# Considerations for Planning Childhood Blood Lead Surveillance

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# Acknowledgments

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#### Disclaimer

This is a living document and will be updated when new or additional relevant information and technologies or products become available.

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# **Abbreviations & Acronyms**

AAS	Atomic Absorption Spectrometry
BLL	Blood Lead Level
CDC	Centers for Disease Control and Prevention (USA)
ETAAS	Electrothermal Atomic Absorption Spectrometry
FAAS	Flame Atomic Absorption Spectrometry
FDA	United States Food and Drug Administration
GFAAS	Graphite Furnace Atomic Absorption Spectrometry
HIV	Human Immunodeficiency Virus
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IQ	Intelligence Quotient
LOD	Limit of Detection
μg/dL	Microgram Per Deciliter
μL	Microliter
mL	Milliliter
NHANES	National Health and Nutrition Examination Survey
ULAB	Used Lead Acid Battery
U.S.	United States
WHO	World Health Organization

# **Background and Objectives**

Lead is a potent toxin that can severely affect the mental and physical functioning of children and the health of adults. Young children are particularly susceptible to lead poisoning because they absorb far more lead from their environments than adults and because their central nervous systems are still developing.<sup>1</sup> Lead exposure can result in reduced intelligence quotient (IQ), behavioral changes, and reduced educational attainment and lifetime earnings.<sup>2–5</sup> These impacts on children occur at even low levels of lead exposure and affect a child's potential to thrive and succeed in the future.<sup>6</sup> Early detection and prevention of exposure to lead are particularly important as neurological and behavioral impacts due to lead exposure among children are generally irreversible. Blood lead surveillance is an important tool to serve this purpose.

## **Purpose of the document**

This document is meant to be used as a tool to facilitate discussion with national and local government institutions to explore the most suitable lead surveillance model for a given setting. This document provides an overview of options and considerations for designing a national or regional childhood blood lead surveillance. There are several approaches for surveillance strategies and survey platforms. The ultimate selection of an approach should be based on engagement with a broad group of stakeholders. The design options described differ with respect to a variety of goals and priorities for the surveillance, the potential for national and/or local exposure characterization, and the degree to which they rely on and consider existing infrastructure and needed resources. Final decisions and recommendations should be made in collaboration with the ministry of health and other key partners in the surveillance activities.

## Childhood blood lead surveillance

A childhood lead poisoning surveillance system typically involves monitoring the blood lead levels (BLL) among children and collecting other information that may indicate children's risks and sources of lead exposure. It is a critical component of a comprehensive lead poisoning prevention program as effective and comprehensive prevention begins with information obtained from surveillance (see Figure 1). Such

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surveillance can: (1) quantify and clarify the person, place, and time dimensions of lead exposure and health impacts to inform public health policy, priorities, and strategies; (2) serve as an early warning system for impending public health emergencies; and (3) document the impact of an intervention or track progress towards specified goals.

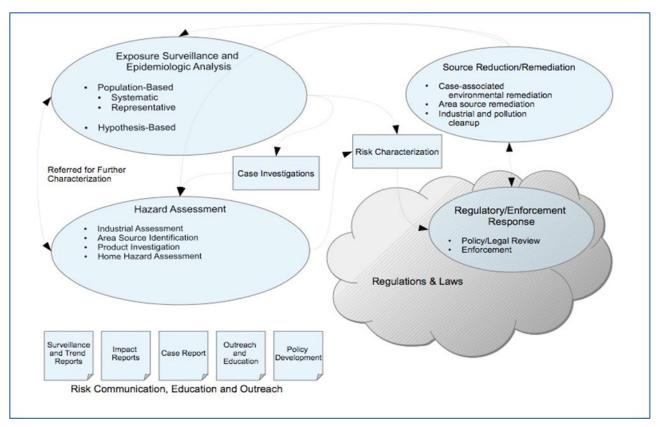


Figure 1: Framework of a comprehensive lead poisoning prevention program

Recognizing the importance and effectiveness of a surveillance system in preventing lead poisoning, several low- and middle-income countries have recently initiated such efforts including Mexico, Peru, Philippines, Georgia, and China. In Table 1, we list a few recent surveillance pilots and their characteristics. Findings from these surveillance systems have been used to establish or update clinical guidelines as well as develop policies to regulate lead contamination in specific products. However, blood lead surveillance and local data on childhood lead exposure are still lacking in many countries. An ongoing study reported that, as of July 2022, only 39 countries have measured the BLLs of children in general populations (Ericson et al., Manuscript in preparation). Building a

blood lead surveillance system to collect local data can be a key step to increase awareness and motivate actions from the government in areas with a limited understanding of lead poisoning. These data would inform the government of the prevalence and severity of lead poisoning among children and the geographic variability in its occurrence and illuminate the most significant sources of exposure. They will also be necessary for planning for future interventions and developing policies and programs to protect the health of children and the nation's future.

