Population Screening Act: Non-invasive prenatal testing (NIPT) as a national population screening programme

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Executive summary

Health Council of the Netherlands

Since 2017, all pregnant women in the Netherlands have been offered non-invasive prenatal testing (NIPT). NIPT involves the screening of maternal blood to estimate the risk for chromosomal abnormalities in the foetus, such as Down syndrome (trisomy 21), Edwards syndrome (trisomy 18) or Patau syndrome (trisomy 13). At present, NIPT is offered as part of a scientific research study, TRIDENT-2 study, which will be completed on 1 April 2023. After that date, the Minister for Health, Welfare and Sport (VWS) wishes to incorporate NIPT into the national prenatal screening programme. The Regional Prenatal Screening Centres have applied for a permit to offer NIPT. In their permit application, the centres proposed that NIPT be offered as part of the prenatal screening programme in a similar way as it is currently offered as part of the TRIDENT-2 study.
At the Minister's request, the Health Council's Committee on Population Screening evaluated the permit application against the requirements of the Population Screening Act (WBO).

Scientific soundness

One of the requirements of the Population Screening Act is that the population screening method must be scientifically valid. The question to be answered here is whether NIPT is a sufficiently reliable and precise testing method. The Committee found that NIPT has good predictive values. The results of the TRIDENT-2 study show that NIPT is good at predicting whether a foetus has trisomy 21, trisomy 18 or trisomy 13. The number of women who are unnecessarily concerned after receiving a false positive NIPT result is very small, and the overwhelming majority of women are provided with quick certainty that trisomy 21, trisomy 18 and trisomy 13 are absent in their foetuses when the test result is negative.

Risk-benefit ratio

The Population Screening Act also stipulates that population screening must have a favourable risk-benefit ratio. In this case, the question to be answered is whether the benefit of NIPT for pregnant women sufficiently outweighs the discomfort caused to the women and the risks posed to them and their foetuses. The Committee considers that, in order to achieve the best possible risk-benefit ratio, certain modifications will have to be made to the way NIPT is to be performed, as compared to how NIPT is currently being performed as part of the TRIDENT-2 study.

First, the Committee recommends that NIPT be performed as part of the regular screening programme without the analysis filter by default. In the TRIDENT-2 study, women can currently opt for NIPT with or without an analysis filter. 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. If NIPT is performed without an analysis filter, abnormalities other than trisomy 21, trisomy 18 and trisomy 13 may be shown to be present. Such findings are referred to as additional findings in the TRIDENT-2 study. In a clinical trial, there may be a justifiable reason as to why participants are given a choice of how

the test is to be performed. The TRIDENT-2 study was partly designed to examine the impact of the use of an analysis filter. However, in the context of a national screening programme, it is not appropriate to allow participants to choose how the test will be performed. The Committee is of the opinion that it is the NIPT provider's responsibility to determine how the screening programme is to be performed, and to select the screening method that has the best possible risk-benefit ratio. Leaving the choice to the participants themselves will result in tests being performed differently on different people, a situation which must be avoided in a screening programme. Moreover, having a choice in this matter will make the decision on whether to undergo screening even more complex than it already is. If NIPT is offered and performed in a uniform manner, it will be easier to provide pregnant women with easily accessed and understandable information and counselling, and thus to help them make a well-informed decision.

Previously, the Health Council advised that secondary findings be reported only if the abnormalities in question are likely or highly likely to result in severe health issues on the child's part, and only if pregnant women can be granted a meaningful way to deal with this information, in the form of a meaningful medical procedure. On the basis of the results of the TRIDENT-2 study, the Committee has judged that this is the case for structural aberrations in the foetus. Foetal structural aberration are chromosomal abnormalities comparable with trisomy 21, trisomy 18 and trisomy 13 in terms of severity. As with trisomy 21, trisomy 18 and trisomy 13, awareness of the presence of a structural chromosomal aberration in the foetus allows pregnant women to make a reproductive decision. The Committee assumes that pregnant women who opt to undergo NIPT do so because they wish to know whether their foetus might have a severe chromosomal abnormality, regardless of what type of abnormality it might be or which chromosome might be involved.

The Committee recommends that structural chromosomal aberrations in foetuses always be reported since this would be in keeping with the objective of prenatal screening (granting pregnant women a chance to make a well-informed decision on whether or not to keep the baby), and also because the risk-benefit ratio is sufficiently favourable (NIPT has proven as suitable for the detection of structural chromosomal aberrations in foetuses as for the detection of trisomy 13). This means that structural chromosomal aberrations will be included in prenatal screening.

In addition to trisomy 21, trisomy 18 and trisomy 13 and structural chromosomal aberrations in foetuses, NIPT can be used to detect rare autosomal trisomies (RATs), or complex aberrant profiles (CAPs). On the basis of the results of the TRIDENT-2 study, the Committee recommends that RATs not be reported, as follow-up examinations have shown that generally, only the placenta is affected by RATs. In certain cases, this may result in foetal growth

retardation or pregnancy complications. However, the Committee is not aware of any interventions that have demonstrably improved the outcome of the pregnancy in such cases, meaning that information on RATs does not really help pregnant women make a decision on a possible medical intervention. As a result, the Committee concludes that RAT reporting does not fall within the scope of prenatal screening for foetal abnormalities. However, the Committee recommends that additional findings concerning CAPs always be reported, as they may relate to a malignant condition in a pregnant woman, such as certain types of cancer.

Rules for medical practice

A third requirement of the Population Screening Act is that population screening must be in line with the legal rules for medical practice. It is vital that the policy changes recommended by the Committee with regard to the use of an analysis filter and what kind of findings to report be incorporated into any information and counselling provided. Furthermore, pregnant women must be informed during their counselling sessions that their personal data (including particularly sensitive personal data) will be processed in electronic health system, Peridos.

Recommendation

The Committee advises that the Minister for Health, Welfare and Sport grant the Regional Prenatal Screening Centres a permit allowing them to incorporate NIPT in the national prenatal screening programme, on the condition that the foregoing recommendations regarding NIPT performance without an analysis filter, reporting findings and additional findings, providing information, counselling and processing personal data be observed. The Committee recommends that screening be referred to as ‘screening for severe chromosomal abnormalities’ from now on. The Committee also recommends that the screening programme (including counselling) continue to be monitored and periodically evaluated.

It is essential that all NIPT results and the results of any follow-up examinations which may be performed be registered.

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