Screening for Elevated Lead Levels in Childhood and Pregnancy: An Updated Summary of Evidence for the U.S. Preventive Services Task Force

Gary Rischitelli, MD, JD, MPH (1, 2)

Peggy Nygren, MA (1)

Christina Bougatsos, BS (1)

Michele Freeman, MPH (1)

Mark Helfand, MD, MPH (1)

From the Oregon Evidence-based Practice Center (1), and the Center for Research on Occupational and Environmental Toxicology (2), Oregon Health & Science University, Portland, Oregon.

Corresponding Author: Gary Rischitelli, MD, JD, MPH, Oregon Health and Science University, Mail Code L606, 3181 SW Sam Jackson Park Road, Portland, Oregon 97239. Email: rischite@ohsu.edu

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Abstract

Background: In 1996, the United States Preventive Services Task Force (USPSTF) provided recommendations for routine screening of asymptomatic children and pregnant women for elevated blood lead levels. This review updates the evidence for the benefits and harms of screening and intervention for elevated blood lead in asymptomatic children and pregnant women.

Methods: We searched MEDLINE, reference lists of review articles, and tables of contents of leading pediatric journals for studies published 1995 or later that contained new information about the prevalence, diagnosis, natural course, or treatment of elevated lead levels in asymptomatic children aged one-five years and pregnant women.

Results: The prevalence of elevated blood lead levels among children and women in the United States, like that in the general population, continues to decline sharply, due primarily to marked reductions in environmental exposure, but still varies substantially among different communities and populations.

Similar to the findings in 1996, our searches did not identify direct evidence from controlled studies that screening children for elevated blood lead levels results in improved health outcomes and there was no direct evidence identified from controlled studies that screening improves pregnancy or perinatal outcomes.

No new relevant information regarding the accuracy of screening for lead toxicity was identified during the update and we did not identify evidence that demonstrates that universal screening for blood lead results in better clinical outcomes than targeted screening. Substantial

new relevant information regarding the adverse effects of screening and interventions was not identified.

Conclusions: There is no persuasive evidence that screening for elevated lead levels in asymptomatic children will improve clinical outcomes. For those children who are screened and found to have elevated levels, there is conflicting evidence demonstrating the clinical effectiveness of early detection and intervention.

Similarly, there are no controlled trials evaluating screening for elevated lead levels in pregnant women, nor are there sufficient data to construct an adequate chain of evidence demonstrating benefit.

Community-based interventions are likely to be more effective than office-based screening, treatment, and counseling.

Keywords: Lead Levels, Children, Pregnancy, Screening, Intervention

Introduction

In 1996, the United States Preventive Services Task Force (USPSTF) recommended screening for elevated blood lead levels at age 12 months in all children with identifiable risk factors, and in all children living in communities in which the prevalence of elevated blood lead levels was high or unknown. There was insufficient evidence, however, to recommend a specific community prevalence below which targeted screening could be substituted for universal screening. The USPSTF found insufficient evidence to recommend for or against routine screening for lead exposure in asymptomatic pregnant women. The USPSTF also found insufficient evidence to recommend for or against trying to prevent lead exposure by counseling families to control lead dust by repeated household cleaning, or to optimize caloric, iron, and calcium intake specifically to reduce lead absorption.[1]

Methods

Problem Formulation

USPSTF members defined the scope of this update, in cooperation with the Agency for Healthcare Research and Quality (AHRQ) and the Oregon Evidence Based Practice Center (EPC) personnel. The USPSTF's goal for this update was to review the literature published since its 1996 recommendation to identify new evidence addressing the previously-identified gaps in the literature, including the accuracy of risk assessment questionnaires in children with varying blood lead levels, the population prevalence at which to change from targeted screening to universal screening, the effectiveness of interventions to lower lead levels, and cost-effectiveness analyses of lead screening programs. (See Appendix 1 and Figure 1 for key questions and analytic framework.)

Literature Review and Synthesis

We developed literature search strategies and terms for each key question (KQ) and then searched MEDLINE, CINAHL, and the Cochrane Library, assisted by a EPC reference librarian, to comprehensively update the literature from 1995 to August 2005 that contained new information about the prevalence, diagnosis, natural course, or treatment of elevated lead levels in asymptomatic children ages 1-5 years and pregnant women. The search was supplemented with reference lists of review articles, references from experts in the field, and reports, guidelines, and recommendations from government, non-government, and medical professional organizations. Inclusion criteria included:

1) The study was an original meta-analysis, prospective cohort study, controlled trial, quasi-experimental study with concurrent controls, or case-control study.
2) The study was not included in the 1996 review.
3) The study was rated at least "fair-quality" using USPSTF criteria (Appendix 2).

Consistent with the scope of USPSTF recommendations, interventions needed to be relevant to primary care and feasible for delivery in primary care or by referral. Interventions were classified as pharmaceutical (chelation), environmental (residential lead paint, dust, or soil abatement), or nutritional. A primary reviewer abstracted relevant information from included studies for each of the intervention categories in KQ 5.

Results

Key Question 1: Screening in Asymptomatic Children and Pregnant Women

Similar to the 1996 findings, our searches did not identify direct evidence that screening children for elevated blood lead levels improved health outcomes. There was also no direct evidence that screening improves pregnancy or perinatal outcomes.

Key Question 2: Prevalence and Risk

The prevalence of elevated blood lead levels among children and women in the United States, like that in the general population, continues to decline sharply, primarily due to marked reductions in environmental exposure to lead (e.g., gasoline, air, dietary sources, and residential paint). These reductions are largely the result of regulatory interventions at the federal, state, and local levels of government. The prevalence of elevated blood lead levels, however, varies substantially among different communities and populations, and children and pregnant women share many of the same risk factors for lead exposure. Correlates of higher blood lead levels at all ages include minority race/ethnicity, urban residence, low income, low educational attainment, older (pre-1950) housing, home renovation or remodeling, pica, use of ethnic remedies, cosmetics, lead glazed pottery, occupational exposures, and recent immigration. Alcohol use and smoking are known risk factors among pregnant women. (See Appendix 3 for a complete discussion.)

Recent observational studies have demonstrated an inverse relationship between historical blood lead levels in children and subsequent measures of behavioral and cognitive performance at blood lead levels of < 10 µg/dL. Observational studies of infants provide preliminary data that prenatal blood lead levels < 10 µg/dL may be associated with

neurodevelopmental delay or impairment. Study design and measurement issues, however, limit interpretation of these studies. Studies also suggest that levels of maternal exposure in this range may be associated with increased risk for spontaneous abortion, hypertension in pregnancy, and adverse effects on fetal growth[3] (Appendix 3).

Key Question 3: Accuracy of Screening Tests

Can screening tests accurately detect elevated blood lead levels?

We identified no new relevant information regarding the accuracy of screening for lead toxicity. Readers are referred to the 1996 USPSTF Statement.[1] Blood lead testing has largely supplanted protoporphyrin levels as a screening tool because of poor performance of the latter at blood lead levels (BLL's) $\leq$ 25 µg/dL.[19]

What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?