Country	Features	
Peru	<ul> <li>Nationally representative active surveillance</li> <li>Clinic-based sampling, with comprehensive neuro- developmental assessment</li> <li>Government-led</li> <li>Field instrumentation for capillary blood</li> <li>Paired with environmental sampling</li> </ul>	
India (states of Bihar and Tamil Nadu)	<ul> <li>Statewide active surveillance</li> <li>Household-based sampling</li> <li>NGO/research institution-led</li> <li>Field instrumentation for capillary blood</li> <li>Paired with environmental sampling</li> </ul>	
Philippines, Georgia	<ul> <li>BLL surveillance paired with the National Nutritional Survey/ National Multiple Indicator Cluster Survey</li> <li>Lab-based venous blood analysis</li> </ul>	

#### Table 1: Examples of recent blood lead surveillance in low- and middle-income countries

## **Surveillance Design**

## Surveillance objectives

The design of a surveillance system should be guided by the main objectives that the government wants to prioritize and achieve. Identifying and agreeing upon these objectives can inform the scope of work and necessary components of the system. For example, if the government aims to understand the major sources of lead exposure in

children with elevated blood lead levels, then conducting household questionnaires paired with blood lead testing will be valuable. Below is a list of objectives that can be achieved through a surveillance system.

- Characterization of the problem: evaluate the magnitude of lead poisoning by assessing blood lead levels and understanding the distribution of lead poisoning in different communities, and, depending on system design, by demographic characteristics, including age, gender, parental occupation, and behavioral and housing characteristics.
- Hotspot identification for effective resource allocation: identify at-risk geographic areas and groups to help prioritize planning of community-based, primary prevention interventions targeted to the highest risk areas (e.g., environmental remediation, health services for early identification and treatment, capacity building).
- Source identification: identify existing and emerging sources of exposure and inform policy and interventions to remove or reduce these sources to ensure safe living environments.
- Measurement of progress and evaluation: evaluate exposure trends over time and determine the effectiveness of existing and future policies and interventions. This can also contribute to evaluating the timeliness and efficacy of case management services available to children with lead poisoning.
- Better case identification and management: improve knowledge and awareness of lead poisoning prevention and treatment in pediatric health care providers and in parents for early detection and timely interventions.

## Surveillance type

There are generally two types of surveillance: passive surveillance and active surveillance. Their strengths and limitations are described below.

 Active surveillance is a system where health care providers or the population are proactively and regularly contacted to <u>collect</u> information about health conditions. This system requires more time and resources but often collects more comprehensive data.

- Example: The U.S. National Health and Nutrition Examination Survey (NHANES) evaluates blood lead levels using a nationally representative sample in multiple cycles. This has been used to establish the BLL reference level and update the reference level in 2012 and 2021. Georgia, Peru, Mexico, and the Philippines have all taken the active surveillance approach, evaluating blood lead levels in a representative sample for the first time, and hope to repeat this effort in a few years.
- Function: Active surveillance provides high-quality data and often representative estimates to describe the problem in the population and provide comparable estimates over time. We suggest to consider a first-time representative BLL study as an "active surveillance" effort if it is designed to be replicable and with strong engagement of the government to inform public health practices.
- Passive surveillance is a system by which a health jurisdiction <u>receives</u> reports submitted from hospitals, clinics, public health units, laboratories, or other sources.<sup>7</sup> This approach often involves a legal mandate for health care providers and laboratories to report ("reportable" or "notifiable"). Reporting is typically accomplished through local collection and passed from the district/province level to the national level.
  - Example: In the U.S., low-income and disabled children with Medicaid insurance are required to get tested for lead before the age of 6. Young children at high risk of lead exposure (often determined through screening questions) are also referred for a blood lead test during doctor visits. Clinical laboratories and doctors' offices are required to report testing results to states and local health departments, which aggregate the data for local analysis and submit them to the <u>national blood lead surveillance database</u> organized by the U.S. CDC.
  - Function: Passive surveillance collects data at multiple levels, but it is often not representative and may be biased due to incomplete screening and reporting. When follow-up actions are required, this system can facilitate the investigation of lead poisoning cases and interventions as needed.

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	Passive Surveillance	Active Surveillance
Advantages	Inexpensive and relatively low effort	More targeted/detailed/consistent
	for health departments once	data
	established	More timely collection of data
		More control over data quality
Disadvantages	Only includes common or high-	Resource-intensive
	priority conditions	Needs dedicated personnel
	Missing/inconsistent data	
	Minimal data on risk factors	
	Delay in reporting	
	Dependent on other organizations	
	and their compliance	
	Difficult if no electronic reporting	
	system is available	
Example	U.S. childhood blood surveillance	NHANES
	Early warning and response system	Annual survey of lifestyle and
	Cancer registry	behavior risk factors

