Original research

Who tests for lead and why? A 10-year analysis of blood lead screening, follow-up and CNS outcomes in a statewide US healthcare system

Aaron Reuben ,[1,2] Ralph Ward,[2] Alex O Rothbaum,[3] Vickey L Cornelison,[2] Sarah Huffman,[2] Lisa M McTeague,[2] Michael G Schmidt,[4] Aaron J Specht,[5] Dean G Kilpatrick[2]

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[1]Department of Psychology and Neuroscience, Duke University, Durham, North Carolina, USA
[2]Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, South Carolina, USA
[3]Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, Georgia, USA
[4]Department of Microbiology and Immunology, Medical University of South Carolina, Charleston, South Carolina, USA
[5]College of Health and Human Sciences, Purdue University, West Lafayette, Indiana, USA

Correspondence to
Dr Aaron Reuben, Duke University, Durham, North Carolina, USA; aaron.reuben@duke.edu

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ABSTRACT

Objectives This study aims to determine (1) which providers in US healthcare systems order lead tests, why and at what frequency and (2) whether current patient population lead levels are predictive of clinical outcomes.

Methods Retrospective medical record study of all blood lead tests in the Medical University of South Carolina healthcare system 2012–2016 and consequent evidence of central nervous system (CNS)-related disease across a potential 10-year window (2012–2022).

Results Across 4 years, 9726 lead tests resulted for 7181 patients (49.0% female; 0–94 years), representing 0.2% of the hospital population. Most tests were for young (76.6%≤age 3) and non-Hispanic black (47.2%) and Hispanic (26.7%) patients. A wide variety of providers ordered tests; however, most were ordered by paediatrics, psychiatry, internal medicine and neurology. Lead levels ranged from ≤2.0 µg/dL (80.8%) to ≥10 µg/dL (0.8%; max 36 µg/dL). 201 children (3.1%) had initial lead levels over the reference value for case management at the time (5.0 µg/dL). Many high level children did not receive follow-up testing in the system (36.3%) and those that did often failed to see levels fall below 5.0 µg/dL (80.1%). Non-Hispanic black and Hispanic patients were more likely to see lead levels stay high or go up over time. Over follow-up, children with high lead levels were more likely to receive new attention-deficit/hyperactivity disorder and conduct disorder diagnoses and new psychiatric medications. No significant associations were found between lead test results and new CNS diagnoses or medications among adults.

Conclusions Hospital lead testing covers a small portion of patients but includes a wide range of ages, presentations and provider specialities. Lack of lead decline among many paediatric patients suggests there is room to improve provider guidance around when to test and follow-up.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Lead is a widely distributed toxicant present in older homes, soils and certain foods. Decisions about when to test patients for lead often fall to individual healthcare providers, but it is not clear whether current testing decisions match guidelines or patient need.

WHAT THIS STUDY ADDS

⇒ Across years in a major US hospital system, only 0.2% of patients were tested for lead each year, although testing represented a wide range of patients ages, presentations and provider specialties. Many high lead-level paediatric patients did not receive follow-up testing in the system (36.3%) and those that did often failed to see levels fall below reference values (80.1%). Non-Hispanic black and Hispanic patients were more likely to see lead levels stay high or go up over time.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Lack of lead testing among elderly patients and lead decline among many paediatric patients suggests there is room to improve provider guidance around when to test and follow-up.

INTRODUCTION

Lead is a neurotoxicant with a significant history of legacy contamination in the USA,[1 2] with ongoing use in multiple industries. Potential exposures to lead—through contaminated products, soil, water, food and dust in old homes—are a concern across the country but are particularly problematic in urban, marginalised and low-income communities with high rates of degrading lead-based water service lines, paints, telecommunication cables, and waste incinerator and lead-industry refuse.[3–5]

Even low-level lead exposure is believed to compromise child brain development[6] and adult mental,[7 8] cardiovascular,[9–11] and cognitive health.[12 13] The US Centers for Disease Control and Prevention (CDC) recommend regular lead exposure surveillance of children and pregnant women at-risk for exposure. In the absence of local surveillance programmes 'responsive to local conditions', the CDC encourages 'universal testing'[14] of blood lead levels among children. The US Occupational Safety and Health Administration (OSHA) meanwhile requires regular testing of blood lead levels among certain adults working in lead-related industries.[15]

Responsibility for US lead exposure surveillance is devolved to states, who report results to the CDC for nationwide compilation.[16] Within states, lead

testing is ordered by healthcare providers and offered by state public health departments.[16–18] With three exceptions, decisions about when and how often to test for lead are left to the decision-making of individual healthcare providers. The first exception is for infants covered by Medicaid, who are required to receive blood lead testing at 12-month and 24-month well visits. The second exception is for children living in 1 of 10 states and the District of Columbia that require universal testing at least once during an early-life well visit (typically age 12 months or 24 months) and for children in 1 of 8 states with 'targeted' testing requirements (typically for children living in 'lead risk' areas with high poverty rates, older homes and other risk factors).[19] The third is for adults working in lead-emitting industries who have been exposed to air lead levels above the 'airborne action level' of 30 $\mu g/m^3$ for ≥30 days/year identified by air-quality testing.[15]

There are potential shortfalls in this system.[20–23] For the past decade, the average Medicaid lead-screening rate among 24-month-old children was only 67.4%.[24] Millions of children live in states without universal or targeted testing requirements. In such states, fewer than 10% of children are estimated to be routinely tested for lead[19] and up to 30% with high exposure may be missed.[23] For vulnerable adults (eg, those >65 years) with potential non-occupational exposure, there are no state screening requirements or surveillance programmes. Thus, it is not clear how many vulnerable individuals not covered by lead testing may have potential exposure to lead. As the CDC notes, 'blood lead testing is initiated by healthcare providers and it is difficult to know why or how healthcare providers decide to test'.[16]

This study aims to help fill this information gap by investigating lead test results and follow-up care across a 10-year window (2012–2022) from a major academic healthcare system in the southeastern US (the Medical University of South Carolina academic medical system, MUSC Health) serving residents from South Carolina and adjacent states, all of which lack universal or targeted testing requirements.

