UK National Screening Committee

Screening for elevated blood lead levels in children aged 1 to 5 years

28 February 2018

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 screening for elevated blood lead levels (BLLs) in children aged 1 to 5 meets the UK NSC criteria for a systematic population screening programme.

Current recommendation

2. The 2013 review of screening for elevated blood lead levels (BLL) concluded that systematic population screening is not recommended. This was because:
    a. No recent data on UK prevalence was found
    b. Screening strategies lacked reliability. Capillary testing had low sensitivity and specificity, mainly due to the chance of contamination via equipment and the skin. Where screening questionnaires had been used, they were found to be no better than chance at identifying elevated BLLs.
    c. There was a lack of a suitable cut-off for screening as there is no "safe" BLL.
    d. There was a lack of proven treatment for those asymptomatic children likely to be identified through screening, with raised blood levels ≥ 10µg/dL to ≤ 45µg/dL (that is, at levels below the threshold at which chelation therapy is recommended)

Evidence Summary

3. Screening for elevated blood lead levels was reviewed in accordance with the triennial review process. https://legacyscreening.phe.org.uk/leadpoisoning

4. The scope of the current review focused on the criteria addressing prevalence (in the UK population), the accuracy of non-invasive screening tests and the benefits/harms

of treating children with lower elevated blood levels (≥ 10µg/dL to ≤ 45µg/dL). The review was undertaken by Bazian Ltd.

5. The main conclusion of the current review is that population screening for elevated blood lead levels in children aged 1 to 5 should not be recommended in the UK. This is because:
    - There is still no UK incidence/prevalence data available. **Criterion 1 not met**
    - Only 2 studies describing the accuracy of non-invasive screening tests for the detection of elevated BLLs have been published since the last UK NSC review. One systematic review reported that screening questionnaires vary widely in their sensitivity and specificity for detecting BLL ≥10 µg/dL, and generally perform poorly at predicting which children are at greatest risk. One cross sectional study provided information on the accuracy of screening questionnaires and found the questionnaire to have low sensitivity, missing nearly half of those children with raised BLLs. However, the results for this study may not represent screening test performance in the general population. **Criterion 4 not met**
    - No studies were identified that assessed interventions for reducing levels of blood lead in lead-exposed children. **Criterion 9 not met**

Consultation

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

7. Responses were received from:
    - Dr Caroline Taylor (Centre for Child and Adolescent Health, University of Bristol)
    - Professor Jean Golding (Centre for Child and Adolescent Health, University of Bristol)

- Dr Carys M Lippiatt, Paramita D Ghosh, and Dr Arnab Seal (Leeds Teaching Hospitals NHS Trust and Leeds Community Healthcare Trust)
- Hesaan Sheridan (Lead Safe World/The Lead Group)
- Simon Abbott (Heritage Testing Limited)
- David Roberts (PHE Lead Exposure in Children Surveillance System (LEICSS) Steering Group)

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

Recommendation

9. The committee is asked to:
   - note the concern articulated in the responses to the review and the need to distinguish between population based screening and public health interventions which may help reduce lead levels in the environment.
   - approve the following recommendation:

     A systematic population screening programme for elevated Blood lead levels in children aged 1 to 5 is not recommended

Based upon the UK NSC criteria to recommend a population screening programme, elevated BLLs 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	Not met ✗

	robust evidence about the association between the risk or disease marker and serious or treatable disease.	
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 stakeholder organisations contacted

1. Faculty of Public Health
2. Royal College of General Practitioners
3. PHE Toxicology Department
4. Lead Paint Safety Association
5. Royal College of Paediatrics and Child Health

Annex B

UK National Screening Committee

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

Name:	Dr Caroline Taylor	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Centre for Child and Adolescent Health, University of Bristol		
Role:	Research Fellow		

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

Yes ☒ **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.*
		Thank you for the opportunity to provide comments on this document.
General/Overall		As with the 2013 review, the reports finds little or no evidence on three key points and rejects the recommendation for screening on this basis. While there are no major issues with the methodology of the review, lack of evidence does not justify a course of no action. Rather it should generate impetus to support and guide studies to gather evidence. Sadly, there is no evidence that the call in the 2013 report for "the introduction and implementation of a comprehensive, co-ordinated primary prevention strategy for raised BLLs in the UK" has been considered in the intervening time. The present report does not even repeat this call in its conclusions. In addition, the aim of the screening is not clear. Is the intention to identify children with levels >45 µg/dl for chelation treatment? Or is it to also identify those between 5 and 45 µg/dl for some other form of treatment/intervention?
General/Overall		1. It is not sufficient or satisfactory for the UK to rely on reports of blood lead levels of children living in other countries – the UK has a particular industrial legacy of lead mining and working over more than 2000 years, as well as high levels of old housing stock (potential sources of contaminated dust (from coal) and old leaded paint). In addition, there has been recent evidence that playground and other paints in south-west England exceed contemporary standards (Turner et al, 2016, 2016), raising the concern that there may be undetected pockets of exposure for children. Population level data from children was last done in the UK in the mid-1990s (Health Survey for England: Primatesta et al.

