Health Council of the Netherlands

Preconception carrier screening

executive summary

Severe hereditary disorders can be passed on to children when both biological parents carry a pathogenic variant in the same gene. Since most people are unaffected by their carrier status, they are usually unaware of this. Carrier status can be detected through genetic testing. The Minister of Health, Welfare and Sport has sought advice from the Health Council of the Netherlands regarding the desirability of a government programme offering expanded preconception carrier screening. This would allow all prospective parents to undergo carrier testing for severe hereditary disorders before planning a pregnancy to determine if they are at elevated risk of having a child with such a disorder. The permanent Committee on Preconception, Prenatal and Neonatal Screening has considered this matter.

Objective: facilitating reproductive choices

The primary objective of expanded preconception carrier screening is to enhance reproductive autonomy. This means providing prospective parents with information so they can make informed choices about their family planning. In cases where both partners carry the severe hereditary disorder, there is a 25% risk for each pregnancy (one in four) that their child will be affected by the disorder. Prospective parents can choose to accept this risk, or they can opt for assisted reproductive technologies that prevent the birth of an affected child (in vitro fertilisation (IVF) with genetic testing of the embryo before transfer to the womb). Another option is for carrier couples to undergo prenatal diagnostics during pregnancy to determine whether their unborn child is affected. Prospective parents may also consider donor sperm or eggs or decide not to have biological children at all.

The objective of expanded preconception carrier screening is not to prevent the births of children with severe hereditary disorders, but to equip prospective parents with the information they need to make informed reproductive choices. A second potential objective of expanded preconception carrier screening, i.e. enabling the early treatment of severe hereditary disorders, is currently not a consideration for the committee. At present there is limited expected health benefit from this, and it would complicate the decision-making process for prospective parents and with that the counselling.

Added value compared to existing types of screening

In the Netherlands, prospective parents who already have a child with a severe hereditary disorder or with proven carrier status within the family are already eligible for carrier screening for that specific disorder, which is covered by their health insurance. The same applies to prospective parents who are known to be at elevated risk of being a carrier couple for one or more severe hereditary disorders. This includes couples with close family relationships (consanguinity) and those from specific ethnic or geographic backgrounds. In 2020, guidelines for healthcare providers were established to facilitate this. Currently, the opportunity for high-risk groups to undergo screening is underutilised. Prospective parents often remain unaware of their increased risk of being carrier couples, and healthcare providers are often unaware of the existence of these guidelines. People can also have carrier screening performed at their own expense, but this option is not very popular in the Netherlands.

According to the committee, offering expanded preconception carrier screening to all prospective parents aligns well with existing prenatal and neonatal screening programmes. It offers various benefits: it informs more carrier couples about their elevated risk and, as screening is performed before pregnancy, it provides more reproductive options to prospective parents. Moreover, expanded preconception carrier screening can identify an elevated risk of severe hereditary disorders that are not detected through existing prenatal screening services. It is worth noting that carrier screening may also be performed during pregnancy. Prenatal carrier screening also provides prospective parents with information about an elevated risk of severe hereditary disorders that cannot be revealed through existing prenatal screening services. However, prenatal carrier screening provides less reproductive choices compared to screening before pregnancy.

Careful consideration of potential risks

While screening holds promise for substantial benefits, there are always potential risks and harms to be considered. Specific risks of expanded preconception carrier screening include the possibility of detecting carrier status for disorders that may not be severe or of which the clinical relevance is uncertain, and confronting prospective parents with complex decision-making.

At a more fundamental level, there are broader societal concerns, some of which align with objections against prenatal screening for severe congenital disorders. These concerns revolve around potential pressure on prospective parents to participate, a growing emphasis on engineering human existence, reduced acceptance of individuals with severe hereditary disorders, and the medicalisation of reproduction. Based on scientific literature – also from the extensive practice of prenatal screening – the committee found no evidence to suggest that a population-wide programme of expanded preconception carrier screening would lead to

undue pressure or discrimination. An essential consideration for the committee is that support for population-wide expanded preconception carrier screening appears to exist not only among prospective parent couples, but also among individuals with severe hereditary disorders and parents of children with such disorders. Another critical point for the committee is that the criteria outlined in the assessment framework for responsible screening, which aim to strike a balance between the benefits and harms, address most societal concerns.