First, we document initial lead test ordering in the MUSC medical record system across a 4-year window (2012–2016) by healthcare provider type, patient demographics and presenting diagnoses. Our goal was to determine 'who orders lead tests and why?' Second, we report rates of repeated lead testing across the 4-year window to determine whether CDC and OSHA monitoring guidelines for paediatric and adult follow-up testing are being satisfied.

Third, we examine the medical record for evidence of central nervous system-related disease (CNS) (developmental, psychiatric and degenerative) following initial lead testing across a 10-year observation window (2012–2022) to determine whether lead levels currently present in clinical populations are predictive of poor outcomes. We also test whether new CNS medications are prescribed during the follow-up period. Results are interpreted to inform clinical guidelines for healthcare practitioners, who must decide when to order lead tests and policy-makers, who must decide where devolution of testing responsibilities is working.

METHODS

Population

The study population included all individuals for whom a lead test was ordered by a healthcare provider between 17 June 2012 and 1 July 2016, at MUSC Health. MUSC Health is a tertiary care system based in Charleston, South Carolina, with sites throughout the state that draw patients from across South Carolina and neighbouring Georgia and North Carolina. In 2022, MUSC had 751 care locations in SC, 2500 in-patient hospital beds, 581 telehealth support sites and >1 million per-year patient encounters. Patients were included in the study if they had at least 6 months of in-system care prior to a first lead test order to ensure baseline diagnoses and medications were observed such that new diagnosis and new medications outcomes could be accurately identified.

Lead testing and exposure

The exposure of interest was a lead test order in the medical record and, secondarily, the lead test result. The lead detection limit available in the hospital system was 2.0 µg/dL; results below this limit were marked '<2.0 µg/dL.' Four exposure groups were established: none low (<2 µg/dL), medium (≥2 to <5 µg/dL), medium-high (≥5 to <10 µg/dL) and high (≥10 µg/dL). No level of exposure is considered safe. During the study period, the CDC recommended repeat testing for children within 3 months when lead levels are ≥5–9 µg/dL (changed to ≥3.5–9 µg/dL in November 2021) and within 1 month for levels 10–19 µg/dL. OSHA standards require semimonthly testing until adult blood lead levels are <40 µg/dL.[15]

CNS disease

Primary outcomes of interest included the provider type requesting each lead test and demographic variables for patients with test orders. Demographics included age (grouped by ages 0–3, 4–12, 13–17, 18–54 and ≥55 years), sex, race and ethnicity (non-Hispanic black, Hispanic, non-Hispanic white and other or missing).

Secondary outcomes of interest included new CNS-related diagnoses and new CNS-related medications received/prescribed following a lead test for up to 10 years (18 June 2012 to 1 July 2022). Given the large variety of diagnoses linked to patients with lead tests in the medical records, we investigated CNS-related diagnoses in broad domains separately for paediatric and adult patients. For patients under age 18 at the time of lead-testing, follow-up diagnoses were grouped by ICD-9-CM and ICD-10-CM codes into the broad domains of (1) neurodevelopmental conditions and (2) psychiatric conditions and the narrower subdomains of (3) attention-deficit/hyperactivity disorder (ADHD) diagnoses and (4) conduct disorder diagnoses. For patients over the age of 18 at the time of lead testing, follow-up diagnoses were grouped into the broad domains of (1) psychiatric, (2) CNS-ageing-related conditions (eg, cognitive disorders) and (3) other CNS conditions (eg, migraine, stroke) and the narrower psychiatric subdomain of (4) substance use disorders. The broad and narrow domains were selected based on CNS disease differences previously associated with lead exposure in other samples.[7 25–31] When a patient received multiple diagnoses over time that fell within a given domain, only the earliest occurrence was retained. Diagnoses that fell before the earliest lead test were considered baseline diagnoses.

New medications were treated in a similar manner to new diagnoses. Medication domains included (1) psychotherapeutic and (2) other CNS medications; these were identified based on the therapeutic classification variable included in the hospital's electronic health record (EHR) data system (online supplemental table 1). Only medications prescribed at MUSC and recorded in the EHR were included.

Table 1 Demographic details of patients with lead test orders during the 4-year test observation window (2012–2016)

Demographic variable	Level	Patient age					Row total
		0–3 years	4–12 years	13–17 years	18–54 years	≥55 years	
Group size N (%)		5502 (76.6)	831 (11.6)	175 (2.4)	334 (4.7)	339 (4.7)	7181
Sex, N (% by age group)	Female	2702 (49.1)	393 (47.3)	99 (56.6)	165 (49.4)	160 (47.2)	3519 (49.0)
	Male	2800 (50.9)	438 (52.7)	76 (43.4)	169 (50.6)	179 (52.8)	3662 (51.0)
Race and ethnicity, N (% by age group)	Hispanic	1703 (31.0)	187 (22.5)	18 (10.3)	6 (1.8)	3 (0.9)	1917 (26.7)
	Non-Hispanic black	2673 (48.6)	448 (53.9)	83 (47.4)	102 (30.5)	82 (24.2)	3388 (47.2)
	Non-Hispanic white	782 (14.2)	134 (16.1)	63 (36.0)	218 (65.3)	246 (72.6)	1443 (20.1)
	Other or missing	344 (6.3)	62 (7.5)	11 (6.3)	8 (2.4)	8 (2.4)	433 (6.0)
Baseline blood lead level, N (% by age group)	≥5.0 µg/dL	172 (3.1)	28 (3.4)	1 (0.6)	4 (1.2)	14 (4.1)	219 (3.1)
	≥3.5 µg/dL	287 (5.2)	48 (5.8)	1 (0.6)	5 (1.5)	21 (6.2)	362 (5.0)
Repeat lead testing, N (% of patients by age group with repeated testing)	Repeat tests	2046 (37.2)	45 (5.4)	8 (4.6)	17 (5.1)	17 (5)	2133 (29.7)

