.*
> *Lastly, I would like the CCB to also look into the ethical and deontological aspects of offering these genetic tests online. In relation to the latter issue, there is no specific deadline.* "

In view of the fact that the fourth mandate came to an end at the end of January 2014, the Committee was unable to give its opinion in time. Thus, the issue was discussed at the

Committee's first plenary session of 8 September 2014, and it was decided to have it analysed by a select committee (CR 2014-4).

I. Introduction

These days, many pregnant women opt for prenatal screening for trisomy 21 (Down syndrome) in the form of a combined test during the first trimester (of the pregnancy). This test, which is performed between the 11th and 13th week of gestation, calculates the risk of giving birth to a baby with trisomy 21 by examining the age, the hormonal values and the result of the nuchal translucency measurements. After the test, the women know whether they are deemed to be at a high or low risk. High-risk women can then opt for an amniotic fluid test or for chorionic villus sampling. An amniotic fluid test, or amniocentesis, is a prenatal examination where a sample of the amniotic fluid is taken through the abdomen of the pregnant woman. Chorionic villus sampling involves taking a sample of the "villi" or placental tissue. Both techniques facilitate the detection of any chromosomal aberrations or the performance of a molecular review and, hence, to reliably diagnose trisomy 21. Yet, both techniques entail a risk of miscarriage which is assessed at about 0.5-1%.

Recently, another method to test for trisomy 21, in parallel with the combined test, has become available: non-invasive prenatal testing (NIPT). This method allows the DNA of the foetus to be obtained via the blood plasma of the pregnant woman. In technical terms, this is referred to as cell-free fetal DNA or cffDNA. Cell-free fetal DNA mainly comes from the placenta and consists of short DNA fragments that circulate in the mother's blood. In practice, NIPT is often performed as of the 11th week of gestation, but it can also be performed earlier.

NIPT offers a higher detection rate than the combined test, and it produces less false positives. Another significant advantage of NIPT is that there is no longer any need to, in first instance, take a sample of the amniotic fluid or to resort to chorionic villus sampling to detect possible genetic or chromosomal aberrations in the foetus. As a result, these invasive procedures and the associated risk of miscarriage can, by and large, be avoided. So, only in cases of an abnormal result, an amniocentesis or chorionic villus sampling will be required to confirm the diagnosis.

In the present opinion, the Committee examines the ethical issues posed by the use of NIPT

for trisomies 21, 13 and 18.[1] This issue needs to be addressed in light of the wider debate within society about the appropriateness of using NIPT to detect abnormalities and the criteria that must support an appropriate use of NIPT. The Committee is aware of the tremendous technical possibilities NIPT has to offer and of the associated ethical issues which go beyond the focus of this opinion. This opinion also features within the framework of a lively international debate various stakeholders (1-9) and bodies (such as the European Society of Human Genetics and the Nederlandse Gezondheidsraad) are involved in.

In terms of the terminology used, the opinion in general refers to 'pregnant women'. However, the Committee wishes to emphasise that reproductive choices are by and large made by pregnant women and their partner together. From a legal point of view, pregnancy-related decisions pertain to the pregnant woman however.

II. State of the art at a scientific level

Traditionally, the main criterion to screen for chromosomal abnormalities, and in particular trisomy 21, was basically the mother's age (10-12). As the risk of chromosomal abnormalities (trisomies 21, 18 and 13) increases with the age of the mother, pregnant women over the age of 35 were given the option of having an amniocentesis. In fact, 5 % of amniocenteses resulted in a 30 % detection rate of foetuses with trisomy 21.

What's more, as we know that foetuses with a chromosomal abnormality die prematurely in the womb more often than normal foetuses, the detection rate of chromosomal abnormalities decreases with gestational age. Thus, the individual baseline risk or "a priori" risk of chromosomal abnormalities will not only depend on the age of the mother but also on the gestational age. (10;12)

This "a priori" risk is then adjusted in function of the ultrasound markers for chromosome abnormalities (nuchal translucency, the presence or absence of nasal bones, blood flow at tricuspid valve or ductus venosus level) and by means of biochemistry (blood tests during the