		1998, Bost et al. 1999; epidemiological data from ALSPAC at about the same time: Golding et al. 1998, Chandramouli et al. 2009) and is very overdue to be repeated to inform current policy. Similarly there needs to be a thorough evaluation of blood spot tests if it is felt that venous sampling is not acceptable (although this is done successfully in other countries such as the USA and other European countries).
General/Overall		2. Although I recognise that for practical purposes there needs to be a 'cut-off' value for population screening tests, the use of the word 'poisoning' rather than 'toxicity' does not encompass that there are adverse effects of lead at all levels of exposure – not just at acute levels. This is recognised in the CDC's approach.
General/Overall		3. The report skips between 5 and 10, and sometimes 45 µg/dl as being of interest. This is partly a consequence of focusing on chelation as being the only treatment available. There are other means of 'treatment' for levels <45 µg/dl that involve surveying the child's environment and providing remediation and/or advice, which should be considered.
Introduction		The report considers the potential sources of lead for a child without mentioning diet and smoking – diet and water are now considered to be among the major sources of lead exposure in European countries (EFSA, 2010). The contribution of passive smoking is also of great importance for children. There are some factual errors. Lead has not been banned in petrol worldwide – there are still a handful of countries that use it and petrol additive is exported from a manufacturing plant in the UK. Many countries have not banned lead in paint. Avgas plane fuel contains also contains lead. Any reduction in blood lead levels is largely documented in developed countries – although this is not to

		say that it does not still cause adverse effects there. There are still many developing countries where it is a major problem (Nigeria, China, Mexico, Iran, etc.), sometimes with fatalities in children. Typo: should be Center**s**
		Social inequalities are often assumed to be a risk factor for environmental exposures but this may not always be the case (Vjijheid et al. 2012). The UK ALSPAC study in the early 1990s higher blood lead levels in pregnant women were associated with higher maternal educational attainment (Taylor et al. 2013). Local conditions and demographics may be important.
p. 7	Basis for current recommendation	Point 1 acknowledges that there are no recent data on BLL in the UK, so it is not correct to state that the prevalence of elevated BLLs in the UK is low – in the absence of any recent population-level data we do not know.
p. 7	Basis for current recommendation	The perceived lack of the suitable cut-off seems unreasonable in the light of a US CDC recommendation that is based on thorough research. Why can this not be adopted? Alternatively there are other European countries that have their own recommendations (e.g. Germany).
p. 7	Basis for current recommendation	The lack of proven treatment has not been thoroughly investigated here so this statement is not justified.
p. 11	Appraisal against UK NSC criteria	Para 2. Reference 3 (Drinking Water Inspectorate) not accessible – but a primary source of evidence would be preferable. Similarly reference 2 in this para doesn't seem to contain the right information here.
p. 11	Appraisal against UK NSC criteria	You state that you rejected studies where the country was dissimilar from the UK (no criteria for this decision are supplied). However, it could be argued that the US has a very different environmental exposure context to that of the UK (much younger housing stock, different industrial history, greater

		public health information and awareness on lead, monitoring, etc.).
p. 17	Description of the evidence	This is an example from an earlier point about the indecision on a 'cut-off' of interest. Why was 10 µg/dl chosen as a marker of elevation instead of 5 µg/dl (US CDC level of action)?
p. 18	Criteria 9 not met.	There are plenty of studies that assess interventions. See for example: Nussbaumer-Streit et al. on dust control (2016); Shao et al. (2017) for impact of lead hazard control treatment in the USA; Greene et al. (2015) on targeted media campaigns; etc.
References	1	This is not in the preferred format for a Cochrane Database reference.
	3	Not accessible
	6	Typo: World Health Organi**z**ation
		References Bost L, Primatesta P, Dong W, Poulter N (1999) Blood lead and blood pressure: evidence from the health Survey for England 1995. J Hum Hypertens 13: 123-8. Chandramouli K, Steer CD, Ellis M, Emond AM (2009) Effects of early lead exposure on academic performance and behaviour of school age children. Arch Dis Child 94: 844-848. European Food Safety Authority Panel on Contaminants in the Food Chain (2010) Scientific opinion on lead in food. EFSA Journal 8:1570-1717. Golding J, Smith M, Delves HT, Taylor H (1998) The ALSPAC study of lead in children. In: IEH report on recent UK blood lead surveys, Report R9, pp. 35-39 (ed. D Gompertz). MRC/IEH: Norwich. Greene D, Tehranifar P, deMartini DP, Faciano A, Nagin D (2015) Peeling lead paint turns into poisonous dust. Guess where it ends up? A media campaign to prevent childhood lead poisoning in New York City. Health Educ Behav 42:409-21. Nussbaumer-Streit B, Yeoh B, Griebler U, Pfadenhauer LM, Busert LK, Lhachimi SK, Lohner S, Gartlehner G. Household

		interventions for preventing domestic lead exposure in children. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD006047. DOI: 10.1002/14651858.CD006047.pub5. Primatesta P, Dong, W, Bost L et al. (1998) Survey of blood lead levels in the population of England, 1996. In: IEH report on recent UK blood lead surveys, Report R9, pp. 9-34 (ed. D Gompertz). MRC/IEH: Norwich. Turner A, Kearl ER, Solman KR (2016) Lead and other toxic metals in playground paints from South West England. Sci Total Environ 15:544 Turner A, Solman KR (2016) Lead in exterior paints from the urban and suburban environments of Plymouth, South West England. Sci Total Environ 15:547 Shao L, Zhang L, Zhen Z (2016) Interrupted time series analysis of children's blood levels: a case study of lead hazard control program in Syracuse, New York. Plos One 12(2):e0171778 Taylor CM, Golding J, Emond A (2014) Lead, cadmium and mercury levels in pregnancy: the need for international consensus on levels of concern. J Dev Origins Health Dis 5:16-30. Taylor CM, Golding J, Hibbeln J, Emond AM (2013) Environmental factors predicting blood lead levels in pregnant women in the UK: the ALSPAC study. PlosOne 8:e72371 Vrijheid M, Martinez D, Aguilera I, Ballester F, Basterrechea et al. (2012) Socioeconomic status and exposure to multiple environmental pollutants during pregnancy: evidence for environmental inequity? J Epidemiol Commun Health 66: 106-113.