Statistical analysis

Summary statistics were used to compare patients by age and lead exposure groups (<2, ≥2 to <5, ≥5 to <10 and ≥10 µg/dL) using χ^2 tests, Fisher's exact tests, Wilcoxon rank-sum or t-tests, as appropriate. Follow-up analyses among patients with high baseline lead levels compared those with repeat lead testing who demonstrated flat or positive test result slopes (eg, lead levels did not improve during surveillance) to those with negative slopes. Next, associations of lead exposure levels with new CNS diagnoses or medications during the follow-up window were estimated using generalised linear models with general estimating equations. Multiple lead test results per patient were accounted for using the repeated statement in SAS PROC GENMOD (V. 9.4, SAS Institute). Results are reported as OR with corresponding 95% CIs. Significance tests were two tailed, $\alpha=0.05$. This report follows RECORD (REporting of studies Conducted using Observational Routinely-collected Data) reporting guidelines.

RESULTS

Who orders and receives lead tests?

Table 1 presents summary statistics for patients who received lead testing. Across the 4-year study window (2012–2016), 9726 lead

Table 2 Provider types ordering lead tests, by specialty and patient age

(A) Paediatric patients

Patient ages 0–3 (N=5502)		Ages 4–12 (N=831)		Ages 13–17 (N=175)	
Authorising provider	**N (%)**	**Authorising provider**	**N (%)**	**Authorising provider**	**N (%)**
Paediatrics	4139 (75.2)	Paediatrics	526 (63.3)	Psychiatry	74 (42.3)
Paediatric orthopaedic surgery	334 (6.1)	Paediatric oncology	47 (5.7)	Paediatrics	47 (26.9)
Internal medicine	281 (5.1)	Nurse practitioner	42 (5.1)	Nurse practitioner	21 (12.0)
Nurse practitioner	227 (4.1)	Paediatric orthopaedic surgery	42 (5.1)	Paediatric gastroenterology	9 (5.1)
Paediatric oncology	139 (2.5)	Internal medicine	37 (4.5)	Paediatric emergency medicine	7 (4.0)
Family medicine	112 (2)	Family medicine	35 (4.2)	Paediatric neurology	5 (2.9)
		Psychiatry	34 (4.1)	Family medicine	3 (1.7)
		Paediatric gastroenterology	15 (1.8)	Internal medicine	2 (1.1)
		Paediatric neurology	11 (1.3)		

(B) Adult patients

Ages 18–54 (N=334)		Ages ≥55 (N=339)	
Authorising provider	**N (%)**	**Authorising provider**	**N (%)**
Internal medicine	81 (24.3)	Internal medicine	137 (40.4)
Neurology	72 (21.6)	Neurology	91 (26.8)
Psychiatry	53 (15.9)	Family medicine	23 (6.8)
Family medicine	30 (9.0)	Psychiatry	20 (5.9)
Emergency medicine	11 (3.3)	Pulmonary disease	8 (2.4)
Obstetrics and gynecology	8 (2.4)	Cardiology	7 (2.1)
Hematology and oncology	7 (2.1)	Emergency medicine	5 (1.5)
Neurosurgery	6 (1.8)	Gastroenterology	5 (1.5)
Pulmonary disease	6 (1.8)	Anaesthesiology	4 (1.2)
Cardiology	5 (1.5)	Neurosurgery	4 (1.2)
Gastroenterology	5 (1.5)		
Hospitalist	5 (1.5)		
Rheumatology	5 (1.5)		
Nephrology	4 (1.2)		

