

**Do Non-Invasive Prenatal Tests promote discrimination against people with Down-Syndrome? -
What should be done?**

NIPT and discrimination of people with Down-Syndrome

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Abstract

By implementation non-invasive prenatal testing (NIPT) for the diagnosis of Down syndrome (DS) in maternity care, an ethical debate is newly inflamed how to deal with this information. Fears of the consequences of an increased use of NIPT are justified with the same arguments when amniocentesis and preimplantation genetic diagnosis were introduced decades ago. It can be expected that the prevalence of people with DS would significantly increase in Western societies as a result of the increasing age of pregnant women and the improved medical care for people with DS. The net effect as to whether an increasing uptake of NIPT will result in more abortions of fetuses with trisomy 21 cannot be reliably estimated. This holds true since more and more couples will use results of NIPT for information only, but will not opt for termination of pregnancy. Although parents love their children with DS, in a society where reproductive autonomy is seen as an achievement, access to NIPT cannot be limited. On this background, comprehensive and qualified pretest counselling is vital, also to avoid possible stigmatization of people with DS and as the resulting consequence to avoid feared deterioration in their living conditions, for which, however, there is no evidence to date. The personal view of a mother of a child with DS illustrates the complexity in dealing with NIPT, which does not allow simple answers and must be understood as a challenge for society as a whole.

Key words

Non-invasive prenatal testing, Down syndrome, discrimination, reproductive autonomy, genetic counselling

List of abbreviations

NIPT: non-invasive prenatal test

DS: Down-Syndrome

PND: Prenatal diagnosis

In 2001, long before non-invasive prenatal testing (NIPT) was available, the German Parliament discussed about "Law and Ethics of Modern Medicine and Biotechnology". Andrea Fischer (Member of Parliament) made a statement which is 20 years later still valid and should also apply in the current discussion about the ethical implications of NIPT: *"None of us should arrogantly place our own morals above others. Each of us should let ourselves be unsettled by the arguments of the other in this discussion."*[1] This statement sheds light on the complexity of the ethical debate which was initiated with the introduction of amniocentesis more than 50 years ago. In this manuscript, new and old aspects are summarized for a better understanding of an ongoing discussion.

The age of mothers giving birth to their children and the number of nonselective pregnancies with trisomy 21 is increasing

Mother's age at birth in western societies is steadily increasing. The average age of birth of the first child in Germany increased from about 24 years in 1970 to more than 30 years in 2015, while the average number of children per woman decreased in this period from more than 2 to about 1.5. Fewer children are born at more advanced maternal age. The single pregnancy moves more into the center of life. Due to increasing age of pregnant women the expected number of pregnancies with Down syndrome (DS) in Western societies is steadily increasing from 12.5 in 1981-1985 to 21.7 per 10.000 (73.6%) in 2011-2015 in Europe and from 11.6 to 19.2 per 10.000 (65,5%) in the US. [2]

More and more parents who refuse abortion use NIPT for information only

Hill et al. [3] showed in their literature review of 14 studies that termination rates following NIPT were unchanged or decreased when compared with the termination rates after invasive prenatal chromosome analysis prior to the introduction of NIPT. The studies included many women who would like to receive additional information about the health of their baby that will not necessarily be used for decision making about termination of pregnancy. This is most likely due to the fact that NIPT is not associated with a risk of miscarriage as this is the case after invasive prenatal diagnosis (PND). The authors concluded that, where termination rates fall, NIPT may have a minimal impact on live birth rates for DS. Comparison of reported termination rates prior and after the introduction of NIPT suggest that in many settings the implementation of NIPT may not alter the overall number of children born with DS.

The often stated figure of termination rates of more than 90% after PND of DS should no longer be anticipated for pregnancies with a NIPT disclosing trisomy 21 (= positive NIPT).

Will there soon be no more children with DS – false alarm?