[1] Trisomy 21 (or Down syndrome) is characterised by delayed development and mental deficiencies. In 50% of cases, this condition also comes with an (operable) heart defect. Related medical issues often manifest themselves during adulthood and the average life expectancy is 60 years. The risk of having a baby with Down syndrome for women under the age of 30 years is less than 1 per thousand. At the age of 35, that risk increases to 1 per 350, at the age of 40, to 1 per 100 and at the age of 45, to 1 per 25. Trisomy 18 (Edwards syndrome) is a genetic disorder characterised by severe cerebral (mental deficiencies) and cardiac malformations. The average survival rate is 14 days. The average prevalence is 1 in 8500 births. Trisomy 13 (Patau syndrome) is a chromosomal condition associated with severe cerebral, cardiac, renal and intestinal abnormalities. The average life expectancy is 7 days. The average prevalence is 1 in 17000 births.

first or second trimester of the pregnancy). This "a priori" risk of the pregnant woman is then multiplied by the relative risk calculated on the basis of the results of each of these ultrasound markers and by the biochemical examinations to establish the final risk.

Measuring nuchal translucency[2], during the first trimester of pregnancy (between week 11 and 14 of amenorrhoea) allows 80 % of foetuses affected by trisomy 21 to be detected in cases where the nuchal translucency value is higher than the expected percentile 95 for a given craniocaudal length[3] of the foetus. When adding the biochemical value results (β-HCG and PAPPA-A measurements during the first trimester), the screening rate comes in at about 90 % for trisomy 21 in 5 % of the false-positive results.(10;11)

Since the 2000s, certain centres have been using new ultrasound markers to perform an ultrasound during the first trimester which enhanced the screening rate for trisomy 21, resulting in a detection rate of about 98 %, with a 5 % rate of false positives. (12-14) This efficiency in ultrasounds can only be achieved if the ultrasound technicians performing the scans are trained and are subjected to continuous external auditing to guarantee the quality of their measurements. Incidentally, in our country, at least 20 % of pregnant women do not benefit from early follow-up and do not get the 12-week ultrasound.

The development of NIPT

In 1997, the research team of Dr Dennis Lo in Oxford demonstrated that cell-free fetal DNA (cffDNA) could be found in the mother's blood during pregnancy (15). This cffDNA comes from the placenta (trophoblast cells) and consists of small fragments of about 150-200 base pairs, which represent the entire fetal genome, and can be detected in the maternal plasma as early as 4 weeks into the pregnancy. The fetal fraction (ratio between cell-free fetal DNA and cell-free maternal DNA) increases as the pregnancy goes on, culminating in 10 % on average (16). Various factors associated with the mother or the foetus can affect this fraction (e.g. obesity, a twin pregnancy, in vitro fertilisation, etc.). These DNA fragments have a short half-life: two hours after delivery, cffDNA can no longer be detected in the mother.

Ever since that discovery, finding methods that would facilitate a non-invasive prenatal diagnosis, and more specifically a method to screen for the most common trisomies (13, 18

[2] Nuchal translucency is established with the help of an ultrasound examination of the foetus, performed between weeks 11 and 14 of gestation, and measures the thickness of the nuchal translucency zone. Nuchal translucency is a collection of fluid under the skin at the back of the baby's neck. All foetuses have it during the first trimester of the pregnancy but is subsequently disappears.
[3] A foetus's craniocaudal length is the length between the cranium and the coccyx.

and 21), became focus of attention. But it wasn't until new sequencing technologies - massive parallel sequencing or high-throughput sequencing - were developed and implemented that it became possible to screen for fetal trisomies with a high degree of sensitivity. (17;18)

Massive parallel sequencing allows us to read and quantify the cffDNA fragments. This quantification forms the basis of the current NIPT test: millions of tiny fragments are read so as to detect any subtle changes in the fetal DNA. By reading and counting the millions of tiny fragments, the number of DNA molecules, e.g. of chromosome 21, in the test sample can be compared against a reference scale. Any statistically significant increase in the number of reads, connected to for instance chromosome 21, points to a fetal trisomy. Various algorithms have been developed to analyse this quantification statistically. (19)

The majority of these NIPT tests have a genome-wide approach, and sequence all chromosomes. However, genome-wide sequencing does not mean that all sequences are analysed. In most of the tests, only the analyses of trisomies 21 and 18 have been validated because they are the most common aneuploidies. On the other hand, NIPT tests could simply be limited to chromosomes 13, 18 and 21, in which case we talk about "targeted" tests.