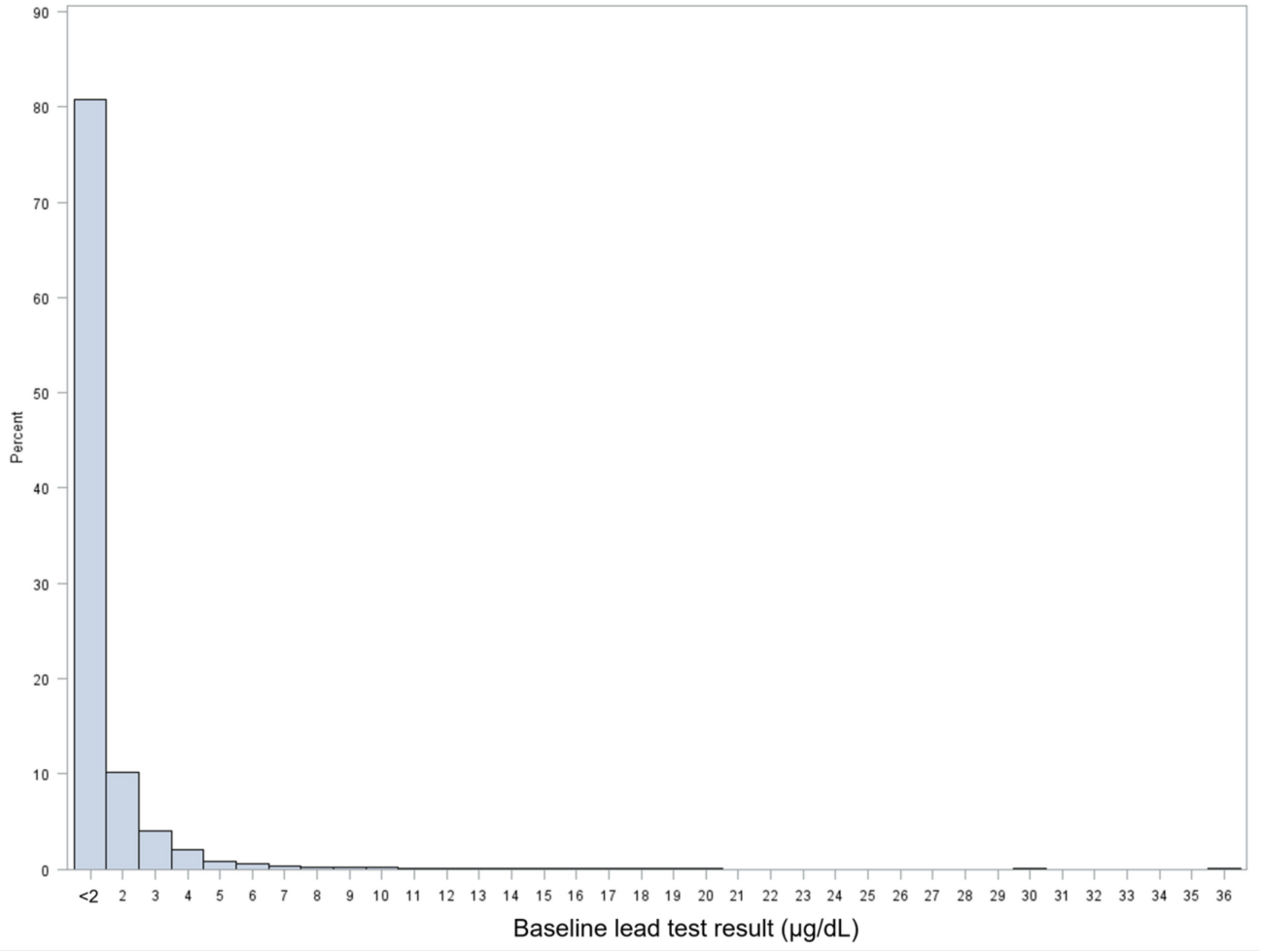

Figure 1 Distribution of initial lead test scores (blood lead levels) across the Medical University of South Carolina healthcare system from 2012 to 2016.

test orders resulted for 7181 patients (49.0% female; ages 0–94 years), reflecting 2133 patients (29.7%) who received multiple tests. Most tests were ordered for paediatric patients (76.6% were aged ≤3 years) and for non-Hispanic black (47.2%) and Hispanic (26.7%) patients.

Table 2 presents provider-type for lead test orders by patient age. Lead test orders came primarily from paediatrics providers for patients aged 0–12 years, from psychiatry providers for patients aged 13–17, and internal medicine, neurology and psychiatry providers for adult patients (≥18 years).

Online supplemental table 2 presents the most common principal diagnoses for visits with initial lead tests orders. For children ≤12 years, routine immunisations and well visits were the most common 'diagnoses' used for visit billing, with 'screening for chemical poisoning', anaemia, foster care status and ADHD as the next most common diagnoses. For children aged 13–17, psychiatric diagnoses (unspecified psychosis, suicidal ideation, 'anxiety state' and depressive disorder) were most common, with anaemia, ADHD and health checks the next most common. Among adults aged 18–54, diagnoses were primarily for psychiatric symptoms (substance use disorder, anxiety, malaise and fatigue) and hypertension. Among adults age ≥55, hypertension, hyperlipidaemia and 'other malaise and fatigue' were most common.

Do lead follow-up testing rates match guidelines?

Initial lead test results in the full patient population ranged from below the detection limit of 2.0 µg/dL (80.8% of patients) to ≥10 µg/dL (0.8% of patients) (figure 1). As shown in online supplemental table 3, there were lead differences by gender and race and ethnicity among paediatric patients but not adults (who were a substantially smaller group). Paediatric males were more likely to have baseline results between 2 and 10 µg/dL, while paediatric females were more likely to have results ≥10 µg/dL ($p=0.022$). Paediatric non-Hispanic black patients were substantially more likely to have lead test results in all detectable categories (≥2 µg/dL and above) compared with other groups ($p<0.0001$).

There were 201 paediatric patients (3.1%) with initial lead test results over the reference value for case management action at the time of testing (5.0 µg/dL) and 362 (5.6%) with results over the current reference value (3.5 µg/dL) (table 1). No adults tested over the OSHA-clinical target for repeat testing of 40 µg/dL.

Overall, 2133 patients received repeated lead testing, of whom 90.7% had a result below the detection limit at every test. Of the 201 paediatric patients with initial lead test scores ≥5.0 µg/dL, only 128 (63.7%) received one or more follow-up tests in the MUSC system. Figure 2 presents the trajectories for the 160 paediatric patients with repeated testing for whom initial or final results were ≥5 µg/dL; all were age ≤3 at initial testing. Within this group, 44 (27.5%) had flat or positive slopes (ie, blood lead levels did not decline) and 60 (37.5%) had final scores above ≥5 µg/dL (ie, follow-up was terminated before lead levels fell below reference value). Non-Hispanic black and Hispanic patients were much more likely to experience flat or