#### Table 2: Summary of characteristics and examples of two surveillance types

Different types of surveillance systems can be selected based on the objective of surveillance, existing knowledge and awareness, and available resources and infrastructure. An ideal active surveillance model will be government-led and implemented using a representative sample at a national or regional level. This is particularly important in countries where the baseline BLL is unknown and local data on childhood blood lead levels is lacking. This surveillance could be conducted routinely (every three to five years) to provide an up-to-date understanding of lead exposure among the general child population and inform policy decisions. The major challenge for establishing this type of surveillance is to get government buy-in when little is known, recruit a representative sample, and build it in a way that sustains future cycles after the end of the program (most likely through incorporating it into government-owned surveys or programs). An approach that may help address some of these challenges is to incorporate blood lead surveillance into existing active surveillance efforts, such as multicycle national health surveys. Many countries started with active childhood blood lead

surveillance because they needed high-quality data to understand the severity of the issue to help improve awareness and engage public interest.

While passive surveillance can be less costly, the system often takes a long time to establish. There are three main criteria to be assessed before planning a passive surveillance system: political will and mandate, screening/testing capacity, and adoption of lead screening protocols in clinical practice. This requires government buy-in since mandates or guidelines on screening and reporting of lead exposure or blood lead level by the local health authorities are necessary. This needs to be followed by building respective local, regional, or national blood lead testing capacity and developing effective screening tools (e.g., risk screening questionnaire). Adopting universal lead screening during routine pediatric visits by medical professionals is one means by which such passive surveillance can occur, but it could also be piloted on a smaller scale. This may require both policy changes (e.g., clinical guidelines and insurance coverage for BLL testing) and education for doctors. Follow-up actions on children with elevated levels detected in this surveillance should also be planned to maximize its benefit.

## Surveillance sites and population

While a national-level surveillance program with sampling sites across the country is ideal, this can be difficult for countries with complex geography, diverse population characteristics, and overburdened health systems with limited resources. Piloting surveillance at a smaller scale (e.g., province, city, and district level) can be a good way to assess the need for wider surveillance and engage further political interests.

We recommend that surveillance prioritize children ages 1 through 5 years old because this age group is most vulnerable to health impacts caused by lead. Clear inclusion criteria should be established to determine who will be eligible for enrollment in the surveillance. Some common factors to consider in the inclusion criteria include age, length of time at residence, general health condition, and parental consent to participate.

## **Sampling strategies**

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A nationally representative sample is highly recommended for blood lead surveillance to understand BLLs among children. There are two ways to obtain this representative sample. If there are existing health surveys involving a nationally representative sample of children, then it will be most cost-effective to incorporate the surveillance activity into future waves of these surveys. If this is not possible, then a nationally representative sample can be obtained using novel recruitment and data collection via a complex, multistage sampling strategy.

#### Adding to existing national surveys or routine surveillance

Many countries regularly conduct national or regional surveys or surveillance to understand the demographic, health, nutrition, and behavior of the population using a representative sample. Identifying appropriate surveys will help save time and human resources in recruiting participants for blood lead surveillance. There are several factors to consider when selecting candidates from existing surveys or surveillance.

- Target population: Ideally, the survey/surveillance should sample children of the same age range in each cycle since blood lead levels generally decrease as age increases.
- Sample collection: Does the survey collect blood samples or does it rely on some health outcome assessment (e.g., body mass index, weight) in person rather than conducting the survey online or through phone calls?
- Relevant health information: Does the survey collect information on the nutrition or health status (e.g., anemia, stunting, underweight, wasting) of the children, so that these factors can be linked with lead exposure?
- Agency in charge: Is the survey organized by a government agency with a strong connection to the ministry of health?

In addition to adding blood lead testing to the next cycles of existing national surveys or surveillance, the country can also consider testing lead levels in stored blood samples. Previous studies and surveillance may have collected blood samples for health conditions related to vector-borne, vaccine-preventable, or other infectious diseases; routine laboratory diagnostics; and during antenatal care for HIV testing, blood sugar testing, and hemoglobin estimation. If additional blood samples are accessible after the initial tests

and proper consent can be obtained, they can be considered for testing lead toxicity or other heavy metals toxicity. This will only involve accessing and evaluating stored blood samples and testing them at certified labs. However, this may not be representative of the population if only people with suspected health conditions were assessed.

#### Establishing a new sample

If incorporating childhood lead exposure into a national survey is not possible, then the government can establish new representative samples following our recommended steps below at the national or provincial levels using a multi-stage, stratified, probability sampling design to enroll participants for surveillance.\*

- Step 1: Define the surveillance area. Theis involves specifying provinces and regions that should be included or excluded based on the surveillance goal, target population, and success in recruitment (e.g., reachability, safety). Sample size can be calculated using the WHO STEP
- Step 2: Define and randomly select a subset of clusters. The surveillance area will need to be divided into clusters which can be administrative areas (e.g., districts, towns, and villages) or areas used for census (e.g., census block, census enumeration areas). A subset of these clusters will be randomly selected. During the selection, we recommend taking into consideration the child population of each cluster. Other important factors to consider include urbanicity and socioeconomic status and whether there is a need to oversample certain communities or a desire to stratify findings by these factors.
- Step 3: Randomly select households/participants. We list a few common methods below and summarize their strengths, limitations, and cost considerations.
  - Simple random sampling: Obtain a list of all households with eligible children living in the study area and their contact information. Participants will be randomly selected from the list.