De Graaf et al. [2] estimated for Europe 8.031 annual live births of children with DS in 2011–2015, which would have been more than doubled without selective terminations (around 17.331 births annually). The estimated reduction of live birth prevalence was on average 54%, ranging from 0% in Malta to 83% in Spain. Improvement of medical care dramatically increased life expectancy of people with DS and as a consequence their prevalence in the population. The mean age of death of people with DS in the USA increased from below 10 years in 1960 up to nearly 50 years in 2000 [4]. As of 2015, De Graaf et al. [2] estimated 417.000 people with DS are living in Europe and without elective

terminations about 572.000, which corresponds to a population reduction rate of 27%. The authors, however, assume that with the introduction of NIPT higher termination rates will follow. The effect on the prevalence of DS with increasing maternal age and a possible decrease of termination rates cannot be predicted, which also applies to the fact that neither all pregnant women will demand for NIPT nor will all women with a positive NIPT decide to terminate pregnancies. Since there is strong evidence that termination rates can be influenced by counselling and improvement of the framework, much will depend on these parameters.

Pregnant women's views on prenatal diagnosis

In a systematic study of the German Federal Centre for Health Education, women who underwent prenatal diagnosis were asked on their views on prenatal diagnosis in 2007. 82% of women stated: *"PND leads to relief because it can take away the worry of illness in the child"* and 74%: *"PND makes pregnancy safer for women"*. [5] These statements can be interpreted in such a way that pregnant women want to experience an undisturbed pregnancy above all. The aim of PND was not explicitly mentioned in order to prevent disabled living. Since a negative result of NIPT nearly excludes DS in early pregnancy, the increasing utilization of NIPT can be understood in this sense.

Lack of knowledge about prenatal risks

In a survey performed until 2005 we asked more than 2000 persons and later in addition medical students in their first year of studies the following question: "What is the risk for a 40 year old pregnant women to give birth to a child with Down syndrome?" The results indicate a severe deficit of knowledge with a serious overestimation of risks, which was even more pronounced in the student's group. [6] **(Fig.1)** Similar observations have been made by Strauss et al. with 67% of 237 women who overestimated their specific risk more than twofold [7]. The overestimation of fetal risks leads to increased fear and, as a result, to an increasing demand for prenatal testing.

Who should be offered prenatal diagnosis?

In their paper entitled "Who should be offered prenatal diagnosis? A 35 year old question" Kuppermann et al. (1999) discussed an old question which is still actual [8]. While the risk of a miscarriage after invasive diagnosis been an argument for limiting invasive prenatal tests to women older than 35 years, the authors believed that it was time to eliminate strict age- or risk-based cutpoints. Instead the authors argued in favour of the preferences of the well-informed individual and summarized: *"Strong consideration should be given to adapting policies to permit assess to prenatal diagnostic services for all women whose preferences indicate that such testing would be appropriate."* Carroll et al. (2013) [9] came to similar conclusions in their survey about the attitudes of woman and health care providers toward changes about maternal age-based prenatal screening for chromosomal disorders. Limiting a non-invasive prenatal test to women with high genetic risk is in their view no longer justified. Several recommendations have no rational basis for restricting NIPT to a specific age group or to women with an increased genetic risk. The German Ethics Council, for example, stated in "The future of genetic diagnostics - from research to clinical application" (2013):

"The majority of the members are of the opinion that a non-invasive prenatal genetic diagnosis should only be carried out if there is an increased risk of a genetic disease or malformation." [10]

Recently, the Federal Joint Committee in Germany made the decision that NIPT should only be covered by the general health insurance, if the pregnant woman has special genetic risks or to clarify abnormalities in individual cases. It is suggested that *"..... a NIPT can be used at the expense of the health insurance if the question arises as part of the medical care for pregnant women whether a fetal trisomy could be present and this represents an unreasonable burden for the pregnant woman."* [11] An exclusively statistically justified risk of a trisomy - for example due to the age of the pregnant woman - is therefore not sufficient to have NIPT reimbursed by the general health insurance. Due to lack of clear in- or exclusion criteria these statements are difficult if at all to understand.

What do relatives of family members with DS think about DS and NIPT?