In communities where there is a low prevalence of elevated blood lead levels, screening will identify few cases and yield a significant proportion of false-positive tests. Older cross-sectional studies in urban and suburban populations showed that one or more positive responses to five questions (about exposures to deteriorated paint from older or renovated housing, to other lead-poisoned children, or to lead-related hobbies or industry) detected 64-87% of children with blood lead levels $\geq$ 10 µg/dL.[1] Higher sensitivities (81-100%) for blood lead levels $\geq$ 15-20 µg/dL were reported,[1] but none of these studies evaluated the ability of questionnaires to detect levels above 20 µg/dL, in part because so few patients had levels so high. Specificity among the studies ranged from 32% to 75%. False negative results were predictably low (0.2-3.5%) in low-

prevalence (2-7%) samples, but increased to 19% when the population prevalence of elevated lead levels was higher (17-28%). Questionnaires, therefore, may have greater utility in identifying children at low risk of elevated blood lead (negative predictive value) where the population prevalence is low and local risk factors are known. Negative predictive values of 96 – 100% have been reported in these settings.[1, 51]

More recent studies of questionnaires in urban and rural settings, however, demonstrated a low prevalence of elevated blood lead levels and poor sensitivity and specificity.[52-55] Studies of questionnaires modified for local use provide some evidence of improved clinical utility for identifying children with elevated blood lead levels,[55-57] when compared to the panel of screening questions recommended by the CDC in 1991.[108]

Other studies have reported high false-positive rates for questionnaires[53, 55] and that resource considerations[52] are important when formulating a screening program. A population-based follow-up study (n=31904) showed that raising the action level for screening to 15 µg/dL in this sample would have eliminated the unnecessary follow-up of 5162 children, 3360 of whom were falsely identified as having elevated lead levels.[58]

A recent study identified housing risk factors associated with elevated blood lead levels ($\geq$ 10 mcg/dL) among 481 children residing in Rochester, New York. Housing characteristics including rental status, lead-contaminated floor dust, and poor housing condition were all associated with elevated blood lead levels (EBLL) (sensitivity 47-92%, specificity 28-76%, positive predictive value 25-34%, negative predictive value 85-93%), suggesting that housing characteristics and floor dust lead levels can be used to identify homes where a lead hazard may exist before or during occupancy.[59]

Prenatal screening with questionnaires

A maternal survey using four questions recommended by the CDC was evaluated in a study of 314 new prenatal patients. The prevalence of elevated maternal lead levels (at or greater than 10 µg/dL or 0.483 µmol/L) was 13%. Subjects with a positive response to at least one question were more likely to have elevated blood lead than those who answered negatively to all four questions (relative risk = 2.39, 95% confidence interval 1.17-4.89; P = .01). The CDC questionnaire had a sensitivity of 75.7%. Among women who answered "No" to all 4 questions, the probability of having an elevated lead level was reduced from 13% to 6.9% (negative predictive value of 93.1%). The most predictive single item was "home built before 1960." The study also identified a high prevalence of elevated blood lead among children living with women with elevated blood lead levels.[6]

Key Questions 5: Effectiveness of Early Detection

Detecting elevated blood lead levels before the development of clinical manifestations allows a clinician to recommend interventions to limit further exposure and, when necessary, begin medical treatment with chelating agents. Early detection may also result in interventions that prevent lead exposure in other children (the child with elevated blood lead level acting as a sentinel for a hazardous environment). There is relatively little convincing evidence, however, that these interventions effectively improve health outcomes. First, most available studies in asymptomatic children evaluate the effects of various interventions on blood lead levels rather than on clinical outcomes. Second, blood lead levels in childhood, after peaking at about two years of age, decrease without intervention,[1, 5] a result attributable in part to regression to the

mean, random variation, laboratory error, and redistribution of lead from blood to other tissue compartments. Studies must account for these changes over time, preferably by using controls who do not receive the intervention, to adequately evaluate the interventions' effects on blood lead levels or health outcomes.

Effect of screening on clinical outcomes

EPC staff did not identify evidence demonstrating that universal screening for blood lead results in better clinical outcomes. The 1996 USPSTF recommendation cited several older studies that reported intensive screening programs targeting children in high-risk neighborhoods reduced case fatality rates, mortality rates, and proportions of children detected with very high blood lead levels or who developed symptomatic lead poisoning.[1] Lacking concurrent controls, however, it was possible that the reported reductions in mortality and case fatality rates were due to other factors, such as advances in medical care, rather than the effect of screening. The reduction in mean blood lead levels in the US population is primarily the result of diminishing exposure in the environment through regulatory interventions. The available evidence regarding the efficacy of screening programs, therefore, is weak.

Do interventions for elevated lead levels result in improved health outcomes?

While chelating agents benefit children with symptomatic lead poisoning, no studies have demonstrated clinical benefits of chelation therapy in asymptomatic children. The Treatment of Lead-Exposed Children (TLC) Trial, a large multicenter randomized controlled trial sponsored by the U.S. National Institute for Environmental Health Science (NIEHS), enrolled children from 1994-97 to assess the effect of oral chelation therapy with succimer on IQ in young children with

venous blood lead concentrations of 20-45 µg/dL.[60] Follow-up testing at 36 months demonstrated a mean IQ one point lower, and poorer parental ratings of behavior, among the succimer group, compared to placebo. Although succimer treated children did slightly better on a test of learning ability, none of the differences between groups were statistically significant.[61] Reanalysis of the same data using the change in blood lead level as the independent variable demonstrated a 4.0 point improvement in cognitive scores for every 10 µg/dL reduction in blood lead level, but only in the placebo group, suggesting that factors other than declining blood lead contributed to cognitive improvement, or that treatment had an adverse effect on cognitive performance.[62] Assessment of neurobehavioral outcomes at seven years of age revealed no statistically significant differences on a battery of neurobehavioral tests except that the succimer group had worse attention-executive function scores.[63] Treatment also appeared to have an adverse effect on mean height.[64] The TLC Group concluded that chelation therapy was not indicated for children with blood lead levels <45 µg/dL.[61, 63]

Despite evidence of efficacy in lowering blood lead on a short-term basis, there is little evidence confirming a clinical benefit from chelation therapy for children with lead levels <45 µg/dL.

We found no studies evaluating clinical outcomes after environmental or nutritional interventions.

Effects of chelation therapy on blood lead levels

In the previously cited NIEHS-sponsored RCT of oral chelation in young children with venous blood lead concentrations of 20-45 µg/dL (TLC Study) reporting no effects of chelation on IQ[60-63, 65] (Tables 1 and 2), blood lead levels fell steeply in the treatment group in the first

week (mean 11 µg/dL lower), but rebounded after. Blood lead levels also dropped in the placebo group but more slowly. Blood lead levels were 77% of baseline in the succimer group (88% of baseline among placebo) at seven weeks after initiation of therapy. Mean blood lead levels among the treatment group were 4.5 µg/dL and 2.7 µg/dL, at six and twelve months respectively, but the difference between treatment and placebo groups at 24 months was not significant.[65]

Chelating agents have demonstrated short-term reductions in blood lead levels in children whose pretreatment values ranged from 20 to 70 µg/dL in studies where chelation therapy was often combined with environmental interventions, but these reductions were not sustained over longer periods in the absence of repeated or continuing chelation therapy or environmental interventions.[1, 66-68]

These data provide good evidence that chelating agents may result in short-term reductions in blood lead levels in children, but suggest that these reductions may not be sustained over longer periods in the absence of repeated or continuing chelation therapy or environmental interventions. Further, there is no evidence that these reductions result in improved neurobehavioral or health outcomes.

Effect of residential lead hazard control on blood lead levels

Recent studies of household dust and paint hazard control through cleaning, abatement, and education have mixed results. Of the eight controlled studies published since 1995, one has shown a modest, but significant, decline, five have shown non-significant declines, and two have shown non-significant elevations in blood lead levels among children. Reduced blood lead levels were seen among children with higher baseline lead levels (15+ or 20+ µg/dL) in two studies (one meta-analysis, one retrospective chart review with no comparison group), but not in

children with lower baseline levels. Recent studies differ from older studies in that newer paint hazard control techniques result in lower lead-dust levels. Population venous lead levels have decreased over time, and lead-poisoned children in older studies had higher mean blood lead levels than in recent studies. (See Tables 3 and 4 and Appendix 4 for a detailed assessment.)

Effect of counseling and education interventions on blood lead levels

Overall, the evidence to determine whether education and counseling improve outcomes among children with moderately elevated blood lead levels is weak and conflicting (see Appendix 5 for a detailed assessment).