Several studies have shown that NIPT is accurate and offers a high, both positive and negative, predictive value for the group of pregnant women at high risk of trisomy 21 (>1/300). In the population of pregnant women not considered to be at high risk of aneuploidies, detection rates are equally promising (>99%), with very few false positives (<0.1%) for all three trisomies. (20-23) That having been said, NIPT can never be 100 % accurate in view of the fact that cell-free fetal DNA comes from the placenta and there is always a possibility of placental mosaicism[4]. So, the only way to confirm an abnormal NIPT with absolute certainty is to undergo an amniocentesis to check whether the foetus itself has indeed been affected.

Thus, by analysing the cell-free fetal DNA in the maternal blood (NIPT), the detection rate for mainly trisomy 21 can be increased to as much as 99.5% while the numbers of false positives also reduce dramatically (to less than 0.1%) (24). As to the debate about the reliability of NIPT, we refer to the report by the Superior Health Council (25) and the Belgian Health Care Knowledge Centre. (26)

[4] Placental mosaicism: the presence of two (or more) cell lines with different chromosomal complements in an individual.

III. Legal framework

The legal and deontological framework within which non-invasive prenatal screening can be organised is relatively clear and coherent. Prevailing texts all put the emphasis on the information to be provided and on respect for patient autonomy.

The Medical Deontological Code insists on patients being correctly informed, in general terms, about any diagnostic or therapeutic measure they are offered, and in particular in relation to any issues relating to reproduction and to maternal or fetal pathologies. In this particular area, the Code unequivocally requires that the persons concerned are given all the relevant information (art. 85), that the female patient is fully informed, that her autonomy is respected and that her informed consent is obtained (art. 86).

The Law of 3 April 1990 on the termination of pregnancy must also be taken into account because screening by means of NIPT may bring untreatable fetal conditions to light. This law provides for two situations where a pregnancy can be terminated, both of which conceivably within the realm of trisomies detected via NIPT. The first possible scenario is the distress of a pregnant woman who is not yet in the 13th week of gestation ("before the end of the twelfth week after conception", as the law states); this highlights the need to offer NIPT from week 11. However, that situation is rare because the NIPT result will still need to be confirmed by an amniocentesis, which isn't performed until the 15th week of gestation at the earliest. In the second situation, termination after the 13th week can be invoked in cases where the trisomies are untreatable and particularly serious.

The Law of 22 August 2002 on the rights of patients among other matters stipulates that patients are entitled to

- A qualitative service that meets their needs and this, with full respect for their human dignity and autonomy and without distinction of any kind (art.5);
- Receive all the relevant information they need to understand the state of their health and its likely evolution (art.7);
- Freely consent to any intervention by a professional practitioner subject to having been informed beforehand. The law deals at length and in detail with the concept 'information prior to any intervention' and includes "the purpose, the nature, the degree of urgency, the duration, the frequency, the contraindications, the secondary effects and risks inherent to the intervention and relevant to the patient, the aftercare, the possible alternatives and the financial repercussions". It also stipulates that the information must be provided beforehand and timely (art. 8) ;
- Have their privacy ensured (art. 10).

The Law on the rights of patients defines health care extremely broadly: “services provided by a professional practitioner with a view to promoting, determining, preserving, restoring or improving patients’ state of health, changing their physical appearance for mainly aesthetic reasons or accompanying them at the end of their life”.(art. 2)

This legal and deontological framework would not be complete however without a reminder of the right of practitioners “to take decisions based on science and their conscience only”. (Medical Deontological Code, art. 32)

A differently formulated conscience clause also features in the Law of 3 April 1990 quoted above: “No doctor, nurse or paramedic is obliged to help terminate a pregnancy”. It is clear that the conscience clause, the right of practitioners, does not in any way release them from their obligation to advise and inform the patient about every aspect, including the option to have an abortion.

