JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Screening for Elevated Blood Lead Levels in Childhood and Pregnancy

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Elevated blood lead level is associated with serious, often irreversible, health consequences.

OBJECTIVE To synthesize evidence on the effects of screening, testing, and treatment for elevated blood lead level in pregnant women and children aged 5 years and younger in the primary care setting to inform the US Preventive Services Task Force.

DATA SOURCES Cochrane CENTRAL and Cochrane Database of Systematic Reviews (through June 2018) and Ovid MEDLINE (1946 to June 2018); surveillance through December 5, 2018.

STUDY SELECTION English-language trials and observational studies of screening for and treating elevated lead levels in asymptomatic children and pregnant women.

DATA EXTRACTION AND SYNTHESIS Independent critical appraisal and data abstraction by 2 reviewers using predefined criteria.

MAIN OUTCOMES AND MEASURES Elevated blood lead level, morbidity, mortality, clinical prediction tools, test accuracy, adverse events.

RESULTS A total of 24 studies (N = 11 433) were included in this review. No studies evaluated the benefits or harms of screening vs no screening in children. More than 1 positive answer on the 5-item 1991 Centers for Disease Control and Prevention (CDC) screening questionnaire was associated with a pooled sensitivity of 48% (95% CI, 31.4% to 65.6%) and specificity of 58% (95% CI, 39.9% to 74.0%) for identifying children with a venous blood lead level greater than 10 µg/dL (5 studies [n = 2265]). Adapted versions of the CDC questionnaire did not demonstrate improved accuracy. Capillary blood lead testing demonstrated sensitivity of 87% to 91% and specificity greater than 90%, compared with venous measurement (4 studies [n = 1431]). Counseling and nutritional interventions or residential lead hazard control techniques did not reduce blood lead concentrations in asymptomatic children, but studies were few and had methodological limitations (7 studies [n = 1419]). One trial (n = 780) of dimercaptosuccinic acid (DMSA) chelation therapy found reduced blood lead levels in children at 1 week to 1 year but not at 4.5 to 6 years, while another trial (n = 39) found no effect at 1 and 6 months. Seven-year follow-up assessments showed no effect on neuropsychological development, a small deficit in linear growth (height difference, 1.17 cm [95% CI, 0.41 to 1.93]), and poorer cognitive outcomes reported as the Attention and Executive Functions subscore of the Developmental Neuropsychological Assessment (unadjusted difference, −1.8 [95% CI, −4.5 to 1.0]; adjusted P = .045) in children treated with DMSA chelation. Evidence was too limited to determine the accuracy of screening questionnaires or benefits and harms of treatment in pregnant women.

CONCLUSIONS AND RELEVANCE Screening questionnaires were not accurate for identifying children with elevated blood lead levels. Chelating agents in children were not significantly associated with sustained effects on blood level levels but were associated with harms.

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Lead causes a number of adverse health effects primarily affecting the central nervous, hematopoietic, hepatic, and renal systems.[1] Many health effects associated with chronic exposure to elevated blood lead levels are irreversible, with the nervous system being the most important.[1] The severity of lead toxicity is correlated with higher blood lead levels, but manifestations may vary. Elevated blood lead levels in children are associated with IQ deficits, attention-related behaviors, and poor academic achievement.[2,3] Lead exposure during pregnancy is associated with spontaneous abortion,[4] reduced fetal growth, premature birth, blood pressure elevation,[5] and cognitive deficiencies in the child.[4]

Elevated blood lead level is defined as greater than 5 µg/dL, according to the Centers for Disease Control and Prevention (CDC).[3] Reference ranges are based on population levels from the National Health and Nutrition Examination Survey blood lead distribution; these do not define safe lead levels but are the level at which further clinical monitoring and treatment is recommended. The reference range may change with population prevalence.

In 2006, the US Preventive Services Task Force (USPSTF) found insufficient evidence for screening asymptomatic children at increased risk for elevated blood lead levels (I statement) and recommended against routine screening in asymptomatic pregnant women and children aged 1 to 5 years at average risk (D recommendations).[6] Recommendations of other organizations are summarized in eTables 1 and 2 in the Supplement. This systematic review was commissioned by the USPSTF to update the prior review[7] by synthesizing evidence on the benefits and harms of screening for elevated blood lead levels in asymptomatic pregnant women and children 5 years and younger.

Methods

Scope of the Review

Using established methods,[8] this review addressed key questions (KQs) as shown in the analytic framework in **Figure 1** and **Figure 2**. Methodological details, including study selection, search strategies, excluded studies, data analysis methods, and detailed results are available in the full evidence report at http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/elevated-blood-lead-levels-in-childhood-and-pregnancy-screening.[9,10]

Data Sources and Searches

Cochrane CENTRAL, the Cochrane Database of Systematic Reviews (through June 2018), and Ovid MEDLINE (1946 to June 2018) were searched, including all studies from prior reviews and reference lists of included studies.[7] Since June 2018, we continued to conduct ongoing surveillance through article alerts and targeted searches of high-impact journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and therefore the related USPSTF recommendation. The last surveillance was conducted on December 5, 2018, and identified no relevant new studies. Search strategies are listed in eAppendix 1 in the Supplement.

Study Selection

Populations of asymptomatic children 5 years and younger and asymptomatic pregnant women were included, regardless of risk for elevated blood lead levels. Testing approaches included studies of screening questionnaires and venous or capillary blood lead testing. Comparisons for KQ1 were screening vs no screening; for KQ2a, a questionnaire against a reference standard (ie, venous lead level); for KQ2b, capillary vs venous blood lead level testing; and for treatment questions, treatment vs no treatment, placebo, or inactive control. Intermediate outcomes (eg, blood lead levels) were included, as well as clinical outcomes using validated measures of cognitive or neurobehavioral outcomes in children. Other outcomes were measures of diagnostic accuracy (KQ2) and harms of testing (eg, anxiety, distress, pain, or discomfort related to testing) and treatment. English-language articles were eligible for inclusion. Included studies were randomized clinical trials (RCTs), nonrandomized controlled intervention studies, and observational studies (for questions on screening and treatment); studies on the diagnostic accuracy of screening questionnaires or capillary sampling; and trials and observational studies of harms. Studies conducted in countries with a "very high" Human Development Index[11] that evaluated interventions that focused on the individual or family (ie, counseling, nutritional interventions, residential hazard control techniques, and chelation therapy) were included. Studies of policies, laws, or community-based interventions focused on primary prevention of lead exposure were excluded.

Data Abstraction and Quality Rating

Data about study design, patient population, setting, screening method, interventions, analysis, and results were abstracted. Predefined criteria were used to assess the quality of individual controlled trials and observational studies using criteria developed by the USPSTF[8]; studies were rated as "good," "fair," or "poor." For harms, results of poor-quality studies were included when no higher-quality studies were available (quality-rating methods are reported in eAppendix 2 in the Supplement). For each study, data abstraction and quality assessment were subject to dual review by study investigators. Disagreements were resolved by consensus.

Data Synthesis

Studies were qualitatively synthesized based on methods developed by the USPSTF[8] and are summarized narratively. For diagnostic accuracy of clinical questionnaires, comparable studies were pooled using a random-effects model using the *metandi* command in Stata version 14.2 (StataCorp), and hierarchical summary receiver operating characteristic (ROC) plots were created using the *metandiplot* function.[12,13] Forest plots without a summary measure and summary ROC plots were also created using Review Manager 5.3 (Cochrane Community).[14] There were too few treatment studies to perform meta-analysis. Studies included in prior reviews were reviewed for consistency with current results; however, lack of studies and differences in scope, key questions, and inclusion criteria limited aggregate synthesis with the updated evidence.

The overall strength of evidence was determined using methods described by the USPSTF.[8] Based on the number, quality, and size of studies, consistency of results, and directness of evidence, overall evidence was rated "insufficient," "low," "moderate," or "high." The applicability of the findings to US primary care populations and settings was also assessed.

Results

Two reviewers evaluated 3147 unique citations and 233 full-text articles based on predefined criteria (eTables 3 and 4 in the Supplement). A total of 24 studies were included in this review (N = 11 433) (**Figure 3** and **Figure 4**).

Screening and Treatment in Children 5 Years and Younger

Effectiveness of Screening

Key Question 1. Is there direct evidence that screening for elevated blood lead levels in asymptomatic children 5 years and younger improves health outcomes (ie, reduced cognitive or behavioral problems or learning disorders)?

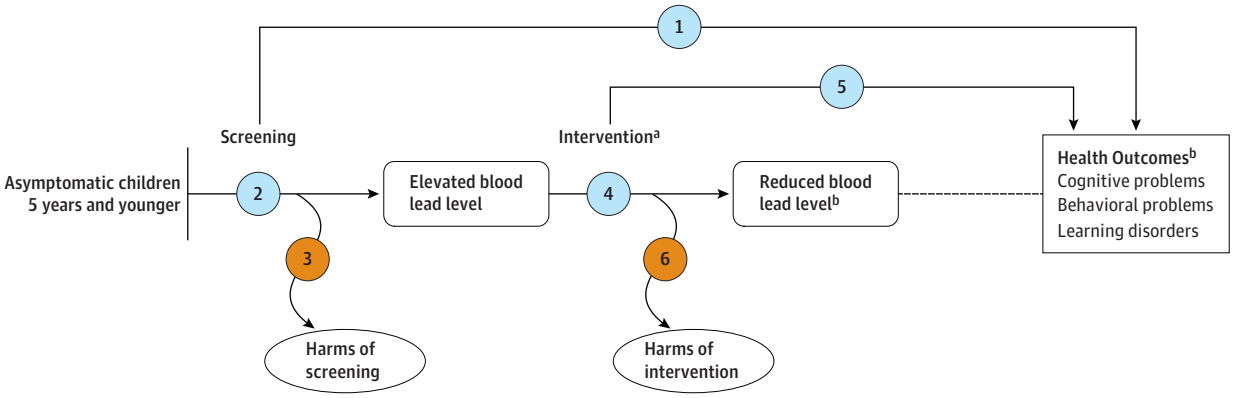
No studies directly compared the effectiveness of screening vs no screening for elevated blood lead levels.