<sup>&</sup>lt;sup>\*</sup> While childhood blood lead surveillance is emphasized in this document, there is a strong rationale for better understanding adult exposure as well. Countries may consider supplementing childhood monitoring with adult monitoring if it adopts an integrationist approach with one or more of these existing national surveys.

- Health clinic cluster sampling: Obtain a list of eligible children and their contact information using records from a local clinic in the selected area and randomly select final participants using this list.
- Health camp cluster sampling: Organize a health camp in the selected area on a specific date. Local health workers will inform all households about this health camp and invite households with eligible children to this health camp. A random sample will be drawn from all eligible children who visited the health camp.

Option	Strength	Limitation
Simple random	If a list exists, then simple to	A complete list of all eligible
sampling	implement.	households and/or children may not
		be available; the sample is spread
		over a large area and may be hard
		to contact.
Health clinic cluster	A centralized recruitment	Need to identify and establish a
sampling	location; may be easier to	relationship with community health
	obtain consent.	centers; a child who has not visited
		the selected clinic has no
		probability of being sampled.
Health camp cluster	Centralized location and time	Will need to obtain support from
sampling	for all recruitment and sample	local health authorities and involve
	collection. Will not be biased	local health workers in community
	by the child's health status or	mobilization before the camp day.
	utilization of health services	Subject to non-representative
	(e.g., visits to a specific	participation bias based on the
	clinic).	perceived likelihood of risk.
Kindergarten or	Centralized location and time	The sample may be biased as
school-based	for all recruitment and sample	certain age and demographic
sampling	collection. Easy to obtain a list	groups may not be captured (e.g.,
	of eligible children.	children under the age of 2;
		households far away or cannot
		afford school costs).

#### Table 3: Summary of methods to sample households/participants

### **Blood sample collection**

Measuring lead levels in blood is the most widely accepted tool for screening and diagnostic testing of lead poisoning. Although other human tissues and fluids, such as hair, nail, urine, and bone also reflect lead exposure, they are subject to contamination, uncertain exposure time frames, and without standardized levels linked to outcomes.

We list the strengths and limitations of three common blood sample types below, summarizing observations from previous studies and WHO's guidelines on analytical methods for measuring lead in blood.<sup>8</sup> Capillary samples are typically drawn from lanced fingertips. Venous samples are typically drawn from arm veins and are of higher volume than capillary samples. At present, dried blood spots have limited application in blood lead surveillance, especially in low-resource settings. This method is vulnerable to environmental contamination, and laboratories that can certify filter papers and analyze dried blood spot samples are almost exclusively located in North America and Europe.<sup>9</sup> There are several factors to consider when choosing between capillary and venous blood to determine the most suitable blood sample type.

- Purpose of the testing: Overall, capillary blood is recommended for screening purposes. If a concerning blood lead level is reported, then a venous blood sample is recommended for diagnostic testing.
- Paired analytical method: Capillary blood samples are generally paired with a portable analyzer due to the small sample volume (200-500 µL). While capillary blood samples can be analyzed using a laboratory-based approach with more advanced equipment and a highly controlled laboratory environment, many laboratories we identified in low- and middle-income countries only accept venous blood samples. In contrast, venous blood should not be analyzed by a portable analyzer (i.e., LeadCare). In 2017, the U.S. FDA cautioned against this after an investigation found that LeadCare tends to underestimate blood lead levels in venous blood samples due to a substance released from the rubber cap of tubes used to collect venous blood samples.
- Participant recruitment: There is suggestive evidence that participation rates will be greater, and less biased, when parents are offered less invasive testing. This

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may be particularly important when conducting surveillance in the general population as parents may be less willing to test their child compared to parents living in high-risk areas. More invasive testing also likely requires more time and effort from the local field team to mobilize participants.

- Environmental contamination: Capillary blood is overall more vulnerable to environmental contamination, so venous blood should be prioritized if environmental contamination is a particular concern (e.g., when low blood lead levels are expected).
- Sample collection, storage, and transportation: Collecting venous blood from young children often requires more experienced personnel (e.g., certified nurses and phlebotomists). Collection may fail if a child has a small or deep vein, dehydration, or certain health conditions (e.g., anemia), or is hard to keep calm. It's important to ensure the availability of experienced personnel for surveillance conducted in low-resource or remote areas. As venous blood samples are generally analyzed in a designated laboratory, it is also important to evaluate if the local team can provide suitable storage conditions, and assess whether there is a system that allows timely transport of samples. Capillary blood samples are generally analyzed on-site with a portable analyzer, so no storage and transportation are required.
- Additional testing: Because of the larger sample volume, a venous blood sample should be considered if there are other blood tests required (e.g., hematology tests, coupling lead analysis with that of other heavy metals).

