Supplementary Online Content

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This supplementary material was provided by the authors to give readers additional information about their work.

eAppendix 1. Search Strategies

Screening

Database: Ovid MEDLINE (R) 1946 to March Week 2, 2017
1 exp Lead/
2 exp Lead Poisoning/
3 1 or 2
4 exp mass screening/
5 exp "Surveys and Questionnaires"/
6 exp risk/
7 4 or 5 or 6
8 3 and 7
9 limit 8 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)")
10 exp pregnancy/
11 exp pregnancy complications/
12 exp fetus/
13 exp prenatal care/
14 exp Prenatal Exposure Delayed Effects/
15 exp Prenatal Injuries/
16 exp "Embryonic and Fetal Development"/
17 10 or 11 or 12 or 13 or 14 or 15 or 16
18 8 and 17
19 9 or 18
20 ((test* or assay* or sampl* or detect* or surveil* or screen* or questionnair* or survey* or (risk* adj3 (assess* or predict* or determin* or measur* or calculat*))) adj5 (lead or pb) adj7 (infan* or fetus or fetal* or prenat* or pregnan* or baby or babies or child* or toddler*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
21 19 or 20
22 exp diagnosis/
23 3 and 22
24 17 and 23
25 limit 24 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)")
26 24 or 25
27 ((test* or assay* or sampl* or detect* or surveil* or screen* or questionnair* or survey* or (risk* adj3 (assess* or predict* or determin* or measur* or calculat*))) adj5 (lead or pb) adj7 (infan* or fetus or fetal* or prenat* or pregnan* or baby or babies or child* or toddler*)).mp.
28 17 and 27
29 limit 27 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)")
30 28 or 29
31 26 or 30
32 21 or 31
33 limit 32 to humans
34 limit 33 to english language
35 limit 33 to abstracts
36 34 or 35
37 remove duplicates from 36
38 limit 37 to yr="2002 -Current"
39 limit 37 to yr="1902-2001"

Treatment

Database: Ovid MEDLINE (R) 1946 to March Week 2, 2017
1 exp Lead Poisoning/dh, dt, nu, su, th [Diet Therapy, Drug Therapy, Nursing, Surgery, Therapy]
2 exp Lead/ae, to [Adverse Effects, Toxicity]
3 ((treat* or therap* or interven* or counsel* or antidot* or remed* or cure or cured or curing or cures or chelat*) adj7 (lead or pb) adj5 (poison* or toxic* or intoxic* or ((high* or elevat*) adj3 level*))).mp.
4 exp Lead Poisoning/ or exp Lead/
5 3 and 4
6 1 or 5
7 exp Therapeutics/
8 (th or dt or dh).fs.
9 exp counseling/
10 exp health education/
11 7 or 8 or 9 or 10
12 4 and 11
13 6 or 12
14 limit 13 to humans
15 limit 14 to english language
16 limit 14 to abstracts
17 15 or 16
18 remove duplicates from 17
19 limit 18 to ("all infant (birth to 23 months)" or "preschool child (2 to 5 years)")
20 exp Pregnancy/
21 exp Pregnancy Complications/
22 exp fetus/
23 exp prenatal care/
24 exp Prenatal Exposure Delayed Effects/
25 exp Prenatal Injuries/
26 exp "Embryonic and Fetal Development"/
27 20 or 21 or 22 or 23 or 24 or 25 or 26
28 14 and 27
29 19 or 28
30 18 not 29

Screening and Treatment

Database: Cochrane Database of Systematic Reviews 2005 to April 19, 2017
1 ((treat* or therap* or interven* or antidot* or remed* or cure or cured or curing or cures or chelat*) adj7 (lead or pb) adj5 (poison* or toxic* or intoxic* or ((high* or elevat*) adj3 level*))).mp.
2 ((screen* or ((routin* or annual* or yearly) adj5 (test* or diagnos* or assay* or exam*))) adj7 ((lead or pb) adj5 (poison* or toxic* or intoxic* or ((high* or elevat*) adj3 level*)))).mp. [mp=title, abstract, full text, keywords, caption text]
3 1 or 2