Diagnostic Accuracy of Questionnaires or Clinical Prediction Tools

Key Question 2a. What is the accuracy of questionnaires or clinical prediction tools that identify children who have elevated blood lead levels?

Nine fair-quality studies reported the diagnostic accuracy of questionnaires or clinical prediction tools for identifying asymptomatic children with elevated blood lead levels, defined as greater than 10 µg/dL (**Table 1**; eTable 5 in the Supplement).[15-23,25] All studies used a blood lead level of 10 µg/dL or greater as the reference standard. Five studies evaluated the accuracy of the 1991 CDC questionnaire and 4 evaluated modified versions of the CDC questionnaire for specific populations and settings.[15-23] The CDC questionnaire is a 5-question survey developed in 1991 that aims to assess residential, household, occupational, and personal risk factors for lead exposure in children. Sample sizes ranged from 167 to 2978 (total n = 6873). Where reported, mean age range was 9 to 31 months.[18,19] Seven studies were conducted in urban or suburban communities, and 3 studies were from rural communities. Two studies identified the population as high risk[16,23] and others did not specify risk

Figure 1. Analytic Framework: Screening and Treatment of Blood Lead Levels in Children



Key questions

1. Is there direct evidence that screening for elevated blood lead levels in asymptomatic children age 5 years and younger improves health outcomes (ie, reduced cognitive or behavioral problems or learning disorders)?
2. a. What is the accuracy of questionnaires or clinical prediction tools that identify children who have elevated blood lead levels?
   b. What is the accuracy of capillary blood lead testing in children?
3. What are the harms of screening for elevated blood lead levels (with or without screening questionnaires) in children?
4. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy reduce blood lead levels in asymptomatic children with elevated blood lead levels?
5. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy improve health outcomes in asymptomatic children with elevated blood lead levels?
6. What are the harms of interventions in asymptomatic children with elevated blood lead levels?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions (KQs) that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes. A dashed line depicts a health outcome that follows an intermediate outcome. Refer to the USPSTF Procedure Manual for further details.[8]

[a] Interventions include counseling families to reduce lead exposure, nutritional interventions, residential hazard control techniques, and chelation therapy.

[b] Included outcomes measured in family members (eg, siblings, pregnant women in the same household) subsequently identified as having elevated blood lead levels after the index family member was found to have an elevated blood lead level during screening.

level; however, many of the populations surveyed were from public programs, such as Medicaid or public health clinics. The prevalence of blood lead level 10 µg/dL or greater ranged from 0.6%[15] to 29%.[15] All studies were rated fair quality. Methodological shortcomings included unclear enrollment methods and exclusion of some patients from analysis. One poor-quality retrospective study was excluded from this analysis and was not included in the total number of studies.[25]

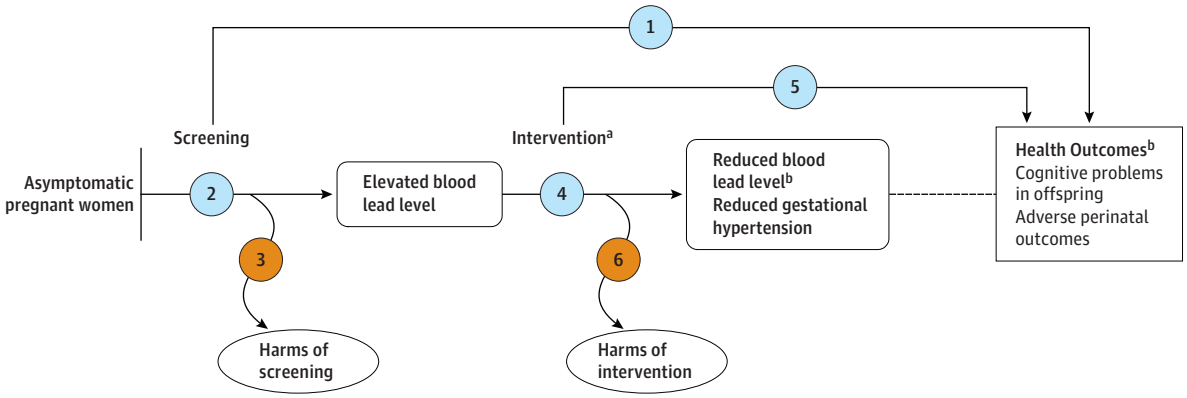
Five studies (n = 2265) conducted in mostly urban settings reported sensitivity of the CDC questionnaire that ranged from 32% to 83% and specificity that ranged from 32% to 80% (Table 1). The pooled sensitivity was 48% (95% CI, 31%-66%) and the pooled specificity was 58% (95% CI, 39%-74%) (**Figure 5**),[15,16,19,21,23] for a positive likelihood ratio of 1.15 and a negative likelihood ratio of 0.89. Four studies[17,18,20,22] (n = 4608) evaluated the 1991 CDC questionnaire modified to address local risk factors or adapted for specific populations. Two studies from urban settings had poor accuracy (sensitivity, 57%-68%; specificity, 51%-58%) for identifying children with elevated blood lead levels (Table 1).[17,18] Two studies conducted in rural settings[20,22] found that the adapted questionnaires had low accuracy (sensitivity, 25%; specificity, 49%) for detecting children with elevated blood lead levels (Table 1).

Diagnostic Accuracy of Capillary Blood Lead Testing in Children

Key Question 2b. What is the accuracy of capillary blood lead testing in children?

Four fair-quality cohort studies assessed the diagnostic accuracy of capillary testing compared with venous sampling for elevated blood lead levels (**Table 2**).[26-28,30] All 4 studies were conducted in the urban United States and were published between 1994 and 1998. Sample sizes ranged from 124 to 513 (total n = 1431). Female participants comprised 41% to 47% of the sample in 3 studies; the fourth study did not report sex. Two studies predominately enrolled black children,[26,30] and 1 study evaluated a more diverse study population (38% white, 28% black, 21% Hispanic, and 6% Asian[27]); the fourth study did not report race or ethnicity.[28] Among the 3 studies reporting baseline lead levels, the proportion of children

Figure 2. Analytic Framework: Screening and Treatment of Blood Lead Levels in Pregnant Women



Key questions

1. a. Is there direct evidence that screening for elevated blood lead levels in asymptomatic pregnant women improves health outcomes (ie, reduced cognitive problems in offspring, adverse perinatal outcomes, and adverse maternal outcomes)?
   b. Does the effectiveness of screening in asymptomatic pregnant women vary by gestational age?
2. What is the accuracy of questionnaires or clinical prediction tools that identify pregnant women who have elevated blood lead levels?
3. What are the harms of screening for elevated blood lead levels (with or without screening questionnaires) in asymptomatic pregnant women?
4. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy reduce blood lead levels and rates of gestational hypertension in asymptomatic pregnant women with elevated blood lead levels?
5. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy improve health outcomes in asymptomatic pregnant women with elevated blood lead levels?
6. What are the harms of interventions in asymptomatic pregnant women with elevated blood lead levels?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions (KQs) that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes.

[a] Interventions include counseling families to reduce lead exposure, nutritional interventions, residential hazard control techniques, and chelation therapy.
[b] Included outcomes measured in family members (eg, siblings, pregnant women in the same household) subsequently identified as having elevated blood lead levels after the index family member was found to have an elevated blood lead level during screening.

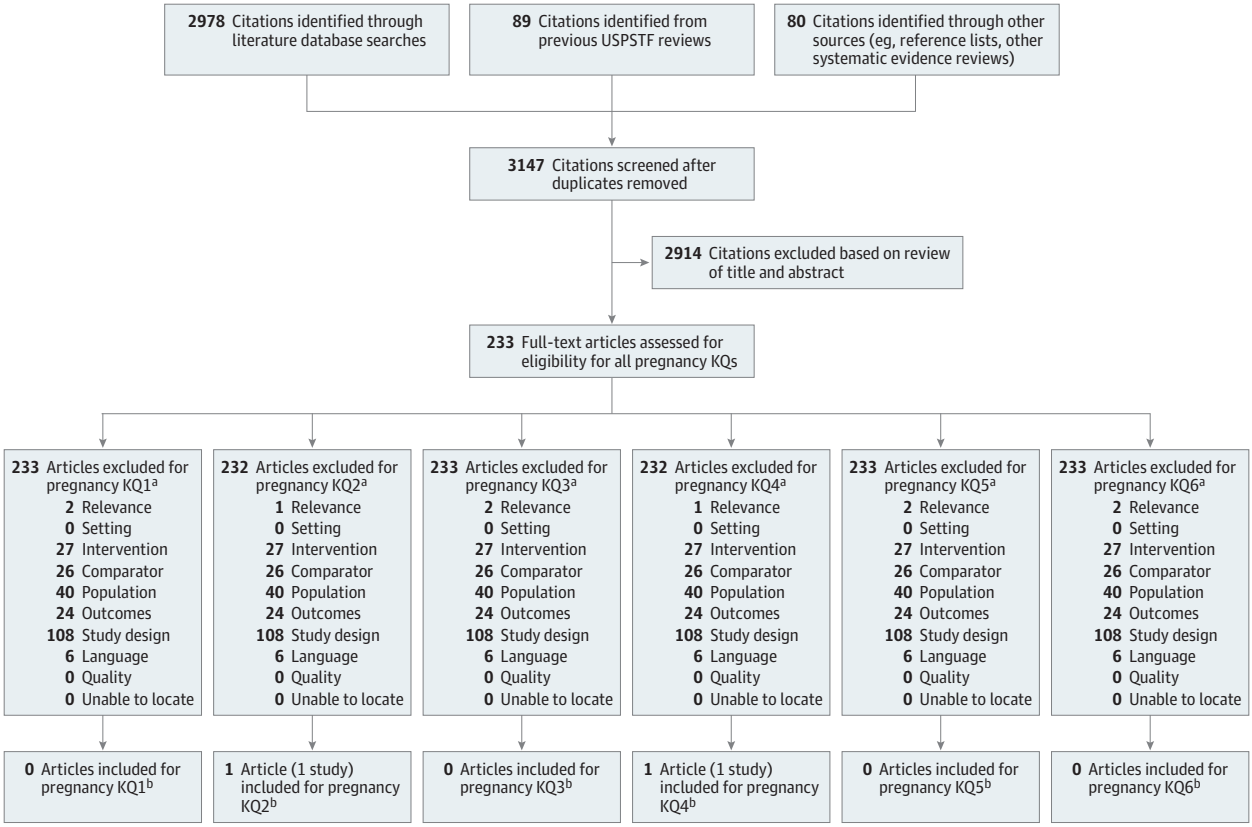
Figure 3. Literature Search Flow Diagram: Childhood Key Questions

KQ indicates key question; USPSTF, US Preventive Services Task Force.