Effect of soil abatement on blood lead levels

Recent studies of soil remediation in residential areas have shown only modest or non-significant effects.[80, 85, 86] Soil remediation in communities near lead mining, milling, or smelting operations may have a beneficial effect, but was not considered within the scope of review (see Appendix 6 for a detailed assessment).

Effect of nutritional interventions on blood lead levels

There is conflicting evidence whether nutritional interventions are an efficacious way to lower children's blood lead levels. Depending on the nutritional intervention under investigation, findings are limited, preliminary, and somewhat contradictory (Tables 5 and 6 and see Appendix 7 for a detailed assessment).

Key Questions 4 and 6: Adverse Effects of Screening and Intervention

We identified no substantial new relevant information regarding the adverse effects of screening and interventions for lead toxicity. The most common adverse effects of screening for elevated lead levels remain those identified in the 1996 USPSTF Statement[1] (i.e., false-positive results and the associated anxiety, inconvenience, work or school absenteeism, and financial costs of return visits and repeat tests). Adverse effects of environmental interventions may include transient elevation in blood levels, inconvenience associated with abatement work or relocation, and cost-benefit considerations.

Reported adverse effects of treatment with succimer (meso-2, 3-dimercaptosuccinic acid, or DMSA) include mild gastrointestinal (vomiting and diarrhea) and systemic symptoms, rashes, transient hyperphosphatasemia, neutropenia, eosinophilia, and elevations in serum transaminases. These effects occurred in up to 10% of cases.[1, 60-63, 65]

Evidence Synthesis and Conclusions

There is no direct evidence that screening for elevated lead levels in asymptomatic children at increased risk for lead exposure will improve clinical outcomes (Table 7). Because there have been no controlled trials directly evaluating screening for elevated lead levels, this conclusion is based on a chain of evidence constructed from studies of weaker design. First, in young asymptomatic children, blood lead levels as low as 10 µg/dL, and perhaps lower, are associated with measurable neurodevelopmental dysfunction. Therefore, a relevant threshold level for screening and subsequent intervention cannot be specified based on clinical evidence.

Second, the national prevalence of elevated lead levels has declined dramatically in the past two decades, although high prevalence persists in some communities, particularly poor urban communities in the Northeast and Midwest. Third, although current interventions (e.g., residential lead hazard control and chelation therapy) can reduce blood lead levels in children identified with levels ≥25 µg/dL, the quality of evidence supporting their effectiveness is weak and a beneficial effect on IQ or other clinical outcomes has not yet been demonstrated. Further, well-designed, randomized controlled trials do not support beneficial effects and suggest adverse effects of chelation therapy for asymptomatic children with levels <45 µg/dL.

For those children who are screened and found to have initial blood lead levels <25 µg/dL, there is no evidence regarding the effectiveness of early detection and intervention, or of repeated screening to detect further increases in blood lead. Longitudinal and cross-sectional studies suggest that in children ≥2 years, such levels will decline naturally with time, but elevated levels may persist in children who are chronically exposed.

There is no direct evidence comparing the outcomes of universal screening with the outcomes from targeted screening for elevated lead levels. Recent studies indicate that the prevalence of elevated blood levels in the US has declined dramatically in the past two decades, but local prevalence is highly variable, with more than 10-fold differences between communities. In a community with a low prevalence of elevated blood lead levels, universal screening may result in disproportionate risks and costs relative to benefits. The prevalence level at which targeted screening can replace universal screening is a public health policy decision requiring consideration beyond the scientific evidence for effectiveness of early detection, such as available resources, competing public health needs, and costs and availability of alternative approaches to reducing lead exposure. Clinicians can consult their local or state health

departments regarding appropriate screening policy for their populations. (See Appendix 8 for recommendations of other groups.)

In communities where data suggest that universal screening is not indicated, there may be some children who are at increased risk of blood lead levels in the range for which individual intervention by chelation therapy or residential lead hazard control has been demonstrated to be effective. In addition to risks from housing, these children may have had exposure to other lead sources such as lead-based hobbies or industries, traditional ethnic remedies, or lead-based pottery. Selective blood lead screening of such high-risk children is appropriate even in low-prevalence communities.

Questionnaires that have been locally validated and are of known and acceptable sensitivity and specificity can assist in identifying those at high risk. In several studies, the CDC[108] and similar questionnaires correctly identified 64% to 87% of urban and suburban children who had blood lead levels $\geq$ 10 µg/dL. Because of frequent false positives in low prevalence communities, questionnaires may have greater utility in identifying children at low risk of elevated blood lead (negative predictive value) where the population prevalence is low, and local risk factors are known. Locale-specific questionnaires inquiring about likely local sources of lead exposure may lead to improved prediction.

There are no controlled trials evaluating screening for elevated lead levels in pregnant women, and there are insufficient data to construct an adequate chain of evidence demonstrating benefit. The prevalence of levels >15 µg/dL appears to be quite low in pregnant women. There is some evidence that mildly-elevated lead levels during pregnancy are associated with small increases in antepartum blood pressure, but only limited evidence that these levels have important adverse effects on reproductive outcomes. An extensive literature search failed to

identify studies evaluating screening or intervention for lead exposure in pregnant women. There are potentially important adverse effects of chelation therapy on the fetus and of residential lead hazard control on both the pregnant woman and fetus if they are not performed according to established standards. While removal to a lead-free environment would theoretically be effective in reducing lead exposure, it has not been specifically evaluated in pregnancy.

Community-based interventions for the primary prevention of lead exposure are likely to be more effective, and may be more cost-effective, than office-based screening, treatment, and counseling.[21] Evaluating the effectiveness of community-based interventions, and recommendations regarding their use, are important areas of future research.

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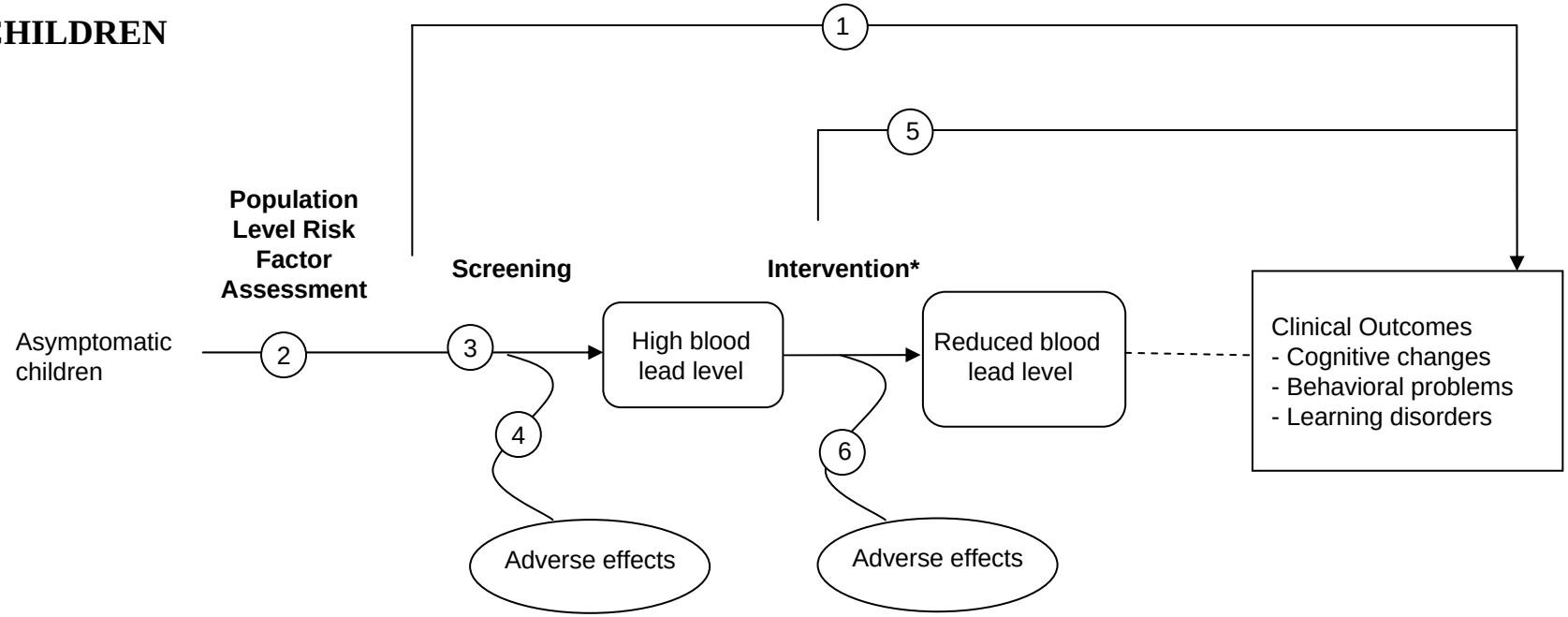
Figure 1. Analytic Frameworks and Key Questions.
The analytic frameworks represent an outline of the evidence review and includes patient populations, interventions, outcomes, and adverse effects. The key questions examine a chain of evidence about the effectiveness, accuracy, and feasibility of screening asymptomatic children for elevated blood lead levels in primary care settings, prevalence rates and risk factors, adverse effects of screening, effectiveness of interventions for children identified with elevated blood lead levels, adverse effects of interventions, and cost effectiveness issues.