Database: EBM Reviews - Cochrane Central Register of Controlled Trials through March 2017
1. ((treat* or therap* or interven* or antidot* or remed* or cure or cured or curing or cures or chelat*) adj7 (lead or pb) adj5 (poison* or toxic* or intoxic* or ((high* or elevat*) adj3 level*))).mp.
2. ((screen* or ((routin* or annual* or yearly) adj5 (test* or diagnos* or assay* or exam*))) adj7 ((lead or pb) adj5 (poison* or toxic* or intoxic* or ((high* or elevat*)
3. 1 or 2

eAppendix 2. United States Preventive Services Task Force Quality Rating Criteria

Criteria for Assessing Internal Validity of Individual Studies

The Methods Work Group for the US Preventive Services Task Force (USPSTF) developed a set of criteria by which the internal validity of individual studies could be evaluated. The USPSTF accepted the criteria, and the associated definitions of quality categories, that relate to internal validity at its September 1999 meeting.

This appendix describes the criteria relating to internal validity and the procedures that topic teams follow for all updates and new assessments in making these judgments.

All topic teams use initial "filters" to select studies for review that deal most directly with the question at issue and that are applicable to the population at issue. Thus, studies of any design that use outdated technology or that use technology that is not feasible for primary care practice may be filtered out before the abstraction stage, depending on the topic and the decisions of the topic team. The teams justify such exclusion decisions if there could be reasonable disagreement about this step. The criteria below are meant for those studies that pass this initial filter. Presented below are a set of minimal criteria for each study design and then a general definition of three categories: "good," "fair," and "poor," based on those criteria. These specifications are not meant to be rigid rules but rather are intended to be general guidelines, and individual exceptions, when explicitly explained and justified, can be made. In general, a "good" study is one that meets all criteria well. A "fair" study is one that does not meet (or it is not clear that it meets) at least one criterion but has no known "fatal flaw." "Poor" studies have at least one fatal flaw.

Systematic Reviews

Criteria:

- Comprehensiveness of sources considered/search strategy used.
- Standard appraisal of included studies.
- Validity of conclusions.
- Recency and relevance are especially important for systematic reviews.

Definition of ratings from above criteria:

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.

Fair: Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies.

Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

Randomized Controlled Trials and Cohort Studies

Criteria:

- Initial assembly of comparable groups:
- For RCTs: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups.
- For cohort studies: consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts.
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination).
- Important differential loss to follow-up or overall high loss to follow-up.
- Measurements: equal, reliable, and valid (includes masking of outcome assessment).
- Clear definition of interventions.
- All important outcomes considered.
- Analysis: adjustment for potential confounders for cohort studies, or intention to treat analysis for RCTs.

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention to treat analysis is done for RCTs.

Poor: Studies will be graded "poor" if any of the following fatal flaws exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.

Case-Control Studies

Criteria:

- Accurate ascertainment of cases.
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both.
- Response rate.
- Diagnostic testing procedures applied equally to each group.
- Measurement of exposure accurate and applied equally to each group.
- Appropriate attention to potential confounding variables.

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, adequately described.
- Study uses a credible reference standard, performed regardless of test results.
- Reference standard interpreted independently of screening test.
- Handles indeterminate results in a reasonable manner.
- Spectrum of patients included in study.
- Sample size.
- Administration of reliable screening test.

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.

Poor: Has fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum of patients.

Reference: U.S. Preventive Services Task Force. Procedure Manual. 2017; www.uspreventiveservicestaskforce.org/Page/Name/procedure-manual.