Please return to the Evidence Team at screening.evidence@nhs.net **by Tuesday 9th January 2018.**

UK National Screening Committee

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

Name:	xxxx xxxx	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Centre for Child and Adolescent Health, University of Bristol.		
Role:	**Research into the effects of the environment on health and development**		

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.*
throughout		I've read the report, and am afraid I am not impressed. There is seemingly an acceptance that there is not enough evidence, therefore nothing needs to be done. This is very defeatist. Surely the report could recommend that an effort be made to assess the current state of affairs. A further suggestion is to investigate whether other biological samples such as teeth, hair or toenails may be useful in monitoring lead levels. This would be cheaper than employing

		someone to collect blood. The samples could even be collected by post.
		See also attached letter

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xxxx xxxx

UK National Screening Committee

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

Name:	Dr Carys M Lippiatt(1) , Dr Paramita D Ghosh(2), Dr Arnab Seal(3)	**Email address:**	xxxx xxxx xxxx xxxx xxxx xxxx
Organisation (if appropriate):	Leeds Teaching Hospitals NHS Trust (1), Leeds Community Healthcare Trust (2,3).		
Role:	**Consultant Clinical Scientist in Biochemistry (1), Consultant Paediatrician (2,3)**		
Do you consent to your name being published on the UK NSC website alongside your response?			

Yes x		
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.*
P6 (Introduction) and P7 (Basis for current recommendation	‘Chelation therapy is the main treatment used for children with BLLs greater than 45.0 µg/ dL. This reduces the risk of death due to severe acute lead encephalopathy, although the lead sequestered in bone cannot be removed, and neuropsychological effects cannot be reversed .1 ’ Basis for current recommendation: 1. The prevalence of elevated BLL is low…..There was however, no recent data on the prevalence of raised BLLs in the UK. 4. There was a lack of proven treatment for those asymptomatic children likely to be identified through screening, with raised blood levels ≥ 10µg/dL to ≤	Agreed that the current available treatments are not applicable to children with blood lead up to 45 ug/dL but effective interventions are available for children with blood lead concentrations >5 ug/dL and <45 ug/dL; such as rigorous checks to identify the source of exposure, removal from further exposure, treating iron deficiency if found, sibling & family screening, ongoing monitoring and follow-up and providing information and education to parents, carers and schools. These interventions can mitigate the risk of chronic exposure and prevent further harm that would result from continued exposure. It is known that many cases elude detection until children are symptomatic. Therefore, there is a case for targeted screening, in children with risk factors such as pica, anaemia, older housing, living in an industrial area, to identify children with elevated blood lead to enable early intervention.

	45µg/dL (that is, at levels below the threshold at which chelation therapy is recommended)	A pilot screening study would allow more accurate determination of the prevalence of high BLLs. If prevalence is found to be high, there would be a greater impetus to support research into more effective treatments and treatments with a better safety profile than the currently available chelation therapy.
P12 (Description of the evidence)	One UK study was identified, but this was available as an abstract only. Full details of the methods were not available and the research would not have undergone full peer review.7 Most importantly, it analysed a small sample of children (n=104) with unexplained developmental delay and learning difficulties (in whom elevated lead levels may be more common), so is not representative of the wider general population or of asymptomatic children. Therefore it was excluded from the analysis.	It is recognised that there is a paucity of UK studies into lead poisoning in children. It is also recognised that BLLs as low as 5ug/dL can have a detrimental effect on children's neurological development, learning and attention. The UK study cited here demonstrated that the potential number of cases in the 5-10ug/dL range is high and that the impact on the individual child and the population on the whole is large. It is also the case that we see fatal cases of lead poisoning in the UK still (manuscript submitted to BMJ cases). Therefore, it would be negligent to ignore this issue. It is critical that we conduct rigorous studies in the UK to address the ongoing potential for lead poisoning and to increase healthcare professionals' awareness that death can still occur from lead poisoning in the UK today.

		A pilot screening study would raise awareness within public and medical circles and would allow earlier recognition of potentially severe toxicity at an earlier stage in exposure.
P19 (Conclusions)	The volume, quality and direction of evidence published since 2012 does not indicate that screening for elevated BLLs should be recommended in the UK. Several uncertainties remain across key criteria, including: • lack of evidence that elevated BLLs in children is an important health problem in terms of UK prevalence • lack of evidence on accuracy of non-invasive screening tests for the detection of elevated BLLs. No optimum screening strategy could be identified • lack of evidence of a benefit or harm of treating children with lower elevated BLLs	Following a fatal case of lead poisoning in a xxxx xxxx year old xxxx xxxx in xxxx xxxx in xxxx xxxx, a serious case review was performed. xxxx xxxx xxxx xxxx (contributor to this comments form) worked with a xxxx xxxx xxxx xxxx at xxxx xxxx to educate GPs and paediatricians about the risks of lead exposure to children in the UK currently and to create an intervention on the electronic blood test requesting system for primary and secondary care at xxxx xxxx. The details of the intervention, the effect of the intervention on the number of requests for blood lead measurement in children living in xxxx xxxx, the number of cases found with elevated blood lead and the effect of follow-up of these cases, is being prepared for publication currently. It is clear to us that a strategy for identifying exposed children early is extremely valuable. Population screening is probably not appropriate. Given the range of ages at which children present with lead poisoning in

