Correspondence from NSC to Head of communications at HEART UK

From: UKNSC.AnnualCall [mailto:UKNSC.AnnualCall@phe.gov.uk]
Sent: 04 September 2017 17:56
To: Head of Communications (HEART UK)
Subject: Annual Call for topics: FH submission

Many apologies for the delay in getting back to you about your submission on screening for familial hypercholesterolaemia in children aged between 1 – 2 years.

From previous correspondence you are aware that this topic is already on the UK NSC's list of recommendations. Because of this, the submission was not within the remit of the Annual Call for Topics.
This process invites proposals on new topics which are not already on the list. However the Committee
agreed to consider the submission as a proposal for an early update of the existing screening recommendation.

The submission focused on a universal 'child-parent' screening strategy as an alternative to the cascade testing
currently approach recommended by NICE. To support the proposal one published reference was submitted. This was:

'Child–Parent Familial Hypercholesterolemia Screening in Primary Care', David S. Wald, F.R.C.P., Jonathan P. Bestwick, M.Sc., Joan K. Morris,
Ph.D., Ken Whyte, Lucy Jenkins, F.R.C.Path., and Nicholas J. Wald, F.R.S. N Engl J Med 2016; 375:1628-1637 October 27, 2016

The assessment of early updates centres on whether the submitted publications alter the overall recommendation
of the most recent UK NSC evidence review. If this is the case, the Committee would bring the next review update forward.
If not then the submitted papers will be considered for inclusion in the scheduled triennial update.

For this proposal, we commissioned two external assessments to summarise the Wald paper and to consider the
way in which it impacts on the previous review. These documents are attached. The assessments, and their
recommendations on whether to bring the FH review forward, were considered by the Chair and Vice Chair of the
UK NSC, the Chair and members of the Committee's Fetal, Maternal and Child Health Reference Group and PHE's Director of Screening.

The consensus was that the overall recommendation of both assessments, that an early update of the FH review
is not warranted, is correct. The main reasons for this were:

- although the child-parent screening strategy is intrinsically interesting the paper did not address important issues which were

identified in the previous review. In particular there is an absence of information on the management of children with FH identified by screening, the acceptability of the strategy was only evaluated in those with positive results and clinical and cost effectiveness compared with current practice is not addressed. Because of this, the study does not alter the overall recommendation of the previous review.

- the assessments point out that the study authors considered the observed strategy to be insufficiently reliable in terms of the detection of FH.

The proposed strategy is based on modelling using a lower total cholesterol threshold to prompt further testing for FH mutations. In addition, a different approach to genetic testing and a different approach to those with negative genetic test results was assumed in the model. Rather than providing a basis for policy making, it may be that the modelled results provide a hypothesis for a further study in which a broader range of issues could be explored.

For example the assessments point out that the number of false positives would increase in the modelled strategy compared to the observed strategy. The parents of a large number of very young children are likely to be informed that, although their child does not have FH, he or she has a total cholesterol level sufficiently high to justify further testing. It is unclear what information would be fed back to parents at different points in the pathway but the potential for anxiety seems very real here. Similarly the arrangements for post test management in this group, should it be required, were not described in the paper.

This kind of issue, as well as those raised in the first bullet point, would need to be studied before it could be said that the strategy, as proposed, was acceptable.

Although the review of screening for FH in children aged between 1 – 2 years will not be brought forward, the Wald paper will be considered for inclusion in the next review. This will take place in the financial year 2018 – 2019. In addition to this the strategy raises some interesting ethical issues which have been touched on above. The UK NSC is in the process of convening an ethics task group and we will ask the group to consider some of the issues arising from the reflex testing strategy as part of its work.

Many thanks for submitting the proposal and, once again, apologies for the delay in getting back to you.

Best wishes,

Evidence Lead
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