eTable 1. Current Childhood Screening Recommendations From Other Organizations

Organization, Year	Screening Recommendation
American Academy of Family Physicians (AAFP) 2006[1]	The AAFP adopted the 2006 USPSTF recommendations for children. Recommendations state that evidence is insufficient to recommend for or against routine screening for elevated BLLs in asymptomatic children ages 1 to 5 years who are at increased risk. The AAFP recommends against routine screening for elevated blood levels in asymptomatic children ages 1 to 5 years who are at average risk.
American Academy of Pediatrics (AAP) 2016[2]	Providers should test asymptomatic children for elevated blood lead concentrations according to federal, local, and state requirements. Immigrant, refugee, and internationally adopted children also should be tested for blood lead concentrations when they arrive in the United States due to increased risk. Recommends targeted screening of children 12 to 24 months of age living in communities with ≥25% of housing built before 1960 or a prevalence of children's blood lead concentrations ≥5 µg/dL of ≥5%; children who live in or visit a home or child care facility with an identified lead hazard; children living in a home built before 1960 in poor repair or renovated in the past 6 months.
American Academy of Pediatrics (AAP)/Bright Futures[3] 2012	Screening for lead poisoning should be done in accordance with state law as applicable. For children who live in states that do not have a state-screening program in place, the AAP recommends universal screening for children at ages 12 and 24 months.
American College of Preventive Medicine (ACPM) 2001[33]	Screening for elevated lead levels via venous or capillary blood lead testing should be conducted for children age 1 year, only if they are identified as being at high risk for elevated BLLs. Criteria for being at high risk include receipt of Medicaid or WIC, living in a community with ≥12% prevalence of BLLs at ≥10 µg/dL, living in a community with ≥27% of homes built before 1950, or meeting one or more high-risk criteria of a lead-screening questionnaire. This questionnaire should include both questions suggested by CDC in their 1997 guidelines and questions developed for and tailored to specific communities. These questions may pertain to use of home remedies and cosmetics, country of origin, and behavioral risk factors. Risk assessment for lead exposure should be performed beginning during prenatal visits and continuing until 6 years of age.
Centers for Disease Control and Prevention (CDC) 2010[4]	Guidelines emphasize primary prevention of lead poisoning and recommend that clinicians educate families about prevention of lead exposure and provide environmental assessments to identify sources of lead exposure before testing children for lead poisoning.

Organization, Year	Screening Recommendation
Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) 2012[4]	Blood lead screening remains necessary to identify children for whom primary prevention is unsuccessful. Screening for lead poisoning should be done in accordance with state law as applicable. For children who live in states that do not have a state-screening program in place, the ACCLPP recommends universal screening for children at ages 12 and 24 months.

Abbreviations: AAFP = American Academy of Family Physicians; AAP = American Academy of Pediatrics; ACCLPP = Advisory Committee on Childhood Lead Poisoning Prevention ACPM = American College of Preventive Medicine; BLL = Blood lead level; CDC = Centers for Disease Control and Prevention; USPSTF = United States Preventive Services Task Force

eTable 2. Current Recommendations for Screening in Pregnancy From Other Organizations

Organization, Year	Screening Recommendation for pregnant women
American Academy of Family Physicians (AAFP) 2006	The AAFP recommends against routine screening for elevated blood levels in asymptomatic pregnant women.
Centers for Disease Control and Prevention (CDC), 2010	Universal screening is not recommended. Blood lead testing for pregnant and lactating women is recommended with one or more important risk factors for lead exposure and increased BLLs: • Recent immigration (from an area where ambient lead contamination is high) • Living near point source of lead (e.g., lead mines, smelters, battery recycling plants, home remodeling) • Pica (i.e., compulsive eating of nonfood items) • Occupational exposures (e.g., painters, those exposed to batteries or radiators, living with someone who works in lead industry) • Environmental exposures (e.g., lead-contaminated soil, water, or food) • Use of lead-containing cosmetics • Cooking/storing in lead-glazed pottery • Use of herbal/alternative medicines (e.g., some Chinese herbs, Ayurvedic medicines)
American College of Obstetricians and Gynecologists (ACOG), 2012	Blood lead testing of all pregnant women in the United States is not recommended. Obstetric health care providers should consider the possibility of lead exposure in individual pregnant women by evaluating risk factors for exposure as part of a comprehensive health risk assessment and perform blood lead testing if a single risk factor is identified. Assessment of lead exposure should take place at the earliest contact with the pregnant patient. The ACOG guidelines refer to CDC recommendations regarding risk factors for exposure.