		our experience it would be difficult to determine an age at which population screening would be beneficial. Furthermore, lead exposure is dynamic and depends on both behavioural and exposure factors, which can change with time. Work in xxxx xxxx has identified that there is an opportunity to identify some exposed children by targeting children with learning and behavioural difficulties and children with pica behaviour. At the very least, there needs to be a UK-wide strategy to increase awareness that blood lead measurement should be considered for children with these risk factors. We would be very happy to provide further details of our as yet unpublished work on targeted screening of children with pica and our previous work on screening children under 5 years presenting with developmental delay.

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Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

Document used for comments:

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years
External review against programme appraisal criteria for the UK National Screening Committee (UK NSC)
Version: Consultation document
Bazian Ltd. April 2017

Comments version issue 1.3, 9th January 2018

Name:	Hesaan Sheridan ☒	**Email address:** ☐	xxxx xxxx
Organisation (if appropriate):	Lead Safe World / The Lead Group		
Role:	**Secretary and UK Branch Member**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes** **No**			

NSC UK National Screening Committee

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.*
Plain English Summary, Page 3	"potential sources of lead"	The University of Southern California has produced a document titled 'Where Lead Hides' [Ref 1]. This lists many more possible sources of environmental lead contamination than listed in the review and illustrates the ubiquity of lead in the environment.
Plain English Summary, Page 3	"some paint"	The term "some paint" could be "most paint". Lead based components in lead and varnish, although labelled as such from the 1960s, were not formally banned in the UK until 1992 [Ref 2]. The Public Health England National Poisons Information Service (PHE NPIS) reports that "Despite the toxicity of lead being well known, lead exposure remains a cause of morbidity not only in industry, but also to members of the public, particularly to children". Paint-stripping is identified as the most common source of exposure [Ref 3].
Plain English Summary, Page 3	"there are few children with raised blood levels (it is rare)"	On what data is the statement based? The latest data we have appears to come from the Avon Longitudinal Study in the early 1990s. Analysis of these data found that: 27% of 30 month olds had BLLs > 5 µg/dL [Ref 4] and 14.4% of pregnant women had BLLs > 5 µg/dL [Ref 5] Ref 4 includes the statement "These data suggest that the threshold for clinical concern should be reduced to 5 µg/dl". 5 µg/dl is also the level at which the CDC recommends public health actions be initiated [Ref 6]. Ref 5 concludes "The mean BLL in this group of pregnant women is higher than has been found in similar populations in developed countries"

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.*
Plain English Summary, Page 3	"there are ways of stopping children getting raised blood levels in the first place"	This is true, but without screening how will parents and carers know that children are being exposed to lead? As noted by Ossiander, 2013 (Reference 13 in the external review) "Lead screening questionnaires …performed little better than chance at predicting lead poisoning risk among children." This suggests that other means, such as blood tests, are required. Evaluation of a pilot surveillance system in 2014 to 2015 showed that timeliness of case reporting was dramatically improved, enabling earlier public health investigations. Where venous blood lead tests were carried out, they identified new cases and enabled faster action by the public health protection teams to investigate and remove the source of exposure [Ref 7]. The current surveillance system is however reactive; it only addresses children who are already symptomatic, whereas screening would allow asymptomatic children to be identified and protected. Preventative programmes based on public health legislation, abatement, and education require resources to be allocated to them. Without a screening programme, how will we be able to justify the allocation or monitor the effectiveness of those initiatives?
Plain English Summary, Page 3	"the test misses lots of children with raised lead levels"	Testing seem to be adequate in the USA and achieves over 66% coverage of eligible children. [Ref 8]. The National Committee for Quality Assurance also states that "Screening for lead is an easy way to detect an abnormal blood lead level in children".

UK National Screening Committee

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Plain English Summary, Page 3	"the evidence does not say what level of blood lead should be treated"	The monograph of the US National Toxicology Program titled "Health Effects of Low-level Lead Evaluation" states that "The evidence provides support for adverse health effects in both children and adults at blood lead levels below 10 µg/dL, and, for some effects, below 5 µg/dL." [Ref 9]. This would seem to clearly state a BLL at which interventions should be initiated. Screening would enable preventative measures to be implemented before symptoms are apparent and before blood lead reaches a level of over 5 µg/dL. However, it should be noted that the UK Teratology Information Service factsheet on lead states that "a lead measurement of less than 20 micrograms per litre (2 micrograms per decilitre) of blood is considered acceptable in the UK." [Ref 10].
Plain English Summary, Page 3	"there is no treatment for the majority of cases (very low levels of raised blood lead levels) that would be identified by screening"	The NHS screening guidelines focus on "effective intervention" not "medical treatment": "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." [Ref 11]. There is nothing here that states the intervention has to be medical. Removing the exposure to lead is "an effective intervention". Screening may also allow other correlations in data to be identified, e.g. are higher blood lead levels associated with children who live in areas which have water fluoridation schemes? Do calcium deficient children have higher BLLs? Procedures that can be put in place to reduce exposure could include those publicised by the United States Environmental Protection Agency [Ref 12]. A CDC report describes appropriate interventions and states that "children negatively affected by lead exposure [should] receive services designed to compensate for lead's effect on the brain and behavior of children". [Ref 13]