Method	Strengths	Potential challenges
Capillary	Easier to obtain consent, less invasive	Vulnerable to environmental
	and painful for children, shorter	contamination; only collects a small
	procedure and time, and trained	volume of blood. Most commonly paired
	nurses and phlebotomists are not	with portable analyzer but occasionally
	required. If analyzed by portable	used with laboratory-based analytical
	analyzers, immediate results can be	methods.
	shared with caregivers, reducing the	
	follow-up burden on the study team.	

#### Table 4: Comparison of different types of blood samples

Vanaua	Essier to obtain a larger emount of	Dequires a trained medical professional
Venous	Easier to obtain a larger amount of	Requires a trained medical professional,
	blood; less likely to be contaminated;	more invasive, harder to obtain consent,
	sufficient volume to sub-sample for	possible to fail. Delay in reporting of
	lead isotopes to support source	findings. Uncertain national laboratory
	identification.	capacity for timely analysis. Venous
		blood samples can be paired with
		different laboratory-based analytical
		methods. Based on an FDA warning,
		venous blood should not be paired with a
		portable analyzer due to the risk of
		underestimation.
Dried blood spot	Minimal pain; stable and easy to store	Both filter and sampling processes are
Dried blood spot	Minimal pain; stable and easy to store and transport; no local laboratory	Both filter and sampling processes are highly vulnerable to origin and field
Dried blood spot		
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field contamination, no immediate result, and
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field contamination, no immediate result, and heterogeneous distribution may bias
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field contamination, no immediate result, and heterogeneous distribution may bias results. Likely needs to be shipped to a
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field contamination, no immediate result, and heterogeneous distribution may bias results. Likely needs to be shipped to a lab outside of the country (except for
Dried blood spot	and transport; no local laboratory	highly vulnerable to origin and field contamination, no immediate result, a heterogeneous distribution may bias results. Likely needs to be shipped to lab outside of the country (except for North America and Europe). Dried blo

## Analytical methods to measure lead in blood

We provide a table below to compare the strengths and limitations of several common methods to analyze BLLs based on observations in our previous projects and the brief WHO report.<sup>8</sup> On one hand, laboratory-based devices employing atomic absorption or ICP-MS technology are gold standards for evaluating blood lead levels because they have a wider detection range and operate free from environmental constraints. On the other hand, the portable analyzer (i.e., LeadCare) approved by the U.S. FDA has comparable accuracy with laboratory-based methods for BLL between 3.3 and 65  $\mu$ g/dL.<sup>10</sup> It is comparatively cost-effective, easy to operate, and can report instant results on-site using a small amount of blood (50  $\mu$ L) that requires no preservation or special handling. It is also possible to pair the portable analyzer and laboratory testing in surveillance to ensure data quality, such as using a portable analyzer to analyze most samples with a subset of samples (e.g., 10%) being validated by laboratory testing.

However, it is important to note that this often requires collecting both capillary and venous blood samples from a participant. Here are a few important things to discuss and consider when making the final decisions.

- Purpose of the surveillance: If the surveillance aims to screen and identify the proportion of children with elevated BLL (e.g., % of children with BLL above 5 µg/dL) a testing method with a higher limit of detection (LOD), such as the portable analyzer, may be chosen. However, if the surveillance aims to understand blood lead levels at all exposure levels, then it will be important to choose laboratory-based methods that generally have lower LODs.
- Expected BLL levels among children: It is important to note that the FDA-certified portable analyzer LeadCare (3.3 µg/dL) has a higher LOD than laboratory-based methods (often between 0.01-1.5 µg/dL). This can be a problem in areas where the BLLs of most children are expected to be lower than 3.3 µg/dL. The expected blood lead level can be estimated by reviewing previous studies that measured BLL among children (ideally among those without known pollution sources) in the area and modeled average blood lead levels from the Global Burden of Disease study or systematic reviews.
- Existing laboratory capacity: It is important to evaluate laboratory capacity for blood lead testing by identifying existing local laboratories and evaluating their characteristics. Several important characteristics to consider include analytical methods and LOD, quality management system, maximum testing capacity, standard turnaround time, and testing costs. Knowing the affiliation of the laboratories is also important as it may not be accessible to all organizations and the government may have concerns about using private laboratories. It often takes months to years to expand the capacity and improve the proficiency of laboratories. This must be taken into consideration when planning surveillance.
- On-site or local testing ability: Results of blood lead levels are available in minutes using a portable analyzer; results from laboratories will only be available in weeks or months. Getting testing results on-site can be a high priority if the government plans to provide education or recommendations for the participants based on their blood lead levels. A portable analyzer can also be distributed to allow testing locally in

remote areas since it is simple to use, and a community health worker can be trained to use it properly after a short amount of time.