For example, the framework stipulates that screening must always target severe disorders, preventing the pursuit of ‘designer babies’ by screening for increasingly milder disorders. Furthermore, participation will always remain voluntary, as prospective parents are completely free not to participate in the programme.

Population-wide programme meets responsible screening criteria

The committee believes that expanded preconception carrier screening can meet at least the first four criteria of the assessment framework for responsible screening. Firstly, there is a pressing health issue: parents are often unexpectedly faced with a child affected by a severe hereditary disorder, causing substantial suffering for both child and family. Additionally, the average likelihood of both parents being carriers for one or more severe hereditary disorders is relatively high, around 1%. These couples face a 25% risk for each pregnancy (one in four) that their child will be affected. Secondly, the screening provides meaningful options for action: it enables parents to make informed reproductive choices. Thirdly, reliable and valid carrier tests are readily available. Fourthly, voluntary participation based on informed consent can be ensured. Based on these factors, the committee concludes that the benefits of preconception carrier screening outweigh the potential harms and risks. How well preconception carrier screening aligns with principles of justice (the fifth and final criterion) will depend on how the screening is made available to the target population, particularly in terms of accessibility and efficiency.

Challenge: a programme that is accessible and efficient

The committee anticipates that the mode of delivery will determine the screening programme’s accessibility and efficiency. Equitable access implies that the target group – all prospective parents in the Netherlands – should have equal opportunity to undergo expanded preconception carrier screening. However, identifying and reaching this target group is no easy task. There is no way of knowing who the prospective parents are in advance. As such, a suitable context for offering preconception carrier screening could be during a preconception care consultation. People who make an appointment for this consultation already have an active desire for parenthood at the very least. During the preconception care consultation, prospective parents receive information about various aspects related to a healthy pregnancy. In this context, including information about screening for carrier status of severe hereditary

disorders would make sense. A combined approach might be more efficient than a stand-alone screening programme. The primary challenge is the current absence of actively offered preconception care, as envisioned by the committee in its best-case scenario. And even if that option did exist, it would still need to be determined whether an approach primarily centred on the preconception care consultation would genuinely enhance the accessibility and efficiency of carrier screening and whether it would be effective and practically feasible.

Given the challenges surrounding the primary offer of preconception care, with carrier screening as a part of it, the committee can also imagine an alternative approach: one with a primary focus on the screening, where prospective parents can also opt to receive general preconception care if they so desire. The advantage of such an approach is that the screening is not dependent on a preconception care consultation. However, the feasibility and effectiveness of such an approach would need to be investigated as well.

Recommendation: pilot study on feasibility and effectiveness

The committee envisions significant value in a combined approach of preconception carrier screening and preconception care. The committee has no data that would allow it to infer which approach would have the best benefit-risk ratio in practice. Such data is rarely available before implementing a screening programme, especially with regard to screening for rare disorders. According to the committee, a pilot study would serve as a middle ground between implementation with post-hoc evaluation on the one hand and pre-emptively forgoing further exploration due to a lack of data on the other. As such, the committee recommends initiating a pilot study to evaluate the effectiveness and feasibility of a population-wide offer of preconception carrier screening. It is important to have data to substantiate which approach is likely to be more effective: one with a primary focus on preconception care or one primarily centred on preconception carrier screening. Aspects that require special attention in the pilot study include the extent to which prospective parents make informed choices, equitable access for all groups in society, technical feasibility, efficiency and the psychological impact on approached and participating prospective parents. In the meantime, the committee recommends raising awareness about the possibility of pre-conception carrier screening among high-risk prospective parents and care providers, as it appears to be relatively unknown in general.

Finally, the committee emphasises that even if the screening proves to be efficient, the question remains as to how efficient interventions should be prioritised amongst each other. The committee recognises that difficult choices must be made more and more often, given the limited resources and capacity in healthcare. Determining the priorities between interventions that have proven to be efficient is a matter for political consideration.

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