[a] Reasons for exclusion: Relevance: Study aim not relevant to key question. Setting: Study not conducted in a country relevant to US practice. Intervention: Study of an excluded intervention or screening approach. Comparator: Study lacked appropriate comparator group. Population: Study not conducted in an average-risk population. Outcomes: Study did not have relevant outcomes or had incomplete outcomes. Design: Study did not use an included design. Language: Study published in non-English language. Quality: Study did not meet criteria for fair or good quality. Unable to locate: Full-text article could not be located.

[b] Articles could appear in more than 1 KQ.

Figure 4. Literature Search Flow Diagram: Pregnancy Key Questions



[a] Reasons for exclusion: Relevance: Study aim not relevant to key question. Setting: Study not conducted in a country relevant to US practice. Intervention: Study of an excluded intervention or screening approach. Comparator: Study lacked appropriate comparator group. Population: Study not conducted in an average-risk population. Outcomes: Study did not have relevant outcomes or had incomplete outcomes. Design: Study did not use an included design. Language: Study published in non-English language. Quality: Study did not meet criteria for fair or good quality. Unable to locate: Full-text article could not be located.

[b] Articles could appear in more than 1 KQ.

with blood lead level 10 µg/dL or greater ranged from 21% to 31%.[26-28] Methodologic shortcomings included unclear enrollment methods and exclusion of some patients from analysis.

Three of 4 studies reported diagnostic accuracy of capillary sampling at a blood lead level cutoff of 10 µg/dL or greater (n = 1136) (Table 2). Sensitivities ranged from 87% to 91% and specificities ranged from 92% to 99%.[26-28] For a blood lead level cutoff of 15 µg/dL or greater, 3 studies (n = 1136) reported sensitivities ranging from 36% to 83% and specificities from 95% to 98%.[26-28] For a blood lead level cutoff of 20 µg/dL or greater, 3 studies (n = 918) reported sensitivities ranging from 78% to 96% and specificities from 91% to 100%.[26,27,30]

One study (n = 295) evaluated different preparation methods for capillary blood sampling.[30] Using a capillary sampling threshold of greater than 20 µg/dL, the most commonly used sampling method (ie, soap and water plus alcohol) had the highest specificity (100%) compared with the other methods and similar sensitivity (88%) (Table 2).

Harms of Screening

Key Question 3. What are the harms of screening for elevated blood lead levels (with or without screening questionnaires) in children?

No studies evaluated the harms of screening vs not screening children for elevated blood lead levels.

Effectiveness of Interventions to Reduce Blood Lead Levels

Key Question 4. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy reduce blood lead levels in asymptomatic children with elevated blood lead levels?

Seven RCTs[31-40] (reported in 10 publications) evaluated the effects of interventions to reduce blood lead concentrations in asymptomatic children with elevated blood lead levels (**Table 3**). Two studies evaluated chelation, 3 studies evaluated home abatement, and 2 evaluated nutritional supplementation. Sample sizes ranged from 39 to 780 (total n = 1419). Mean age of participants was 1.6 to 3.6 years, with balanced sex distributions in the 3 studies that reported sex. One study was rated good quality, 4 fair quality, and 2 poor quality. Methodological limitations in the poor-quality studies included high loss to follow-up or failure to describe randomization, allocation concealment, or masking methods.

Chelation

Two trials (n = 819) found inconsistent effects of dimercaptosuccinic acid (DMSA) chelation therapy on blood lead level in asymptomatic children with baseline levels of 20 to 45 µg/dL (Table 3).[31,34,35,37,38] Duration of follow-up was 6 years in 1 trial and 6 months in the other.

Table 1. Characteristics and Results of Questionnaire Screening Studies[a]

Source	Setting	Screening Test	Definition of Positive Screening Examination	Sample Size, No.	Proportion With Condition, No./Total (%)	Population Characteristics	% (95% CI)	
							Sensitivity	Specificity
Childhood Studies								
Casey et al,[15] 1994	Urban general pediatric department, United States	CDC Risk Assessment Questionnaire	≥1 positive answer	167	BLL ≥10 µg/dL: 48/165 (29) BLL 10-14 µg/dL: 36/165 (22) BLL 15-19 µg/dL: 7/165 (4) BLL 20-44 µg/dL: 4/165 (2.5) BLL 46 µg/dL: 1/165 (0.5)	Mean age (low vs high risk): 10 mo vs 9 mo Female (low vs high risk): 50% vs 50% Ethnicity (low vs high risk): African American, 29% vs 33%; white, 62% vs 62%	Overall: 19/48 (40) [25.77-54.73] By screening question: Peeling paint: 15 Renovation: 31 Sibling with lead: 6[b] Adult's job with lead: 2[c] Lives near lead industry: 6	Overall: 70/117 (60) [50.36-68.78] By screening question: Peeling paint: 76 Renovation: 75 Sibling with lead: 99[b] Adult's job with lead: 97[c] Lives near lead industry: 98
Dalton et al,[16] 1996	Medical center, United States	CDC Risk Assessment Questionnaire; additional behavioral risk factor questions	≥1 positive or equivocal answer	516	BLL ≥10 µg/dL: 101/463 (22) BLL ≥15 µg/dL: 28/463 (6)	Mean age: NR (range, 6-72 mo) Female: NR Ethnicity: NR	CDC risk factors (overall): 70.3 (60.39-78.98) Behavioral risk factors (playing near outside of house): 74.2 (64.60-82.44)	CDC risk factors (overall): 31.8 (27.00-36.84) Behavioral risk factors (playing near outside of house): 54.1 (28.05-37.98)
France et al,[17] 1996	Multisite primary care network, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	≥1 positive or equivocal answer	2978	Mean BLL: 4.19 µg/dL BLL ≥10 µg/dL: 85/2978 (2.9)	Mean age: NR (range, 5 mo to 6.5 y) Female: NR Ethnicity: NR	CDC questions: 57 (45-69) CDC + additional questions: 59.7 (48-72)	CDC questions: 51 (49-53) CDC + additional questions: 36 (34-38)
Holmes et al,[18] 1997	Continuity clinic at a children's hospital, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	Unclear	754	BLL ≥10 µg/dL: 25/801 (3.1)	Mean age: 28.44 mo (range, 9-72 mo) Female: 46% Ethnicity: Hispanic, 39%; black, 39%; white, 18%	68 (46.50-85.05)	58 (53.93-61.23)
Kazal,[19] 1997	Rural clinic, Navajo Reservation, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	Unclear	368	BLL ≥10 µg/dL: 8/368 (2.2)	Mean age: 30.5 mo Female: 49% Ethnicity: Navajo, 98%	CDC questions: 42.9 (9.90-81.59) CDC + additional questions: 42.9 (NR)	CDC questions: 68.52 (68.52-78.50) CDC + additional questions: 66.1 (NR)
Muñiz et al,[20] 2003	Rural clinic, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	≥1 positive or equivocal answer	171	BLL ≥10 µg/dL: 4/171 (2.3)	Mean age: NR (range, 9-24 mo) Female: NR Ethnicity: NR	CDC questions: 25 (NR) CDC + additional questions: 50.0 (6.76-93.24)	CDC questions: 49% (NR) CDC + additional questions: 49.70 (41.88-57.53)
Robin et al,[21] 1997	Urban and rural Medicaid recipients, United States	Modified Health Care Financing Administration questionnaire	≥1 positive answer	967	BLL ≥10 µg/dL: 6/967 (0.6)	Mean age: NR (range, 2-6 y) Female: 51.3% Ethnicity: Alaska native, 60%; white, 28%; black, 5%	83.3 (35.88-99.58)	38.6 (35.50-41.77)
Schaffer et al,[22] 1996	Rural clinic, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	≥1 positive or equivocal answer to the CDC questions	705	BLL ≥10 µg/dL: 59/705 (8.4)	Mean age: NR (range, 6-72 mo) Female: NR Ethnicity: NR	CDC + additional questions: 75 (NR) Condensed questionnaire from 4 most likely to correctly identify patients: 88 (NR)	CDC + additional questions: NR Condensed questionnaire from 4 most likely to correctly identify patients: NR

(continued)

Table 1. Characteristics and Results of Questionnaire Screening Studies[a] (continued)

Source	Setting	Screening Test	Definition of Positive Screening Examination	Sample Size, No.	Proportion With Condition, No./Total (%)	Population Characteristics	% (95% CI)	
							Sensitivity	Specificity
Snyder et al,[23] 1995	Public clinics, United States	CDC Risk Assessment Questionnaire; additional risk factor questions	≥1 positive answer	247	BLL ≥10 µg/dL: 19/247 (7.7)	Mean age: NR (range, 6-72 mo) Female: NR Ethnicity: NR	CDC questions: 31.6 (12.58-56.55) Additional questions: 89.5 (66.86-98.70) CDC + additional questions: 89.5 (66.60-98.70)	CDC questions: 79.8 (74.02-84.83) Additional questions: 37.3 (30.99-43.91) CDC + additional questions: 31.6 (25.6-38.0)
Pregnancy Study								
Stefanak et al,[24] 1996	Prenatal clinics, United States	CDC Lead Poisoning Risk Questionnaire	A positive response to any of the 4 relevant CDC questions	314	Prevalence of elevated BLL: 13%	Mean age: NR Race: white, 66%; black, 28%	75.7 (NR)	46.2 (NR)
		Three questions regarding housing, smoking, and consumption of canned foods	A positive response to any of the 3 relevant additional questions				89.2 (NR)	96.4 (NR)

Abbreviations: BLL, blood lead level; CDC, Centers for Disease Control and Prevention; NR, not reported.