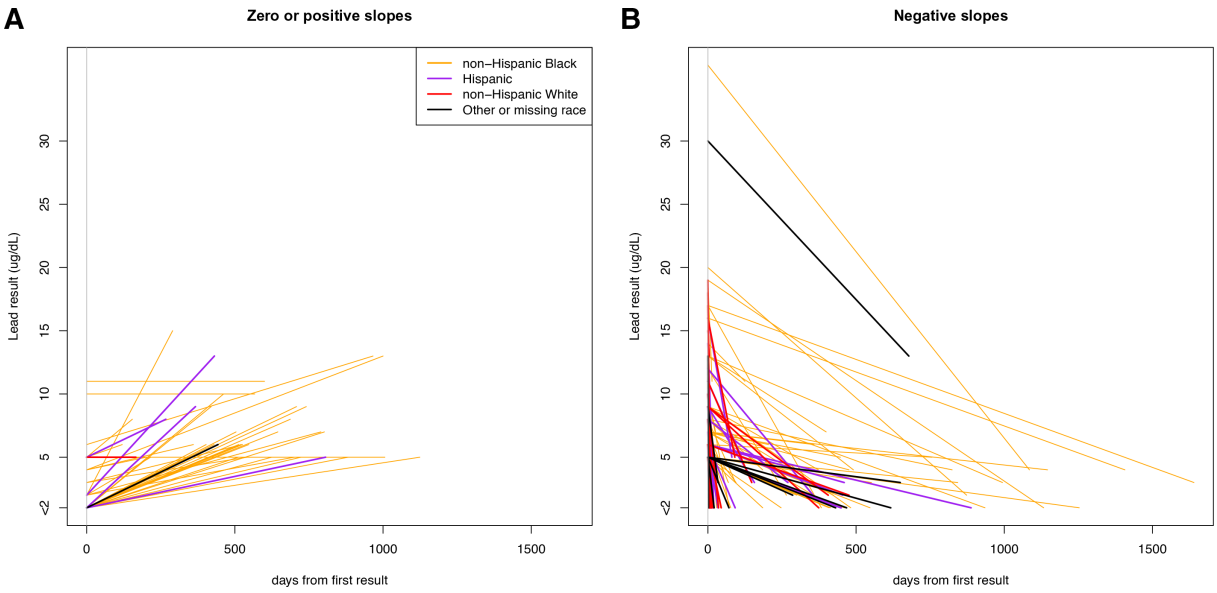

Figure 2 Blood lead level trajectories (lead test intercepts and slopes) for the 160 paediatric patients with repeated testing for whom initial or final results were above the reference value (≥5 µg/dL). (A) Patients with flat or increasing lead levels across follow-up, by race and ethnicity. (B) Patients with declining lead levels across follow-up, by race and ethnicity. All 160 patients were aged 3 or younger at baseline testing. All depicted trajectories are linear as, for clarity, only first and final results are shown. Within this group, 44 children (27.5%) had flat or positive slopes (ie, blood lead levels did not decline) and 60 (37.5%) had final scores above ≥5 µg/dL (ie, follow-up was terminated before lead levels fell below reference level).

positive slopes than non-Hispanic white patients (35.0% for black and 25% for Hispanic patients compared with 4.8% for non-Hispanic white patients, p=0.011). Non-Hispanic black and Hispanic patients were also much more likely to have test scores ≥5 µg/dL at their final test (45.0% and 35.7%, respectively) compared with non-Hispanic whites (14.3%), p=0.03.

Are lead test scores predictive of greater CNS disease during follow-up?

Diagnoses

35.4% of lead tested paediatric patients received a new CNS disease diagnosis during the study time frame; 17.7% received a new diagnosis within 1 year. Table 3 presents results from models estimating the association of blood lead values with subsequent risk for a new CNS diagnosis. These models, all adjusted for sex, age group and race and ethnicity, produced mixed findings (full model results found in online supplemental tables 4,5 reports counts of new diagnoses over follow-up for patients at each level of lead test score). In comparison to paediatric patients with low lead levels (<2 µg/dL) those with moderate levels (≥2 µg/dL to <10 µg/dL) were not more likely to receive any new developmental or psychiatric disorder diagnosis writ large (p=0.8 and p=0.9, respectively). However, they had more than 20% greater risk for specific diagnoses in the narrower domains of ADHD and conduct disorder (HRs of 1.22 and 1.37, respectively, p<0.05). Children with the highest lead values (≥10 µg/dL) had more than twice the risk of receiving an ADHD diagnosis over follow-up compared with low-level peers (HR 2.08, 95% CI 1.37 to 3.15); results for other diagnosis categories were not significant, although HRs were greater than 1.0 in all cases, suggesting a possible trend towards association in this smaller high exposure group (only 65 of 6505 paediatric patients had any test result ≥10 µg/dL).

Among adult patients, 73.6% received a new CNS disease diagnosis during the study time frame; 48.6% received a new diagnosis within 1 year of lead testing. No significant associations between higher lead test results and new diagnoses were found in the adult group (table 3).

Medications

Among paediatric patients, 16.1% received new relevant medications during the study time frame, of which 14.1% were psychotherapeutic medications and 4.0% were CNS related (eg, for migraine). Table 3 presents results from models testing the association of initial blood lead levels with risk for a subsequent new psychotherapeutic or CNS-related medication. Online supplemental table 5 reports counts of new medications over follow-up for patients at each level of lead test score). Similar to the models for new diagnoses, these were adjusted for sex, age group, and race and ethnicity, and again produced mixed findings.

In comparison to paediatric patients with low lead levels (<2 µg/dL) those with moderate levels (≥2 µg/dL to <10 µg/dL) were more likely to receive new psychotherapeutic or other CNS medications over time (HR 1.21, 95% CI 1.02 to 1.44, p=0.03). Among the highest exposure group (≥10 µg/dL) results did not reach significance (HR 1.83, 95% CI 0.82, 4.1, p=0.14), potentially due to the small number of patients in the category (N=94). There was also a trend towards significance for receipt of psychotherapeutic medications among paediatric patients with moderate and high lead levels (p values=0.06 and 0.11, respectively).

Among adult patients, 73.5% received new medications during the study time frame, of which 65.2% were psychotherapeutic medications and 45.6% were CNS related. No significant associations between higher lead test results and new medications were found in the adult group (table 3).