IV. Ethical considerations

IV.1. Prenatal screening: an ethically sensitive issue

The Committee recognises the ethical sensitivity associated with prenatal screening.
Firstly, prenatal screening is always associated with the societal debate on the protection of the embryo. In its opinion no. 18 (27), the Committee already exhaustively dealt with the various points of view on the embryo. These various points of view on the protection of the embryo give rise to a range of perspectives on prenatal screening and the termination of a pregnancy. In this context, also the issue of what qualifies as a “serious” condition is relevant.
Secondly, the ethical debate on prenatal screening is associated with discussions around the value judgments that the termination of a pregnancy entails for people suffering from these conditions. (28) Some of the protagonists in this debate fear that prenatal screening and the termination of a pregnancy will have a discriminatory effect on people suffering from this condition and may lead to a dismantling of the social support and solidarity for the care extended to this population. (29) Certain patient groups have pointed out that a prenatal test and the termination of a pregnancy on grounds of their particular condition can be perceived as a rejection of their right to existence and worth, which is at odds with the non-discrimination principle. (30) However, others argue that the termination of a pregnancy on grounds of the disability the foetus is affected by can prevent a lot of suffering in the long term. Some believe that, where possible, we have a moral obligation to prevent any such future suffering and to ensure that the child is born with the best possible chances in life, thereby assuming that the life of a child without a disability is better than that of a child with a disability. (31)

Thirdly, the ethical debate relates to the social impact of prenatal screening. Some believe that prenatal screening fuels the idea that pregnancy and having children is a controllable and manageable process that gives parents significant control over the genetic characteristics of their offspring. (32) Critics claim that this development could create social pressure to opt for prenatal screening. That could ultimately induce the perception that having a child with a disability is irresponsible because this could have been avoided in the first place.

This fundamental debate about the appropriateness of prenatal screening is beyond the scope of this opinion but, unquestionably, forms part of the wider societal debate NIPT fuels. It is also worth noting that prenatal screening is seen as a means to enable women and couples to exercise their reproductive autonomy. This reproductive autonomy does not merely entail that they can decide themselves whether they want a child, but, to a certain extent, also that they can learn about the health of their child. Having a child with a severe disability takes a heavy toll on many couples' lives and often means a serious restriction on the life plans the people in question may have. The specific advantages of NIPT, in comparison to other prenatal diagnostic methods, means that couples will henceforth be able to find out about the health of their future child with far fewer chances of miscarriage and a reduction in the psychological burden that comes with an invasive test.

In this context, the Committee wishes to emphasise that prenatal tests, in general, and NIPT for trisomies 13, 18 and 21 in particular, must meet a number of specificcriteria for responsible offer.

Contrary to the other types of screening (for instance: screening for bowel cancer or neonatal screening), which are designed to detect a condition that can be prevented or cured, the purpose of prenatal screening for fetal abnormalities (like trisomies 21, 13 or 18) is to inform pregnant women about the health of the foetus so that they can make autonomous reproductive choices.

For that reason, the use of the term "preventive" in the context of prenatal screening for trisomies 21, 13 and 18 is inadequate. (33) From the authorities' point of view, the purpose of prenatal screening is not to prevent certain conditions, but to offer "participants practical courses of action" (33) and to allow them to make informed choices. The prevention of certain conditions is a possible consequence of the choices individual citizens make. This distinction is as subtle as it is important. In fact, the authorities cannot impose reproductive choices on their citizens.

The authorities' involvement in facilitating prenatal screening is a highly sensitive issue to say the least. Some believe that organising or reimbursing prenatal screening for trisomies 21,

18 or 13 can never be seen as neutral. This is for instance clear from the torrent of reactions to the question whether screening for trisomy 21 is appropriate.(34) Hence the criticism that there is social, political and medical pressure not to allow certain children to be born (for instance children with Down syndrome). In this debate, the concept 'eugenics' is bandied about on a regular basis. The fact that the authorities provide funding to finance a screening programme could be interpreted as a eugenic measure because it might suggest that people suffering from one condition or another are not welcome in our society. Yet, the word 'eugenics' is used incorrectly in this context because this concept relates to situations where an authority imposes reproductive choices. The Committee is of the opinion that the public authorities can play an important role in offering pregnant women access to safe and reliable tests which provide them with the information they need to make the reproductive choices that suit them in all freedom. As such, they should be able to bank on satisfactory counselling and support.

