Elevated Blood Lead Concentration in Children

Prevalence Study Discussion Document

Document Control

Version	Date	Author	Contents
d0.1	3rd August 2021	Tim Pye LEAPP Alliance	Initial draft

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Introduction

Inception

At the Lead Exposure In Children Surveillance System (LEICSS) steering group meeting on 30th June 2021 it was agreed that the number one priority for the group is a prevalence study of lead levels in the child population and that a sub-group would be formed to take this forward.

The actual text of the option presented for prioritisation was

Support/set up/get funding for a population survey of blood lead levels including an economic evaluation.

Prof Alan Emond and Tim Pye were provisionally identified as volunteers for the sub-group.

Purpose

The purpose of this document is to propose some ideas for discussion. It is expected that any, or all, of these will be revised.

Aims

The Lead Exposure In Children Surveillance System (LEICSS) has two aims:

1. To facilitate timely public health action for individual cases, as the mainstay of treatment for cases of lead exposure is rapid removal of the putative source of exposure.
2. The system should also meet population level surveillance objectives, to inform public health action to reduce the incidence of lead exposure in children in England, such as by identifying at risk geographic areas or populations, and identification of current and emerging sources of exposure.

This discussion document relates to the second aim.

Background

A recent Unicef report estimated that there are between 180 and 280 thousand children under 19 in the UK with an elevated blood lead concentration. (The Toxic Truth, 2020). In the USA the CDC estimate that there are 535,000 under 6s, which would equate to around 109,000 in the UK given the same lead exposure. The USA and UK have had a similar history of the use of lead, but the USA has had lead poisoning prevention programmes for the last 20 years (Dignam et al, 2019). There has been no measurement of the prevalence of elevated blood lead concentrations since the mid-1990s.

Abbreviations

BLC	Blood lead concentration
eBLC	Elevated blood lead concentration
LEICSS	Lead Exposure In Children Surveillance System
LEAPP	Lead Exposure and Poisoning Prevention
NIHR	National Institute for Health Research

Study Design

Objectives

The objectives of the prevalence study would be to estimate the number of participants with blood lead concentrations above, or equal to, the new intervention limit of 5µg Pb/dL whole blood.

Purpose

The purpose of this study is as much political as scientific. Depending on the findings, this may have a pivotal impact on the following:

- The National Screening Committee review of screening lead in children
- Health policy including the:
  - NHS Long Term Plan
  - “Giving every child the best start in life” programme
  - “Building our Future: Laying the Foundations for Healthy Homes and Buildings” white paper produced by the Healthy Homes and Buildings All Party Parliamentary Group
- Political will to address the problem of lead exposure and toxicity

Scope

The scope of the study would be:

- Children aged less than 72 months
- Total whole blood lead concentration
- England, plus identified high risk areas

Demographics

To estimate the prevalence across the English population the sample set should be as random as possible. However, from experience in the USA, it is known that lead exposure is more prevalent in deprived urban areas, or areas with a history of industrial processing or use of lead.

It would seem that two participant populations are needed:

a) As random as possible using multiple study centres
b) Selected worse case study centres in at risk population locations

Data

The prevalence study does not need much data about each participant, just the blood lead concentration would be enough to answer the basic question of how many children have eBLCs. However, the output would be more valuable if some demographic information could be included and analysed, but within the limits of ethical and data privacy considerations.

This data may include:

- Age
- Gender
- Race
- Postcode, perhaps only the outward code
- Age of home
- Type of home (house, flat, ..)
- Tenure of home (owned, rented)
- Occupation of the parents
- Hobbies of the parents
- Diagnosed health conditions using ICD10 coding

Sample Size

The sample size needs to be large enough to provide an estimate of the national population. A sample size calculator is provided by Creative Research Systems. The following inputs were used to calculate the sample size:

Parameter	Value	Reason
Confidence level	95%	Commonly used confidence interval
Population size	3,876,394	Number of children under 72 months. Derived from ONS data with an adjustment to remove data from Wales.
Percentage, specificity	2%	Prevalence of eBLCs in the USA is around 2%.
Margin of error, confidence interval	1%	Assuming the same prevalence in the UK an estimate in the range 1% to 3% would be adequate
Result	**760**	**Sample size needed**

Subsets selected by demographic attributes would be for smaller populations so require smaller sample size. If the specificity is larger, then a larger sample size would be needed to achieve the same confidence level.