All parents of children with DS love their children as do their siblings. They express the joy the child with DS has brought to the family, as do all parents of handicapped children including the most severely affected children. There are many studies of family members evaluating the family perspective of DS. The overwhelming majority of parents of different studies report that they are happy with their decision to have a child with DS. They universally indicate that their sons and daughters are great sources of love and pride for their families. In a recent publication How et al. [12] expresses the message in the title of their paper: *"We would have missed out so much, had we terminated: What fathers of a child think about current non-invasive prenatal testing for Down syndrome"*. Van Schendel et al. [13] explored the attitudes of Dutch parents of children with DS towards NIPT. Although safety, accuracy and earlier testing were seen as advantages of NIPT, some participants were critical about the routine implementation in maternity care. The participants acknowledged that NIPT enables people to know whether the fetus is affected and to prepare for the condition without risking miscarriage. Many parents fear uncritical use of NIPT and more abortions for DS including the consequences for the acceptance of and facilities for children with DS. Kellogg et al. (2014) [14] studied the attitudes of 73 mothers of children with DS. The majority of mothers agreed that NIPT should be made available to all pregnant women. In their view NIPT is a good instrument because it allows people to prepare themselves for a child with DS but expected NIPT to cause an increased pressure to test and a social stigma for having a child with DS. In a study of Bryant et al. (2005) [15] including 78 women who had a sibling with DS, about one-third of participants would still consider PND and termination if they were expecting a child with DS. They expressed a negative impact on their own well-being and that of their families by the fact that they had a sibling with DS, although they overall had a positive experience with DS. One weakness of many of these studies is a possible ascertainment bias since the majority of families have been contacted through self-support groups with different response rates, which therefore might not be representative.

The effect of routinization and its implication for people with DS

Kater-Kuipes et al. [16] conducted a literature search regarding the different interpretations of routinization in prenatal screening. With regard to NIPT, routinization could have major negative consequences for people with a disability. It is obvious that this might depend on the number of children born with DS in the future, which, however, cannot be predicted today. Although the fear of

negative consequences of PND for living people with DS has been expressed already with the introduction of amniocentesis more than 50 years ago, the living conditions of people with DS have improved since that to a great extent. There is so far little supporting empirical evidence for an increase in social pressure to take part in screening or to terminate affected pregnancies. No studies exist indicating possible negative effects of stigmatization with the consequence of worsening the living conditions of people with DS. Rubeis and Steger [17] analyzed the so-called burden assumption which claims that children with disabilities are necessarily a burden to others, especially to their parents and other family members. If this were the case, this would exert pressure on women to decide against the birth of children with disabilities, thus undermining women's autonomy. The authors claim that such an attitude, which they feel is wrong, can be avoided without restraining reproductive autonomy. They argued that such an attitude is mostly based on misinformation and a false understanding of disability and can be challenged through an advanced genetic counseling as a combination of empirical evidence with narratives from a first-person perspective.

Counseling is essential and a major key for responsible use of NIPT

In the 1980ies the Dutch Patient Alliance for Rare and Genetic Diseases (VSOP) imposed with advertisement for genetic counseling in newspapers with headlines like "Life begins before birth. Medical care before conception" resulting in the message GENETIC COUNSELLING MAKE SURE YOUR WAY. By contrast, the relationship between geneticists and representatives of self-support groups in Germany remains difficult [18]. Informing about the real life of people with hereditary diseases in genetic counseling is challenging. In Rubeis' and Steger's [17] opinion advanced genetic counseling can address the burden assumption. They emphasize that sound and evidence-based information on the quality of life with disabilities is necessary. In order to achieve the goal, more empirical research about the quality of life of children with disabilities and their family members is needed. In addition, information material should be offered to pregnant women (??) that includes the views of people with disabilities and their family members. V. Schendel et al. [13] report that nearly all participants in their study found that improving information provision is important for informed decision-making in order to avoid routinization. Many other statements emphasize the importance of qualified counseling before performing NIPT as well as after receiving the diagnosis of DS and mention the value of information material. Criteria for written information have been defined [19].

