UK National Screening Committee

UK National Screening Committee (UK NSC)

Screening for classic galactosaemia as part of the newborn bloodspot

Date: 28 October 2020

Contents

Aim

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in the evidence review, whether or not newborn screening for classic galactosaemia meets the UK NSC criteria for a systematic population screening programme.

Current Recommendation

2. The UK NSC currently does not recommend a systematic population screening for classic galactosaemia in newborns. The Committee based this recommendation on the evidence provided by the 2015 UK NSC review carried out by Bazian Ltd. The 2015 UK NSC review concluded the following:

    a. Most babies would develop symptoms before the screening process is completed

    b. A screening programme may identify cases of uncertain clinical significance

    c. There was a lack of evidence that early treatment, as a result of screening, would improve outcomes compared with treatment following clinical detection.

3. Although none of the stakeholders disagreed with the conclusion of the review, that population screening should not be recommended, they suggested that screening should be considered as a means of improving prevention and management of acute neonatal presentation and the reduction of neonatal mortality; and that focusing on the published literature excludes

the contribution of the patient and public voice and the experience of practicing clinicians.

Evidence Review

4. The 2020 UK NSC evidence review was undertaken by Bazian Ltd., in accordance with the triennial review process.

5. The aim of the 2020 UK NSC evidence review was to assess the evidence published since 2015 on the age of clinical presentation of classic galactosaemia, accuracy of screening tests and effectiveness of early initiation of treatment on short-term and long-term outcomes.

6. The conclusion of the 2020 UK NSC evidence review is that the current recommendation not to introduce newborn screening for classic galactosaemia should be retained. This is because:

    a. The new evidence is in agreement with the 2015 UK NSC evidence review conclusions showing that a large proportion of screen-detected cases will be symptomatic by the time screening results are confirmed and diagnosis is made. This review concluded that the age of clinical presentation of classic galactosaemia was around 7 days. All studies (n=5) were case series and only 2 of them were judged to be good quality.

        - **Criterion 1 met.**

    b. The uncertainties around the optimum screening approach remain. Two retrospective screening programme evaluations conducted in Italy and the Netherlands were identified. There was insufficient evidence to establish an optimal screening test because screening programmes used different index tests and cut-off values of GALT/total galactose. While the sensitivity values were high, PPV was low, however, this is common for rare conditions. The Dutch study was judged to be at low risk of bias whereas the Italian study had some uncertainties regarding the reference standard and patient flow and timing.

        - **Criteria 4 and 5 not met.**

    c. The effectiveness of early initiation of treatment on short-term and long-term outcomes is unclear. Three studies, a systematic review of randomised controlled trials (RCTs) and 2 cases series, were identified. The Cochrane systematic review found no RCTs that compared short-term and/or long-term outcomes for screened with non-screened individuals. One case series study analysing the data from the International Galactosaemia Network registry (n=509 individuals, n=15 countries) found that newborn screening (NBS)

compared to no NBS and galactose-restriction within the first week of life compared to galactose restriction after the first week of life were associated with a reduced risk of neonatal complications. Two case series showed inconsistent findings for long-term outcomes. Case series studies were judged to be low quality as comparative studies with various uncertainties and gaps in the data.

- **Criterion 9 not met.**

7. In response to the comments of the previous public consultation, the review aimed to identify any background information on the number of classic galactosaemia cases detected through phenylketonuria screening, which is currently included in the NHS newborn blood spot screening programme. No published evidence was identified through the retrieved literature. Contact with the Public Health England screening data and management team confirmed that such information is not routinely documented.

Consultation

8. A three-month consultation was hosted on the UK NSC website from 11 June to 3 September 2020. Direct emails were sent to 22 stakeholders (*see Annex A*).

9. Comments were received from 1 stakeholder – the Royal College of Paediatrics and Child Health. The stakeholder informed that they did not receive any comments. *See Annex B for comments.*

Recommendation

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

A population screening programme for classic galactosaemia in newborns is not recommended in the UK.

11. The evidence on this condition will be reconsidered in 3 years therefore this condition should remain on the UK NSC's conditions list.

Criteria (only include criteria included in the review)	Met/Not Met
Criteria for appraising the viability, effectiveness and appropriateness of a screening programme	
Aetiology	
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.	**Met**
The Test	
4. There should be a simple, safe, precise and validated screening test. 5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.	**Not Met**
The treatment	
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.	**Not Met**

UK National Screening Committee

Annex A

List of organisations and individuals contacted

1. British Association of Perinatal Medicine
2. British Inherited Metabolic Disease Group
3. Clinical Genetics Society
4. Colin Pavelin - DH rare diseases
5. Faculty of Public Health
6. Galactosaemia Support Group
7. Genetic Alliance UK
8. Institute of Child Health
9. Mark Bale - DH rare diseases
10. Metabolic Support UK
11. MetBio
12. PHE ANNB Screening Programmes
13. Rare Disease UK
14. Royal College of General Practitioners
15. Royal College of Midwives
16. Royal College of Paediatrics and Child Health
17. Royal College of Physicians
18. Royal College of Physicians and Surgeons of Glasgow
19. Royal College of Physicians of Edinburgh
20. Save Babies Through Screening Foundation UK
21. Tom Fowler - Genomics England/ PHE
22. UK Newborn Screening Laboratories Network

UK National Screening Committee

Annex B

Newborn screening for classic galactosaemia

Consultation comments

1. Royal College of Paediatrics and Child Health

Name:	xxxx xxxx	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Royal College of Paediatrics and Child Health		
Role:			

Do you consent to your name being published on the UK NSC website alongside your response?

Yes - Organisation name only

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
General	General	Thank you for inviting the Royal College of Paediatrics and Child Health to comment on the Galactosaemia screening in newborns consultation. We have not received any responses for this consultation.