Additional findings from non-invasive prenatal testing (NIPT)

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Executive summary

Health Council of the Netherlands

Since 2007 the combined test has been available to all pregnant women in the Netherlands as part of the national programme of prenatal screening for Down's syndrome, Edwards' syndrome and Patau's syndrome (also known as trisomy 21, 18 and 13 respectively). Several years ago non-invasive prenatal testing (NIPT) was introduced. NIPT involves the screening of maternal blood to estimate the risk for chromosomal abnormalities in the foetus. Pregnant women in the Netherlands can choose to receive NIPT as an alternative to the combined test within a scientific research study, called TRIDENT-2. This study will continue until 1 April 2023. NIPT is more reliable than the combined test, meaning that fewer pregnant women are referred for in hindsight unnecessary invasive follow-up diagnostic testing, which is associated with a slight risk of miscarriage.

Within TRIDENT-2, 0.48% of pregnant women have been identified as having a high-risk for trisomy 21, 18 and 13 with NIPT. TRIDENT-2 uses a technique that is based on the analysis of the whole genome (genome-wide NIPT). As part of the study, pregnant women can indicate whether they would like to be informed about any other chromosomal abnormalities in addition to trisomy 21, 18 and 13. In the context of a screening programme for trisomy 21, 18 and 13 these abnormalities are deemed to be 'additional findings'. If women do no opt for the reporting of additional findings, a filter is used so that only abnormalities on chromosomes 21, 18 and 13 are visible. Of the pregnant women who chose to be informed about additional findings, 0.36% were identified as having a high-risk for chromosomal abnormalities other than the common trisomies. There are also NIPT techniques available that exclusively target chromosome 21, 18 and 13. Such targeted tests do not expose potential abnormalities on other chromosomes.

The minister of Health, Welfare and Sport (VWS) has yet to decide whether NIPT will be included in the nationwide prenatal screening programme once TRIDENT-2 is completed. One of the questions that have to be addressed beforehand is to what extent chromosomal abnormalities other than trisomy 21, 18 and 13 should be detectable and if detected, reported. The answer to that question will affect which NIP tests are eligible for the Dutch prenatal screening programme. The minister of Health, Welfare and Sport has requested advice on this issue from the Health Council of the Netherlands. The Committee NIPT Additional Findings was established to address this question.

In principle, the preferred test for screening is one in which the likelihood of additional findings is minimised. However, additional findings from genome-wide NIPT may indicate a high risk for severe genetic disorders in the foetus. Such findings could be of importance to the pregnant woman's reproductive decision-making, as is the case for trisomy 21, 18 or 13. Some additional findings therefore could be considered to lie within the scope of the objectives of prenatal screening. The committee recommends the use of a genome-wide technique in the case that NIPT is included in the Dutch prenatal screening programme. This technique allows for potentially expanding prenatal screening in the future to cover additional genetic disorders.

Based on the available evidence, no general assertions can be made about the overall risk-benefit ratio of reporting findings other than the common trisomies detected by genome-wide NIPT. In TRIDENT-2, some NIPT results were known to be associated with severe congenital disorders, while for others clinical significance was considered unknown, limited or of no relevance to reproductive or clinical decision-making. As such, the committee upholds that results of additional findings from NIPT should only be reported to the pregnant woman as per her own choice, as is currently the case within TRIDENT-2. To maximise benefits and minimise potential risks, the committee recommends attaching a number of conditions to the reporting of additional findings.

If the pregnant woman indicates she wants to be informed about any additional findings, only those additional findings will be reported that (1) are known to cause or likely to cause disease, and (2) have severe consequences for the health of the child if the finding were to be confirmed by diagnostic testing. The pregnant woman must also be clearly informed about the available decision options and their consequences during pre-test counselling.
If the minister decides to include NIPT as part of the Dutch prenatal screening programme, the professional organisations involved and other stakeholder groups should jointly establish a protocol based on these conditions that specifies the reporting of additional findings and follow-up procedures. The protocol should take into account advances in scientific evidence on additional findings, including the views and experiences of participants in TRIDENT-2.
The protocol should be applied uniformly across the country. Additional findings indicative of maternal cancer should always be reported, as is the case within TRIDENT-2. The committee advises further investigation during the preparatory phase leading up to 1 April 2023 into whether unsolicited reporting of these findings is justified given the particular risks and benefits.

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