[a] All childhood studies were fair quality; the pregnancy study was poor quality. Quality was assessed using criteria outlined in the US Preventive Services Task Force Procedure Guide.[8]

[b] Sibling or close contact monitored or treated for lead poisoning (BLL >15 µg/dL).

[c] Living with adult exposed to lead through work or hobbies.

The Treatment of Lead-Exposed Children (TLC) study, a good-quality RCT (n = 780), evaluated children aged 12 to 33 months with blood lead levels between 20 and 44 µg/dL.[31,34,35,38] All children received nutritional supplements and had home inspections with lead abatement. Children were randomized to treatment with DMSA (1050 mg/m^2 per day for 7 days, then 700 mg/m^2 per day for 19 days) or placebo and could be treated up to 3 times with a goal blood lead concentration of less than 15 µg/dL. DMSA was associated with a blood lead level at 1 week that was mean difference of 11 µg/dL lower than that of children in the placebo group (Table 3). However, blood lead levels increased once DMSA was discontinued, and at 52 weeks the blood lead level for the treatment group was only a mean difference of 2.7 µg/dL lower than that of the placebo group (95% CI, 1.9-3.5 µg/dL).[38] In a follow-up study of 7-year-old TLC study participants (83% of original study population) 4.5 to 6 years after treatment, mean levels were similar in both groups (8.0 µg/dL).[34]

A small, fair-quality study (n = 39)[37] randomized children aged 2.5 to 5 years with mean blood lead level between 30 and 45 µg/dL to 1 course of DMSA or control. DMSA was dosed according to weight and was administered 3 times daily for 5 days followed by twice daily for 14 days. There were no significant differences in mean blood lead level at 1 month (27.4 µg/dL [SD, 7.5] vs 33.2 µg/dL [SD, 10.3], P = .16) or 6 months (28.8 µg/dL [SD, 6.4] vs 25.1 µg/dL [SD, 6.8], P = .06) (Table 3).

Nutritional Interventions

Two poor-quality studies provided insufficient evidence to determine the effects of calcium or iron nutritional supplementation interventions on blood lead level in children.[36,39]

Residential Lead Hazard Control Techniques

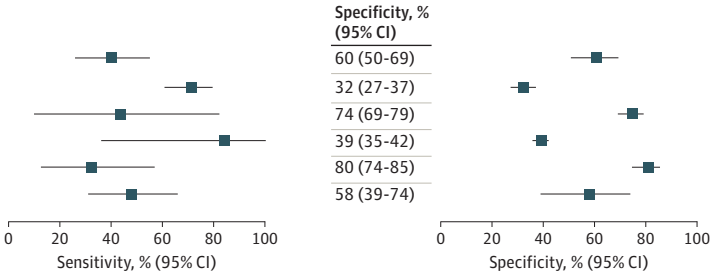
Three fair-quality RCTs found no clear effects of home lead abatement in lowering blood lead concentrations in asymptomatic children with elevated blood lead levels at baseline (Table 3).[32,33,40] One trial (n = 175) randomized children younger than 28 months in Rhode Island with blood lead levels of 15 to 19 µg/dL[33] to a home-based intervention or control. Blood lead levels in both groups decreased overall, but there was no significant difference between the intervention and control groups at 3, 6, or 12 months after baseline. A fair-quality trial (n = 90)[32] randomized age-matched pairs of 12- to 60-month-old children with mean blood lead levels 15 to 30 µg/dL to home remediation and lead abatement or delayed intervention for 1 year. Despite reductions in home lead concentrations after the intervention, the effects of remediation on mean blood lead levels were small (17.5 vs 17.9 µg/dL; mean change, 1% [95% CI, −11% to 11%]), with no significant difference between groups. A fair-quality trial (n = 84)[40] conducted in Florida enrolled asymptomatic children from the Women, Infants, & Children and Head Start programs with blood lead levels 3 to 10 µg/dL (mean, 5.29 µg/dL [range, 3.0-9.3 µg/dL]). Participants were randomized to receive an educational brochure, a home cleaning kit, or a formal home inspection and abatement. A passive control group received no intervention or information. All groups experienced a decrease in blood lead level of 2.26 to 2.99 µg/dL over 6 to 12 months, with no significant difference between groups.

Effectiveness of Interventions to Improve Health Outcomes

Key Question 5. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy

Figure 5. Meta-analysis of Sensitivity and Specificity for the Centers for Disease Control and Prevention Questionnaire

Study	Positive		Negative		Sensitivity, % (95% CI)	Specificity, % (95% CI)
	True	False	True	False		
Casey et al,[15] 1994	19	47	29	70	40 (26-55)	60 (50-69)
Dalton et al,[16] 1996	71	247	30	115	70 (60-79)	32 (27-37)
Kazal,[19] 1997	3	83	4	233	43 (10-82)	74 (69-79)
Robin et al,[21] 1997	5	587	1	369	83 (36-100)	39 (35-42)
Snyder et al,[23] 1995	6	46	13	182	32 (13-57)	80 (74-85)
Pooled	104	1010	77	969	48 (31-66)	58 (39-74)



The *metandi* command in Stata version 14.2 cannot be used to formally investigate heterogeneity or to compare the accuracy of 2 or more tests because it does not have an option for including a covariate in the bivariate model.

improve health outcomes in asymptomatic children with elevated blood lead levels?

The TLC[34,35,38] trial of DMSA chelation therapy vs placebo (n = 780) was the only study to evaluate the effect of interventions for lowering elevated blood lead level on health outcomes by measuring children's neuropsychological outcomes (Table 3). At 36 months, there were no significant differences between chelation therapy and placebo in the Wechsler Preschool and Primary Scale of Intelligence–Revised, the Developmental Neuropsychological Assessment (NEPSY), or the Conners Parent Rating Scale–Revised. In a follow-up study[34] of the same children at age 7 years (4.5-6 years after treatment), chelation was associated with lower (worse) scores on the adjusted Attention and Executive Functions subscore of the NEPSY (unadjusted difference, −1.8 [95% CI, −4.5 to 1.0]; adjusted *P* = .045). There were no statistically significant effects on any other cognitive, neuropsychiatric, or behavioral outcome.

Harms of Interventions for Children With Elevated Blood Lead Levels

Key Question 6. What are the harms of interventions in asymptomatic children with elevated blood lead levels?

One good-quality RCT (Table 3) and 1 poor-quality study reported adverse effects of chelation therapy. The TLC trial (n = 780) compared DMSA chelation therapy with placebo in children aged 12 to 33 months with blood lead concentrations between 20 and 44 µg/dL.[38] DMSA was associated with a small but statistically significant decrease in height growth over 34 months (difference, 0.35 cm [95% CI, 0.05-0.72 cm]) and slightly poorer scores on attention and executive function (unadjusted difference, −1.8; adjusted *P* = .045 for effect) tests at age 7 years.[34] There were no significant differences in laboratory values, including neutrophil count, platelet count, aminotransferase concentrations, and alkaline phosphatase concentration after chelation.[31,38] One poor-quality study[42] reported adverse events associated with the less-commonly used chelator d-penicillamine, including leukopenia, thrombocytopenia, rashes, urinary incontinence, and gastrointestinal symptoms. No study identified harms of counseling, nutritional interventions, or residential lead hazard control techniques.

Screening and Treatment in Pregnancy

Evidence to determine effects of lead screening during pregnancy was extremely limited. There were no studies of screening in pregnant women and no studies reported health outcomes of interventions to reduce blood lead levels in asymptomatic pregnant women. One study reported the diagnostic accuracy of a clinical questionnaire for pregnant women,[24] and 1 study reported effects of a nutritional intervention during pregnancy.[41]

Effectiveness of Screening

Key Question 1a. Is there direct evidence that screening for elevated blood lead levels in asymptomatic pregnant women improves health outcomes (ie, reduced cognitive problems in offspring, adverse perinatal outcomes, and adverse maternal outcomes)?

Key Question 1b. Does the effectiveness of screening in asymptomatic pregnant women vary by gestational age?

No studies directly evaluated clinical benefits and harms of screening pregnant women for elevated blood lead levels vs no screening or how effectiveness of screening varies according to the gestational age at which screening is performed.

Diagnostic Accuracy of Questionnaires or Clinical Prediction Tools

Key Question 2. What is the accuracy of questionnaires or clinical prediction tools that identify pregnant women who have elevated blood lead levels?