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.*
Plain English Summary, Page 3	"there is no research comparing screening with usual methods of identifying and treating children in the UK"	The CDC states that "Because lead exposure often occurs with no obvious symptoms, it frequently goes unrecognized." [Ref 14]. Screening would mean that elevated BLLs would be identified when otherwise they would not be. Although the CDC Morbidity and Mortality Weekly Report (2014) states that "evidence is insufficient to recommend for or against routine screening" it does add that "children who are at risk for lead exposure need to be tested to determine if their exposure is high". This includes children who are "living in poverty, and living in older housing". The report concludes that "Screening and early identification of children at risk for lead exposure has the potential to prevent permanent neurologic damage and behavioral disorders in hundreds of thousands of young children across the United States." [Ref 15].
Plain English Summary, Page 3	"This review could not find evidence about: • the number of children with raised blood levels in the UK"	The CDC estimates that there are 535,000 children age 1-5 with elevated BLLs [Ref 16]. Assuming similar exposure, this would equate to around 100,000 children in the UK at any one time. The total number of referrals in the UK from screening last year was 460,000. The potential number of children with elevated BLL could increase the success of screening by a large proportion of this and is not 'very few' [Ref 17]. The lack of evidence is simply because of the lack of any prevalence studies since the early 1990s. A pilot screening programme could address this.

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.*
Plain English Summary, Page 3	"This review could not find evidence about: • an acceptable screening test"	As stated above, BLL screening is routinely performed in the USA. In the USA in 2010 over 4 million tests were performed on children [Ref 15]. In the UK, the NHS, and private services [Ref 18], provide blood lead analysis. The Control of Lead At Work act requires employers to provide BLL tests and a number of laboratories are available to conduct tests [Ref 19]. There would appear to be acceptable and available screening tests.
Plain English Summary, Page 3	"This review could not find evidence about: • how well treatment works"	There is widespread information about reducing lead exposure. For example, from Defra [Ref 20] A biokinetic model has been developed which predicts BLL based on exposure [Ref 21]. This also includes examples of the effectiveness of remedial actions [Ref 22] The National Toxicology Program monograph referenced [Ref 9] discussed the evidence for elevated BLLs and health impacts. In combination, it is shown that reducing exposure is an effective treatment.
Executive Summary, Page 4	"1 No studies report the prevalence of elevated BLLs in the UK"	This is why we are calling for a pilot screening study.

UK National Screening Committee

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.*
Executive Summary, Page 4	"US studies had the potential for selection bias"	The US studies referenced in the review do not seem to support this statement: Reference 9 concluded: "living in older houses (presumably containing lead paint) was associated with higher BLLs in children". Lead paint was not banned in the UK until 1992 meaning that over 80% of homes could contain some lead paint and 55% pre-1960s home probably contain lead paint [Ref 23]. Reference 10 included analysis of the whole of the US so is not entirely selective. The letter in reference 11 noted possibility of bias in one study, but the letter writer's own study still found 5% of children with elevated BLLs. Reference 13 notes bias in some cases, but is an analysis of the effectiveness of interventions, not a study of the prevalence of elevated BLLs. Reference 14 is an analysis of the effectiveness of screening questionnaires so not relevant to this question
Executive Summary, Page 5	"2. There was little evidence on the acceptability of non-invasive screening methods."	Based on reference 14 in the review this is agreed, but why not use an invasive method, i.e. blood tests including fingerstick tests as described by Schonfeld et al [Ref 24].

NSC UK National Screening Committee

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Executive Summary, Page 5	"3. No studies had assessed the benefit of treatment in children exposed to lead."	A 2004 CDC report, titled "Preventing Lead Exposure in Young Children" describes housing based approaches [Ref 25].
Results of studies looking at prevalence of raised blood lead levels, Page 12	"In France, a cross-sectional survey included 3,831"	France may not be generalizable to the UK because: 1) White lead paint was banned in 1909 [Ref 26] 2) All properties built before1949 need to be tested for lead paint on sale [Ref 27] These rules may have reduced the
Criterion 1 not met, Page 13	"Therefore UK prevalence is still unknown"	Because the most recent data we have suggested that a large number of toddlers and pregnant mothers had elevated BLLs [Ref 4 and 5] it would seem appropriate to conduct a pilot screening exercise to resolve this important unknown.
Criterion 4 not met, Page 17	"non-invasive screening"	The summary focusses on non-invasive screening. Venous blood sampling is rejected because it would be "less likely to be practical or feasible", but no reason or reference is given for this assumption. It is difficult to understand why tests used routinely in the USA, and used electively in the UK, could not be used for screening.

