

UK National Screening Committee

Newborn Screening for Tyrosinaemia Type 1

23 June 2017

Aim:

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in this document, whether or not newborn screening for Tyrosinaemia Type 1 meets the UK NSC criteria to support the introduction of a population screening programme.

This document provides background on screening for Tyrosinaemia Type 1 in the neonatal population.

The document provides a summary of the responses received from the public consultation on the review of newborn blood spot screening for tyrosinaemia type 1 (TYR1) in the UK.

Current recommendation

2. Screening for TYR1 is not currently recommended. The previous review was completed in 2014. This considered TYR1 as one of several disorders of amino acid metabolism. The review, and the subsequent consultation, identified TYR1 as a potential screening candidate. Further review work was required to address outstanding questions relating to the epidemiology in the UK, the use of succinylacetaone (SUAC) as the marker for screening and the outcomes from early treatment with Nitisinone compared to late treatment.

Evidence review

3. The evidence review examined three key questions relating to the effectiveness and appropriateness of newborn screening for TYR1 by measuring SUAC levels using tandem mass spectrometry. The questions related to:

- the number of babies born every year (incidence) with TYR1 in the UK.

No studies were found to give firmer estimates of the incidence of TYR1 in the UK.

Criterion 1 not met

- the accuracy of screening for TYR1 using SUAC as the primary marker.

Studies of screening, while reporting very good test performance, were at high risk of bias so it wasn't possible to be confident in the results. In addition there were concerns about the applicability of the studies to the UK setting.

Criterion 5 not met

- the advantages of early treatment following screening versus later treatment following the onset of the illness.

There was some suggestion that treatment with nitisinone results in improved outcomes in TYR1 cases. But there were a number of problems in how the research had been carried out which made it difficult to be sure that there was more benefit from early rather than late treatment.

Criterion 9/ 13 not met

The review document has also been considered at two FMCH meetings

Consultation

4. A three month consultation was hosted on the UK NSC website. The document was sent directly to 17 individuals or organisations. **Annex A**
5. Five responses were received; an individual response from, Dr Mick Henderson, (Laboratory Director, Willink Biochemical Genetics Unit, Manchester Centre for Genomic Medicine and Biochemical Genetics, St James's University Hospital), and four organisations: Save Babies Through Screening Foundation UK, on behalf of the UK Patient Advocates for Newborn Screening Working Group (PANS), Royal College of Paediatrics and Child Health, British Inherited Metabolic Diseases Group, and Genetic Alliance UK.

All the submissions favoured the introduction of newborn screening for TYR1 in the UK, with a number of the submissions emphasising the positive impact that early treatment can have. The following themes were common:

- an acknowledgement of the review's conclusion that there are gaps in research. This means that some of the UK NSC criteria on which the key review questions are based have not been met,
- that the outstanding questions can only be answered either as a result of a national research study (which may be impractical) or a pilot newborn screening programme for TYR1,
- that the level of evidence demanded by the UK NSC criteria is unlikely to be achieved without a pilot screening programme and that the emphasis on published evidence excludes the patient voice from the decision making process.

Workshop

6. A workshop was held in January 2017 to discuss the review with stakeholders. A note of the meeting has been circulated with the meeting papers. The main conclusion of the meeting was that TYR1 remained a candidate for inclusion in the Newborn Blood Spot Screening Programme. However, before considering a UK pilot of screening further work was required to explore a range of issues relating to TYR1 cases detected within current UK practice. In particular:
 - seek further information on the false negative screening results from the authors of some of the test accuracy papers
 - request a reanalysis of the outcomes data in the largest study of nitisinone treatment
 - undertake a modelling exercise to estimate the benefit of screening over and above current UK practice

Recommendation

7. The Committee is asked to approve the following recommendation:

A systematic population screening programme for newborn screening for TYR1 is not recommended and that further work is undertaken to address the areas of uncertainty.

The Committee will revisit screening for Tyr1 as an early update if the above work has been completed before the regular three year cycle.

Based on the 20 UK NSC Criteria set to recommend a population screening programme, evidence was appraised against the following criteria:

Criteria		Met / Not met
The condition		
The Test		
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease	Not met ✘
The intervention		
9	There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered.	Not met ✘
13	The benefit gained by individuals from the screening programme should outweigh any harms for example from overdiagnosis, overtreatment, false positives, false reassurance, uncertain findings and complications.	Not met ✘



List of individual/ organisations contacted:

1. Barbara Howe – NHSE
2. British Inherited Metabolic Disease Group
3. Children Living with Inherited Metabolic Diseases
4. Clinical Genetics Society
5. Colin Pavelin –DH rare diseases
6. Faculty of Public Health
7. Genetic Alliance UK
8. Institute of Child Health
9. Mark Bale –DH rare diseases
10. MetBio
11. Rare Disease UK
12. Royal College of General Practitioners
13. Royal College of Midwives
14. Royal College of Paediatrics and Child Health
15. Save Babies Through Screening
16. Tom Fowler –Genomics England / Public Health England
17. UK Newborn Screening Laboratories Network