CHILDREN



KQ1: Is there direct evidence that screening in asymptomatic children for lead results in improved health outcomes (i.e. cognitive changes, behavioral problems, learning disorders)?

KQ2: What is the prevalence of elevated lead in children? Are there population-level risk factors that identify children at higher risk for elevated lead levels (i.e. geography, racial/ethnicity, SES, age)?

KQ3: Can screening tests accurately detect elevated blood lead level?
A. What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?
B. What is the optimal frequency for screening? What is the optimal frequency for repeat testing?

KQ4: What are the adverse effects of screening?

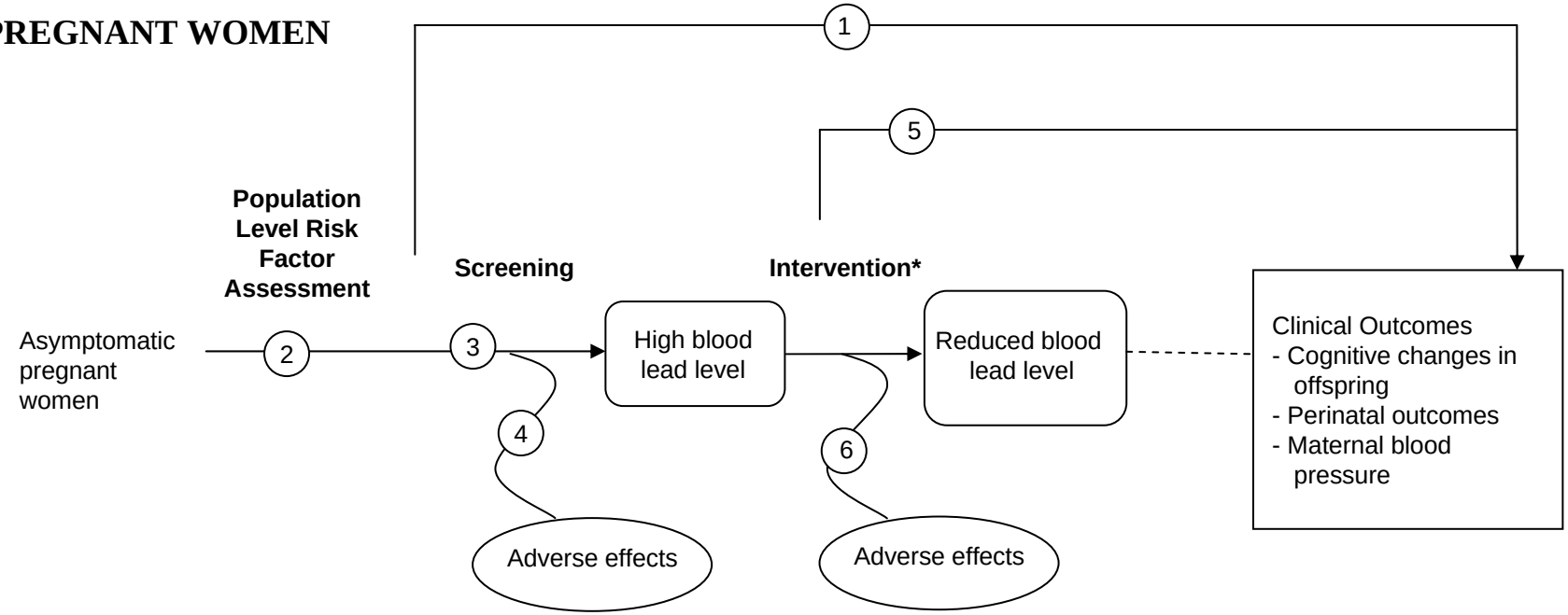
KQ5: Do interventions (i.e. counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?

KQ6: What are the adverse effects of the interventions?

KQ7: What are the cost effectiveness issues?

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

PREGNANT WOMEN



KQ 1: Is there direct evidence that screening in asymptomatic pregnant women for lead results in improved health outcomes (i.e. cognitive changes in offspring, perinatal outcomes including birth weight/preterm delivery etc, maternal blood pressure)?

KQ 2: What is the prevalence of elevated lead in asymptomatic pregnant women? Are there population-level risk factors that identify pregnant women at higher risk for elevated lead levels (i.e. geography, racial/ethnicity, SES, age)?

KQ 3: Can screening tests accurately detect elevated blood lead levels? What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?

KQ 4: What are the adverse effects of screening?

KQ 5: Do interventions (i.e. counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?

KQ 6: What are the adverse effects of the interventions?

KQ 7: What are cost effectiveness issues?

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

Table 1. Chelation Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Besunder, 1995[66]	Chelation with DMSA and abatement of domestic lead hazards	46 treated, 18 excluded, N=28	Referral population, 35% African American, 10% Hispanic	25-49 µg/dL	80 days	BLL: post-treatment (day 18) -43% (±20.8%), 80 Days -31% (±20.2%). ZPP post-treatment (day 18) -12% (±21.7%), 80 days -32% (±21.9%).	Neutropenia (N=1)
Chisolm, 2000[68]	Chelation with DMSA, relocation to lead-safe housing	59	Children age 12-65 months	25-70 µg/dL	21 days	Mean BLL decreased to below 35% of pretreatment value after 4 weeks of DMSA treatment; rebounded to 58% of pretreatment level 2-3 weeks after termination of treatment	Elevated alkaline phosphate levels (n=2), eosinophilia (N=1)
Dietrich, 2004[63] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 random-ized	Children age 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	6 years (until 7 years of age)	No statistically significant difference in neurobehavioral outcomes except DMSA-treated children did worse on attention/executive functions	No statistically significant difference compared to placebo. Excess noted: trauma, scalp rashes, neutropenia/thrombocytopenia, elevated ALT.
Liu, 2002[62] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 randomized, results from 741 reanalyzed for this study	Children age 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	36 months	6 months after treatment, BLL had fallen a similar amount in both DMSA and placebo groups. There was no association between change in BLL and change in cognitive test score. BLL continued to fall, but at 36 months after treatment, cognitive test scores improved 4.0 points for every 10 µg/dL drop in BLL in the placebo group only.	No statistically significant difference compared to placebo. Excess noted: trauma, scalp rashes, neutropenia/thrombocytopenia, elevated ALT.