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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 9 not met, Page 17	"did not have elevated BLL (≥10µg/dL)"	It has been established that the current level of concern should be BLL ≥5µg/dl so this exclusion criterion would not seem to be appropriate. If treatment is widened to include prevention of further exposure then, as described above, there are studies that show interventions can be effective.
Criterion 9 not met, Page 18	"No studies were identified that assessed interventions for reducing levels of blood lead in lead-exposed children."	The CDC lists many preventative measures to reduce lead exposure [Ref 28]. Dixon et al. (2008) described how lowering floor dust lead standards would impact blood lead levels in children [Ref 29]. Lanphear et al. (2016) stated that "Evidence-based guidance is available for managing increased lead exposure in children, and reducing sources of lead in the environment, including lead in housing, soil, water, and consumer products, has been shown to be cost-beneficial." [Ref 30]. The conclusions in reference 13 (Woolfenden et al, 2012) in the review are noted. However, the range of floor dust levels stated in the table on page 3 is very low at 1.65 to 2.28 µg/ft^2, with small variations in intervention groups. These are well below the current HUD clearance level of 10 µg/ft$^{2.}$ [Ref 31] This would suggest that many homes in these studies were already relatively 'lead-safe' with regard to floor dust and any exposure could be from other sources. What is needed are studies which show the impact of reducing floor dust lead levels from above to below the defined clearance levels.

Please return to the Evidence Team at screening.evidence@nhs.net **by Tuesday 9th January 2018.**

UK National Screening Committee

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UK National Screening Committee

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

Name:	Simon Abbott	**Email address:**	xxxx xxxx
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Role:	**Data Scientist**		

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

Yes ☒ **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.

Page 3, Plain English Summary, Condition	“There has been concerns that low levels of lead within the environment are causing a number of problems, including developmental and behavioural conditions.”	Health Canada have compiled several tables derived from research projects which show evidence that even blood lead levels as low as 3 µg/dl are detrimental and a cause for concern [2]. Lead has no known function in the human body, unlike many other heavy metals that are useful at trace levels. “The pre-industrial blood lead level in people is estimated to have been about 0.016 µg/dl” [1].

Page 6	“There are a number of other potential sources of lead in the environment, including industry, leaded petrol, some paint, water piping and hobbies that use lead.”	Architectural lead paint is widely regarded today as the most likely source of elevated blood lead levels. Architectural lead paint was formally banned in the UK in 1992 (one of the last countries to do so). Children can also be affected via parental occupational exposure (particularly construction and painting) [4, 5]. However, lead has been found within the paint and materials of manufactured goods such as new playground equipment [3] and toys. The US Consumer Products Safety Commission identifies around 500 to 700 items a year with unacceptable levels of lead aimed at children particularly toys and clothing. The EU-wide alert system finds around 20 per year. International purchases by consumers directly from countries such as China (enabled by internet markets such as eBay) may be an additional source of unregulated and undocumented exposure. The food chain is another potential source; lead poisoning in cattle [6] is the primary form of livestock poisoning in the UK (often associated with lead paint and lead acid batteries) and has been for a long time [7]. There have also been concerns raised by the European Food Standards Agency on environmental lead exposure in food crops [8]. Lead flashing is the most widely used and most common form of architectural rainwater protection in the UK. This gives rise to the possibility of high levels of lead in collected rainwater for use in gardens and allotments. Residential chicken eggs may also be another potential unregulated source.

Page 6	"The Centre for Disease Control in the USA currently recommend a BLL of 5 µg/ dL to be used as a threshold for initiating educational programmes, environmental investigations, and medical monitoring."	The US has been monitoring BLLs in its general population since the 1970s and currently reviews what it calls Blood Lead Reference Value (BLRV) every 4 years to consider what is achievable, which has been the 95th percentile, but now in 97.5th percentile [10]. Without UK screening data, we cannot judge what is achievable in the UK and therefore cannot work towards the ideal – which would be as low as achievable. The US CDC lowered the threshold value to 5 µg/ dL in 2012 and in 2017 agreed in principal to lower the BLL to 3.5 µg/dL [9] in order to maintain its preventative stance, however the UK retains a 'reactive' threshold value of 10 µg/ dL. The review assumes that US BLL's are comparative to the UK, but does not attempt to address the discrepancies between the two countries.
Page 7, Basis for current recommendation	1. The prevalence of elevated BLLs is low. The number of people affected has been in decline for many years, due to primary prevention measures, and so very few children in the UK were thought to be affected. There was, however, no recent data on the prevalence of raised BLLs in the UK.	This assumption is paradoxical: There is no data because there is no screening; however there is no screening because there is no data.

Page 7, Basis for current recommendation	2. Current screening strategies lacked reliability.	Blood testing is routinely employed within other NHS screening programmes, and blood lead testing is the most widely researched and used method due to its reliability.
Page 7, Basis for current recommendation	3. There was a lack of a suitable cut-off for screening as there is no “safe” BLL.	The purpose of screening is to gather data that would assist with public health policy. The “safe” BLL would naturally be defined by the limit of detection (LoD) or reporting limit of the analytical methods used. Current NHS patient test results indicate the latter to be at or around 2 µg/ dL – however there are indications that the achievable LoD could be far lower than this reporting limit.
Page 7, Basis for current recommendation	4. There was a lack of proven treatment for those asymptomatic children likely to be identified through screening	NHS screening criteria is for “effective intervention” [11]. It does not specify that it must be a “treatment”. Identifying and removing the lead source is a highly proven effective ‘preventative’ intervention for asymptomatic children likely to be identified through screening. Ensuring good nutrition including adequate calcium levels is another.

