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CHAPTER 4



**Changing attitudes towards
termination of pregnancy for
trisomy 21 with non-invasive prenatal
trisomy testing: a population-based
study in Dutch pregnant women**



The aim of providing testing for chromosomal conditions is enabling reproductive choice with respect to carrying to term, or terminating the pregnancy of a child with a serious disorder or disability. Except for a few countries such as Denmark and Hong Kong, the uptake of screening for fetal trisomy is relatively low, ranging from 25% (The Netherlands) to around 50% in many other Western countries. Reasons for refraining from screening include a number of perceived disadvantages of current screening programs, of which the risk of iatrogenic miscarriage associated with follow-up testing with invasive diagnostic procedures (0.5 to 1%) is an often reported one.

At present, the vast majority of women confronted with a confirmed diagnosis of fetal trisomy request termination of pregnancy (TOP). In the Netherlands, 93% of women receiving the diagnosis fetal T21 terminate the pregnancy (according to the 2010 annual report on prenatal diagnosis), which is similar to published European data.¹ A recently published systematic review presented evidence of decreasing termination rates in the USA (67%), which was speculated to be associated with progress in the medical management of Down syndrome children.² Another study underlines women's strong preference for tests with no risk of miscarriage demonstrating that consideration for safety of the fetus is paramount in decision making.³ With the newly developed non-invasive prenatal testing (NIPT) approach using cell-free fetal DNA obtained from maternal plasma, decision-making in prenatal screening is likely to change. Both the sensitivity and specificity of NIPT exceed 99%.⁴ However, ethical debates revolve around the issue of a possible consequence of this increased testing rate: 'Will the world be without children with Down syndrome in a few years?' There is also concern that increased testing with likely reduced numbers of live-born children with T21 may lead to a reduction in scientific progress, and funding, aiming for treatment of children with Down syndrome. We sought to evaluate whether and how the assumed increased rate of detection with the introduction of NIPT would influence the rate of TOP for affected pregnancies. This information may aid in the planning of new screening strategies.

In two hospitals and nine community midwife practices, self complete questionnaires were administered to pregnant women shortly after women received counseling for first trimester combined test (FCT) by their own midwife or doctor between 1 August 2011 and 31 December 2011. All women received information about prenatal screening for trisomies following the current guidelines. Questionnaires were given to all women, independent from their expressed interest in prenatal screening. All questionnaires were handled anonymously. The questionnaire addressed questions regarding prenatal screening in the current pregnancy and regarding NIPT if available. Background information about NIPT was included prior to questions to determine the attitude of women towards NIPT. Participating women were asked to indicate the likelihood that they would choose the option of terminating their pregnancy should their fetus be diagnosed with Down syndrome based on a visual analog scale (VAS).



The VAS is a graphic tool with a 100mm horizontal line with the left end marked as 'very uncertain' and the right end marked as 'very certain'. The subject is asked to mark the point that is corresponding most with their feeling about the subject questioned. The last part of the questionnaire included sociodemographic questions (age, educational level, religion, and income). The Dutch legislation does not require informed consent for a prospective study using questionnaires when results are treated anonymously. Data were analyzed using SPSS version 17. Completed questionnaires were received from 147 (43%) of the 340 women who were sent a questionnaire. In this group of responders, 79/147 (54%) opted for FCT in their current pregnancy; 82% (121/147) of the women answered they would elect to undergo NIPT if it were available. There were no women opting for FCT in the current pregnancy and declining NIPT, if available. The data of the women who preferred (82%) or declined (18%) NIPT were analyzed separately. Figure 1 shows the frequency distribution of the likelihood of TOP among the 121 women with a positive attitude towards NIPT. Among women electing to receive NIPT if available, those who elected to undergo FCT in their current pregnancy were more likely to request TOP (median likelihood score of 70, range: 0–100) than those not performing FCT in their current pregnancy (median score of 34, range: 0–100). Women who chose not to perform either FCT or NIPT were extremely unlikely to terminate a pregnancy of a T21 fetus, with a median score of 0 (range: 0–95). Women currently electing FCT were more likely to terminate a T21 pregnancy than those who currently rejected FCT but elected for NIPT screening for T21 ($p=0.03$). In both groups, the attitude towards TOP was not related to age, education level, income, or religion.

Our study suggests that implementing NIPT may result in a higher uptake of prenatal screening. The percentage of women who opt to terminate their pregnancy upon detecting T21 will likely be reduced if NIPT becomes available for all. With the introduction of NIPT, nearly complete elimination of iatrogenic miscarriages due to invasive prenatal diagnosis, and in particular the fear of women for these risks, will lead to more balanced, autonomous reproductive choices. We speculate that the main and important difference with the current screening programs will be that, unlike now, most live-born children with T21 will be born in families who made the deliberate choice not to test for fetal trisomy, or to accept and care for a child with T21. Most women wish to be reassured regarding the health of their baby, as reflected by the high number of women who choose to undergo a mid-trimester structural anomaly scan.