One fair-quality observational study[24] evaluated the accuracy of a questionnaire for identifying pregnant women with elevated blood lead levels using 4 questions from the 5-question 1991 CDC questionnaire designed to identify children at risk (n = 314). Women with a positive response to at least 1 of the 4 questions were more likely to have elevated blood lead levels than those who answered negatively to all 4 questions (relative risk, 2.39 [95% CI, 1.17 to 4.89]; *P* = .01) (Table 1). However, diagnostic accuracy was poor, with a sensitivity of 75.7% and specificity of 46.2%. The single most predictive item was having a "home built before 1960."

Harms of Screening

Key Question 3. What are the harms of screening for elevated blood lead levels (with or without screening questionnaires) in asymptomatic pregnant women?

No study directly compared the harms of screening pregnant women for elevated blood lead levels in a screened vs an unscreened population.

Table 2. Characteristics and Results of Capillary Screening Studies

Source	Quality[a]	Setting	Definition of a Positive Screening Examination	Sample Size, No.	Proportion With Condition, %	Population Characteristics, %	% (95% CI)	
							Sensitivity	Specificity
Holtrop et al,[26] 1998	Poor	Urban clinic, United States	≥10 µg/dL, ≥15 µg/dL, ≥20 ug/dL	124	BLL ≥10 µg/dL: 31/120 (26)	Mean age: NR Female: 41 Ethnicity: black, 97	≥10 µg/dL: 94 (NR) ≥15 µg/dL: 75 (NR) ≥20 ug/dL: 78 (NR)	≥10 µg/dL: 99 (NR) ≥15 µg/dL: 98 (NR) ≥20 ug/dL: 100 (NR)
Parsons et al,[27] 1993	Fair	County health clinics and university hospital, United States	≥10 µg/dL, ≥15 µg/dL, ≥20 µg/dL, ≥25 µg/dL	499	≥10 µg/dL: 30.5 ≥15 µg/dL: 16.7 ≥20 µg/dL: 9.9 ≥25 µg/dL: 6.6	Mean age: NR (range, 0-12 y) Female: 43 Race/ethnicity: white, 38; black, 28; Hispanic, 21; Asian, 6	≥10 µg/dL: 87.5 (81.8-91.9) ≥15 µg/dL: 83.0 (74.8-89.5) ≥20 µg/dL: 81.8 (70.4-90.2) ≥25 µg/dL: 82.5 (67.2-92.3)	≥10 µg/dL: 93.2 (90.0-95.6) ≥15 µg/dL: 95.3 (92.8-97.2) ≥20 µg/dL: 97.3 (95.3-98.6) ≥25 µg/dL: 98.5 (96.9-99.4)
Sargent and Dalton,[28] 1996; Sargent et al,[29] 1995	Fair	Urban clinic, United States	≥8 µg/dL, ≥10 µg/dL, ≥12 µg/dL, ≥15 µg/dL	513	BLL ≥10 µg/dL: 20.5% Elevated BLL ≥20 µg/dL: 2.3%	Population characteristics NR	≥8 µg/dL: 100 (NR) ≥10 µg/dL: 91 (NR) ≥12 µg/dL: 63 (NR) ≥15 µg/dL: NR	≥8 µg/dL: NR ≥10 µg/dL: 92.2 (NR) ≥12 µg/dL: NR ≥15 µg/dL: NR
Schlenker et al,[30] 1994[b]	Poor	Urban health department and clinics, United States	≥20 µg/dL	295	Elevated BLL: NR	Mean age: 3 y Female: 47 Ethnicity: black, 88	Method 1: 95 (NR) Method 2: 96 (NR) Method 3: 88 (NR) Method 4: 86 (NR)	Method 1: 94 (NR) Method 2: 96 (NR) Method 3: 100 (NR) Method 4: 91 (NR)

Abbreviation: NR, not reported.

[a] Quality was assessed using criteria outlined in the US Preventive Services Task Force Procedure Guide.[8]

[b] Study compared 4 methods of capillary screening (method 1: alcohol wipe; method 2: alcohol + silicone; method 3: soap and water + alcohol; method 4: soap and water, alcohol, and 1% nitric acid solution).

Effectiveness of Interventions to Reduce Blood Lead Levels and Gestational Hypertension

Key Question 4. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy reduce blood lead levels and rates of gestational hypertension in asymptomatic pregnant women with elevated blood lead levels?

One fair-quality RCT (n = 670) of healthy pregnant women (mean baseline lead level, ≈4 µg/dL) in Mexico found calcium supplementation associated with reduced blood lead levels vs placebo (difference, 11%; *P* = .004; levels in each group not reported) (Table 3).[41] Effects were more pronounced in women with baseline blood levels of 5 µg/dL or greater. Women were not required to have elevated blood levels at baseline. Limitations included unclear allocation methods, unblinded design, and some baseline between-group differences, including dietary calcium intake. Loss to follow-up was 14% (46/334) in the calcium group and 18% (59/336) in the placebo group. No harms were reported.

Effectiveness of Interventions to Improve Health Outcomes

Key Question 5. Do counseling and nutritional interventions, residential lead hazard control techniques, or chelation therapy improve health outcomes in asymptomatic pregnant women with elevated blood lead levels?

No studies reported health outcomes after interventions to reduce blood lead levels in asymptomatic pregnant women.

Harms of Interventions for Pregnant Women With Elevated Blood Lead Levels

Key Question 6. What are the harms of interventions in asymptomatic pregnant women with elevated blood lead levels?

One RCT on the effects of calcium supplementation on blood lead levels in pregnant women did not report harms (Table 3).[41]

Discussion

A summary of the evidence for this updated review is shown in **Table 4** and **Table 5** (summary of evidence tables from the full USPSTF reports are available in eTables 6 and 7 in the Supplement). Consistent with the prior USPSTF review,[7] no evidence was found that directly evaluated benefits or harms of screening children for elevated blood lead levels compared with no screening. Based on studies available at the time of the prior USPSTF review, instruments to identify children at higher risk of elevated blood levels to guide targeted screening have poor diagnostic accuracy. This update confirms there are no clear effects of interventions for lowering elevated blood levels in affected children or to improve neurodevelopmental outcomes. Evidence to determine benefits and harms of screening or treating elevated lead levels during pregnancy remains extremely limited.

Given the decreased prevalence of elevated blood lead levels identified in the US pediatric population (from 88% between 1976 and 1980 to 0.8% from 2007 to 2010), targeted screening strategies have been suggested.[2] The most commonly used risk assessment instrument is the CDC questionnaire; however, studies of this instrument or adapted versions have found poor diagnostic accuracy, with results that are not informative.[17,18,20,22,43] Furthermore, the CDC questionnaire was created in 1991 and no study on its accuracy has been published since 1997, potentially limiting the applicability of available

Table 3. Characteristics and Results of Randomized Clinical Trials of Treatment[a]

Source	Setting	Inclusion Criteria	Interventions (No.)	Study Duration	Patient Characteristics	Main Findings		
						Intermediate Outcomes	Clinical Health Outcomes	Adverse Events
Childhood Trials								
Boreland et at,[32] 2009	Lead-mining neighborhood, Australia	Children aged 12-60 mo with BLL 15-29 µg/dL	A: Immediate home lead abatement (n = 45) B: Delayed home lead abatement (n = 45)	Mean, 13 mo	Mean age: 3.5 y Race: NR Female: 58% BLL 15-19 µg/dL: 28% BLL 20-24 µg/dL: 23% BLL 25 to 29 µg/dL: 37% BLL >30 µg/dL: 12%	BLL, µg/dL (A vs B): 17.5 vs 17.9 (mean change, 1% [95% CI, −11% to 11%])	NR	NR
Brown et at,[33] 2006	Rhode Island Department of Health, United States	Children aged <28 mo with BLL 15-19 µg/dL	A: 5 home visits from a nurse (n = 92) B: Usual care, including educational outreach about lead poisoning (n = 83)	1 y	Mean age: 19.1 mo (A) vs 18.8 mo (B) Race (A vs B): white, 47% vs 39; Hispanic, 40% vs 49; black, 8% vs 10% Sex: NR BLL, µg/dL (A vs B): 16.5 vs 16.6	BLL: No significant difference between groups at 3, 6, or 12 mo (data only reported in a figure) Last available BLL >10 µg/dL (A vs B): 51% vs 51% (*P* = NR) Any BLL >20 µg/dL (A vs B): 8% vs 11% (*P* = NR)	NR	NR
Nicholson,[40] 2017	Urban children's hospital, United States	Low-income families with children aged <6 y and BLL 3-9.9 µg/dL	A: Professional lead inspection and cleaning kit B: Professional lead inspection C. Cleaning kit D. EPA lead exposure pamphlets	6 mo	Age: 3.94 y Race: NR Sex: NR BLL, µg/dL (A vs B vs C vs D): 5.18 vs 5.75 vs 5.25 vs 5.02	Change in BLL at 6 mo, µg/dL (A vs B vs C vs D): −2.54 vs −2.99 vs −2.46 vs −2.26; no significant differences	NR	NR
O'Connor and Rich,[37] 1999	Urban children's hospital, United States	Children aged 2.5-5 y with BLL 30-45 µg/dL	A: DMSA chelation 100-200 mg 3× daily (dose weight-dependent) (n = 19) B: Placebo (n = 20)	6 mo	Age: 39.8 vs 40.8 mo Race: NR Female: 68% vs 35% Mean BLL: 34.9 vs 33.0 µg/dL	1 mo (A vs B): mean BLL, 27.4 vs 33.2 µg/dL (*P* value NR) 6 mo (A vs B): mean BLL, 28.8 vs 25.1 µg/dL (*P* = .06)	NR	NR
TLC Trial Group,[31] 2000 See also: Rogan et al,[38] 2001 Liu et al,[35] 2002 Dietrich et al,[34] 2004	Multiple urban clinics, United States	Children aged 12 to 33 mo with BLL between 20 and 44 µg/dL	A. DMSA, dose-dependent on body surface area (n = 396) B. Placebo (n = 384)	3 y	Age: 24 vs 24 mo Race (A vs B): black, 78% vs 76%; white, 12% vs 11%; Hispanic, 6% vs 7%; other, 4% vs 6% Female: 45% vs 43% BLL: 26 vs 26 µg/dL	6 mo: BLL, mean difference: −4.5 (95% CI, −3.7 to −5.3) µg/dL 12 mo: BLL, mean difference: −2.7 (95% CI, −1.9 to −3.5) µg/dL Age 7 y: BLL >10 µg/dL: 25% vs 27% (*P* value NR)	36 mo: No significant differences in WPPSI-R, NEPSY, or CPRS neurodevelopment scales or any of their subscales[38] No significant difference or change in WPPSI-R or Bayley Scale of Infant Development cognitive scale scores.[35] No significant differences in WISC-III, NEPSY, or WLPB-R cognition scales; BASC behavior scales; CVLT-C learning and memory scales; CPT attention scale; or CPT or NESS neuromotor scales[34]	3 mo: Hospitalizations (A vs B): 5.6% vs 3.9% (difference, 1.6% [95% CI, −2.0% to 6.3%]); no significant differences in rates of any adverse event. 36 mo: No significant difference between groups in any category of adverse events (data NR in article but available online)[35]; height at age 7 y shorter in DMSA-treated patients by 1.17 (95% CI, 0.41 to 1.93) cm