Page 11	“The current evidence summary aims to establish whether elevated BLLs in children aged 1 to 5 years is an important health problem, looking at the prevalence and incidence in the UK or comparative settings... UK studies were prioritised with other studies from Western populations that are comparable to those in the UK”.	The US CDC attributes its success of lowering blood lead levels in its population with legislation (banning of lead paint, lead pipes, leaded petrol etc) and “ongoing screening of children and educational efforts, and lead paint abatement programs” [10]. The UK has lagged behind most other nations in terms of lead-specific environmental and public health legislation (particularly lead paint, but also leaded petrol), currently has no screening programme, and has no lead abatement programmes. A comparison with other countries therefore does not appear possible.

Page 11	“Ideally the study should have included a sample of 500 children or more and be representative of the general population, though studies reporting the incidence or prevalence in specific populations were also considered. . . One UK study was identified, but this was available as an abstract only. Full details of the methods were not available and the research would not have undergone full peer review. Most importantly, it analysed a small sample of children (n=104) with unexplained developmental delay and learning difficulties (in whom elevated lead levels may be more common), so is not representative of the wider general population or of asymptomatic children. Therefore, it was excluded from the analysis.”	The UK study mentioned [12] is of relevance and should have been included as it is consistent with international research that BLL’s as low as 5 µg/ dL should be investigated and not the current UK investigative limit of 10 µg/ dL.

Page 12	France is not a comparable country regarding blood lead levels.	Taking lead paint as an example, France banned white lead paint for residential use in 1909, whereas the UK banned white lead paint for residential use in 1992. Over 80% of English housing stock was built before 1992. Old lead paint is widely perceived to be the primary source of lead exposure in most countries today. The UK would therefore be expected to have higher BLL's than France.
Page 12	The US is not a comparable country regarding blood lead levels.	Taking lead paint as an example, the US banned lead paint in 1978 and has been proactively monitoring and taking action on lead levels ever since [10]. The UK banned white lead paint for residential use in 1992.The Royal Commission on Environmental Pollution [13] reported the US was already far ahead in 1983 and many of the recommendations have still not been implemented. In the absence of UK data, it would be more appropriate to assume that the UK has higher levels of blood lead than the US.
Page 14	"The most commonly used screening test for BLL is the capillary test"	The most commonly used test for BLL is blood testing. This is the most relevant and useful as it is accurate, identifies recent exposure, and is still at a stage where effective intervention is possible. The second most widely used biomarker is urine, although is more commonly used for regular long-term monitoring (occupationally or during chelation therapy) as opposed to one-off testing or screening.

Page 14	Potential viability of saliva testing	There have been several studies into saliva testing, however it appears to be unreliable [14].
Page 16	Usefulness of questionnaires	The usefulness of questionnaires stems from well-thought out questionnaire design, being properly understood and completed, and appropriate interpretation of the answers. The CDC questionnaire failed in its design, whereas more localised questionnaires were more successful. The potential sources of lead exposure do make a comprehensive questionnaire unwieldy. On the other hand, this adds to the case that blood testing needs to be carried out.
Page 17	"The previous UK NSC review states "Chelation is not advised for BLLs less than 45 µg/dL. It is this level that would be mainly identified in a screening programme. For children identified at the lower level removal from the source of lead is advised and primary prevention interventions to remove the source long term." . . . The current evidence summary aims to establish the benefits/harms of treating children with lower elevated blood levels (≥ 10µg/dL to ≤ 45µg/dL)."	The NHS criteria for appraising screening programmes states: "There should be an **effective intervention** for patients identified through screening [11]". Effective intervention includes identifying and removing sources of lead, not just medical treatments such as chelation therapy. There is plenty of evidence that identifying and removing sources of lead is an effective intervention for patients identified with having elevated blood lead levels, even at levels as low as 5µg/dL.

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UK National Screening Committee

Screening for elevated blood lead levels in asymptomatic children aged 1 to 5 years – an evidence review

Consultation comments pro-forma

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Organisation (if appropriate):	On behalf of the Public Health England Lead Exposure in Children Surveillance System (PHE LEICSS) Steering Group		
Role:	**Epidemiologist**		

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

Yes ☒ **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.

Page 12	Results of studies looking at prevalence of raised blood lead levels (including <10 µg/dL)	Your literature search aimed to detect studies that could be used to estimate the prevalence of elevated blood lead concentrations in children in the UK (1-5 yr old general population), in order to determine whether lead poisoning is an 'important health problem'. Your results included a cross-sectional study from France (Etchevers et al), 2 sub-national surveillance studies from the US (Jackson, and Kennedy), and McClure et al, a US study (50 states plus District of Columbia) containing mainly surveillance data. You then state that the findings from the latter 3 are difficult to generalise, as they will suffer selection bias and not reflect the wider population. You also gave the same remark about Etchevers, as they selected their survey population from children attending hospitals for blood tests. You concluded that there was an absence of applicable evidence to determine whether lead poisoning was an 'important public health problem' in the UK. We would like to highlight a study which has none of these limitations: [1]Man-Fung Tsoi et al, who report a time series of USA National Health and Nutrition Examination and Survey data from 1999-2014, which includes blood lead concentrations of surveyed 1-5y children, selected in a manner so as to be representative of the US noninstitutionalized population. Prevalence estimates from 2013/14 reveal a blood lead