Table 1. Chelation Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
O'Connor, 1999[67]	Chelation with DMSA, domestic cleaning and repair	39	Low-income African-American inner-city children 2.5-5 years old	30-45 µg/dL	6 months	DMSA: baseline 34.9 ±4.7 µg/dL, 1 month 27.4 ±7.5 µg/dL, 6 months 28.8 ±6.4 µg/dL. Placebo: baseline 33.0 ±6.2 µg/dL, 1 month 33.2 ±10.3 µg/dL, 6 months 25.1 ±6.8 µg/dL (p=0.06). Differences in BLL between groups were not statistically significant (p=0.16 at 1 month, p=0.06 at 6 months)	ND
Peterson, 2004[64] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 randomized	Children age 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	34 months	Difference in mean change in height, DMSA vs. Placebo: 0-9 months: -0.27 cm (CI -.42, -.11) 0-34 months: -0.43 cm (CI -0.77, -0-.01)	Small, marginally significant decrease in height among treatment group compared to placebo. Excess noted: trauma, scalp rashes, neutropenia/thrombocytopenia, elevated ALT.
Rogan, 1998[60] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 randomized	Children age 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	36 months	Description of baseline measurements, group characteristics, study methodology.	ND

Table 1. Chelation Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Rogan, 2000[65] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 randomized	Children age 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	12 months	DMSA group: BLL 11 µg/dL lower at one week. Rebound began at 1 week, and at 7 weeks DMSA group mean BLL was 72% of baseline (placebo group mean BLL was 88% of baseline). During the 6 months after initiation of treatment, the DMSA group had a mean BLL 4.5 µg/dL lower than the control group. At 12 months mean DMSA group BLL was 2.7 µg/dL lower than the control group, but confidence intervals overlap. At 12 months groups are similar.	No statistically significant difference compared to placebo. Excess noted: trauma, scalp rashes, neutropenia/thrombocytopenia, elevated ALT.
Rogan, 2001[61] TLC	Chelation with DMSA after domestic cleaning with HEPA vacuum and damp cloth wiping	1,854 evaluated, 780 randomized	Children ages 12-33 months, 77% African-American. Most had poor, single mothers and lived in older, poorly maintained residences.	20-44 µg/dL	36 months	First 6 months: DMSA mean BLL 4.5 µg/dL lower than placebo. At 36 months, DMSA group scored on average 1 IQ point lower than the control group, and had slightly worse behavior by parental rating compared to the placebo group. The placebo group fared slightly better on a developmental neuropsychological battery of tests. Overall, there was no statistically significant difference.	No statistically significant difference compared to placebo. Excess noted: trauma, scalp rashes, neutropenia/thrombocytopenia, elevated ALT.

Abbreviations: ALT=Alanine transferase; BLL= Blood lead level; CBC=Complete blood count; DMSA=Dimercaptosuccinic acid; HEPA=High efficiency particulate air; ND= Adverse events not described; TLC=Treatment of Lead-exposed Children study; WBC=White blood cell count; ZPP=Zinc protoporphyrin

Table 2. Summary of Chelation Interventions

Author, Year (Quality)	Study Design	Type of Intervention	Years Conducted	N	Age	Duration of Follow-up	Baseline BLL	BLL Results	Summary of Effect
Rogan, 1998[60]; Rogan, 2000[65]; Rogan, 2001[61]; Liu, 2002[62]; Dietrich, 2004[63]; Peterson, 2004[64]; TLC study (Good)	Randomized multicenter, placebo controlled, double-blind trial	DMSA lasting 26 days, dose based on body surface area; treatment repeated up to 3 times for persistently elevated blood lead level; domestic cleaning with HEPA vacuum and damp cloth wiping	NR	1,854 evaluated 780 randomized 741 of randomized reanalyzed for Liu 2002 (cognitive function)	Children 12-33 months	At 12 months following initiation of treatment, test BLL; at 36 months, planned behavioral, cognitive, and biochemical tests; retest at 72 months (to age 7); also, at 9 and 34 months, test height-weight	20-44 µg/dL	DMSA vs. Placebo 1 wk: BLL 11 µg/dL lower in DMSA. 7 wks: 72% vs. 88% of baseline. First 6 months: BLL 4.5 µg/dL lower in DMSA. 12 months: groups are similar.	DMSA produced short-term reduction in BLL; rebound began at 1 week and 7 weeks. Followup outcomes do not support the hypothesis that lead-induced cognitive defects are reversible by chelation therapy. DMSA group scored worse on some measures.
Besunder, 1995[66] (N/A)	Retro-spective case series	DMSA 10 mg/kg every 8 hours for 5 days, followed by 10 mg/kg every 12 hours for 14 days; and abatement of domestic lead hazards	June 1991 to May 1993	46 treated, 18 excluded, N=28	Children Age NR	80 days	25-49 µg/dL	BLL post-treatment: 18 days: -43% (± 20.8%) 80 days -31% (± 20.2%) ZPP post-treatment 18 days: -12% (±21.7%) 80 days: -32% (±21.9%)	No control group. Cannot exclude other intervention effects (abatement of domestic lead hazards).

Table 2. Summary of Chelation Interventions

Author, Year (Quality)	Study Design	Type of Intervention	Years Conducted	N	Age	Duration of Follow-up	Baseline BLL	BLL Results	Summary of Effect
Chisolm, 2000[68] (N/A)	Open-label case series	DMSA 1,050 mg/m^2/day, divided in three doses for 5 days, followed by 700 mg/m^2/ day, divided in two doses for 21-23 days; and relocation to lead-safe housing	NR	59	Children 12-65 months	21 days	25-70 µg/dL	BLL post-treatment 1 day: below 35% of pretreatment level 2-3 weeks: rebounded to 58% of pretreatment level	No control group. Cannot exclude other intervention effects (abatement of domestic lead hazards).
O'Connor, 1999[67] (Fair)	Randomized placebo-controlled double-blind trial	DMSA (child weight <15 kg) 1,000 mg tid for 5 days, followed by 100 mg bid for 14 days DMSA (child weight >15 kg) 200 mg tid for 5 days, followed by 200 mg bid for 14 days	NR	39	Children 2.5-5 years	6 months	30-45 µg/dL DMSA group 34.9 ±4.7 µg/dL Placebo group 33.0 ±6.2 µg/dL	DMSA vs. Placebo 1 month: 27.4 ±7.5 µg/dL vs. 33.2 ± 10.3 µg/dL 6 months: 28.8 ±6.4 µg/dL vs. 25.1 ±6.8 µg/dL	Both treatment and control groups demonstrated significant BLL reductions. Differences between groups were not significant.

Abbreviations: Bid=Two times per day; BLL= Blood lead level; DMSA=Dimercaptosuccinic acid; HEPA=High efficiency particulate air; NR = Not reported; TID=Three times per day; TLC=Treament of Lead-exposed Children Study; ZPP= Zinc protoporphyrin

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Aschengrau, 1994[85] Aschengrau, 1997[86]	Soil and interior dust abatement, and loose paint stabilization	152	Children <4 years	7-24 µg/dL	2 years	BLL and change (µg/dL)(95% CI) Phase I, mixed interventions: pre 13.10, post 10.65; change -2.44 (CI -3.32, -1.57) Phase II, soil abatement for homes not already deleaded: Group A: pre 12.94, post 7.69; change -5.25 (CI -6.51, -3.99) Group B: pre 10.54, post 9.15; change -1.30 (CI -4.03, +1.26) All groups, all phases combined: pre 12.66, post 9.77; change -2.89 (CI -3.64, -2.13) Soil lead reduction of 2,060 ppm is associated with a 2.25-2.70 µg/dL decline in BLL. Low levels of soil recontamination 1-2 years following abatement indicate the intervention is persistent. Paint hazard remediation alone was associated with a BLL increase of 6.5 µg/dL (p=0.05). Paint hazard remediation combined with soil abatement suggested an insignificant increase of 0.9 µg/dL (p=0.36).	ND
Aschengrau, 1998[72]	Dust, domestic cleaning with HEPA vacuum, wash window surfaces, seal flaking paint, and repair holes in wall	63	Children <=4 years	16.9 µg/dL	6 months	BLL and change (µg/dL) Automatic intervention group (high risk): pre 17.5, post 9.1; change -8.4 Randomized intervention group: pre 17.6, post 11.5; change -6.2 Randomized control group: pre 16.3, post 10.4; change -5.9 Relative change, Treatment vs. Control: -0.3 (95% CI -3.8, +3.3) Automatic Intervention vs. Control: -2.5 (CI -7.0, +2.1)	ND