From an ethical point of view, neither a prenatal test, nor the choice that is made on the basis of that test, should be imposed on pregnant women. Offering women the choice to either or not terminate a pregnancy because the foetus was found to have a condition does not necessarily imply that the life of people suffering from that same condition is less valuable and that it would be better if they had not been born. (35)

On the basis of that point of view, the Committee wishes to put forward a number of criteria of responsible offer in the context of the implementation of NIPT. The failure to meet these requirements could have adverse effects, such as the lack of information or appropriate advice, uninformed or inadequately informed reproductive choices, social pressure or stigmatisation. The Committee points out that these criteria are relevant to all forms of prenatal screening and not only to NIPT.

IV.2. Criteria for a responsible offer of NIPT

IV. 2.1. Clinical and technical challenges and social impact

These days, NIPT is a fairly common clinical practice both internationally (36) and in Belgium (37). More specifically, significant numbers of high-risk pregnant women (because of their age or the result of the combined test) already avail of this test. Furthermore, certain pregnant women also ask for it even though they are not in the high-risk category.
Yet the introduction of NIPT cannot be considered independently from other aspects and techniques used in the prenatal environment, such as monitoring the quality of ultrasounds and combined tests.

The main advantage of NIPT is that the risk of miscarriage, associated with invasive prenatal

tests (and currently assessed at 0.5-1 %), can be avoided. Pregnant women consider this to be the main advantage of NIPT. (38) The invasive test (i.e. amniocentesis) is in fact no longer offered to women unless the NIPT is abnormal. Even though this additional step in the prenatal screening process makes the procedure for the women concerned even longer and more cumbersome, the advantages certainly seem to outweigh the inconveniences. The fact that this test can be performed earlier on in the pregnancy than the combined test is also deemed to be an advantage. That having been said, NIPT cannot completely replace the current prenatal screening process because this could result in relevant clinical information about conditions other than trisomies 13, 18 and 21 being lost. (21) This also applies to cases of multiple congenital abnormalities where an invasive test is preferable to NIPT because each one of the 23 pairs of chromosomes needs to be examined in an indication like this.

It is also worth noting that the risk of having a child affected by trisomy 21, 13 or 18 is not evenly spread across all pregnant women. Generally accepted factors are (1) the advanced age of the pregnant women (in this respect the age of 35 is deemed to be significant); (2) a positive combined test; (3) previous pregnancies with aneuploidies or (4) known genetic risks. (39) As far as the population of women with these risk factors is concerned, NIPT will give a better return in terms of detecting trisomies than in a low-risk population.

However, NIPT is equally valuable for women who are not at high risk of aneuploidies. (40) Firstly, the desire to make personal reproductive choices is not necessarily associated with an increased risk and, *all* pregnant women are entitled to invoke the right to reproductive autonomy and to demand the information they need to exercise this autonomy.

Furthermore, the various studies that have been conducted to validate the clinical use of NIPT in low-risk pregnancies (21, 22, 41) indicate that the implementation of NIPT could improve the detection rates of aneuploidies and limit the number of false positives. This would allow the number of women who unnecessarily undergo an invasive test for trisomy 21 to be reduced. As far as trisomy 13 is concerned, the number of false positives varies in function of the technology used. (42) Thus, it is essential that the test for trisomy 13 is validated if it is to be integrated into NIPT.

IV.2.2. Guaranteeing access to the offer of a test

In Belgium, all pregnant women have, in principle, access to NIPT. That having been said, certain obstacles can prevent effective access to this test. Firstly, the cost, which currently has to be borne by the pregnant women in full. A number of health insurance providers have taken the initiative to partially refund the cost of NIPT. Secondly, it is not altogether sure that the option to avail of NIPT is discussed with all women when they go for a pregnancy check-up.
In that respect it is also worth pointing out that, all too often, pregnant women do not attend

a medical specialist during their pregnancy or do so belatedly. In that light, efforts must be made to guarantee that also the weaker social groups have access to qualitative care during their pregnancy.

The Committee is concerned about the inequalities in health care NIPT is likely to create if NIPT is only available to pregnant women who can afford to pay for it. Considerations of equity prompt the Committee to stress the importance of open access to new and reliable technologies. Obviously, appropriate consideration needs to be made about how public finances can be spent effectively. Reimbursement in function of the risk is, in principle, one option that has its merits, provided it is sufficiently founded of course. However, a serious ethical conflict will raise its head if NIPT is increasingly presented to pregnant women as the safest and most reliable test even though the very access to that test is hampered because it is not refunded or refunded to a limited population only.

