UK National Screening Committee

Screening for iron deficiency anaemia (IDA) in children under 5 years

November 2017

Aim

- To ask, following the three month public consultation on Iron Deficiency Anaemia (IDA), that the Chair of the UK National Screening Committee (UK NSC) makes a recommendation, based on the evidence presented in this document, as to whether or not screening for iron deficiency anaemia in children under 5 years meets the UK NSC criteria for a systematic population screening programme.

- At the October 2017 meeting it was agreed that Chairs action would be taken on this issue and reported to the February 2018 UK NSC meeting. This document was considered and approved by individual members of the UK NSC, the Chair of the Fetal, Maternal and Child Health Reference Group and the Director of Screening.

Previous reviews

- The last review of screening for iron deficiency anaemia in children under 5 years was published in 2012 and the current recommendation is that systematic population screening is not recommended. This is because;

  - A causal relationship between IDA and adverse developmental outcomes was not demonstrated
  - A non-invasive test for population screening was not identified
  - The reported effect of iron supplementation on complications with iron deficiency (ID) in asymptomatic children was conflicting
  - In the absence of screening the emphasis, in terms of prevention, should continue to be placed on primary prevention via good dietary advice.

Evidence Summary

- The current evidence summary was undertaken by Bazian in accordance with the triennial review process https://legacyscreening.phe.org.uk/irondeficiency

- The review looked for studies on the adverse developmental outcomes of iron deficiency (ID)/IDA in children under 5 years, the prevalence and/or the incidence of ID/IDA in children under 5 in the UK, whether there was a non-invasive, simple, safe, precise and validated screening test, and whether treating asymptomatic children detected through screening improved developmental outcomes.

- The main conclusion of the current review is that population screening for iron deficiency anaemia in children under 5 years should not be recommended in the UK. This is because:
    - prevalence estimates for ID/IDA in UK children under 5 years are inconsistent **Criterion 1 not met**
    - no studies assessing whether ID/IDA in children under 5 is associated with later adverse health and developmental outcomes were identified **Criterion 1 not met**
    - no studies assessing a screening test for ID/IDA (invasive, non-invasive or minimally invasive) against a diagnostic reference standard in a non-selected sample representative of the general UK population aged less than 5 years were identified **Criterion 4 not met**
    - although two systematic reviews identified a number of small RCTs assessing treatment, they were in clinically-detected children, inconsistent and inconclusive, and the trials included were published over 25 years ago, and so had limited applicability to a contemporary UK screening population **Criterion 9 not met**

Consultation

- A three month consultation was hosted on the UK NSC website. Direct emails were sent to 5 stakeholder organisations. **Annex A**

- Responses were received from the following 2 organisations;
    - Royal College of Paediatrics and Child Health (RCPCH)
    - Ludwig-Maximilians-Universität Munich

  All comments are in **Annex B**, below.

- The following points were made:

- the RCPCH were supportive of the review conclusions, but suggested a sentence be included in the review. This has been covered in the introduction and background.
- Ludwig-Maximilians-Universität Munich highlighted the possibility of using a non-invasive test for erythrocyte zinc protoporphyrin (ZnPP) an indicator of iron status.

Although the team at Ludwig-Maximilians-Universität are in the process of publishing the results of a study in 100 children the test has not yet been validated in larger groups of children. This potential test should be investigated in the next scheduled 3 yearly update.

Recommendation

- The Chair of the UK NSC is asked to approve the following recommendation:

A systematic population screening programme for iron deficiency anaemia in children under 5 is not recommended.

Based upon the UK NSC criteria to recommend a population screening programme, iron deficiency anaemia did not meet the following requisites;

	Criteria	Met / Not met
The condition		
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 Test		
4	There should be a simple, safe, precise and validated screening test.	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 should not be further considered.	Not met ✗

Annex A

List of organisations contacted:

1. Faculty of Public Health
2. Institute of Child Health
3. Royal College of General Practitioner
4. Royal College of Paediatrics and Child Health
5. Institute of Health Visiting

Annex B

UK National Screening Committee
Screening for iron deficiency anaemia in children under 5 years –an evidence review

Consultation comments pro-forma

Name:	Comments provided on behalf of the following: • Dr Eugen Strehle (Local Paediatric Advisory Group) • Dr Anne livesey (Consultant Community Paediatrician)	**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 ☒ No ☐**			

Section and / or	**Text or issue to which comments relate**	**Comment**

page number		*Please use a new row for each comment and add extra rows as required.*
General		We are happy with this document and have no concerns; however, there should be a sentence along the lines 'paediatricians should have a low threshold for checking the haemoglobin of children under theri care.'

Please return to the Evidence Team at screening.evidence@nhs.net **by Thursday 2nd November 2017.**

UK National Screening Committee
Screening for iron deficiency anaemia in children under 5 years –an evidence review

Consultation comments pro-forma

Name:	Berthold Koletzko	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Ludwig-Maximilians-Universität Munich, Germany, Dept. of Paediatrics, Dr. von Hauner Children's Hosptial		
Role:	Professor of Paediatrics		

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

Yes X **No** ☐

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.*
Criterion 4, Question 3 / p. 23	Is there a non-invasive, simple, safe, precise and validated screening test for ID/IDA in children under 5 years?	Recently, a new technique for the non-invasive detection of erythrocyte zinc protoporphyrin (ZnPP) by an optical measurement on the lower lip has been developed and a first

		evaluation in adult women was published: https://www.nature.com/articles/ncomms10776 In this published study performed in 56 women after childbirth, the non-invasive measurement provides a reliable result in about 1 minute showing good correlation with HPLC reference measurements of ZnPP, with limits of agreement of 19 µmol / mol heme. We have now also completed a study with the same technique in 100 children aged 9 months to 5 years to assess the feasibility of the measurement on children. Here we also mdetermined the correlation of the non-invasive measurement of ZnPP with the HPLC reference and compared the measured ZnPP to other iron status markers (ferritin & soluble transferrin receptor). We achieved the following results (manuscript is prepared for publication): • The non-invasive measurement is feasible in children aged less than 5 years. • The limits of agreement between the non-invasive method and reference HPLC measurements are 20 µmol/mol heme. • Sensitivity and specificity of ZnPP (threshold 50 µmol / mol heme) against soluble transferrin receptor are 83% and 93%, respectively. We see great potential for the non-invasive measurement of ZnPP as a simple, safe, and precise screening test for ID in children under 5 years. Further validation studies in larger

		groups of children are planned.

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