[1] http://www.sciencedirect.com/science/article/pii/S0002934316306003

		concentration (BLC) ≥ 5 µg/dL = 0.5% for 1-5 year olds (0.9% in 1-2 year olds; 0.3% 3-5 year olds). In 2007-8 estimates were 3.1% for 1-5 year olds (confirming a continued fall in prevalence of elevated BLC amongst 1-5 year olds). These are higher, but not dissimilar to Etchever's findings of BLC ≥ 5 µg/dL = 1.5%, and BLC ≥ 10 µg/dL = 0.09%, on survey in 2008/9. We note however, that the context of exposure to lead in the USA may not be directly applicable to that in the UK. Overall, these findings must be interpreted with caution. Additionally, caution must be used if further stratifying by sub-groups where the number of surveyed participants may be small. It should also be noted that at-risk populations are likely to have higher prevalence of elevated BLC: children 1-2 years, children from ethnic minorities, children living in poverty, and children with pica/age-inappropriate mouthing, commonly secondary to conditions such as autism. This is supported by Man-Fung Tsoi's findings of a consistently higher than average prevalence of BLC ≥ 5 µg/dL in these groups (other than children with pica/age-inappropriate mouthing, who were not specifically surveyed). For example, in 1.6% of non-Hispanic Black 1-5 year-old children in 2013/14 (a figure to be regarded with caution due to smaller numbers, the previous years' were 7.1%, 3.8% and 3.2%). Note also the much higher prevalence in 1-5 year-old boys (2.4%), and in 1-5 year-olds in low income families

		compared to average/high income families (1.1% compared to 0%, respectively). Other studies cited and summarised in your review also point out the increased prevalence in areas with lead industry. Other significant sub-populations of children, particularly those with special educational needs who are likely to have age-inappropriate mouthing and/or pica behaviour, were not included in the study, but based on our preliminary surveillance findings[2], we would consider it highly likely they would also have a higher prevalence of elevated BLC. We are not aware of work that has established the nature of exposure amongst ethnic minority children in the UK, but we would also be concerned a variation in risk by ethnicity analogous to that observed in the USA is possible in the UK. Evidence on prevalence is limited in terms of extent and generalizability to the UK, particularly for sub-groups of children who may be at higher risk. The evidence available supports a conclusion of a falling and very low prevalence of raised BLC in the general UK paediatric population. However, prevalence is likely higher in at risk populations, in whom lead exposure may be a public health concern.
Page 17	Literature search for evidence of effective	The current NSC review aimed to 'establish the benefits/harms of

[2] Crabbe, H., Dabrera, G., Close, R., Morris, J., Keshishian,C., Leonardi, G., Ruggles, R. (2016) Lead poisoning in children; evaluation of a pilot surveillance system in England, 2014-15. In: Abstracts of the 2016 International Society of Environmental Epidemiology (ISEE). Abstract P2-267 | ID: 3829. Research Triangle Park, NC: Environmental Health Perspectives; http://ehp.niehs.nih.gov/isee/2016-p2-267-3829/

	interventions for lead exposed children	treating children with lower elevated blood levels (≥ 10µg/dL to ≤ 45µg/dL)' with a search strategy limited to 2012-17, so as to detect new evidence published since the last published NSC review (literature search January 2007 up to April 2012). A wide variety of primary study designs, and systematic reviews were potentially eligible. The current search found 4 studies (not further described, so we cannot tell which studies they were), all of which were deemed unsuitable for inclusion in your review. On reviewing the previous NSC 2012 review the only evidence relevant to the current aim that is cited included an evidence review by the US Preventive Services Task Force published in 1996. Since then, and not as far as we can see explicitly acknowledged in the current UK NSC review, the Cochrane Collaboration has published a 2016 systematic review of 14 RCTs and quasi-RCTs (published 1993-2011) with settings in the USA and Australia addressing this research question[3]. The findings of the Cochrane review were of high-quality evidence of ineffectiveness of household educational interventions in reducing blood lead levels, that dust control interventions may lead to little or no difference in blood lead levels (moderate to low quality evidence), and insufficient evidence to draw conclusions about the effectiveness of soil abatement or combination interventions. We

[3] http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006047.pub5/full

		realise this will not necessarily change your conclusions, but are concerned the NSC reviews (2012 and current) findings may have never explicitly considered this Cochrane Review and/or therefore several relevant RCTs, and may not accurately reflect the availability of evidence on the subject.
Page 19	Conclusions	Related to our discussion above, we would welcome an explicit recognition that some groups of children are more likely to have elevated blood lead compared to the background population. These children may benefit from targeted public health interventions, such as surveillance and public health case management of children with significantly elevated blood lead as already conducted by PHE, though we acknowledge such interventions for sub-populations were not the subject of this review.
Page 36	References	The aforementioned Cochrane review is referenced, but only for the background/introduction statements such as 'Lead poisoning is a serious health hazard that can lead to severe health problems, especially in young children', a subject on which the review provides no primary evidence. This is essentially referencing a study that summarizes other references. Better practice would be to reference the primary studies or reviews of such studies e.g. by the WHO[4] or AAP[5].

Please return to the Evidence Team at screening.evidence@nhs.net **by Tuesday 9th January 2018.**

[4] http://www.who.int/ceh/publications/leadguidance.pdf
[5] https://www.cdc.gov/nceh/lead/ACCLPP/Oct%202005/Documents/DOCUMENT%202%20AAP%20PEDIATRICS.pdf