This statement also holds true for women who choose not to terminate after receiving an antenatal diagnosis of T21 because they value the certainty of the diagnosis during pregnancy and trust their ability to prepare themselves adequately. Although we acknowledge that because of cultural differences, our results cannot be extrapolated to all countries, the introduction of NIPT must be designed carefully and its implications addressed thoroughly

by healthcare workers and policy makers. Counseling for prenatal screening to facilitate informed reproduction choices should maintain the fundamental basis of prenatal screening programs. Specifically, women should retain their 'right not to know'. Caregivers should be aware of the undesirable situation that these prenatal tests may be performed 'routinely', in the sense that the possible consequences are not considered before testing. In our experience, in the current situation of offering FCT, many pregnant women are poorly informed regarding the implications of Down syndrome itself. The counseling is focused on explaining the test rather than on the condition itself. With the introduction of NIPT, counseling about the test will be easier, and more time will be available to inform the expectant parents regarding Down syndrome. Health issues common among children with Down syndrome and variability in the degree of intellectual disability are essential elements of this information. In addition, parents should be informed that individual medical and neurodevelopmental outcomes cannot be predicted antenatally.

Korenromp et al. reported that when Down syndrome is diagnosed, medical caregivers are among the most important individuals to the woman in guiding her decision whether to terminate the pregnancy.⁵ A shift will likely occur following the introduction of NIPT among the selected group of women who mainly have a positive attitude towards TOP, leading to a more diverse group containing a larger proportion of women who will continue their pregnancy of a fetus with Down syndrome. In either situation, the woman must be accompanied by supportive counselors. Preparing for a life with a child with Down syndrome requires up-to-date information regarding Down syndrome, an explanation of potential ultrasound abnormalities, and - if desired - a referral, for example, to a patient support group. On the other hand, for many women, the choice to terminate the pregnancy is associated with long-lasting psychological issues. As we have described, NIPT has many advances compared with current testing; therefore, it can even be perceived as unethical to withhold it from pregnant women. However, NIPT needs to be carefully incorporated into a well-designed screening program that is based on informed decision-making. A non-directive-based counseling approach by healthcare workers will be as important as ever. Limitations in our study are the relatively small sample size and the limited response rate. The difference between the national uptake of FCT (around 30%)⁶ and the uptake in our study population (54%) may be explained by the fact that women who perform FCT are more willing to complete a questionnaire about FCT than women who reject FCT. A study with a larger sample size or with choice experiments should be undertaken to obtain more information about this important topic.

In conclusion, the reproductive choices of pregnant women will likely change following the introduction of NIPT. The uptake of prenatal screening will likely increase. However, this does not necessarily mean that the abortion rate of T21 fetuses will rise similarly. Our



study shows that the introduction of NIPT is likely to cause a shift in decision-making in which more women will choose prenatal screening to gain knowledge without the intention to terminate the pregnancy. NIPT needs to be carefully incorporated into a well-designed screening program that is based on informed decision-making.



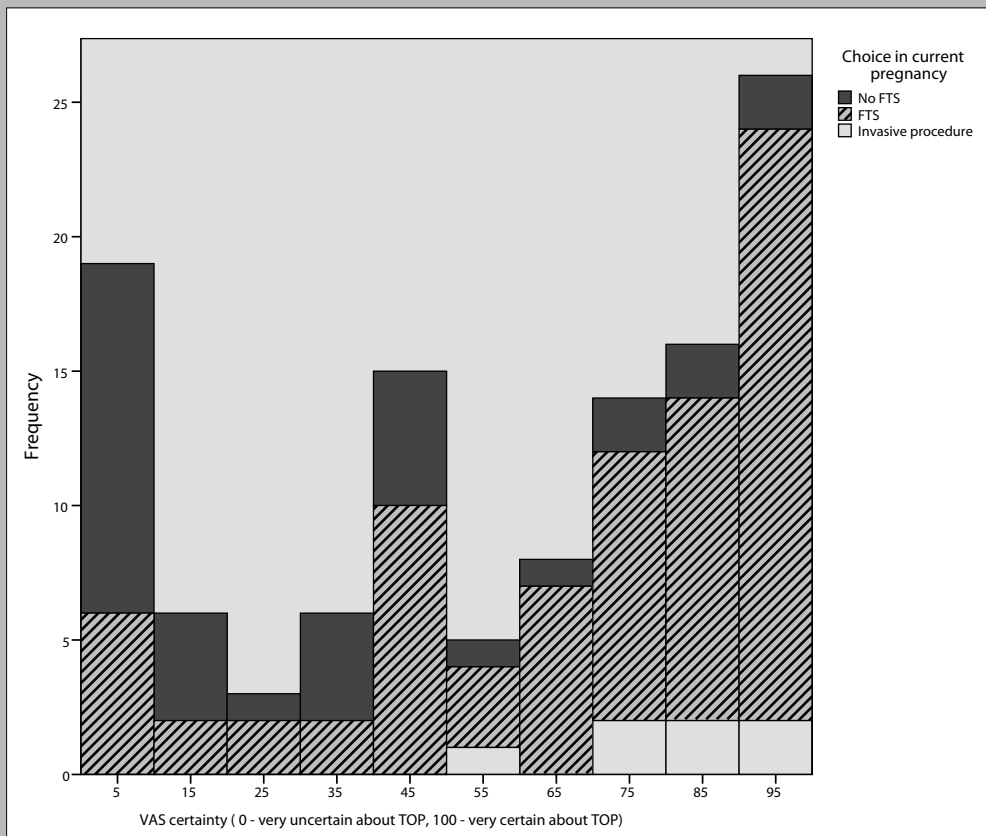


Figure 1. Likelihood of termination of pregnancy (TOP) for T21 in pregnant women who would opt for NIPT if available. The number of women for the 3 different groups (frequency; y-axis) is plotted against VAS certainty (x-axis). A VAS score of 0 indicates high uncertainty regarding TOP and a VAS score of 100 indicates high certainty regarding TOP.



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