DISCUSSION

This retrospective medical record study generated five primary findings. First, the lead testing rate at a major tertiary academic

Table 3 Associations of blood lead values with risk for new CNS disease during the 10-year observation window

(A) Paediatric patients (N=6508 patients)					
		Lead test result (ref= <2 µg/dL, N=7092 tests)			
		≥2 to < 10 µg/dL (N=1821)		**≥ 10 µg/dL (N=94)**	
New diagnoses		**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Broad disorder domains					
	Developmental disorders	1.02 (0.87 to 1.2)	0.80	1.16 (0.81 to 1.66)	0.42
	Psychiatric disorders	0.99 (0.80 to 1.21)	0.91	1.26 (0.75 to 2.1)	0.38
Narrow disorder domains					
	ADHD	1.22 (1.01 to 1.47)	0.04	2.08 (1.37 to 3.15)	<0.001
	Conduct/antisocial problems	1.37 (1.06 to 1.77)	0.02	1.11 (0.49 to 2.48)	0.80
New medications		**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Broad domains					
	New psychotherapeutic or other CNS medication	1.21 (1.02 to 1.44)	0.03	1.83 (0.82 to 4.1)	0.14
Narrow domains					
	Psychotherapeutic medications	1.18 (0.99 to 1.39)	0.06	1.99 (0.86 to 4.58)	0.11
	Other CNS medications	1.02 (0.77 to 1.36)	0.86	0.69 (0.17 to 2.76)	0.60
(B) Adult patients (N=673)					
		Lead test results <2 µg/dL (N=552) vs ≥2 µg/dL (N=147)			
New diagnoses		**HR (95% CI)**			**P value**
Broad disorder domains					
	Age-related cognitive disorders	1.26 (0.64 to 2.48)			0.50
	Psychiatric disorders	0.98 (0.58 to 1.67)			0.96
	Other CNS conditions	1.38 (0.86 to 2.22)			0.18
Narrow disorder domains					
	Substance use disorders	1.53 (0.72 to 3.24)			0.27
New medications		**HR (95% CI)**			**P value**
Broad domains					
	New psychotherapeutic or other CNS medications	1.13 (0.76 to 1.69)			0.54
Narrow domains					
	Psychotherapeutic medications	1.08 (0.72 to 1.61)			0.71
	Other CNS medications	0.81 (0.53 to 1.23)			0.32

Analyses adjusted for sex, age group, and race and ethnicity.
ADHD, attention-deficit/hyperactivity disorder; CNS, central nervous system.

healthcare centre in the southeastern USA (MUSC Health) was just over 2400 tests a year for approximately 1800 patients. This represents approximately 0.2% of the patient encounters seen each year at MUSC and 0.04% of the 5.2 million residents of South Carolina. The majority of tests were ordered for populations of concern, including children ≤3 years (76.6% of test orders) and for non-Hispanic black and Hispanic patients (47.2% and 26.7% of test orders, respectively).

Second, provider specialties found to order lead tests varied by patient age. Appropriately, paediatrics was most likely to order lead tests for preadolescent patients, psychiatry for adolescent patients and internal medicine for adults. Lead test orders were not restricted to these specialties, however: neurology, oncology, gastroenterology, cardiology, family medicine and emergency medicine also requested lead tests, although at low rates. In an effort to reach more at-risk patients with lead surveillance, future research could use mixed methods (eg, surveys, focus groups) to determine what training about lead risks these specialties receive and what motivates less-common specialties to order tests.

Notably, past surveys (now three decades old) of paediatricians[32] and paediatric residents[33] identified sex, regional and practice-setting-based differences in provider lead test ordering in an era when CDC guidelines called for universal screening of children under age 6. Paediatrics providers who were male, practising in suburban and rural areas, and living in the South or West were less likely to follow universal screening guidelines. Those who had graduated from medical school more recently (<10 years) were more likely to universally screen, as were those who had read the CDC guidance and believed that their state required testing.[32 33] While no surveys of lead testing beliefs or motivations have been conducted among other provider specialties to the best of our knowledge, evidence suggests that state testing requirements, guidance from government agencies and training/guidelines from professional associations may significantly increase provider test ordering, particularly for higher-risk patients.[32 33]

Why are lead tests ordered? One answer lies in the diagnoses that accompany lead test orders. For young paediatric patients these included, appropriately, health checks, 'screening for chemical poisoning', anaemia, and ADHD, and, for older paediatric patients, psychiatric diagnoses. These diagnoses suggest that paediatric providers are aware of the extensive body of evidence linking lead to these specific conditions.

Diagnoses most likely to accompany adult lead test orders included primarily psychiatric diagnoses, malaise and fatigue, and, in adults aged 55 and older, hypertension and hyperlipidaemia. In this regard, the emerging evidence linking low-level lead exposure to cardiovascular disease (CVD), particularly coronary heart disease, warrants specific mention. While heart disease was not evaluated in this CNS-focused study, lead has recently been identified by the American Heart Association as a 'significant contributor' to CVD worldwide,[11] with specific lead-related differences in arterial stiffness, blood pressure, lipid metabolism, inflammation and endothelial function identified in mechanistic studies.[11] Epidemiological evidence has, meanwhile, linked adult blood lead levels to excess CVD morbidity and mortality in multiple studies in the USA, Europe and Asia.[9–11] Notably, while hypertension and hyperlipidaemia were the diagnoses most likely to accompany lead tests orders in adults aged 55 and over in this study, such tests were rarely ordered by cardiology providers, who only ordered 12 lead tests in total over the 4-year observation window (representing 1.8% of all adult lead test orders). Lead-associated risk for adult bone[34] and kidney[35] disease was likewise under-represented in the ordering provider specialties. Finally, a lack of diagnoses related to cognitive conditions and dementing illnesses suggests that lead exposure, a putative risk for neurodegenerative disease,[12 13 36] is not yet 'on the radar' of geriatricians, at least in this investigated medical system.

Third, one-fifth of patients (19.2%) had blood lead levels above the detection limit of 2.0 µg/dL. This matches national blood lead level rates in the USA during the study period[37] and indicates that lead exposures were, as anticipated, ongoing in the wider South Carolina community. Among paediatric patients, 3.1% of tested children exceeded the previous reference value (5 µg/dL) and 5.2% exceeded the current reference value (3.5 µg/dL). These lead-level rates match those reported by South Carolina's child-lead-tracking programme, which reported elevated paediatric lead-level rates from 3% to 4% depending on the year of study.[38] SC-state tracking indexed between 15 000 and 20 000 paediatric lead tests statewide on average during the study period—an approximate 4% statewide paediatric lead-screening rate.[38] No study adults tested over the OSHA clinical target of 40 µg/dL.