Information about DS should be realistic

Although nearly all parents of children with DS love their children, many thought there was lack of good counselling and up-to-date balanced information about DS, which is portrayed as being either too negative or too optimistic. A statement in a flyer of a DS self-support organization about mental development in DS like "*There are the first university graduates in Europe.*" is unrealistic and misleading and must lead to disappointment if this goal cannot be achieved. Realistic information about several risks, like the fact that about 70% of adults with DS older than 35 years have dementia, are often not adequately addressed. The concern of caring for people with DS in advanced age is a major concern for all parents. A statement of a 70 year old father of a 40 year old son with DS "*We wish that our son would die only one day earlier than ourselves.*" expresses this ongoing concern.

Reproductive autonomy vs. right to live – no solution

The German Ethics Council (Ethik-Rat) (2013) [10] stated in their minority statement: *“The ethical analysis should be based on the reality of people’s lives.”* One major aspect is that reproductive autonomy has long becoming reality in Western societies. In Germany, there were 100.893 legal abortions in 2019, while only 3.875 (3.8%) were performed according to a medical indication.[20] Access to abortion in the Republic of Ireland is possible now due to legislation followed from the 66.4% “Yes” vote in the referendum in May 2018. **(Fig. 2)** Argentina legalized abortions not until 2020. In Poland huge protest against restrictive regulation of abortion law is evident. A very similar ethical discussion took place with regard to preimplantation genetic diagnosis (PGD). The Ethics Committee of the Giordano-Bruno Foundation voted for approval of PGD within extended limits in 2011: *“Choosing a healthy embryo with PGD is by no means linked to a downgrading of the disabled. The assumption that the destruction of fertilized egg cells with genetic defects leads to discrimination against the disabled is just as absurd as the demand for the abolition of vaccination against polio could result in discrimination against people with polio. Anyone who takes a rational, humanistic point of view should be aware that the disabled and the sick deserve our full support, but disability and illness do not.”* [21] Do these arguments also apply to NIPT?

Letter from a mother of a child with DS as a touchstone for our own opinion on NIPT

We did not use (non-invasive) PND for DS abortion....we wanted to rule out severe organ damage and I wanted to know which gender the child has. I wanted to know if it has DS in order to prepare myself for it and to welcome my child that was already in the belly... The advice in the hospital ...was excellent...and first thing the doctors said was "we don't see ourselves as a DS prevention center", which I thought was great. Dealing with the questions of PND was an important part of my late journey to being pregnant and becoming a mom.... They helped me cope with the demands of giving birth.

I do not want to go into details as regards the long medical history of my son. But I want to share with you my thoughts which are based on my experiences as a DS mother and in the DS self support group here on site: I don't think it helps to create and hold a place for DS people by hiding the different sides of the coin. The distorted image of DS is wrong in both directions: It suppresses the positive aspects (apart from the usual "Mongo romanticism" - "they are always so nice and happy" etc.), but it also underexposes that some DS children die in the first few years (especially those with heart defects), and how much time, energy or money it "costs" to create "flagship downies". I know wonderful mothers with DS children of considerable handicap who suffer a lot from the silent insinuation that they do less right than those mothers whose DS children already walk with two and speak well with four.

What we need to avoid is a "it-is-not-so-bad" rhetoric, but a positive acceptance of the unavoidable fate, let it be good or bad. This not only relevant for DS, but for everything sick, dying, disabled, restricted ... This also means that I would not blame mothers, who decide to opt for the extreme step of abortion, across the board of egoism. I cannot accuse them, even if I would not have an abortion for the reason of DS myself. BUT !!!! I find it terrible that advances in PND are likely to lead to increased abortions in sick and DS people UNLESS we make significant changes on two major "fronts"....:

First, we need better and comprehensive advice in maternity care which specifically addresses the greatest fears and worries of the pregnant woman and her family.

