

# Health Council of the Netherlands

## Preconception Carrier Screening

### Introduction

Children can be born with a serious hereditary condition if both biological parents are carriers of a disease-causing variant in the same gene. People are often unaware that they are carriers because this gene variant does not cause any symptoms in them. Carrier status can be detected through genetic testing. The Minister of Health has asked the Health Council to advise on the desirability of a government-sponsored preconception carrier screening program. This would mean that all prospective parents would have the opportunity to be tested for carrier status of serious hereditary conditions before a potential pregnancy to determine whether they have an increased risk of having a child with this condition. The Committee on Screening Around Pregnancy and Childbirth has considered this question.

### Goal: Offering Choices Regarding Reproduction

The goal of preconception carrier screening is to increase reproductive autonomy. This means that prospective parents receive information that allows them to make choices regarding their reproduction. If both are carriers of a serious hereditary condition, they run a 1 in 4 (25%) risk of their child having the condition with each pregnancy. Intended parents can choose to accept this risk or use reproductive technologies that can prevent an affected pregnancy (in vitro fertilization (IVF) with genetic testing of the embryo before transfer). Another option is for carrier couples to use prenatal diagnosis during pregnancy to determine whether the unborn child actually has the condition. Intended parents can also choose to use donor sperm or eggs, or they can forgo having biological children altogether.

The goal of preconception carrier screening is not to prevent the birth of children with a serious illness, but to enable intended parents to make informed choices about reproduction. According to the committee, a second potential goal of preconception carrier screening, namely enabling early treatment of serious hereditary conditions, is not currently being addressed. For the time being, only limited health benefits are expected from this, while it complicates the intended parents' decision-making (and thus the counseling process).

### Added value compared to existing screening options

In the Netherlands, intended parents with a child with a serious hereditary condition or a proven carrier in the family already have an indication for carrier testing for this specific condition. They are reimbursed for this testing by their health insurance. This also applies to intended parents who are known to have a higher-than-average risk of being a carrier couple for one or more serious hereditary conditions. This includes couples where the partners are related (consanguineous) and couples with a specific ethnic or geographical origin. Guidelines for healthcare providers were developed for this in 2020. Currently, limited use is being made of the screening option for high-risk groups. Intended parents are often unaware that they have an increased risk of being a carrier couple, and healthcare providers are insufficiently aware of the guideline's existence. It is also possible to have genetic carrier testing performed at one's own expense. This is also being used to a limited extent.

According to the committee, offering preconception carrier screening to all intended parents would complement the existing screening offered around pregnancy and birth. The added value is multifaceted: more carrier couples can be informed about their increased risk, and because screening takes place before pregnancy, there are more reproductive treatment options for intended parents. Moreover, preconception carrier screening can reveal an increased risk of serious hereditary conditions that cannot be detected with current prenatal screening. Carrier screening is also possible during pregnancy. In that case, too, it provides future parents with information about an increased risk of serious hereditary conditions that cannot be detected with current screening. However, the treatment options are more limited than when screening takes place before pregnancy.

### **Carefully address potential disadvantages**

Screening not only has advantages, but also disadvantages. Specific disadvantages of preconception carrier screening include the risk of finding carriers of conditions that are not serious or whose clinical course is uncertain, and the risk that prospective parents may face difficult decisions.

More fundamental disadvantages include societal concerns, which partly overlap with the objections to prenatal screening for serious congenital conditions. These concerns include pressure on prospective parents to participate, a growing perception of control over their own lives, less acceptance of people with serious hereditary conditions, and the medicalization of the desire to have children. The committee has not yet found any evidence in the scientific literature—not even from the longer-established practice of prenatal screening—that a population-wide offering of screening leads to pressure or discrimination. A key finding for the committee is that support for population-wide preconception screening appears to exist not only among prospective parents, but also among people with serious hereditary conditions and parents of a child with a serious hereditary condition. Another key finding for the committee is that the criteria from the assessment framework for responsible screening, which safeguard the balance between benefits and harms, address most societal concerns. For example, screening should always focus on serious conditions—preventing a feared pursuit of perfect children by screening for increasingly milder conditions. And participation is always voluntary; Intended parents are completely free not to be tested.

### **Population-wide screening can meet criteria for responsible screening**

According to the committee, screening can at least meet the first four criteria of the assessment framework for responsible screening. First, there is a significant health problem: parents are often unexpectedly confronted with a child with a serious hereditary condition, which can cause significant distress for both the child and the family. Furthermore, the average chance of being a carrier couple for one or more serious hereditary conditions is considerable, approximately 1%. These couples have a 1 in 4 (25%) risk of having an affected child with each pregnancy. Second, screening offers meaningful options: parents can make meaningful reproductive choices. Third, reliable and valid carrier tests are available. Fourth, voluntary participation based on an informed choice could be guaranteed. Based on this, the committee concludes that the benefits of a potential preconception carrier screening program could outweigh the disadvantages. The extent to which preconception carrier screening meets the requirements of fairness (the fifth and final criterion) will depend on the format in which the screening is offered. This specifically concerns the accessibility and effectiveness of the program.

### **Challenge: accessible and effective programs**

The committee expects that the format in which the screening is offered will determine the accessibility and effectiveness of the program. Equal access means that the target group—all intended parents in the Netherlands—have the opportunity to be screened. However, identifying and approaching the target group is not easy. It is not known in advance exactly who the intended parents are. A good context for offering preconception carrier screening would therefore be the preconception care consultation (also known as a fertility clinic). People who make an appointment for this consultation certainly have an active desire to have children. In a preconception care consultation, intended parents receive information about various aspects related to healthy pregnancy. In this context, screening for carrier status of serious hereditary conditions could be offered. A combined offering could potentially be more effective than a standalone screening program. The main challenge is the current lack of actively offered preconception care, as the committee ideally envisions. However, even if such a program were available, it would still be necessary to investigate whether a program primarily focused on the preconception care consultation actually increases the accessibility and effectiveness of carrier screening, and whether it is effective and feasible.

Given the challenges surrounding a primary offering of preconception care, with carrier screening as a component, the committee can also envision an alternative approach. Namely, a program primarily focused on screening, in which prospective parents, if they so desire, also receive general preconception care. The advantage of such a program is that screening is not dependent on a visit to the preconception care consultation. The feasibility and effectiveness of such a program would also need to be investigated first.

### **Recommendation: Pilot study on feasibility and effectiveness**

The committee sees great value in a combined offer of preconception carrier screening and preconception care. Data to be able to investigate There are no clear guidelines for determining which method of delivery will outweigh the disadvantages in practice. Such data is rarely available before a screening program is implemented, especially in the case of screening for rare diseases. According to the committee, a pilot study offers a middle ground between implementation with subsequent evaluation, on the one hand, and refraining from further exploration due to a lack of data, on the other. Therefore, the committee recommends conducting a pilot study into the effectiveness and feasibility of a population-wide offer of preconception carrier screening. It is important to be able to substantiate with data which strategy is more effective: an offer primarily focused on preconception care or one primarily focused on preconception carrier screening. Aspects requiring special attention in the pilot study include the extent to which prospective parents make an informed choice, accessibility 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 of the possibility of preconception carrier screening among high-risk prospective parents and healthcare providers, as it appears that there is still little awareness about this topic.

Finally, the committee emphasizes that even if screening proves effective, the question remains how (proven) effective interventions should be prioritized among themselves. The committee recognizes that, given the scarcity of resources and capacity in healthcare, increasing numbers of choices must be made. How these choices should be made among (proven) effective interventions is a political decision.