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Campbell, 2003[75]	Dust, second cleaning follows 18-21 months after TLC study cleaning	73 treatment 86 control	Toddlers age 12-34 months	20-44 µg/dL	6 months	BLL declined in both treatment and control groups Geometric mean BLL, adjusted for month and child, declined monotonically among 73 children whose homes were cleaned a 2nd time. BLL of the 86 children whose homes did not receive a 2nd cleaning also declined over time, although there was an unexplained increase at the 3-mo post cleaning follow-up visit. BLL before the cleaning were higher among children in high-exposure homes (GM 18.1 µg/dL), compared with those in low-exposure homes (GM 14.5 µg/dL). Stratified by randomized treatment, there were only small differences in BLL: 18.3 µg/dL and 17.1 µg/dL for children in chelation vs. placebo, in high exposure homes; and 14.5 vs. 13.5 µg/dL for chelation vs. placebo, in low-exposure homes.	ND
Clark, 2004[69]	Lead-based paint and dust hazard control program and survey	869 children	HUD hazard control program participants in 14 states	ND	6 weeks	Post-intervention, 81 (9.%) participants had BLL increases $\geq$5 µg/dL (range 5-25; average 8.4). Logistic regression analysis indicated four factors were significantly associated with increases: (a) child's age at pre-intervention (p=0.006), (b) female caregiver's education (p=0.002) (c) general exterior building condition (p=0.0071), and (d) second season of blood-sample collection (p<0.001). Odds ratio of BLL increase decreased sharply as child's age increased. Where female parent had not completed high school, likelihood of BLL increase was 2.5 times higher than families where female parent had completed high school.	ND
Farrell, 1998[80]	Soil	Enrolled 408 children in 263 houses; 187 completed study	Children age 6 months to 6 years	Baseline 11 µg/dL 54% of properties had soil samples >1000 ppm.	1 year	1 year post-abatement: BLL in both groups fell below baseline. Differences between treatment and control groups were not significant in any of the cross-sectional or longitudinal models. 2 years post-abatement: soil sampling showed significant lead re-accumulation.	ND

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Galke, 2001[78]	Dust	240 children 1,212 dwellings	Children age 6 months to 6 years	Median 10 µg/dL (range 2-48)	12 months	12 months post-intervention: BLL declined from 11.0 to 8.2 (-2.8) µg/dL, a 26% reduction.	ND
Haynes, 2002[74]	Dust, meta-analysis	4 studies, total subjects= 533	NR	6.7-16.9 µg/dL	6-48 months	Weighted mean change in BLL: -0.62 µg/dL (95% CI -1.55, 0.32). No significant difference between intervention and control groups, combined from educational dust control and professional dust control trials.	ND
Jordan, 2003[82]	Education	594 mothers and 378 of their children	Inner-city, poor, ethnically diverse (78% non-Caucasian)	Before intervention, all levels were <10 µg/dL	2 years	Intervention vs. Control Maintained BLL <10 µg/dL: 81% vs. 73% (p=0.08). >90% completed 19-20 sessions. Half completed first year of follow-up sessions; <5% completed second year.	ND
Lanphear, 1999[83]; Lanphear, 2000[34]; Lanphear, 2002[93]	Education	275	Children age 6 months	2.9 µg/dL (95% CI 2.7-3.1) at age 6 months	48 months	No significant difference in BLL by intervention status at 24 months or 48 months. Intervention vs. Control BLL: Age 24 months: 7.3 vs. 7.8 µg/dL Age 48 months: 5.9 vs. 6.1 µg/dL Dust lead levels declined sharply in both the treatment and control groups. There was no significant difference in dust lead levels at 24 months by group, nor a difference in change in dust lead levels from 6 to 24 months by group. Other results (Lanphear, 2002): Dietary iron intake, but not calcium intake, was inversely associated with BLL (p<0.05). Also, BLL was over 50% higher in black than in white children (p=0.0001).	ND

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Lanphear, 2003[87]	Soil	198 in first survey; 215 in second survey	Children	Mean 5.6 µg/dL with soil >500 ppm (11% >=10 µg/dL) Mean 3.0 µg/dL with soil <500 ppm (3% >=10 µg/dL)	N/A	BLL change (µg/dL) before and after soil abatement: Intervention group: pre 5.6, post 3.0; change -3.6 (p=0.0001) Nonintervention group: pre 3.0, post 2.6; change -1.4 (p=0.06) Stratified by age, and adjusted for mouthing behavior score, and socioeconomic status: Age 36-72 months: change -2.3 µg/dL (NS) Age 6-36 months: change -2.5 µg/dL (p=0.03)	ND
Leighton, 2003[73]	Lead paint hazard remediation	221	Lead-poisoned children	20-44 µg/dL	10-14 months	BLL declined significantly for all groups, 24.3 µg/dL at baseline, to 12.3 µg/dL at 10-14 month followup: a 50% decline (p<0.01). Intervention (n=146) vs. Nonintervention (N=75): BLL reduction 53% vs. 41%, relative reduction ±20% (p<0.01). After adjusting for confounders, remediation effect was 11% (NS). Race was the only factor that confounded the relationship. African American children had higher BLL in followup after remediation. Mean BLL for white and Asian children was 30% lower than African American children (p<0.01). Effect of remediation appeared to be stronger in younger children (10-36 months) than in older children (36-72 months) (p=0.06). Timing of remediation produced no significant effect on BLL.	ND
Rhoads, 1999[70]	Dust	113 enrolled; final blood levels obtained from 99	Children mean age 1.7 years	Intervention mean 12.4 µg/dL (SD 5.7) Control mean 11.6 µg/dL (SD 6.2)	1 year	Significant effect on BLL (µg/dL) change. Intervention: pre 12.4, post 10.3; change -2.1 (17%) Control: pre 11.6, post 11.6; change +0.1 (+1%) Estimated intervention effect= -1.9 µg/dL (p<0.05). Mother's final knowledge score was not a highly significant predictor of BLL change. The contribution of the educational intervention could not be clearly distinguished from the effects of cleaning.	ND

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Schultz, 1999[84]	Education	187	African American, Caucasian, Native American, Asian, other	20-24 µg/dL	6 months	Intervention vs. Reference group BLL decline (µg/dL) significant: 4.2 (±21%) vs. 1.2 (±6%); net reduction 3.1 µg/dL (p<0.001).	ND
Strauss, 2005[79]	Paint	1,179	Children age <=36 months	Pre-intervention means (µg/dL) Untreated 4.5 Treated 7.0	From 1 year pre-interventio n to 3 years post-inter-vention	Comparison of case vs. control change in BLL (µg/dL) showed significant differences, adjusted for time, seasonality, age, and gender. Controls matched on housing criteria only: HUD-treated: 7.04 (42.7%) vs.3.54 (13.2%) Untreated control: 4.57 (19.7%) vs. 3.45 (10.0%) (p<0.001) Controls matched on combination of pre BLL and housing information: HUD-treated: 7.07 (42.8%) vs. 3.57 (12.5%) Untreated control: 5.76 (29.1%) vs. 3.96 (15.9%) (p=0.116) Controls matched on pre-intervention BLL information: HUD-treated: 7.07 (42.9%) vs. 3.59 (12.6%) Untreated control: 6.62 (36.9%) vs. 4.28 (16.0%) (p=0.015)	ND
Swindell, 1994[76]	Paint; dust	132	Children with high BLL, mean age 35 months, range 12-91 months 52% boys	Pre-abatement level = 26.0 (+-6.5) µg/dL	2 wks to 6 months following abatement	BLL declined significantly: 26.0 µg/dL to 21.2 µg/dL (p<0.001). BLL reduction varied by baseline BLL: 97% with BLL >=30 µg/dL had reductions within 1 year 81% with BLL 20-29 µg/dL had reductions 35% with BLL <20 µg/dL had reductions; in this group, BLL increased following abatement, 16.7 to 19.2 µg/dL (p=0.053) There was no meaningful change in pre- to post-abatement levels by calendar year of abatement.	ND

