European Cystic Fibrosis Society

Journal of Cystic Fibrosis
The Official Journal of the European Cystic Fibrosis Society

Cystic Fibrosis Research News

Title:

NEWBORN BLOOD SPOT SCREENING FOR CYSTIC FIBROSIS WITH A FOUR-STEP SCREENING STRATEGY IN THE NETHERLANDS

Authors:

Jeannette E. Dankert-Roelse[1], Marelle J. Bouva[2], Bernadette S. Jakobs[3], Hettie M. Janssens[4], Karin M. de Winter-de Groot[5], Yvonne Schönbeck[6], Johan J.P. Gille[7], Vincent A. M. Gulmans[8], Rendelien K. Verschoof-Puite[9], Peter C.J.I. Schielen[10], Paul H. Verkerk[6].

Affiliations:

[1]School for Public Health and Primary Care, Department Pediatrics, Maastricht University Medical Centre, Debyelaan 25, 6229 HX Maastricht, the Netherlands

[2]Reference Laboratory for Neonatal Screening, Centre for Health Protection, National Institute for Public Health and the Environment (RIVM) Postbus 1, 3720 BA Bilthoven, The Netherlands

[3]Department of Clinical Chemistry and Haematology, Elisabeth-Twee Steden (ETZ) Hospital Hilvarenbeekseweg 60, 5022 GC Tilburg, The Netherlands

[4]Department of Pediatric Pulmonology, Erasmus Medical Center, Sophia's Children's Hospital, Wytemaweg 80, 3015 CN al, Rotterdam, The Netherlands

[5]Department of Pediatric Pulmonology, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht University, Lundlaan 6, 3584 EA Utrecht, The Netherlands

[6]TNO, Department Child Health, Schipholweg 77, 2316 ZL Leiden, The Netherlands

[7]Department of Clinical Genetics, VU University Medical Centre, de Boelelaan 1118, 1081 HV Amsterdam, The Netherlands

[8]Dutch Cystic Fibrosis Foundation (NCFS), doctor Albert Schweitzerweg 3, 3744 MG Baarn, The Netherlands

[9]Department of Vaccine Supply and Prevention Programmes, National Institute for Public Health and the Environment (RIVM), Postbus 1, 3720 BA Bilthoven, The Netherlands

[10]Reference Laboratory for Neonatal Screening, Centre for Health Protection, National Institute for Public Health and the Environment (RIVM) Postbus 1, 3720 BA Bilthoven, The Netherlands

What was your research question?

Does the novel Dutch newborn screening strategy for cystic fibrosis (CF) in use since May 2011 perform as required? Requirements are that: screening identifies 95% of babies with CF, the

diagnosis of CF is made within 30 days in 50% of the affected babies, a positive test predicts a risk of at least 30% for CF.

Why is this important?

Newborn screening for CF is important for babies with CF to ensure an early diagnosis, because early treatment leads to an improved prognosis. It becomes even more important now new drugs are being developed that correct the underlying defect. An important negative side-effect of screening is that healthy newborns may have a positive (abnormal) screening-test. Excluding CF can be difficult as sweat-tests often fail in young babies. This may lead to a long period of anxiety among the parents. Therefore, Dutch Health authorities require that the number of healthy newborns identified by newborn screening should be as low as possible.

What did you do?

We looked at the results of newborn blood spot screening for CF in the period from May 1, 2011 and January 1, 2016. Our screening approach consisted of four steps. The first two were biochemical markers from the pancreas (a large gland behind the stomach which secretes digestive enzymes into the small intestine). If concentrations of these markers were elevated, a standard analysis of 35 CF-mutations followed, and in selected cases an extended CF-gene analysis. Screening for CF was positive if two CF mutations were found. After two CF babies were missed, tests were also positive with only one identified disease-causing CF-mutation. We compared our results with other novel screening strategies and standard requirements.

What did you find?

If we considered screening positive when one disease-causing mutation was found, 192 newborns out of 819,879 had positive screening. CF was confirmed in 120, 37 were considered healthy CF-carriers, in 28 CF was not confirmed nor excluded, in 7 newborns CF was unlikely. Sixteen babies with CF were missed by newborn screening. In 50% of the babies the diagnosis was made at the age of 22 days. A total of 63% of babies with positive screening were diagnosed with CF, considerably higher than recommended and as found in other novel screening strategies. The screening strategy identified 90% (≥95% required) of babies with CF.

What does this mean and reasons for caution?

The novel screening approach is achievable within the Dutch newborn screening program. The number of healthy newborns and CF-carriers with a positive screening test is greatly reduced compared to other strategies. This is most probably due to including the second

biochemical pancreatic marker instead of using only one. Even with the use of four steps a diagnosis of CF can be made in most babies with CF within 30 days. The goal to identify at least 95% of the babies was not achieved. Most of those missed by screening had concentrations of one of the biochemical markers below the cut-off levels.

What's next?

The screening approach was adapted. Since July 2016 other cut-off values for the two biochemical markers are used and the R117H-7T/9T mutation is now considered as non-pathogenic. These changes may lead to the identification of around 95% of babies with CF, and positive screening may predict a risk of 60% for CF.

Original manuscript citation in PubMed

https://www.ncbi.nlm.nih.gov/pubmed/?term=NEWBORN+BLOOD+SPOT+SCREENING+FOR+CYSTIC+FIBROSIS+WITH+A+FOUR-STEP+SCREENING+STRATEGY+IN+THE+NETHERLANDS