Fourth, one-third of children (36.3%) with elevated blood lead levels failed to receive follow-up testing during the study window, at least within the MUSC system. For children with elevated levels that did receive follow-up testing within MUSC: one-fourth (27.5%) had flat or positive lead test slopes, indicating a failure lead abatement; one-third (37.5%) had final scores above the reference value, indicating a failure of follow-up to extend until lead abatement was successful. Non-Hispanic black and Hispanic patients were significantly more likely than non-Hispanic white patients to experience these negative outcomes. Future work should investigate where in the chain of care improvements can be made to promote health equity. As noted below, it is possible that children received additional testing outside MUSC Health (eg, at public health departments), which should be taken into account in future investigations.

Fifth, in confirmation of past studies on lead exposure implications for brain development,[6 39 40] children with detectible lead levels were more likely to receive new developmental and psychiatric diagnoses as well as new related medications across up to 10 years of follow-up. Specifically, children with moderate lead levels (≥2 µg/dL to<10 µg/dL) were 22% and 37% more likely to receive new ADHD and conduct disorder diagnoses, respectively, and 21% more likely to receive new psychotherapeutic or CNS-related medications. In comparison to children with levels at or below the detection limit, children with the highest lead levels (≥10 µg/dL) had twice the risk of later receiving an ADHD diagnosis. No statistically significant associations between higher lead test results and new diagnoses or medications were found among adult patients, a finding that may reflect the relatively small number of adults who received lead testing during the study window (ie, positive point estimates did not achieve significance owing to wide CIs). While study results are observational and cannot establish causation, lead is believed to elevate rates of neurodevelopmental and psychiatric conditions through a variety of brain and non-brain-based mechanisms that diminish emotional and behavioural regulation capacity, including neuroinflammation, abnormal brain-derived neurotrophic factor expression, mitochondrial dysfunction and oxidative stress.[6]

This study has limitations. First, as noted above, we do not know what decision-making contributed to provider lead test ordering. Future studies should consider mixed methods to approach this question. Second, we do not know whether specific lead abatement case management interventions followed test results. Third, it is possible that patients received additional lead testing after the observation window at public health departments or other health systems. Future studies could extend the observation window to confirm current results and incorporate multiple health systems where possible. Fourth, blood lead tests are a measure of acute exposure (across the proceeding 4–6 weeks) and cumulative exposure across time was unknown. Future studies should consider the potential utility of cumulative, bone lead assessments among high-risk patients. Fifth, this study considered only one population living in one region of the USA who received care at one care system; results should be replicated in other hospital systems, regions and countries. Sixth, the study is based solely on data from the electronic medical record, which may not capture all relevant information, including family or patient home or occupational information that could be used to identify potential routes of lead exposure, or information about other exposures that can influence the CNS (eg, mercury, polycyclic aromatic hydrocarbons). Finally, the study was observational and cannot establish causation.

CONCLUSIONS

While lead exposure rates continue to decline in the USA and other countries,[2 3] lead remains a hazard for both children and adults.[2 5 23] In one major southeastern healthcare system investigated across the past 10 years, we determined that lead testing covered only a small portion of the hospital population but nevertheless represented a wide range of patient ages, presentations, and provider specialties, from paediatrics and psychiatry to neurology and oncology. Often, paediatric patients found to have blood lead levels above reference values for case management did not experience improvements, with lead monitoring proving either unsuccessful, unrepeated or terminated prematurely. Often, paediatric patients with elevated lead levels went on to experience deteriorations in their health, as identified by new developmental and psychiatric diagnoses and the use of new related medications.

In many US states, responsibility for lead testing is delegated to individual healthcare providers. There remains room for improvement in the systems guiding provider decision-making around when to test and how to follow up on positive results.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants but as a study of deidentified medical records designed to evaluate care practice, this study was determined by the MUSC Institutional Review Board to fall under a quality improvement designation exempt from ethics review.