Cost consideration: The cost of different analytical methods can vary based on the sample size, the purchase location, and available resources. For the portable analyzer, the cost is generally the sum of the initial purchase price of equipment (often between US\$2,000 and \$8,000) and the cost of testing kits (between US\$8 and \$30 per test). To establish or expand the capacity of a testing laboratory, the total cost will be a combination of the purchase of equipment, operating and maintenance costs (e.g., reagents, gases, electricity), and personnel costs. Generally, these costs are the highest for an ICP-MS laboratory because it requires more expensive instruments, a stable operating environment, and highly skilled technicians. Often, the cost per sample of a portable analyzer will be lower if there is no established laboratory or only private laboratory-based approach can be lower if there are established government or public health laboratories or by seeking discounted rates with a private laboratory.

Option	Strengths	Limitations
Portable	<ul> <li>Portable, battery-operated</li> </ul>	<ul> <li>Limited analytical working range</li> </ul>
analyzer	<ul> <li>Small blood volume (50 μL)</li> </ul>	(3.3–65 µg/dL)
(LeadCare II)	<ul> <li>Can be used at non-laboratory sites</li> </ul>	Higher risk of sample contamination
	<ul> <li>Uses capillary sample</li> </ul>	<ul> <li>Risk of low-biased results on</li> </ul>
	<ul> <li>Simple to use, does not require</li> </ul>	venous blood collected with certain
	skilled laboratory personnel	evacuated blood tubes
	<ul> <li>Low purchase and running costs</li> </ul>	<ul> <li>Unstable at high altitudes (above</li> </ul>
	Report results on-site within three	2,400 meters)
	minutes	
	<ul> <li>Has comparable accuracy with</li> </ul>	
	laboratory-based methods (U.S. FDA	
	validated and approved)	

#### Table 5: Comparison of different analytical methods

Flame atomic	<ul> <li>Short analysis time (seconds)</li> </ul>	<ul> <li>Large sample volume is often</li> </ul>
absorption	<ul> <li>Relatively easy to use</li> </ul>	needed (typically in mL) but the cup
spectroscopy	<ul> <li>Relatively few interferences</li> </ul>	method can allow the use of 50-100
(FAAS)	<ul> <li>Relatively low capital and running</li> </ul>	μL samples
	costs	<ul> <li>Relatively high LOD (5 μg/dL)</li> </ul>
		<ul> <li>Cannot be left unattended</li> </ul>
		(flammable gas)
		<ul> <li>Results cannot be obtained on-site</li> </ul>
		(only available after sending samples
		back to the laboratory for analyses)
Electrothermal	• Low LOD (< 1 μg/dL)	<ul> <li>Limited analytical working range</li> </ul>
Atomic	Can analyze small volume samples	<ul> <li>Requires some laboratory expertise</li> </ul>
Absorption	(50–100 μL)	<ul> <li>Longer analysis time</li> </ul>
Spectroscopy	<ul> <li>Can be fitted with autosampler so</li> </ul>	<ul> <li>Results cannot be obtained on-site</li> </ul>
(ETAAS)	multiple samples can be processed	(only available after sending samples
	<ul> <li>Well-documented applications</li> </ul>	back to the laboratory for analyses)
	<ul> <li>May be left unattended</li> </ul>	
	<ul> <li>No need for sample preparation</li> </ul>	
Inductively	• Very low LOD (0.02 μg/dL)	High purchase and running costs
coupled	Can analyze small volume samples	<ul> <li>Require highly skilled and certified</li> </ul>
plasma mass	(50–100 μL)	laboratory staff
spectrometry	• Very fast analysis time (< 1 minute)	<ul> <li>Analysis of a large number of</li> </ul>
(ICP-MS)	<ul> <li>Wide analytical working range</li> </ul>	samples is cheaper than ETAAS
	<ul> <li>Multi-element capabilities and can</li> </ul>	• Results cannot be obtained on-site
	be economical if used for large	(only available after sending samples
	sample runs	back to the laboratory for analyses)
	Potential to perform isotopic ratio	
	analyses with some forms of ICP-MS,	
	which may help to identify the source	
	of the lead	

## **Risk assessment of lead exposure**

There are several tools that we recommend using along with blood lead testing to screen a child's risk of lead exposure and understand potential sources of exposure. A risk assessment questionnaire is often conducted with the caregiver to collect information on factors related to a child's lead exposure including household demographics, home and surrounding environment, use of consumer products, and children's behavior and nutrition status. Analyzing the association between these factors and blood lead levels can help understand the important factors that help predict blood lead levels in this population and inform the design of future risk screening tools. In areas with limited blood lead testing ability, the questionnaire can also be conducted before blood lead testing to evaluate a child's risk and prioritize testing for high-risk children.