Abbreviations: AAFP = American Academy of Family Physicians; ACOG = American College of Obstetrics and Gynecologists; BLL = blood lead level; CDC = Centers for Disease Control and Prevention

eTable 3. Inclusion Criteria for Childhood

	Include	Exclude
Populations	Asymptomatic children age ≤ 5 years	All other populations[a]
Screening tests	KQs 1, 3: Measurement of BLL (using any method) with or without screening questionnaires or risk prediction tools KQ 2a: Questionnaires or risk prediction tools that identify children who are more or less likely to have elevated BLLs (defined by a minimum threshold of 5 µg/dL) KQ 2b: Measurement of BLLs using capillary blood sampling	All other screening tests, including point-of-care BLL assays that are not approved by the U.S. Food and Drug Administration and are not available in the U.S.
Interventions	KQs 4–6: Studies assessing interventions aimed at reducing BLLs, including one or more of the following: counseling families to reduce lead exposure, nutritional interventions, residential hazard control techniques, and chelation therapy	Policies, laws, or community-based interventions focused on the primary prevention of lead exposure
Comparisons	KQs 1, 3: Screened vs. nonscreened groups KQ 2a: Measurement of BLLs using venous blood sampling KQ 2b: Studies on accuracy of capillary sampling to detect elevated BLLs must include a comparison with venous sampling KQs 4–6: Treatment vs. placebo, inactive control, or no treatment	All other comparisons, including head-to-head comparisons of two different interventions
Outcomes	KQs 1, 5: Validated measures of cognitive and neurobehavioral outcomes in children, including assessment of IQ or development[b] KQ 2a: Sensitivity, specificity, discrimination, and calibration KQ 2b: Sensitivity, specificity, discrimination, calibration and measures of diagnostic accuracy KQ 3: Anxiety, distress, pain, or discomfort related to venous or capillary blood sampling; false-positive results or BLLs < 5 µg/dL, leading to repeat testing, unnecessary treatment, or both KQ 4: BLLs[b] KQ 6: Anxiety or distress; inconvenience associated with intervention (e.g., school absenteeism associated with followup testing); morbidity attributed to chelation therapy (e.g., renal toxicity, sensitivity reactions)	All other outcomes, including measures of household lead dust
Study designs	KQ 1, 4: RCTs KQ 2a: Observational studies assessing the accuracy of screening questionnaires for predicting elevated BLLs KQ 2b: Observational studies assessing the accuracy of capillary sampling to measure BLLs KQ 3: RCTs, CCTs, and cohort studies KQ 5: RCTs and CCTs KQ 6: RCTs, CCTs, prospective cohort studies with a concurrent control group, and case-control studies	Systematic reviews,[c] case series, case reports, or comparison with historical controls
Quality	Studies rated good or fair quality	Studies rated poor quality

	Include	Exclude
Clinical Setting	Settings applicable to U.S. primary care settings, including pediatric outpatient clinics, community health clinics, and school-based clinics KQs 4–6: The above plus settings referable from primary care settings	All other settings, including community health case-finding (e.g., BLL monitoring after known environmental exposure)
Country Setting	KQs 1-3: Research conducted in the U.S. or in populations similar to U.S. populations with services and interventions applicable to U.S. practice (i.e., countries with a United Nations Human Development Index of "very high" or "high" when no other evidence is available) KQs 4-6: Any country	KQs 1-3: Research not relevant to the U.S. or conducted in countries with a Human Development Index other than "very high"
Language	English language	Languages other than English

Abbreviations: BLLs = blood lead levels; CCT = controlled clinical trials; IQ = intelligence quotient; KQ = key question; RCTs = randomized controlled trials; U.S = United States of America.