Note that the National Screening Committee will only consider data with at least 500 participants.

Existing Sources

Instead of collecting new blood samples, consideration could be given to utilising existing sources. Some cohort studies have retained samples of blood and teeth. However, the blood samples may only be serum and it needs to be established whether this would be a reliable surrogate for whole blood in estimating prevalence of eBLCs. The same applies to deciduous teeth. Some studies only included adults and it may not be appropriate to infer child BLCs from adult data.

Known, or potential, sources of retained samples are:

- Blood
    - Blood Spot Screening
        - It has been suggested that a measure of BLC could be included in neonatal screening, but this is far from being implemented
    - Generation Scotland
        - Adult serum and whole blood samples
    - Born in Bradford
        - The children in the cohort are now aged around 12
    - UKBioBank
        - Only adult blood samples
    - Northern Ireland Cohort
        - Unknown
    - ONS Longitudinal Study
        - Unknown
    - National Diet and Nutrition Survey
        - Unknown
- Teeth
    - Centre for Longitudinal Studies Every Tooth Tells a Story Project
        - 4000 deciduous teeth collected in 2008

Method

Measurement

Device

Clinical, venous, blood samples in the UK are currently sent to a UKAS accredited laboratory for analysis. For this study this may be unnecessarily invasive. An alternative could be to employ a finger-stick capillary test.

An example of a capillary test is the Magellan Lead-Care II analyser. Results are obtained in 3 minutes per sample. This analyser has a BLC reporting range of 3.3 – 65 µg/dL. Because we only want to know how many samples are above 5 µg/dL this would be adequate.

The cost is low, examples are:

- Price per unit $3,400.00 / Each
- Price per test $532.00 / Pack of 48

Skills

No advanced clinical skills are required for capillary sampling with this analyser. Training can be achieved with a short video and competency test.

Whether a nurse of phlebotomist would be required would be an ethical or regulatory matter.

Sample Collection

Recent CoViD-19 related surveys included participants taking their own blood samples. However, the Lead-Care II system needs blood that is less than 24 hours old so a mail-in procedure would not be appropriate.

It is therefore likely that sampling will need to be done in a specific location where cleanliness requirements can be met. One potential problem with the test is lead contamination on the skin where the prick is applied.

Recording

Results of blood tests should be recorded along side demographic data. This would preferable be electronically in an encrypted file backed up to a password protected cloud service.

A spreadsheet should be sufficient for recording study data which would require a laptop computer. An internet connection, either provided by the study centre or a telephone hotspot would be required to keep the data safe.

Analysis

Data from study centre spreadsheets would be collated for analysis.

Prevalence

The simplest analysis would be how many participants had eBLCs. Other breakdowns by demographic factors could also be performed. Extrapolations from the study data to local or national populations would require appropriate statistical methods to calculate confidence intervals.

Economic

An additional objective is to perform an economic evaluation of the findings. The metrics presented in some existing studies might be utilised for this including

- Attina and Trasande, 2013
- Pichery et al, 2011
- Unicef, 2020
- Landrigan, 2002
- Gould, 2009

Survey Centres

Number and Location

The number and location of survey centres would be defined during more detailed study design. A possible initial aspiration might be 7-10 survey centres with around 100 participants in each.

> Francis J. DiTraglia and Ludovica Gazze of the Departments of Economics, University of Oxford and University of Warwick, respectively, have proposed a study into lead exposure in the UK the first step of which could “construct highly localized projections of lead hazards in the UK”. This would utilise existing data and could help identify areas that would be appropriate for worst case survey centres as well as more typical locations.

Location selection might also be informed by the 360 Dust Analysis programme that is collecting and analysing vacuum cleaner contents for heavy metal contamination as presented on the Map My Environment online facility.