Environmental lead risk assessment can help identify lead contamination in the home environment and understand the contribution from different sources. This is often done through a home visit to test lead levels in environmental samples such as soil, dust, water, paint, and other everyday household products (e.g., food, toys, cookware) collected in and around the household. If environmental assessment cannot be conducted for all households, we suggest prioritizing households with children with elevated blood lead levels. If resources are available, we suggest randomly selecting a subset of all households that participated in blood lead surveillance which will provide information on potential sources of lead exposure for children across all blood lead levels. Overall, the final decision should be made based on knowledge of local BLLs, available resources, and preferred workflow.

## **Health Assessment**

If the goal of surveillance also includes evaluating the health impacts of lead exposure, then health assessments can be conducted along with blood lead testing. This can be done by assessing sub-clinical health symptoms (e.g., headache, abdominal pain) and conducting anemia screening, neurodevelopmental assessment, and nutrition evaluation.

# **Surveillance Implementation**

## Protection of human subjects

Before starting any surveillance sampling, it is necessary to consult government and implementation partners to determine if approval and/or exemption from the ethical review board/committee is needed based on national and local regulations. Informed

consent should be obtained from the children's guardians after providing adequate information on the purpose of this study and potential risks and benefits. Protocols should be developed to protect the participants' privacy and ensure data safety according to national and international standards.

## **Field staff**

We recommend recruiting field staff who are local to the sampling area to improve participation and engagement through their connection and understanding of local culture and norms. Potential candidates for field staff include health workers from primary health care centers, local health department staff, and volunteers from nursing, public health, and medical programs in local colleges. If venous blood samples will be collected, a pediatric phlebotomist or an experienced nurse should be included where possible and follow medical standards of practice.

The responsibility of the field team will include recruiting participants, collecting samples, conducting surveys, and educating the participants. When a portable analyzer is used, one of the field team members will also need to be trained to analyze the blood samples on-site. We provided an example of a team of three with their responsibilities.

- Supervisor (one person): responsible for introducing the team and procedure to the subjects, consent form administration, visit tracking, navigation, blood storage, and coordination between field team members and the local health department. This team member should have some training in public health or epidemiology.
- Interviewer (one person): responsible for questionnaire administration, results sharing, and health education for participants.
- Nurse/phlebotomist (one person): responsible for obtaining the blood sample, conducting the blood lead test (if a portable analyzer is used) and health assessment, and monitoring adverse health events. This team member should have some clinical training.

## **Results sharing and counseling**

A plan for sharing findings and recommendations with participants should be developed in consultation with local stakeholders and health authorities. Sharing the testing results and understandable interpretations with caregivers of tested children is a first step toward effective education in surveillance and is typically an ethical requirement of follow-up and reporting. Using portable analyzers allows participants to receive their results before the end of the visit. If blood samples were sent to be tested in the laboratory, then the surveillance team should maintain the contact information of participants and determine a reliable way to share the results with participants after the visit. Depending on the goal and available resources, different educational information can be provided for different audiences to achieve the goals of the surveillance.

Audience	Educational information	Goal of education
Caregivers of tested	BLL results and interpretation, source of	Provide targeted recommendations
children	lead exposure, recommended actions for	based on BLL levels
	reducing lead exposure and/or seeking	
	treatment	
Community health	Health impacts of lead, source of lead	Increase awareness and
workers	exposure, actions for reducing lead	knowledge of lead poisoning
	exposure	among community health workers
		so they can help educate parents in
		their communities
Primary care	National or WHO guidelines for clinical	Equip local medical professionals
provider/	management of exposure to lead	with knowledge for timely detection,
pediatrician/nurse	exposure in children and pregnant women	diagnosis, and treatment of lead
		poisoning among children and
		pregnant women

#### Table 6: Summary of options for educational efforts during surveillance

A detailed protocol is needed for children with elevated BLLs who require interventions, to effectively communicate risk to parents, and to refer these children to the national and local health care system for further assessment and treatment. This protocol should be in line with the local guidelines as well as the World Health Organization guidelines for clinical management of lead exposure.<sup>6</sup> Consulting local experts such as physicians and clinical toxicologists and identifying specialized facilities for advanced treatment (e.g., chelation therapy) can be helpful in developing the protocol. Depending on the local law

and regulations, cases of lead exposure or poisoning may need to be reported to the local health service or the ministry of health for further evaluation and action.

## **Data management and dissemination**

Surveillance data can be collected in two ways: paper forms and electronic devices such as smartphones or tablets. Generally, electronic data collection is preferred for higher data quality, streamlining interviews, and minimizing transcription errors. As internet access may not be available in remote areas, we recommend using electronic data collection systems that do not require internet access in the field and can upload results once a connection is possible. However, if the area lacks access to electronics or a stable power supply, paper forms can be used and then submitted to a centralized location for data entry. If blood lead surveillance is integrated into an existing program, then data will be collected, stored, and reported based on the program's current approach.