eTable 4. Inclusion Criteria for Pregnancy

	Included	Excluded
Populations	**All KQs:** Asymptomatic pregnant women **KQ 2:** Asymptomatic pregnant women and asymptomatic nonpregnant adults	All other populations
Screening tests	**KQs 1, 3:** Measurement of venous BLL, with or without screening questionnaires or risk prediction tools **KQ 2:** Questionnaires or risk prediction tools that identify adults who are more or less likely to have elevated BLLs (defined by a minimum threshold of 5 µg/dL)	All other screening tests, including point-of-care BLL assays that are not approved by the U.S. Food and Drug Administration and are not available in the U.S.
Interventions	**KQs 4–6:** Studies assessing interventions aimed at reducing BLLs, including one or more of the following: counseling families to reduce lead exposure, nutritional interventions, residential hazard control techniques, and chelation therapy	Policies, laws, or community-based interventions focused on the primary prevention of lead exposure
Comparisons	**KQs 1, 3:** Screened vs. nonscreened groups **KQ 1b:** Women screened early vs. later in pregnancy **KQ 2:** Measurement of BLLs using venous sampling **KQs 4–6:** Treatment vs. placebo, inactive control, or no treatment	All other comparisons, including head-to-head comparisons of two different interventions
Outcomes	**KQs 1, 5:** Validated measures of cognitive and neurobehavioral outcomes in offspring, including assessment of IQ or development[a]; rates of adverse perinatal outcomes (e.g., premature birth, low birth weight); rates of adverse maternal outcomes (e.g., chronic kidney disease, cognitive decline, mortality) **KQ 2:** Sensitivity, specificity, discrimination, and calibration **KQ 3:** Anxiety or distress; false-positive results or BLLs <5 µg/dL, leading to repeat testing, unnecessary treatment, or both **KQ 4:** Reduction in BLL[a]; reduction in gestational hypertension **KQ 5:** Reduction in adverse perinatal outcomes and cognitive problems in offspring **KQ 6:** Anxiety or distress; inconvenience associated with intervention (e.g., need for temporary housing due to home lead abatement, work absenteeism associated with followup testing and treatment); morbidity attributed to chelation therapy (e.g., renal toxicity, sensitivity reactions); adverse effects of nutritional supplements (e.g., nausea)	All other outcomes, including measures of household lead dust
Study designs	**KQs 1, 4:** RCTs **KQ 2:** Observational studies assessing the accuracy of screening questionnaires for predicting elevated BLLs **KQ 3:** RCTs, CCTs, or prospective cohort studies **KQ 5:** RCTs and CCTs **KQ 6:** RCTs, CCTs, prospective cohort studies with a concurrent control group, and case-control studies	Systematic reviews[b], case series, case reports, or comparison with historical controls
Quality	Studies rated good or fair quality	Studies rated poor quality

	Included	Excluded
Clinical Setting	**All KQs:** Settings applicable to U.S. primary care settings where women receive prenatal care, including obstetrics/gynecology outpatient and family medicine clinics **KQs 4–6:** The above plus settings referable from primary care settings	All other settings, including community health case-finding (e.g., BLL monitoring after known environmental exposure)
Country Setting	**KQs 1–3:** Research conducted in the U.S. or in populations similar to U.S. populations with services and interventions applicable to U.S. practice (i.e., countries with a United Nations Human Development Index of "Very High" or "High" when no evidence exists from "Very High" countries) **KQs 4–6:** Any country	**KQs 1–3:** Research not relevant to the U.S. or conducted in countries with a Human Development Index other than "Very High"
Language	English language	Languages other than English

Abbreviations: BLL = blood lead level; CCT = controlled clinical trials; IQ = intelligence quotient; KQ = key question; RCTs = randomized controlled trials; U.S. = United States of America.

eTable 5. Characteristics and Results for Studies of Childhood Screening Questionnaires (From Full Evidence Review)