Second, we need individually adapted help, e.g. trained therapists or midwives who can talk to the mother's parents about what they need to process the diagnosis and assist the DS mom. There should be support programs for employers of DS parents including a partial assumption of salaries. Caring parents could receive preferential doctor's appointments taking care of the special health needs and the limited schedule. The fight for school places should end and the unspeakable ongoing discussion about inclusion needs to change. The injurious and restrictive practice of many health insurance companies with regard to care levels should be changed. and aids approved more easily. Generally speaking, there is specific support required in the first year of life of a child with DS (or other disability). Restructuring everything in the midst of all the chaos is not good for the whole family; there is always something going down the drain (either the external facts or the health of the parents; you can rarely keep the two together).

Since my son was born, I have observed two opposing tendencies in my environment: Based on the experience with my extremely popular son, everyone around me has received a much more positive image of DS people and life with DS. However, the same people say that they are more likely to have an abortion because of DS today than they were before my son was born. After seeing what all this has done to me and my life, my friends rather believe they would not cope to have a child with DS.

TO CONCLUDE: THE BEST "ADVERTISING" AGAINST ABORTION OF DS PEOPLE LIES IN SUPPORTING DS PEOPLE AND THEIR FAMILIES! - SOCIALLY VISIBLE! IT IS NOT THE TEST THAT LEADS TO ABORTION - BUT THE LACK OF SPACE IN SOCIETY EXPECTED BY FUTURE DS PARENTS!

In this context, we should handle the prenatal blood test very differently. All mothers over 18 years should make the test; then all parents would deal with the question - instead of repressing it and see it as the problem of somebody-else. Then the subject would be in the middle of everyone planning to have children. Everyone would think about what life, a successful life, being human is all about and what is important of having children. Maybe that would be a different perspective in life for everyone I consider the question of how to deal with the blood test to be a litmus test. And I think a defense strategy is doomed to fail. So I think other ways have to be found to keep the place for DS socially - for DS people, and for parents who choose (or are surprised by) DS children.... [Content slightly shortend respectively summarized] .

What should be done?

We have to ask about the relation between the cultural appreciation of disabled people and the demand for prenatal diagnosis. NIPT is a serious challenge of society as a whole [6].

Five statements on the challenges of receiving genetic information which are also valid for NIPT:

- We cannot prevent access to genetic information.
- We (rather) have to advocate responsible use of it.

- Our population knows too little about hereditary diseases and disabilities and their origin.
- We need to increase our knowledge about genetic information and improve “neutral” counseling competence.
- As a society we have to be asked again and again, whether we can offer families affected by a hereditary disease the help that enables them to lead a dignified life.

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Fig. 1

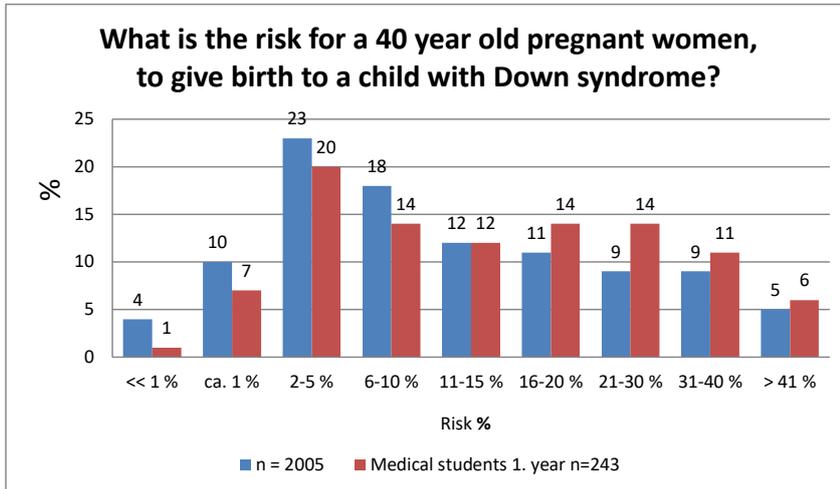


Fig 2



Legend of figures

Fig. 1

Results of a survey in the year ?? in Aachen, Germany about the knowledge about fetal risks for DS [6]

Fig. 2

Placard on the occasion of the referendum amending the Laws on abortion in Dublin, Ireland in June 2016

Photo K. Zerres