A unique identifier assigned to all participants can help link information collected during the surveillance through different components (e.g., BLL testing, risk assessment questionnaire, environmental assessment). Surveillance data should be consolidated, cleaned, and managed centrally, and feedback about improving the quality of data collection should be communicated back to field teams.

Analyzing the surveillance data will also require an experienced epidemiologist or biostatistician and the use of statistical software to account for the complex sampling design and weighting. Descriptive statistics should be used to describe household and child demographics and characteristics of the study population (e.g., average BLLs). Bivariate and multivariate analyses can be used to examine risk factors for elevated BLLs that were obtained from the household survey and environmental sampling.

Aggregated and de-identified data from the surveillance should be linked to other existing databases on lead sources or exposure (e.g., lead levels in drinking water, ULAB recycling, or mining sites). An integrated database can be a helpful tool to assess the regional risk of lead exposure and identify potential high-risk areas for screening and interventions. Some governments have also made such information and findings available online through data portals for the public (see Figure 4).

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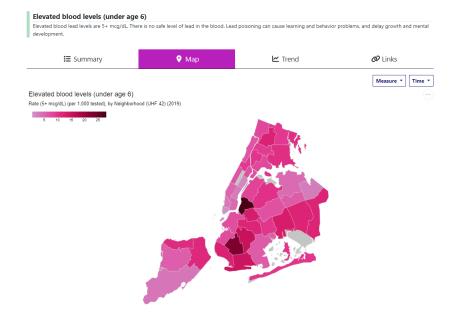


Figure 2: Data portal displaying information collected from blood lead surveillance in New York City. (Link)

Different types of dissemination products can be developed based on the target audience and goals of communication. Below we summarized a list of different audiences, the primary aim of informing these audiences, and some examples of dissemination products. When developing the dissemination products, findings should be discussed and interpreted with key stakeholders to help provide local context and credibility.

Table 7 Dissemination pr	oducts for different audiences
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Audience	Primary Aims	Dissemination Products
Parents/tested people	Education and personal action	Exposure reports, health
		guidance, health referrals
Government officials	Awareness, information for public	Report(s) of findings
	dissemination, prioritization of	Sub-national reports
	interventions and investment	Data exploration and
		visualization portal
Policymakers/civil	Prioritize policy actions to address	Data briefs, data portal,
society stakeholders	leading risks and at-risk populations	policy briefs

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General public	Increase awareness of risk factors,	Social media, press
	drive the public to physicians as	releases, interviews,
	appropriate, build support for policy	infographics
	interventions	
Health care workers	Inform clinical practice, embolden	Clinical alerts, professional
	advocacy	meeting presentations,
		continuing education
Academics	Elevate lead as an issue for further	Research manuscripts,
	study	professional conference
		presentations

# **Stakeholder engagement**

Incorporating blood lead surveillance into a comprehensive approach to prevent lead exposure will require cross-sectoral and multi-level collaboration among different government departments and national and local authorities. Below is a summary of key stakeholders and their suggested roles/functions in developing and implementing surveillance.

- Ministry of health or provincial health department: Depending on the scope of the surveillance (national or provincial), the ministry of health or the provincial health department will be the leading organization in designing the surveillance plan and coordinating the surveillance effort with local health departments.
- Local health department: The local health department will be an important partner in implementing the surveillance effort as they can help identify and mobilize local health workers and resources to implement the surveillance.
- National/regional public and private laboratories: National and regional public health laboratories will be the main implementors to analyze the blood samples if laboratory-based methods are selected. If public laboratories do not have enough capacity to analyze the expected number of samples, then it will be important to explore opportunities to use laboratories in academic institutions and private companies through agreements.
- Primary health care providers: In a passive surveillance system, primary health care providers will be the first level to identify and test children for elevated blood

levels. In a clinic-based active surveillance system, primary health care providers can also be mobilized to be implementation partners for the surveillance. Even if they are not part of the field team, they should be informed of the study and be aware of potential support or treatment they can provide for children with elevated BLLs. They can also be important recipients of educational efforts to increase awareness of lead poisoning and improve its timely detection and treatment.

- Other government departments: Childhood lead poisoning prevention requires coordination and policy strengthening across sectors, therefore, findings from surveillance should be shared to facilitate coordination among agencies in the health, environment, trade and industry, finance, and labor sectors.
- Local and national policymakers: Policymakers should be involved in identifying the main goal of surveillance and considered as the main users of findings from surveillance. Summaries of results should be communicated to policymakers in a manner that helps inform policy decisions such as identifying policies that reduce major sources of lead exposure or strengthening health services for children experiencing lead poisoning.
- Civil society stakeholders: It is also important to identify and engage with key local and international organizations that focus on addressing lead poisoning and/or children's health. Several international organizations that are currently working on lead poisoning prevention with governments in multiple countries include Pure Earth, UNICEF, WHO, and Lead Exposure Elimination Project (LEEP). These organizations can play an important role in helping build connections with the government, disseminating surveillance findings, and advocating for policy actions.

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