Study, year Setting Quality	Screening test Definition of a positive screening exam	Sample size Proportion with condition Population Characteristics	Sensitivity (95% CI)	Specificity (95% CI)
Casey,[5] 1994 United States Urban general pediatric department Fair	CDC Risk Assessment Questionnaire ≥1 positive answer	n=167 Elevated BLL: overall ≥10 ug/dL: 29% (48/165) 10-14 ug/dL: 22% (36/165) 15-19 ug/dL: 4% (7/165) 20-44 ug/dL: 2.5% (4/165) 46 ug/dL: 0.5% (1/165) Low risk vs. High risk Mean age, months: 10 vs. 9 Female: 50% vs. 50% Ethnicity: 29% vs. 33% African-American [illegible]	Overall: 40% (19/48, 95% CI 25.77 to 54.73) By screening question: Peeling paint: 15% Renovation: 31% Sibling with Pb: 6% Adult's job with Pb: 2% Live near Pb industry: 6%	Overall: 60% (70/117, 95% CI 50.36 to 68.78%) By screening question: Peeling paint: 76% Renovation: 75% Sib with Pb: 99% Adult's job with Pb: 97% Live near Pb industry: 98%
Dalton,[6] 1996 United States Medical center Fair	CDC Risk Assessment Questionnaire Additional behavioral risk factor questions ≥1 positive or equivocal answer	n=516 Elevated BLL: overall ≥10 ug/dL: 22% (101/463) ≥15 ug/dL: 6% (28/463) Mean age, months: NR, range: 6 to 72 Female: NR Ethnicity: NR	CDC Risk Factors Overall: 70.3% (95% 60.39 to 78.98) Behavioral Risk Factors Playing near outside of house: 74.2% (95% 64.60 to 82.44)	CDC Risk Factors Overall: 31.8% (95% CI 27.00 to 36.84) Behavioral Risk Factors Playing near outside of house: 54.1% (95% CI 28.05 to 37.98)

Study, year Setting Quality	Screening test Definition of a positive screening exam	Sample size Proportion with condition Population Characteristics	Sensitivity (95% CI)	Specificity (95% CI)
France,[7] 1996 United States Multisite primary care network Fair	CDC Risk Assessment Questionnaire Additional risk factor questions ≥1 positive or equivocal answer	n=2978 Mean BLL: 4.19 ug/dL Elevated BLL ≥10 ug/dL: 2.9% (85/2978) Mean age, months: NR, range: 5 months to 6.5 years Female: NR Ethnicity: NR	CDC + additional questions: 59.7% (95% CI 48 to 72) CDC alone: 57% (95% CI 45 to 69)	CDC + additional questions: 36% (95% CI 34 to 38) CDC alone: 51% (95% CI 49 to 53)
Holmes,[8] 1997 United States Continuity clinic at a children's hospital Fair	CDC Risk Assessment Questionnaire Additional risk factor questions	n=754 Elevated BLL ≥10 ug/dL: 3.1% (25/801)	68% (95% CI 46.50 to 85.05)	58% (95% CI 53.93 to 61.23)
Kazal,[9] 1997 United States Rural clinic, Navajo Reservation Fair	CDC Risk Assessment Questionnaire Additional risk factor questions Unclear definition of positive screening exam	n=368 Elevated BLL ≥1 0ug/dL: 2.2% (8/368) Mean age, months: 30.5 months Female: 49% Ethnicity: 98% Navajo	CDC questions: 42.9% (95% CI 9.90 to 81.59) CDC + additional questions: 42.9% (95% CI NR)	CDC questions: 68.52% (95% CI 68.52 to 78.50) CDC + additional questions: 66.1% (95% CI NR)

Study, year Setting Quality	Screening test Definition of a positive screening exam	Sample size Proportion with condition Population Characteristics	Sensitivity (95% CI)	Specificity (95% CI)
Muniz,[10] 2003 United States Rural clinic Fair	CDC Risk Assessment Questionnaire Additional risk factor questions	n=171 Elevated BLL ≥10 ug/dL: 2.3% (4/171) Mean age: NR, range 9 to 24 months Female: NR Ethnicity: NR	CDC questions: 25% (95% CI NR) CDC + additional questions: 50.0% (95% CI 6.76 to 93.24)	CDC questions: 49% (95% CI NR) CDC + additional questions: 49.70 (95% CI 41.88 to 57.53)
Robin,[11] 1997 United States Urban and Rural Medicaid recipients Fair	Modified Health Care Financing Administration questionnaire	n=967 Elevated BLL ≥10 ug/dL: 0.6% (6/967) Mean age: NR, range 2-6 years Female: 51.3% Ethnicity: Alaska native: 60% White: 28% Black: 5%	83.3% (95% CI) 35.88 to 99.58)	38.6% (95% CI 35.50 to 41.77)
Schaffer,[12] 1996 United States Rural clinic Fair	CDC Risk Assessment Questionnaire Additional risk factor questions	n=705 Elevated BLL ≥10 ug/dL: 8.4% (59/705) Mean age: NR, range 6 to 72 months Female: NR Ethnicity: NR	CDC + additional questions: 75% (95% CI NR) Condensed questionnaire from 4 most likely to correctly identify patients: 88% (95% CI NR)	CDC + additional questions: NR Condensed questionnaire from 4 most likely to correctly identify patients: NR