Health care staff expect the number of women opting for NIPT to exceed the numbers who currently undergo prenatal screening. (43) Some caregivers of a think tank led by Hill et al. (44) believe that NIPT will lead to an increase in the numbers of patients using this test to obtain information about the foetus but without the outcome of the test having any effect on the further course of the pregnancy. They take the view that, precisely because NIPT only poses a minimal risk to the pregnancy, it will be appreciated by those women who want to find out more about their pregnancy but who would refuse to terminate it or who would decline an invasive test because of the risk of miscarriage. (45;46)

IV.2.3. Preventing trivialisation and ensuring informed decision-making

The Committee is of the opinion that all pregnant women should be informed about the possibility to avail of NIPT, and, hence, encourages health professionals to, timely and carefully, discuss the availability of prenatal tests with their patients and to furnish them with the relevant information about the tests and their impact but to respect women's freedom of choice if they accept or decline the offer to have a test. At the same time, the Committee calls for special vigilance to prevent a test like this from being trivialised. By offering it routinely, there is a risk that counselling and the decision to avail of the test will be done in a less considerate manner.

Also in the current context of prenatal screening, various studies have shown that pregnant women did not always understand the importance and implications of prenatal screening and were not always aware that they were undergoing a prenatal screening test. (47-51)

Various studies on NIPT have already highlighted the risk that women can feel social pressure to undergo a test labelled as safe and "easy". (46) The invasive nature of the current prenatal examination makes the step towards this test even harder and makes that pregnant women

will think carefully about the choice they make. The non-invasive nature of NIPT will make the step towards the test easier to take, which may prove to be as much of an advantage as a disadvantage.

If NIPT is introduced as a first-line test, preventing the trivialisation of the test may well prove to be one of the greatest ethical challenges to be faced. (5;7;47) After all, there is a risk that caregivers will present NIPT as a routine test, and that pregnant women will no longer be explicitly given the option not to undergo the test as an informed choice. (7) If NIPT is upheld as a follow-up test however, the risk of the test becoming trivial will decrease because caregivers will give women who tested positive in the combined test the chance to decide whether or not they wish to avail of NIPT. (48)

The Committee is of the opinion that the only way to limit the risk of trivialisation is to pay more attention to the conditions for taking a careful decision. Therefore, pregnant women should be properly informed of the properties, limitations and consequences of NIPT, and of the risks. Proper information is essential if a person is to make an informed decision on whether to agree to or decline a prenatal test. To that effect, pregnant women should have access to leaflets or websites that provide information about NIPT and to caregivers who can provide them with the information they need and who can answer any questions they have.

Surveys amongst pregnant women have brought to light that the information about the current combined test is all too sketchy at times. (49-51) One possible explanation could be that health care staff spend less time informing women deemed to be in the low-risk category and tend to focus more on women deemed to be high risk and who are faced with the choice between chorionic villus sampling or an amniotic fluid test. (52) In terms of NIPT, this is an important finding. In a context where NIPT would only be offered to high-risk women, the information provided is likely to be far better. As it happens, information about the prenatal examination is provided in stages, and each stage comes with a new opportunity to provide information. In the latter scenario, also the group would be relatively small and therefore “manageable” for the health care staff tasked with providing counselling. If, on the other hand, NIPT is offered to all pregnant women, the pressure on the medical staff is likely to increase significantly. This will probably mean that caregivers will have less time for counselling and that patients will have less time to assimilate the information about the test and its implications. (52; 53) The information will in fact have to be provided with the patient’s need for information in mind, with due regard for the patient’s moral considerations and in a non-directive way. This should create the right conditions to allow a pregnant woman to make an informed choice without pressure from outside. The focus on the availability of qualitative information in a patient-friendly way should not only translate into support while the patient is undergoing NIPT but also when the result of the test is given and during any of the subsequent steps the patient

may choose to take.