Table 3. Environmental Interventions

Author, Year	Type of Intervention	N	Population/ Risk Factors	Lead Levels	Duration of Follow-up	Results	Adverse Effects
Taha, 1999[71]	Paint; dust	42 eligible, data analyzed for 37	Children age 1-3 years	28.8 µg/dL	±69 days after abatement	Post-treatment, mean BLL 24.6 µg/dL represented a 6.2 µg/dL reduction (22%). Adjusted for season and age of child, the BLL reduction was 6.0 µg/dL (18%). Adjusted BLL (µg/dL) initial / follow-up / change / percentage change Intervention (n=37): pre 28.8, post 22.8; change -6.0 (-18%) (p=0.05) Control (n=65): pre 31.1, post 29.5; change -1.6 (-1.8%) (NS)	ND

Abbreviations: CI=Confidence interval; BLL=Blood lead level; HUD= US Department of Housing and Urban Development; NS=Not significant; PPM=Parts per million; TLC=Treatment of Lead-exposed Children study

Table 4. Summary of Environmental Interventions

Author, Year (Quality)	Study Design	Type of Inter-vention	Years Con-ducted	N	Age	Duration of Follow-up	Baseline BLL	BLL (µg/dL) Results (Initial / Final / change)	Summary of Effect
Aschengrau, 1994[85]; Aschengrau, 1997[86] (N/A)	Randomized environmental intervention; no untreated comparison group	Soil	1989-1990	152	≤4	2 years	7 to 24 µg/dL	T1: 13.10 / 10.65 / -2.44 (95% CI -3.32, -1.57) T2: 12.94 / 7.69 / -5.25 (95% CI -6.51, -3.99) T3: 10.54 / 9.15 / -1.30 (95% CI -4.03. +1.26) All Ts: 12.66 / 9.77 / -2.89 (95% CI -3.64. -2.13) C: None	N/A
Aschengrau, 1998[72] (Fair)	RCT	Dust, paint	1993-1995	63	≤4	6 months	16.9 µg/dL	T1 (high BLL, not randomized): 17.5 / 9.1 / -8.4 T2 (random): 17.6 / 11.5 / -6.2 C (random): 16.3 / 10.4 / -5.9 T1 vs. C: -0.3 (95% CI -3.8, +3.3) T2 vs. C: -2.5 (95% CI -7.0, +2.1)	No effect
Campbell, 2003[75] (Fair)	Non-randomized controlled trial; follow-up at the Philadelphia site of TLC, a chelation RCT	Dust	NR	73	12-34 months	3-6 months post-treatment	20-44 µg/dL	No significant difference mean BLL at any clinic visit between children whose homes were cleaned vs. those whose homes were not cleaned. BLL declined among both groups.	No effect
Clark, 2004[69] (N/A)	Observational, no untreated comparison group	Dust, paint	NR	869 children	6 months to 6 years	6 weeks	ND	Mean change after intervention +8.4 µg/dL Predictors of BLL increase of >5 µg/dL: Child's age at baseline (p=0.006) Mother's education (p=0.002) Exterior building condition (p=0.007) Season of sample collection (p<0.001)	N/A

Table 4. Summary of Environmental Interventions

Author, Year (Quality)	Study Design	Type of Inter-vention	Years Con-ducted	N	Age	Duration of Follow-up	Baseline BLL	BLL (µg/dL) Results (Initial / Final / change)	Summary of Effect
Farrell, 1998[80] (Fair)	RCT	Soil	1990	408 enrolled in 263 houses; 187 complete d the study	6 months to 6 years	1 year	11 µg/dL	T: 12.1 (1988) / 9.7 (1991) C: 10.9 (1988) / 8.4 (1991) Treatment effect, adjusted for effects of time, seasonality, SES, age, and mouthing behavior T (pre - post): 0.030 (SE 0.034) C (pre - post): 0.075 (SE 0.036) T vs. C: -0.045 (SE 0.037)	No effect
Galke, 2001[78] (N/A)	Descriptive study, no comparison group	Dust	1994-1997	240 children 1,212 dwelling s	6 months to 6 years	12 months	Median 10 µg/dL	T: 11.0 / 8.2 / -2.8 C: none	N/A
Haynes, 2002[74] (Good)	Meta-analysis	Dust, paint; meta-analysis of RCTs	NR	4 studies, total subjects = 533	NR	6 to 48 months	6.7 to 16.9 µg/dL	Weighted mean change, T vs. C (95%CI): 2 educational dust control trials: -0.33 (-1.4, 0.74) 2 professional dust control trials: -1.52 -3.41, 0.37 All trials: % >=10 µg/dL in T vs. C: similar % >=15 µg/dL in T vs. C: 6% vs. 14% (p=0.008) % >=20 µg/dL in T vs. C: 2 vs. 6% (p=0.024)	No effect overall; effects seen at higher lead levels
Jordan, 2003[82] (Fair)	RCT	Education	NR	594 mothers and 378 of their children	Birth to 36 months	2 years	<10 µg/dL	T vs. C % who maintained BLL < 10 µg/dL: 81 vs. 73% (p=ns) % with BLL 10-19.99: 15 vs. 24% (p=ns) % with BLL >20 µg/dL: 4 vs. 2% (p=ns)	No effect
Lanphear, 1999[83]; Lanphear, 2000[34]; Lanphear, 2002[93] (Fair)	RCT	Education	NR	275	6 months	48 months	2.9 µg/dL	Change from age 6 to 24 months: T: 2.8 / 7.3 / +5.6 (sic) C: 2.9 / 7.8 / +6.3 (sic) T vs. C: (p=ns)	No effect

Table 4. Summary of Environmental Interventions

Author, Year (Quality)	Study Design	Type of Inter-vention	Years Con-ducted	N	Age	Duration of Follow-up	Baseline BLL	BLL (µg/dL) Results (Initial / Final / change)	Summary of Effect
Lanphear, 2003[87] (N/A)	Two cross-sectional surveys before and after soil abatement	Soil	1993-1996	198 in first survey, 215 in second survey	6-72 months	N/A (cross-sectional)	5.6 µg/dL	T: 5.6 / 3.0 / -3.6, p=0.0001 C: 3.0 / 2.6 / -1.4, p=0.06 Stratifying by age, adjusted for mouthing behavior score and socioeconomic status: Age 36-72 months: 2.3 µg/dL decline (p=ns) Age 6-36 months: 2.5 µg/dL decline (p=0.03)	Effect seen only in young children who had not been exposed
Leighton, 2003[73] (Good)	Retrospective cohort study	Dust, paint	1994-1997	221	6 months to 6 years	10-14 months	20-44 µg/dL	Decline occurred regardless of remediation: 24.3 / 12.3 / -12 (p<0.01) T: 24.6 / 11.6 -53% C: 23.8 / 13.9 -41% Remediation effect adjusted for race: 11% (p=ns) Effect of remediation tended to be stronger in younger children (10 to <36 months) vs. 36-72 months (p=0.06)	No effect
Rhoads, 1999[70] (Fair)	RCT	Dust	NR	113; final BLL obtained from 99	6-36 months	1 year	12 µg/dL	T: 12.4 / 10.3 / -2.1 C: 11.6 / 11.6 / +0.1 T vs. C: -1.9 µg/dL (p<0.05) Adjustment for baseline BLL	+
Schultz, 1999[84] (Fair)	Retrospective cohort study	Education	1994	187	Mean age 3.35	6 months	20-24 µg/dL	Change in BLL, T vs. C: -4.2 vs. -1.2 (p<0.001)	+
Strauss, 2005[79] (Fair)	Retrospective cohort study	Dust, paint	1993-2002	1179	≤36 months	3 years	4.5-7.0 µg/dL	T vs. C BLL reduction, adjusted for time, seasonality, age, and gender. Matched on pre-intervention BLL: T: 7.07 / 3.59 / -3.48 C: 6.62 / 4.28 / -2.34 (p=0.015) Matched on pre-intervention BLL and housing criteria: T: 7.07 / 3.57 / -3.50 C: 5.76 / 3.96 / -1.80 (p=0.116)	+