Study, year Setting Quality	Screening test Definition of a positive screening exam	Sample size Proportion with condition Population Characteristics	Sensitivity (95% CI)	Specificity (95% CI)
Snyder,[13] 1995 United States Public clinics Fair	CDC Risk Assessment Questionnaire Additional risk factor questions	n= 247 Elevated BLL ≥10 ug/dL: 7.7% (19/247) Mean age: NR, range 6 to 72 months Female: NR Ethnicity: NR	CDC questions: 31.6% (95% CI 12.58 to 56.55) Additional questions: 89.5% (95% CI 66.86 to 98.70) CDC + additional questions: 89.5% (95% CI 66.6 to 98.70)	CDC questions: 79.8 (95% CI 74.02 to 84.83) Additional questions: 37.3% (95% CI 30.99 to 43.91) CDC + additional questions: 31.6% (95% CI 25.6 to 38.0)

Abbreviations: CDC = Centers for Disease Control and Prevention; CI = confidence interval; NR = not reported; Pb = lead.

eTable 6. Summary of Evidence From Full Evidence Review of Childhood Screening

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Strength of Evidence[b]
1	No studies	0	No studies	No studies	Not applicable	No studies	Insufficient
2a	Not previously reviewed[c]	10 cross-sectional studies	All studies conducted from 1994 to 2003; studies used the 1991 CDC questionnaire or a modified version of this survey.	Consistent	Moderate	Five studies that used the threshold of ≥1 positive answers on the 5-item 1991 CDC screening questionnaire reported 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 that used versions of the CDC questionnaire modified for specific populations or settings did not demonstrate improved accuracy (sensitivity range 25% to 68%, specificity range 49% to 58%).	Moderate

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Strength of Evidence[b]
2b	Not previously reviewed[c]	4 observational studies	None	Consistent	Moderate	Four studies conducted in urban areas of the U.S. found capillary BLL testing associated with sensitivity of 87% to 91% and specificity >90% (92% to 99%) for identification of elevated BLL compared with venous sampling.	Moderate
3	No studies	0	No studies	No studies	Not applicable	No studies	Insufficient

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Strength of Evidence[b]
4	Not previously reviewed[c]	7 RCTs or observational studies (in 10 publications)	Poor quality studies of nutritional interventions do no provide adequate data to assess treatment effects.	Consistent	Low to moderate	One large, RCT found chelation therapy with 2,3-dimercaprosuccinic acid (Succimer; DMSA) in children with mean BLL 20 to 45 mcg/dL associated with decreased BLL versus placebo at 1 week, 6 months, and 1 year, but there were no effects at longer term follow-up at 4.5-6 years. One RCT found no differences between chelation versus placebo in BLL at 1 or 6 months. There was insufficient evidence from two studies to determine effects of nutritional supplementation. Three studies of residential lead hazard control techniques found no difference in BLL between intervention or control groups.	Moderate

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Strength of Evidence[b]
5	No clear evidence to support a clinical benefit from chelation therapy in children with elevated BLL at baseline, based on one trial; no studies on effects of environmental or nutritional interventions on health outcomes.	1 RCT (in 3 publications)	Based on one RCT of 780 U.S children, the adjusted treatment effect on one cognitive testing sub-score showed a statistically significant, but small improvement in the placebo group (p=0.045). No other significant outcomes for all other effects of treatment on cognitive, neuropsychiatric, and behavioral testing scores.	Consistent	Moderate	One randomized study found no differences between chelation therapy versus placebo in neuropsychological outcomes, despite a decrease in BLL following 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.	Moderate