IV.2.4. Disclosing incidental information

Every now and again, an examination or certain diagnostic test produces incidental information that may be relevant to the patient even though it is irrelevant to the original issue. Where this information may lead to a preventive or therapeutic intervention, it is important to also share this information with the patient in the context of clinical genetics. The failure to do so may be construed as serious negligence. The current debates about incidental findings made in the course of an analysis of the genome of children and adults also apply to the genetic analysis of the foetus. It is essential that the necessary time be given to genetic counselling before and after the test.

IV.2.5. The role of the authorities in guaranteeing the criteria for responsible offer

From the considerations regarding the purpose of prenatal screening outlined above, it is clear that the public authorities have an important role to play. In fact, the authorities must first of all guarantee that there is the least possible confusion about the purpose of prenatal screening. Screening aims to provide the population with informed choices and that freedom of choice must be safeguarded. (35) On no account should screening become a veil for an underlying eugenic context where couples, in practice, no longer have a choice. This means that the authorities, in collaboration with the medical staff, must see to it that qualitative information is developed that highlights the pros and cons of NIPT.

In the context of prenatal screening, the role of the authorities is a managerial and coordinative one. It is in the very interest of pregnant women that prenatal screening meets strict quality standards. Likewise, the authorities must guarantee the quality of the information, the availability of genetic counselling, the monitoring of the quality of the test offer, the development of care paths, access to the test offer and a targeted use of public resources. In addition, vulnerable people in society and groups at specific risk should be given particular attention. At the same time, pregnant women who wish to continue with their pregnancy should be given proper support. People suffering from a physical or mental disability are every bit as much citizens of our society. This entails that the authorities must ensure that they are given the proper educational support, adequate home help, the proper medical care and residential and non-residential facilities.

Conclusion

The Advisory Committee on Bioethics was asked to give an opinion on the ethical dimensions non-invasive prenatal testing brings into play. The opinion focuses on the ethical dimensions of this test in the context of its implementation in the health care system. In view of the fact that, at this moment in time, and as far as the Advisory Committee on Bioethics can establish, non-invasive testing for trisomies 21, 13 and 18 is not directly offered to consumers via the Internet, that component has been deliberately left out. What's more, the Advisory Committee on Bioethics and the Superior Health Council have already dealt with the issue of genetic self-testing in the past. (54-55) Topic of this opinion was not whether prenatal screening is appropriate as such but rather to identify any urgent issues that need to be addressed if NIPT is to become part and parcel of health care and clinical practice. The Committee came to the following conclusions and recommendations:

1) Prenatal screening is an area that is particularly sensitive from an ethical point of view. In fact, in this area the debates on the right to dignity and the interest of the unborn child, the freedom of choice for pregnant women and the appropriate attitude of medical staff are intertwined. Any form of prenatal screening that may lead to a termination of pregnancy is also potentially topic of an ethical debate. As a result, the Committee wants to put the focus on the fact that any offer of prenatal screening, and NIPT in particular, must also allow pregnant women to take a properly informed decision. On no account should the offer of prenatal screening lead to an obligation to make certain choices.

2) In that light, the public authorities have an important role to play which is to manage and coordinate the implementation of prenatal screening, by paying the necessary attention to the quality of the test offer, the quality of the information, counselling and access to the test offer. This should ensure that vulnerable people in society and groups at specific risk will receive the necessary attention.

3) In the context of NIPT, the risk of trivialisation and social pressure cannot be excluded. The Advisory Committee on Bioethics believes that this risk can only be avoided by ensuring that the conditions to facilitate a careful decision are put in place. Furthermore, pregnant women should be properly informed of the characteristics, the limitations and the consequences of non-invasive prenatal testing.

4) Considerations of equity prompt the Committee to stress the importance of ensuring broad access to a new and reliable technology such as NIPT. Even though the authorities are obliged to assess the cost of the various policy options in matters of health care, an ethical

equity-related problem will arise if NIPT is the safest and most reliable test but the very access to that test is hampered by financial constraints.

5) The Committee also emphasises the importance of providing pregnant women who choose to continue their pregnancy with the necessary support. This also implies that the authorities must put the necessary support in place for people suffering from a physical or mental disability, especially in the areas of education, support staff and residential or non-residential management.

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The working documents of the select commission 2014/4 – the question, personal contributions of the members, minutes of the meetings, documents consulted – are kept at the Committee's documentation center, where they are available to be consulted and copied.

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