(continued)

Table 3. Characteristics and Results of Randomized Clinical Trials of Treatment[a] (continued)

Source	Setting	Inclusion Criteria	Interventions (No.)	Study Duration	Patient Characteristics	Main Findings		
						Intermediate Outcomes	Clinical Health Outcomes	Adverse Events
Pregnancy Trial								
Ettinger et al,[41] 2009 (RCT)	Prenatal clinics, Mexico	Pregnant women <14 weeks gestation, without a high-risk pregnancy	A. Calcium, 1200 mg at bedtime (n = 334) B. Placebo (n = 336)	8 mo	Mean age (A vs B): 26.9 vs 25.9 y ($P < .05$) Race: NR No. of pregnancies (A vs B): 2.0 vs 2.1 Mean BLL (A vs B): 3.8 vs 4.1 μg/dL	BLL: 11% mean reduction in treatment group vs placebo ($P = .04$)	NR	NR

Abbreviations: BASC, Behavior Assessment System for Children; BLL, blood lead level; CPRS, Connors Parent Rating Scale; CPT, Connors Continuous Performance Test; CVLT-C, California Verbal Learning Test-Children's Version; DMSA, dimercaptosuccinic acid; EPA, US Environmental Protection Agency; NEPSY, a developmental neuropsychological assessment; NESS, Neurological Examination for Soft Signs; NR, not reported; NS, not significant; TLC, Treatment of Lead-Exposed Children Trial Group; WISC-III, Wechsler Intelligence Scale for Children-third edition; WLPB-R, Woodcock Language Proficiency Battery-Revised; WPPSI-R, Wechsler Preschool and Primary Scale of Intelligence-Revised.

[a] All trials in table were fair quality except for TLC Trial Group,[31] which was good quality. Quality was assessed using criteria outlined in the US Preventive Services Task Force Procedure Guide.[8]

evidence to contemporary clinical practice. Accurate risk-assessment instruments would be helpful for guided targeted screening strategies. In lieu of accurate screening instruments, potential alternative strategies include universal screening[15,19] or screening targeted at communities with a high prevalence of elevated lead levels.[16] The findings regarding the poor accuracy of the CDC questionnaire are generally consistent with those from another recent systematic review[44] on accuracy of screening questionnaires and with evidence from the prior USPSTF review.[7]

Evidence indicates that capillary sampling is slightly less sensitive than venous sampling, with comparable specificity,[26-28,30] provided that contamination is avoided using standard techniques. Factors that may inform the decision to perform capillary sampling for screening include the trade-offs between slightly worse accuracy and greater convenience or patient preferences. Both methods require confirmation.

There is limited evidence on the effectiveness of interventions for elevated blood lead levels on neurodevelopmental outcomes and longer-term blood lead levels. One trial showed short-term (through 1 year) effects of DMSA chelation on lowering blood levels vs placebo in children with moderately elevated blood levels (20-44 μg/dL) at baseline, but no clear effects on longer-term lead levels or neurodevelopmental outcomes, with some data indicating potential harms.[38] No trial evaluated effects of chelation in children with blood lead levels less than 20 μg/dL, but chelation is not recommended at this level in the absence of severe symptoms. Evidence on residential interventions was limited and showed no clear effects on blood lead concentrations. Evidence on calcium and iron nutritional interventions was poor quality and insufficient to determine effects on blood lead levels or clinical outcomes.

This review focused on evidence of screening and treatment of individuals in primary care settings. Community or public health–based approaches are other important strategies used to address lead exposures. Risk factors for lead exposure include socioeconomic disadvantage, living near lead industry, renovation or deterioration of older lead-painted houses, poor nutrition, and previously living in countries where leaded gasoline is used.[2,45,46] Exposures may occur through water sources, lead pipes, or culturally linked sources, such as folk remedies, imported food and candy, and traditional pottery used for cooking.[47,48] The CDC recommends that public health entities provide clinicians with community-specific risk factors that can be used to determine the need for screening.[49]

Elevated blood lead levels predominantly affect socioeconomically disadvantaged and minority children. Different sources of lead exposure than have been previously considered are emerging in these children, yet research on screening and prevention in these populations remains limited.[47,48,50] Exposures related to community water sources, lead pipes in schools, and factory emissions affecting neighborhood soil quality are some of the relevant factors not captured by current screening questionnaires. Culturally linked sources of lead poisoning, such as imported candy, pottery, traditional medicines, and cosmetics, specific to subpopulations[47,48] living in the United States also may pose additional risk, since little regulation exists to monitor, identify, and control these nonpaint exposures. Additional research is warranted to validate these potential associations in specific geographic locations. Children exposed to less common sources of lead exposure may live in areas with a higher risk for housing-related source exposures.[50] The dual risk associated with these communities suggests a more focused strategy to deal with population-specific risks.

Table 4. Summary of Evidence: Childhood Key Questions

No. of Studies (No. of Participants); Study Design	Summary of Findings	Main Findings From Prior USPSTF Reviews	Consistency/Precision	Limitations	Applicability	Strength of Evidence[a]
KQ1: Direct Evidence for Screening						
0	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ2a: Accuracy of Questionnaires or Clinical Prediction Tools						
9 Fair-quality cross-sectional studies (n = 6873)	Five studies used the threshold of ≥1 positive answers on the 5-item 1991 CDC screening questionnaire had a pooled sensitivity of 48% (95% CI, 31.4% to 65.6%) and specificity of 58% (95% CI, 39.9% to 74.0%) for identifying children with a venous BLL ≥10 µg/dL Four studies of modified versions of the CDC questionnaire did not demonstrate improved accuracy (sensitivity, 25% to 68%; specificity, 49% to 58%)	Not previously reviewed[b]	Consistent; findings reasonably precise	All studies conducted from 1994 to 2003; studies used the 1991 CDC questionnaire or a modified version of this survey	Poor accuracy of questionnaires or clinical tools to predict elevated BLL in rural, urban, low-, and higher-risk settings Modified versions tailored for specific populations did not improve accuracy All studies conducted from 1994-2003 and may not address current risk factors for lead exposure	Moderate
KQ2b: Accuracy of Capillary Blood Lead Testing						
2 Fair-quality and 2 poor-quality observational studies (n = 1431)	Four studies conducted in the urban United States found capillary BLL testing associated with sensitivity of 87% to 91% and specificity >90% (92%-99%) for identification of elevated BLL vs venous sampling	Not previously reviewed[b]	Consistent; precise	None	Diagnostic accuracy studies demonstrate high overall sensitivity and specificity for BLL testing Reference standard during study periods was 10 ug/dL	Moderate
KQ3: Harms of Screening						
0	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ4: Interventions to Reduce BLLs in Asymptomatic Children With Elevated Levels						
1 Good-quality, 5 fair-quality, and 2 poor-quality RCTs (n = 1419)	One large RCT of chelation therapy with DMSA in children with mean BLL 20-45 µg/dL associated with decreased BLL vs placebo at 1 week, 6 mo, and 1 y—but no effects at longer term follow-up at 4.5-6 y One RCT found no significant differences in BLL between chelation vs placebo at 1 or 6 mo There was insufficient evidence from 2 studies to determine effects of nutritional supplementation Three studies of residential lead hazard control techniques found no significant difference in BLL between groups	Not previously reviewed[b]	Some inconsistency between chelation studies; consistency of nutritional and residential hazard control interventions; some imprecision for individual outcomes	Poor quality studies of nutritional interventions do not provide adequate data to assess treatment effects	Limited effectiveness of these interventions limits applicability for implementation of these interventions in clinical settings in the United States	Moderate

(continued)

Table 4. Summary of Evidence: Childhood Key Questions (continued)