Facilities

Survey centres would not require many facilities, but would need the following:

- A room or other confidential location
- A clean table or desk
- Skin cleanser
- A capillary analyser and sampling kits
- Someone to perform the blood tests and record the results
- Participant questionnaires

Possible Types of Centres

Centres could include:

- GP surgeries
- Hospital out-patient departments
- University premises
- Village halls
- Sports centres
- Shopping malls

Centre Recruitment

A general practice surgery would be ideal centre. These could be recruited in various ways:

- Approaching clinicians with a known interest in lead toxicity.
- Asking our own GPs if they would allow use of their practice.
- Advertising in suitable journals, newsletters or magazines.
- Posting on social media appropriate groups

Staffing

It may be best that centres are in a health care setting so that services are available to deal with any emergencies such as fainting. It may be sufficient to have a first aider present or available. If a trained nurse or phlebotomist was required for other reasons then they might be expected to also be able to provide first aid.

Survey Period

The survey period in any one centre will need to be long enough to obtain sufficient samples. Assuming there are enough participants and a target of 100 samples per centre, we might assume the following

- Rate of sampling 6 per hour
- Sampling sessions per day 6 hours
- Samples per day 36
- Number of days 3

Pilot

In order to make assessments of how well the study is received by potential participants, and how sampling operates in real life, it may be appropriate to run a pilot at one survey centre.

Participant Recruitment

Requirement

The study will require a representative sample of the UK population or of a selected area. Methods to attract participants should avoid selection bias on any demographic grounds.

Bias

Selection bias may be a result of concerns about lead exposure. Parents who are aware of this may be more likely to present their child for sampling. However, their awareness may mean that their home is less likely to contain lead risks. For others it may be the first time that they have been made aware of domestic lead risks. Some may then prefer denial and not want to know if their child has an eBLC.

The study design and public materials will need to take this into consideration.

Invitations

Invitation to take part in the study could be provided by several routes

- GP, or other health care professional, consultations
- Posters and leaflets in the health care facility or blood donation clinics
- Posters in the local area – libraries, shops, noticeboards
- Social media posts in local groups

Content

The content of the invitations would need provide information that will attract participants, but not be alarming. It may include the following information:

- Title “Lead Exposure Study - Invitation”
- Organisation owning the study
- Aims
- Why lead exposure is a concern
- How you can help
- Session dates
- Links to online information, with QR code

Indemnity and Insurance

It may be assumed that those responsible for the study will need to indemnify the study centre and participants against any negative outcomes. This would require public liability insurance.

Risk Assessment

The study should provide a risk assessment to both the study centres and participants together with control measures. The study centre and participants should be asked to sign off their acceptance of the risk assessment.

Costs

Project Team

Work to be done by the project team may need to be funded and would include:

- Project management
- Study design
- Presentation to ethical standards authorities
- Design of centre and participant invitations
- Recruitment of survey centres
- Collation and analysis of results
- Authoring a paper for publication

External Costs

Items that may need to be considered when costing the project include:

- Room hire
- Nurse or phlebotomist payment
- Blood analysis device
- Blood analysis consumables
- Printing invitations
- Publishing costs

Funding

It was initially suggested that the National Institute for Health Research (NIHR) could be approached for funding.

Ethical Considerations

What if eBLC is found?

The primary ethical concern may to decide what to do if an eBLC is found in a participant. The obvious next step would be to alert their GP who should request a confirmatory venous blood test. If this confirms an eBLC then the local health protection team should be engaged to investigate the source of exposure.

The participating parent could be given information on how to reduce lead exposure.

Health Protection Team

It may be unlikely, but one potential consequence of the study is that there a localised panic about lead exposure resulting in extra work for the local health protection team and demand for venous blood tests requiring extra capacity in laboratories. The local health protection team should be alerted before the sampling period starts.

Plumbophobia

It is possible that the results of the test, or even the participation invitations, could trigger OCD or anxiety. GPs should be alerted to this so that they are prepared.