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ORCID iD

Aaron Reuben http://orcid.org/0000-0001-5713-4913

REFERENCES

1 McFarland MJ, Hauer ME, Reuben A. Half of US population exposed to adverse lead levels in early childhood. *Proc Natl Acad Sci U S A* 2022;119:e2118631119.
2 Ettinger AS, Ruckart PZ, Dignam T. Lead poisoning prevention: the unfinished agenda. *J Public Health Manag Pract* 2019:S1–2.
3 Dignam T, Kaufmann RB, LeStourgeon L, *et al*. Control of lead sources in the United States, 1970-2017: public health progress and current challenges to eliminating lead exposure. *Journal of Public Health Management and Practice* 2019;25:S13–22.
4 Bihari E, Grewal G, Richter DD. Legacies of Pre-1960S municipal waste incineration in the PB of city soils. *Environ Sci Technol Lett* 2023;10:897–902.
5 Miranda ML, Lilienfeld A, Tootoo J, *et al*. Segregation and childhood blood lead levels in North Carolina. *Pediatrics* 2023;152:e2022058661.
6 Bellinger DC. Very low lead exposures and children's Neurodevelopment. *Curr Opin Pediatr* 2008;20:172–7.
7 Reuben A, Schaefer JD, Moffitt TE, *et al*. Association of childhood lead exposure with adult personality traits and lifelong mental health. *JAMA Psychiatry* 2019;76:418–25.
8 Bouchard MF, Bellinger DC, Weuve J, *et al*. Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in U.S. young adults. *Arch Gen Psychiatry* 2009;66:1313–9.
9 Lanphear BP, Rauch S, Auinger P, *et al*. Low-level lead exposure and mortality in US adults: a population-based cohort study. *Lancet Public Health* 2018;3:e177–84.
10 Chowdhury R, Ramond A, O'Keeffe LM, *et al*. Environmental toxic metal Contaminants and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ* 2018;362:k3310.
11 Lamas GA, Bhatnagar A, Jones MR, *et al*. Contaminant metals as cardiovascular risk factors: A scientific statement from the American heart Association. *J Am Heart Assoc* 2023;12:e029852.
12 Shih RA, Hu H, Weisskopf MG, *et al*. Cumulative lead dose and cognitive function in adults: A review of studies that measured both blood lead and bone lead. *Environ Health Perspect* 2007;115:483–92.
13 Weuve J, Korrick SA, Weisskopf MG, *et al*. Cumulative exposure to lead in relation to cognitive function in older women. *Environ Health Perspect* 2009;117:574–80.
14 Ruckart PZ, Jones RL, Courtney JG, *et al*. Update of the blood lead reference value — United States, 2021. *MMWR Morb Mortal Wkly Rep* 2021;70:1509–12.
15 Occupational Safety and Health Administration. Lead - Overview, Available: https://www.osha.gov/lead [Accessed 28 Nov 2023].
16 CDC. National childhood blood lead surveillance data. 2022. Available: https://www.cdc.gov/nceh/lead/data/national.htm [Accessed 23 May 2023].
17 Lead: adult blood lead epidemiology and surveillance (ABLES) | NIOSH | CDC. 2023. Available: https://www.cdc.gov/niosh/topics/lead/ables.html [Accessed 23 May 2023].
18 Egan KB, Tsai RJ, Chuke SO. Integrating childhood and adult blood lead surveillance to improve identification and intervention efforts. *J Public Health Manag Pract* 2019;25:S98–104.
19 Dickman J. Children at risk: gaps in state lead screening policies. 2017. Available: https://toxicfreefuture.org/research/children-at-risk/state-lead-screening-policies/ [Accessed 13 Jun 2023].
20 Ruckart PZ, Bove FJ, Dallas C. Evaluating the effectiveness of state-level policies on childhood blood lead testing rates. *J Public Health Manag Pract* 2023;29:241–9.
21 Bruce SA, Christensen KY, Coons MJ, *et al*. Using Medicaid data to improve childhood lead poisoning prevention program outcomes and blood lead surveillance. *Journal of Public Health Management and Practice* 2019;25:S51–7.
22 Courtney JG, Chuke SO, Dyke K, *et al*. Decreases in young children who received blood lead level testing during COVID-19 — 34 jurisdictions, January–may 2 020. *MMWR Morb Mortal Wkly Rep* 2020;70:155–61.
23 Kamai EM, Daniels JL, Delamater PL, *et al*. Patterns of children's blood lead screening and blood lead levels in North Carolina, 2011–2018—who is tested. *Environ Health Perspect* 2022;130:67002.
24 NCQA. Lead screening in children. Available: https://www.ncqa.org/hedis/measures/lead-screening-in-children/ [Accessed 23 May 2023].
25 Rhodes D, Spiro A, Aro A, *et al*. Relationship of bone and blood lead levels to psychiatric symptoms: the normative aging study. *J Occup Environ Med* 2003;45:1144–51.
26 Golub NI, Winters PC, van Wijngaarden E. A population-based study of blood lead levels in relation to depression in the United States. *Int Arch Occup Environ Health* 2010;83:771–7.
27 Weisskopf MG, Hu H, Mulkern RV, *et al*. Cognitive deficits and magnetic resonance spectroscopy in adult Monozygotic twins with lead poisoning. *Environ Health Perspect* 2004;112:620–5.
28 Stewart WF, Schwartz BS, Davatzikos C, *et al*. Past adult lead exposure is linked to neurodegeneration measured by brain MRI. *Neurology* 2006;66:1476–84.
29 Brubaker CJ, Dietrich KN, Lanphear BP, *et al*. The influence of age of lead exposure on adult gray matter volume. *Neurotoxicology* 2010;31:259–66.
30 Stokes L, Letz R, Gerr F, *et al*. Neurotoxicity in young adults 20 years after childhood exposure to lead: the bunker hill experience. *Occup Environ Med* 1998;55:507–16.
31 Reuben A, Elliott ML, Abraham WC, *et al*. Association of childhood lead exposure with MRI measurements of structural brain integrity in Midlife. *JAMA* 2020;324:1970–9.
32 Campbell JR, Schaffer SJ, Szilagyi PG, *et al*. Blood lead screening practices among US Pediatricians. *Pediatrics* 1996;98:372–7.
33 Schaffer SJ, Campbell JR, Szilagyi PG, *et al*. Lead screening practices of pediatric residents. *Arch Pediatr Adolesc Med* 1998;152:185–9.
34 Campbell JR, Auinger P. The association between blood lead levels and osteoporosis among adults—results from the third national health and nutrition examination survey (NHANES III). *Environ Health Perspect* 2007;115:1018–22.
35 Harari F, Sallsten G, Christensson A, *et al*. Blood lead levels and decreased kidney function in a population-based cohort. *American Journal of Kidney Diseases* 2018;72:381–9.
36 Weisskopf MG, Proctor SP, Wright RO, *et al*. Cumulative lead exposure and cognitive performance among elderly men. *Epidemiology* 2007;18:59–66.
37 National Center for Health Statistics. Blood lead (2011-2018) [National Report on Human Exposure to Environmental Chemicals]. Atlanta, GA: Centers for Disease Control; 2023. Available: https://www.cdc.gov/exposurereport/data_tables.html [Accessed 1 Dec 2023].
38 South Carolina Environmental Public Health Tracking Program. Demographic risk factors associated with blood lead levels in South Carolina children (2010-2014) [Report No.: CR-011906]. S.C. Department of Health and Environmental Control Columbia; 2014. Available: https://scdhec.gov/sites/default/files/Library/CR-011906.pdf [Accessed 14 Jun 2023].
39 Braun JM, Kahn RS, Froehlich T, *et al*. Exposures to environmental Toxicants and attention deficit hyperactivity disorder in U.S. children. *Environ Health Perspect* 2006;114:1904–9.
40 Braun JM, Froehlich TE, Daniels JL, *et al*. Association of environmental Toxicants and conduct disorder in U.S. children: NHANES 2001–2004. *Environ Health Perspect* 2008;116:956–62.