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Strength of Evidence[b]
6	Adverse effects of environmental interventions included transient BLL, 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 aminotransferases.	1 RCT (in 3 publications) and 1 observational study	One poor quality study reported intermediate outcomes associated with adverse effects of treatment.	Consistent	Moderate to high for harms	One good quality and one 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 months and slightly poorer scores on attention and executive function tests at 7 years of age. One 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.	Moderate

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

Key Question 2a. What is the accuracy of questionnaires or clinical prediction tools that identify children who have elevated blood lead levels?
Key Question 2b. What is the accuracy of capillary blood lead testing in children?
Key Question 3. What are the harms of screening for elevated blood lead levels (with or without screening questionnaires) in children?
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?
Key Question 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?
Key Question 6. What are the harms of interventions in asymptomatic children with elevated blood lead levels?

[b]EPC Assessment of Strength of Evidence" is based on new evidence identified for this update and relevant evidence from the prior report.
[c]Key Questions in this review differ from the previous review and Key Question numbers in this review do not correspond to Key Question numbers in the prior review. For some questions, the number of studies included in the prior review was not precisely reported.
Abbreviations: BLL = blood lead level; CDC = Centers for Disease Control; GI = gastrointestinal; RCT = randomized controlled trial; US = United States.

eTable 7. Summary of Evidence From Full Evidence Review of Screening in Pregnancy

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Overall quality[b]
1a, 1b	No studies	0	No studies	No studies	No studies	No studies	No studies
2	No studies	1 observational study	Questionnaire not designed specifically for pregnant women; used a higher threshold of blood lead than the CDC <5µg/dL. No intention-to-treat analysis. Larger set of investigator-designed questions not reported.	Not applicable	One study conducted in a single setting in Ohio from 1990 to 1992.	One study used 4/5 questions from the CDC questionnaire for children and showed women with a positive response to at least one of the four questions were more likely to have elevated blood lead than those who answered negatively to all four questions (RR 2.39, 95% CI 1.17 to 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.'	Fair
3	No studies	0	No studies	No studies	No studies	No studies	No studies

Key Question[a]	Main findings from Prior USPSTF reviews	Number and type of studies identified for update	Limitations	Consistency	Applicability	Summary of findings	Overall quality[b]
4	No studies	1 RCT	Enrolled any healthy pregnant woman; did not identify an asymptomatic group with elevated BLL at baseline. Limited subgroup analyses of those with elevated lead were available; some findings conflict with overall study results.	Not applicable	One study conducted in Mexico city; high proportion of participants regularly using lead-glazed ceramics for cooking meals (35%).	One RCT of healthy pregnant women (mean baseline lead levels ~ 4 µg/dL) in Mexico found calcium supplementation associated with reduced blood levels versus placebo (difference 11%, p=0.004; levels in each group not reported). In women with baseline BLL ≥5u/dL, calcium supplementation was associated with a 17% greater reduction in BLL versus placebo, compared with a 7% greater reduction in those with lead levels <5 ug/dL at baseline. .	Fair
5	No studies	0	No studies	No studies	No studies	No studies	No studies
6	No studies	0	No studies	No studies	No studies	No studies	No studies

[a] Key Question 1a. Is there direct evidence that screening for elevated blood lead levels in asymptomatic pregnant women improves health outcomes?
Key Question 1b. Does the effectiveness of screening in asymptomatic pregnant women vary by gestational age?
Key Question 2. What is the accuracy of questionnaires or clinical prediction tools that identify pregnant women who have elevated blood lead levels?
Key Question 3. What are the harms of screening for elevated blood lead levels in asymptomatic pregnant women?
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?

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?
Key Question 6. What are the harms of interventions in asymptomatic pregnant women with elevated blood lead levels?
[b]Overall quality" is based on new evidence identified for this update

Abbreviations: BLL=blood lead level; CDC=Centers for Disease Control; RCT=randomized controlled trial; US=United States.

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