
Request for advice

Letter of 9 July 2009 (reference PG/OGZ-2940324) from the Minister of Health, Welfare and Sport to the President of the Health Council of the Netherlands.

Background

In view of recent research and scientific developments a further advisory report is required from the Health Council of the Netherlands on the possible expansion of neonatal heel prick screening to include cystic fibrosis (CF).

On 22 August 2005, at the request of the then State Secretary for Health, Welfare and Sport, the Health Council published an advisory report on neonatal heel prick screening. The advisory report concerned two central topics: should the screening package be expanded and are the criteria for neonatal screening still up-to-date.

The Health Council assessed and discussed 30 disorders and divided them into three categories on the basis of a number of criteria. The Health Council took the view that disorders whereby considerable irreparable damage could be prevented belonged in category 1 and that disorders in cases where the latter was less possible or had not been satisfactorily proven belonged in category 2. The disorders which the Health Council's advisory report recommended should be included in the screening programme were all in category 1.

The Health Council put CF in category 2, with the qualification that it is a borderline case between categories 1 and 2. The Health Council recommended including CF in neonatal heel prick screening as soon as test methods became available with a higher specificity and recommended research into better screening methods.

In November 2005, on the basis of the aforementioned advisory report, the Ministry of Health, Welfare and Sport decided to expand screening with a total of 14 disorders, including metabolic disorders and sickle cell anaemia. In accordance with the Health Council's recommendations, CF was not included in the expansion. Expanded heel prick screening was introduced on 1 January 2007.

CHOPIN pilot study

On 24 February 2006, the Ministry of Health, Welfare and Sport informed the Netherlands Organisation for Health Research and Development of the advisory report and view of the Health Council on the possible expansion of neonatal heel prick screening to include CF. It was pointed out that the intention was to expand neonatal screening to include CF once it had been conclusively proven that early screening for CF provided additional benefits for the health of neonates, was cost-effective and could be performed using adequate test methods.

The Netherlands Organisation for Health Research and Development subsequently funded the implementation of a CF population screening trial, CHOPIN (Cystic fibrosis heel prick screening of neonates in the Netherlands) in Gelderland, Limburg, Noord-Brabant and Utrecht in 2008, including an extension until June 2009. I received the final report on the CHOPIN study on 22 June 2009 and hereby present it to you. You have already been provided with the digital version.

Information on being a carrier

Experience has now been gained with the expanded neonatal heel prick screening programme in general and with the information and 'informed consent' in particular. Experiences relating to sickle cell anaemia are particularly important for this request for an advisory report. The test used in screening for sickle cell anaemia provides information on whether a person is a carrier, while this is not the primary intention of screening. The same applies to CF, although the number of carriers identified depends on the test strategy chosen.

Parents are informed of the possible outcomes of screening before the child's birth and therefore prior to screening; this information includes details of whether the child is a carrier and the possible consequences of that information in relation to whether the parents and their other children are carriers. The 'informed consent' of parents is required prior to screening, before they may be provided with information on being a carrier after screening has taken place. Parents are free to determine beforehand whether they wish to receive the information. Owing to the complicated message that has to be conveyed, difficulties have emerged in practice with regard to the information as well as the required 'informed consent'. It has also emerged in practice that a great deal of misunderstanding arises in parents about the child's health when they are informed of screening results indicating that the child is a carrier (not sick but is a carrier).

An additional problem is anticipated in screening for CF because the disease involves several mutations, some of which are as yet unknown. A need for guidelines on how to handle information on coincidental findings and on being a carrier has arisen in the current practice of performing certain population screening programmes, such as neonatal heel prick screening and prenatal screening. This

need will increase owing to technological developments, such as those which enable various types of genetic screening. Guidelines of this kind are required on providing advice about CF in aid of the possible implementation of screening for CF as part of neonatal heel prick screening.

CHOPIN project group recommendations

The project group concerned with neonatal screening for CF formulated various recommendations. To summarise, the project group calls for adoption of a screening strategy (combination of tests) with the lowest possible number of false-positive starting points, the lowest possible number of children with mild CF variants and the lowest possible number of identified carriers.

Specific advice requested

Please pay particular attention to the following requests for advice:

- 1 What is the Health Council's current advice on adding CF to the diseases covered by neonatal heel prick screening.
 - 2 Has it been established that early screening for CF would provide significant additional benefits with regard to the health of neonates with CF.
 - 3 If the Health Council's advice is affirmative on adding CF to the diseases covered by neonatal heel prick screening, what would be the preferred test method and what are the assessments that form the basis for this preference? Please take the following points into account in making your assessments:
 - Cost aspects and cost-effectiveness;
 - The choice of test method has consequences for the number of CF carriers identified, whereas this is not the primary objective of screening, partly given the project group's recommendations;
 - The consequences for parents with regard to the differences in turnaround times of the screening strategies, whereby in exceptional cases the turnaround time can be up to 87 days from screening to result;
 - Identification of coincidental findings or 'mild variants' in CF screening, also in view of the project group's recommendations.
 - 4 What are the Health Council's recommendations on providing information on being a carrier and on detecting mild variants, given the above and taking into account the Health Council's advice on point three regarding the test method.
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I would also ask you to take into account the relevant social, ethical and legal aspects when forming your opinion.

If possible, please present your advisory report before 15 September 2009.

Kind regards,
the Minister of Health,
Welfare and Sport,
(signed)
Dr A. Klink