No. of Studies (No. of Participants); Study Design	Summary of Findings	Main Findings From Prior USPSTF Reviews	Consistency/Precision	Limitations	Applicability	Strength of Evidence[a]
KQ5: Interventions to Improve Health Outcomes in Asymptomatic Children With Elevated BLLs						
1 Good-quality RCT (n = 780)	One RCT found no significant differences between chelation therapy vs placebo in neuropsychological outcomes, despite a decrease in BLL after chelation There was no evidence on effects of counseling and nutritional interventions or residential lead hazard control techniques on health outcomes in asymptomatic children with elevated BLL at baseline	No clear evidence to support a clinical benefit from chelation therapy in children with elevated BLL at baseline, based on 1 trial; no studies on effects of environmental or nutritional interventions on health outcomes	Consistent; some imprecision	Based on 1 RCT of 780 US children, the adjusted treatment effect on 1 cognitive testing subscore showed a statistically significant but small improvement in the placebo group (P = .045) No other significant outcomes for all other effects of treatment on cognitive, neuropsychiatric, and behavioral testing scores	One large RCT from the United States demonstrates lack of benefit for chelation therapy in asymptomatic children	Moderate
KQ6: Harms of Interventions						
1 Good-quality RCT; 1 poor-quality observational study (n = 855)	One good-quality and 1 poor-quality study reported adverse effects of chelation therapy The good-quality study found that children treated with DMSA had a small but statistically significant decrease in height growth over 34 mo and slightly poorer scores on attention and executive function tests at age 7 y; the poor-quality study reported adverse events associated with the less commonly used chelator d-penicillamine, including leukopenia, thrombocytopenia, urticarial and maculopapular rashes, urinary incontinence, abdominal pain, and diarrhea No study identified harms of counseling, nutritional interventions, or residential lead hazard control techniques	Adverse effects of environmental interventions included transient BLL elevation, inconvenience associated with abatement work or relocation, and cost-benefit considerations Adverse effects after chelation treatment included mild GI and systemic symptoms, rashes, transient hyperphosphatasemia, neutropenia, eosinophilia, and elevations in serum aminotransferase levels	Consistent; precise	One poor-quality study reported intermediate outcomes associated with adverse effects of treatment	One RCT from a single US setting provided evidence of adverse effects after chelation treatment in asymptomatic children	Moderate

Abbreviations: BLL, blood lead level; CDC, Centers for Disease Control and Prevention; DMSA, dimercaptosuccinic acid; GI, gastrointestinal; KQ, key question; RCT, randomized clinical trial; USPSTF, US Preventive Services Task Force.

[a] Evidence-based Practice CenterAssessment of Strength of Evidence is based on new evidence identified for this update and relevant evidence from the prior report.

[b] KQs in this review differ from those in the previous review, and KQ numbers in this review do not correspond to KQ numbers in the previous review. For some questions, the number of studies included in the previous review was not precisely reported.

Table 5. Summary of Evidence: Pregnancy Key Questions

No. of Studies (No. of Participants); Study Design	Summary of Findings	Main Findings From Prior USPSTF Reviews	Consistency/ Precision	Limitations	Applicability	Strength of Evidence[a]
KQ1a: Direct Evidence for Screening						
No studies	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ1b: Effectiveness of Screening by Gestational Age						
No studies	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ2: Accuracy of Questionnaires or Clinical Prediction Tools for Pregnant Women						
1 Fair-quality observational study (n = 314)	One study used 4 of 5 questions from the CDC questionnaire for children Women with a positive response to ≥1 of the 4 questions were more likely to have elevated BLLs than those who answered negatively to all 4 questions (RR, 2.39 [95% CI, 1.17-4.89]; *P* = .01) The CDC questionnaire had a sensitivity of 75.7% in the study and a sensitivity of 46.2%; the most predictive single item was "home built before 1960"	No studies	No studies	Questionnaire not designed specifically for pregnant women; used a higher threshold of blood lead than the CDC <5 µg/dL No intention-to-treat analysis Larger set of investigator-designed questions not reported	One study conducted in a single setting in Ohio from 1990 to 1992	Moderate
KQ3: Harms of Screening						
No studies	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ4: Interventions to Reduce BLLs or Rates of Gestational Hypertension						
1 Fair-quality RCT (n = 670)	One RCT of healthy pregnant women (mean baseline lead levels, ≈4 µg/dL) in Mexico found calcium supplementation associated with reduced BLLs vs placebo (difference, 11%; *P* = .004; levels in each group not reported) In women with baseline BLL ≥5 µg/dL, calcium supplementation was associated with a 17% greater reduction in BLL vs placebo, vs a 7% greater reduction in those with lead levels <5 µg/dL at baseline	No studies	Consistent; imprecise	Enrolled any healthy pregnant woman; did not identify an asymptomatic group with elevated BLL at baseline Limited subgroup analyses of those with elevated BLL were available; some findings conflict with overall study results	One study conducted in Mexico city; high proportion of participants regularly using lead-glazed ceramics for cooking meals (35%)	Moderate
KQ5: Interventions to Improve Health Outcomes in Asymptomatic Pregnant Women						
No studies	No studies	No studies	No studies	No studies	Not applicable	Insufficient
KQ6: Harms of Interventions						
No studies	No studies	No studies	No studies	No studies	Not applicable	Insufficient

Abbreviations: BLL, blood lead level; CDC, Centers for Disease Control; KQ, key question; RCT, randomized clinical trial; RR, relative risk; USPSTF, US Preventive Services Task Force.

[a] Evidence-based Practice Center Assessment of Strength of Evidence is based on new evidence identified for this update and relevant evidence from the prior report.

Elevated blood lead levels are associated with serious, often irreversible, health consequences. Effective screening could identify lead-contaminated residential environments and abate them, not only to improve the health of the individual child but also of others in the household. While remediation of lead exposures in a specific residence may be too late for an individual child who already is exposed, the downstream effect could prevent exposure for subsequent generations of children. Development of questionnaires that incorporate current risk factors for elevated lead levels with validation in contemporary populations of children in the United States is necessary. Research evaluating effectiveness of treatments for elevated lead levels, such as counseling, nutritional interventions, and residential lead hazard control techniques, in trials with adequate sample sizes may also inform treatment strategies. While there is limited evidence on the clinical benefit of nutritional supplementation in reducing lead levels in children, epidemiologic evidence suggests potential benefits and is supported by studies of the toxicokinetics of lead in childhood. Effects of nutrition could be further validated by well-designed research studies. Ideally, randomized trials would recruit children from a range of racial, ethnic, and socioeconomic strata and evaluate the effects of screening on improving health outcomes as well as short- and long-term harms. However, ethical issues of trials in the context of environmental health exposures would limit feasibility. Research on newer methods for testing blood lead levels, such as point-of-care testing, and on the intraindividual and interlaboratory reliability of blood lead level testing would be helpful for informing testing strategies.

Limitations

This review has several limitations. First, there was an overall lack of evidence to address all key questions. Second, despite searching for updated data, the available studies evaluating the effectiveness of the risk-based questionnaires were published between 1994 and 2003 and may not assess contemporary risk factors. Current clinical practice uses a reference blood lead level greater than 5 µg/dL based on updated CDC guidance, but several of the studies included for this review used the older reference value of 10 µg/dL or greater. Third, nonrandomized studies were included to evaluate the effectiveness of interventions for elevated blood levels but are more susceptible to confounding and bias, leading to downgrading of study quality. Fourth, direct correlation of environmental exposures with longer-term health outcomes is difficult to study and characterize, since these exposures often have subtle clinical effects. Fifth, the review focused on screening and treatment of individuals in primary care settings, excluding community and public health approaches that could inform screening practices at the population level.

Conclusions

Screening questionnaires were not accurate for identifying children with elevated blood lead levels. Chelating agents in children were not associated with sustained effects on blood level levels but were associated with harms.

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Acquisition, analysis, or interpretation of data: Cantor, Hendrickson, Blazina, Griffin, Grusing, McDonagh.
Drafting of the manuscript: Cantor, Hendrickson, Griffin, Grusing.
Critical revision of the manuscript for important intellectual content: Cantor, Hendrickson, Blazina, McDonagh.
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REFERENCES

1. Flora G, Gupta D, Tiwari A. Toxicity of lead: a review with recent updates. *Interdiscip Toxicol*. 2012;5(2):47-58. doi:10.2478/v10102-012-0009-2

2. Advisory Committee on Childhood Lead Poisoning Prevention, Centers for Disease Control and Prevention (CDC). Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. CDC website. https://www.cdc.gov/nceh/lead/acclpp/final_document_030712.pdf. Published 2012. Accessed November 15, 2017.

3. Centers for Disease Control and Prevention (CDC). Standard surveillance definitions and classifications. CDC website. https://www.cdc.gov/nceh/lead/data/definitions.htm. Updated November 18, 2016. Accessed February 12, 2019.

4. Centers for Disease Control and Prevention (CDC). Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women. CDC website. https://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf. Published 2010. Accessed November 15, 2017.

5. Sowers M, Jannausch M, Scholl T, Li W, Kemp FW, Bogden JD. Blood lead concentrations and pregnancy outcomes. *Arch Environ Health*. 2002;57(5):489-495. doi:10.1080/00039890209601442

6. U.S. Preventive Services Task Force (USPSTF). Lead levels in childhood and pregnancy: screening. USPSTF website. https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lead-levels-in-childhood-and-pregnancy-screening?ds=1&s=lead. December 2006. Accessed October 22, 2018.

7. Rischitelli G, Nygren P, Bougatsos C, Freeman M, Helfand M. *Screening for Elevated Lead Levels in Childhood and Pregnancy: Update of a 1996 U.S. Preventive Services Task Force Review*. Rockville, MD: Agency for Healthcare Research and Quality; 2006.

8. U.S. Preventive Services Task Force (USPSTF). Procedure Manual. USPSTF website.

https://www.uspreventiveservicestaskforce.org/Page/Name/procedure-manual. Published June 2018. Accessed November 15, 2017.

9. Cantor A, Hendrickson R, Blazina I, Griffin J, Grusing S, McDonagh M. *Screening for Elevated Lead Levels in Children: A Systematic Review for the U.S. Preventive Services Task Force: Evidence Synthesis No. 174*. Rockville, MD: Agency for Healthcare Research and Quality; 2019. AHRQ publication 18-05245-EF-1.

