

UK National Screening Committee

Newborn Screening for Severe Combined Immune Deficiency (SCID)

23rd June 2017

Aim

1. The aim of this document is to ask the UK National Screening Committee (UK NSC) to approve the proposal that the UK NSC consults on a proposal to carry out an evaluation of newborn screening for SCID using polymerase chain reaction (PCR).

Background/ Review

2. The last review of screening for SCID was completed in 2013. At that point the UK NSC's position was that screening was not recommended outside of well-designed evaluations to assess its impact. The rationale for this was that there was insufficient evidence about the:
 - epidemiology of the condition in the UK
 - performance of the test
 - management and outcomes of babies who are detected by screening but do not have SCID and
 - clinical and cost effectiveness of screening compared to current practice

It was hoped that research through the Health Technology Assessment (HTA) or Medical Research Council (MRC) could be initiated to explore the first three themes. However an application for funding was rejected. Following this a SchARR cost effectiveness evaluation was commissioned by the UKNSC and this was presented to the Committee in June 2016. The evaluation estimated that there was a 65% chance of screening being cost effective and that even a small health decrement in the non SCID cases detected by screening may further reduce this likelihood. Because the result was so finely balanced the quality of the health economic work is crucial so a peer review exercise was undertaken and the evaluation was revisited. The resulting document is attached.

The underlying model found that:

- There are approximately 17 SCID cases in the UK each year. 30% (5-6) of whom would be detected through cascade testing (ie would be found without the need for a screening programme)
- The main benefit of screening is to find and treat babies before they become infected. The model estimates that without screening eight babies would die from infections and with screening that would be reduced to around two. The babies found and treated before they become infected would have the same health outcomes as those currently identified through cascade testing
- earlier transplantation would not significantly alter long term outcomes in babies who are currently detected on the basis of symptoms and survive
- approximately 260 families would receive false positive results which would be confirmed by flow cytometry within two weeks
- approximately 26 cases of non SCID T cell lymphopenia of which seven would be likely to be asymptomatic at birth

3. A PCR based screening strategy was estimated to cost £3.2 million / year and to have a high likelihood of being cost effective. Some uncertainties were identified such as the cost of the test.
4. A set of systematic reviews is also attached and this document is intended to provide an update on the 2013 review. The systematic review approach was suggested in the above mentioned peer review exercise as a means of exploring some of the parameter values in the cost effectiveness evaluation.
5. In relation to the test, the main findings of the reviews were that more information on the test cut off, incidental findings and the false positive rate in a UK population was required. In relation to the treatment, although good outcomes were reported from transplantation in a number of studies the long term outcomes were difficult to interpret because of small sample sizes, inter study variation in outcomes and variations in length of follow up.

A workshop was held in May 2017 to discuss the documents. A draft note of the workshop is included in the meeting papers.

Proposal

The UK NSC evidence review process requires a public consultation to be undertaken. To develop the discussion on screening for SCID it is proposed that:

- The reviewers should be asked to update the cost effectiveness document incorporating the analysis of disbenefit in the false positive cases,
- A recommendation to evaluate SCID screening should be the subject of the stakeholder consultation. An evaluation would aim to:
 - i. define a cut off for screening and report on clinical outcomes which are achievable in the timeframe and realistic given the rarity of the condition
 - ii. identify and undertake research priorities, for example to understand more about the impact of false positive results and the viability of alternatives to universal screening
 - iii. clarify the logistics and costs of screening and outcomes monitoring as a basis on which to revisit the cost effectiveness evaluation
 - iv. explore the possibility of international collaboration with ongoing pilots and research projects relating to SCID.

Action

The UK NSC is asked to approve the above proposal.