10. Cantor A, McDonagh M, Blazina I, Griffin J, Grusing S, Hendrickson R. *Screening for Elevated Lead Levels in Pregnancy: A Systematic Review for the U.S. Preventive Services Task Force: Evidence Synthesis No. 175*. Rockville, MD: Agency for Healthcare Research and Quality; 2019. AHRQ publication 18-05245-EF-2.

11. United Nations Development Programme (UNDP). Global human development indicators: country profiles. UNDP website. http://hdr.undp.org/en/countries. 2017. Accessed November 17, 2017.

12. Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med*. 1993;12(14):1293-1316. doi:10.1002/sim.4780121403

13. Liu Z, Yao Z, Li C, Liu X, Chen H, Gao C. A step-by-step guide to the systematic review and meta-analysis of diagnostic and prognostic test accuracy evaluations. *Br J Cancer*. 2013;108(11):2299-2303. doi:10.1038/bjc.2013.185

14. Toft N, Nielsen SS. Summary receiver operating characteristics (SROC) and hierarchical SROC models for analysis of diagnostic test evaluations of antibody ELISAs for paratuberculosis. *Prev Vet Med*. 2009;92(3):249-255. doi:10.1016/j.prevetmed.2009.08.019

15. Casey R, Wiley C, Rutstein R, Pinto-Martin J. Prevalence of lead poisoning in an urban cohort of infants with high socioeconomic status. *Clin Pediatr (Phila)*. 1994;33(8):480-484. doi:10.1177/000992289403300806

16. Dalton MA, Sargent JD, Stukel TA. Utility of a risk assessment questionnaire in identifying children with lead exposure. *Arch Pediatr Adolesc Med*. 1996;150(2):197-202. doi:10.1001/archpedi.1996.02170270079012

17. France EK, Gitterman BA, Melinkovich P, Wright RA. The accuracy of a lead questionnaire in predicting elevated pediatric blood lead levels. *Arch Pediatr Adolesc Med*. 1996;150(9):958-963. doi:10.1001/archpedi.1996.02170340072014

18. Holmes SE, Drutz JE, Buffone GJ, Rice TD. Blood lead levels in a continuity clinic population. *J Toxicol Clin Toxicol*. 1997;35(2):181-186. doi:10.3109/15563659709001190

19. Kazal LA Jr. The failure of CDC screening questionnaire to efficiently detect elevated lead levels in a rural population of children. *J Fam Pract*. 1997;45(6):515-518.

20. Muñiz MA, Dundas R, Mahoney MC. Evaluation of a childhood lead questionnaire in predicting elevated blood lead levels in a rural community. *J Rural Health*. 2003;19(1):15-19. doi:10.1111/j.1748-0361.2003.tb00536.x

21. Robin LF, Beller M, Middaugh JP. Statewide assessment of lead poisoning and exposure risk among children receiving Medicaid services in Alaska. *Pediatrics*. 1997;99(4):E9. doi:10.1542/peds.99.4.e9

22. Schaffer SJ, Kincaid MS, Endres N, Weitzman M. Lead poisoning risk determination in a rural setting. *Pediatrics*. 1996;97(1):84-90.

23. Snyder DC, Mohle-Boetani JC, Palla B, Fenstersheib M. Development of a population-specific risk assessment to predict elevated blood lead levels in Santa Clara County, California. *Pediatrics*. 1995;96(4, pt 1):643-648.

24. Stefanak MA, Bourguet CC, Benzies-Styka T. Use of the Centers for Disease Control and Prevention childhood lead poisoning risk questionnaire to predict blood lead elevations in pregnant women. *Obstet Gynecol*. 1996;87(2):209-212. doi:10.1016/0029-7844(95)00397-5

25. Tejeda DM, Wyatt DD, Rostek BR, Solomon WB. Do questions about lead exposure predict elevated lead levels? *Pediatrics*. 1994;93(2):192-194.

26. Holtrop TG, Yee HY, Simpson PM, Kauffman RE. A community outreach lead screening program using capillary blood collected on filter paper. *Arch Pediatr Adolesc Med*. 1998;152(5):455-458. doi:10.1001/archpedi.152.5.455

27. Parsons PJ, Raciti K, Esernio-Jenssen D. *Evaluation and Improvement of Sample Collection Procedures for the Determination of Blood Lead*. Atlanta, GA: Centers for Disease Control and Prevention; 1993.

28. Sargent JD, Dalton MA. Rethinking the threshold for an abnormal capillary blood lead screening test. *Arch Pediatr Adolesc Med*. 1996;150(10):1084-1088. doi:10.1001/archpedi.1996.02170350086015

29. Sargent JD, Brown MJ, Freeman JL, Bailey A, Goodman D, Freeman DH Jr. Childhood lead poisoning in Massachusetts communities: its association with sociodemographic and housing characteristics. *Am J Public Health*. 1995;85(4):528-534. doi:10.2105/AJPH.85.4.528

30. Schlenker TL, Fritz CJ, Mark D, et al. Screening for pediatric lead poisoning: comparability of simultaneously drawn capillary and venous blood samples. *JAMA*. 1994;271(17):1346-1348. doi:10.1001/jama.1994.03510410058033

31. Treatment of Lead-Exposed Children (TLC) Trial Group. Safety and efficacy of succimer in toddlers with blood lead levels of 20-44 microg/dL. *Pediatr Res*. 2000;48(5):593-599. doi:10.1203/00006450-200011000-00007

32. Boreland F, Lesjak M, Lyle D. Evaluation of home lead remediation in an Australian mining community. *Sci Total Environ*. 2009;408(2):202-208. doi:10.1016/j.scitotenv.2009.10.013

33. Brown MJ, McLaine P, Dixon S, Simon P. A randomized, community-based trial of home visiting to reduce blood lead levels in children. *Pediatrics*. 2006;117(1):147-153. doi:10.1542/peds.2004-2880

34. Dietrich KN, Ware JH, Salganik M, et al; Treatment of Lead-Exposed Children Clinical Trial Group. Effect of chelation therapy on the neuropsychological and behavioral development of lead-exposed children after school entry. *Pediatrics*. 2004;114(1):19-26. doi:10.1542/peds.114.1.19

35. Liu X, Dietrich KN, Radcliffe J, Ragan NB, Rhoads GG, Rogan WJ. Do children with falling blood lead levels have improved cognition? *Pediatrics*. 2002;110(4):787-791. doi:10.1542/peds.110.4.787

36. Markowitz ME, Sinnett M, Rosen JF. A randomized trial of calcium supplementation for childhood lead poisoning. *Pediatrics*. 2004;113(1, pt 1):e34-e39. doi:10.1542/peds.113.1.e34

37. O'Connor ME, Rich D. Children with moderately elevated lead levels: is chelation with DMSA helpful? *Clin Pediatr (Phila)*. 1999;38(6):325-331. doi:10.1177/000992289903800602

38. Rogan WJ, Dietrich KN, Ware JH, et al; Treatment of Lead-Exposed Children Trial Group. The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead. *N Engl J Med*. 2001;344(19):1421-1426. doi:10.1056/NEJM200105103441902

39. Wolf AW, Jimenez E, Lozoff B. Effects of iron therapy on infant blood lead levels. *J Pediatr*. 2003;143(6):789-795. doi:10.1067/S0022-3476(03)00540-7

40. Nicholson JS. A community-based intervention for low-income families to reduce children's blood lead levels between 3–9.9 µg/Dl. *Child Health Care*. 2017:1-18. doi:10.1080/02739615.2017.1370673

41. Ettinger AS, Lamadrid-Figueroa H, Téllez-Rojo MM, et al. Effect of calcium supplementation on blood lead levels in pregnancy: a randomized placebo-controlled trial. *Environ Health Perspect*. 2009;117(1):26-31. doi:10.1289/ehp.11868

42. Shannon M, Graef J, Lovejoy FH Jr. Efficacy and toxicity of D-penicillamine in low-level lead poisoning. *J Pediatr*. 1988;112(5):799-804. doi:10.1016/S0022-3476(88)83212-8

43. Roper WL, Houk VN, Falk H, Binder S; Centers for Disease Control and Prevention. *Preventing Lead Poisoning in Young Children: A Statement by the Centers for Disease Control, October 1991*. Atlanta, GA: Centers for Disease Control and Prevention; 1991.

44. Ossiander EM. A systematic review of screening questionnaires for childhood lead poisoning. *J Public Health Manag Pract*. 2013;19(1):E21-E29. doi:10.1097/PHH.0b013e3182249523

45. Tong S, von Schirnding YE, Prapamontol T. Environmental lead exposure: a public health problem of global dimensions. *Bull World Health Organ*. 2000;78(9):1068-1077.

46. Raymond J, Wheeler W, Brown MJ; Centers for Disease Control and Prevention (CDC). Lead screening and prevalence of blood lead levels in children aged 1-2 years—Child Blood Lead Surveillance System, United States, 2002-2010 and National Health and Nutrition Examination Survey, United States, 1999-2010. *MMWR Suppl*. 2014;63(2):36-42.

47. Centers for Disease Control (CDC). Lead poisoning from Mexican folk remedies—California. *MMWR Morb Mortal Wkly Rep*. 1983;32(42):554-555.

48. Centers for Disease Control and Prevention (CDC). Lead poisoning associated with imported candy and powdered food coloring—California and Michigan. *MMWR Morb Mortal Wkly Rep*. 1998;47(48):1041-1043.

49. Centers for Disease Control and Prevention (CDC). Screening Young Children for Lead Poisoning: Guidance for State and Local Public Health Officials. CDC website. https://www.cdc.gov/nceh/lead/publications/screening.htm. Published 1997. Accessed October 2, 2018.

50. Lanphear BP, Weitzman M, Eberly S. Racial differences in urban children's environmental exposures to lead. *Am J Public Health*. 1996;86(10):1460-1463. doi:10.2105/AJPH.86.10.1460