Table 4. Summary of Environmental Interventions

Author, Year (Quality)	Study Design	Type of Inter-vention	Years Con-ducted	N	Age	Duration of Follow-up	Baseline BLL	BLL (µg/dL) Results (Initial / Final / change)	Summary of Effect
Swindell, 1994[76] (N/A)	Retrospective chart review; no comparison group	Dust, paint	1987-1990	132	Mean 35 months Range 12-91 months	2 weeks to 6 months following abatement	26 µg/dL	T: 26.0 / 21.2 / -4.8 (p<0.001) T group with baseline <20 µg/dL: 16.7 / 19.2 / +2.5 (p=0.053) C: none Stratified by baseline BLL, reductions within 1 year occurred in 97% with baseline >=30 81% with baseline 20-29 35% with baseline <20	+ only if baseline BLL ≥20
Taha, 1999[71] (Fair)	Retrospective cohort study	Dust, paint	1994	42 eligible data analyzed for 37	6 months and 6 years	Mean 69 days after abatement	28.8 µg/dL	Adjusted for season and age of child: T: 28.8 / 22.8 / -6.0 (p=0.05) C: 31.1 / 29.5 / -1.6 (p=NS)	+

Abbreviations: '+'= benefit; C=Control group; NR=Not reported; NS=Not significant; RCT=Randomized-controlled trial; T=Treatment group; TLC=Treatment of Lead-exposed Children study

Table 5. Nutrition Interventions

Author, Year	Nutritional Category	Population	N	Initial Blood Levels	Significant Results	Adverse Effects
Dalton, 1997[88]	Calcium Iron Phosphorus	Infants aged 3.6 - 6 months in Lawrence, MA. High proportion of low income families. Data collected 1991-1993. Majority Latino (> 90%).	103	0.12 µmol/dL - 0.07 µmol/dL	There were no significant differences by treatment group in mean or median change from baseline of serum ferritin, total iron binding capacity, erthrocyte protoporphyrin, or hematocrit at 4 and 9 months after enrollment. Incidence of iron deficiency was similar for both groups and no infant developed iron deficiency anemia during the trial.	ND
Gallicchio, 2002[95]	Calories Carbohydrates Fat Vitamin C	Children, age 1 (approximately), from low income families, living in urban houses built prior to 1950. 85% African American.	205	mean 4.0 µg/dL (range 1-19 µg/dL) 4.9% $\geq$ 10 µg/dL	Statistically significant positive associations ($p<0.05$) were found between blood lead and calories, total fat, saturated fat, and monounsaturated fat. Statistically significant negative associations ($p<0.05$) were found between blood lead and carbohydrates and vitamin C. After multiple linear regression analyses, statistically significant positive associations were found between blood lead and total fat ($p=0.03$) as well as blood lead and saturated fat ($p=0.02$), independent of lead exposure and age of the child. Total caloric intake was found to be a marginally significant effect modifier of the association between lead exposure and blood lead ($p=0.06$).	ND
Hammad, 1996[97]	Iron	Children from 9 months - 5 years old cared for at University of Maryland at Baltimore Pediatric Ambulatory Center. Low income, inner-city families.	299	NA	Average blood lead was 11.4 µg/dL. After adjusting for confounders using multiple linear regression models, a negative association between blood lead and dietary iron intake was found ($p=0.03$). No association was found between blood lead and serum iron.	ND
Haynes, 2003[94]	Calcium Iron	Children living in Rochester, NY and were 5-7 months old at baseline visit. Low income families. (same participants in Lanphear, 2002)	275 (245 at 24 months, 239 with adequate blood samples)	NA	Calcium intake was inversely associated with children's blood lead ($p=0.03$) in a multivariate model that included VDR Fok 1 genotype as an independent variable.	ND

Table 5. Nutrition Interventions

Author, Year	Nutritional Category	Population	N	Initial Blood Levels	Significant Results	Adverse Effects
Lanphear, 2002[93]	Iron Calcium Vitamin C Vitamin D	Children living in Rochester, NY and were 5-7 months old at baseline visit. Low income families. (same participants in Haynes, 2003)	249	2.9 µg/dL (95% CI, 2.7-3.1)	At 24 months of age, BLLs were 7.5 µg/dL. 82 (33%) had BLLs ≥10 µg/dL; 32 (13%) had BBLs ≥15 µg/dL; 14 (6%) had BBLs ≥20 µg/dL. Dietary iron intake was inversely associated with BLLs (p=0.03) during first year of life. Calcium intake was not associated with BLL concentration.	ND
Lee, 2005[10]	Calories Fat Thiamine Pyridoxine Vitamin E Ascorbic acid Folate Calcium Phosphorus Iron	Women 20-49 years old from National Health and Nutritional Survey (NHANES III)	4,394 (3,716 had complete data for all variables in study)	NA	Average BLL of reproductive age woman was 1.78 µg/dL. Inverse associations (p<0.05) between BLL and thiamine and serum folate. Positive associations (p<0.05) between BLL and iron, pyridoxine intake, and folate.	ND
Lucas, 1996[96]	Calories Fat	Children ages 9-6 years, cared for at University of Maryland at Baltimore Pediatric Ambulatory Center. Low income, inner-city families.	296	NA	Average blood lead was 11.4 µg/dL. After adjusting for confounders using multiple linear regression models, significant positive associations with blood lead were found independently for total caloric intake (p=0.01) and dietary fat (p=0.05).	ND
Markowitz, 1996[81]	Iron	Moderately lead poisoned children referred to Montefiore Medical Lead Clinic from 1986-1992 with BLLs 25-55 µg/dL. Low income, inner-city families, living in pre-1960 housing. 2/3 Hispanic, 1/3 African American.	79	NA	BLLs declined 27% on average over 6 months. Two thirds < 25 µg/dL, 7% < 15 µg/dL. However, iron status did not account for change in BLLs.	ND
Markowitz, 2004[89]	Calcium	Children ages 1-6 referred to Montefiore Medical Center with BLLs between 10-44 µg/dL	88	10-44 µg/dL	No significant differences between BLLs in either group. Ca supplementation of 1800 mg/day for 3 months or 6 months did not reduce BLLs.	Abdominal pain complaints occurred infrequently in both groups.

Table 5. Nutrition Interventions

Author, Year	Nutritional Category	Population	N	Initial Blood Levels	Significant Results	Adverse Effects
Sargent, 1999[90]	Calcium Iron Phorphorus	Infants aged 3.6 - 6 months in Lawrence, MA. High proportion of low income families. Data collected 1991-1993. Majority Latino (> 90%).	103; complete lab data collected for 81 (78.6%) of original random assignment	< 25 µg/dL	There was no significant difference between groups in the mean ratio of urinary calcium to creatinine, serum calcium and phosphorus, or change in iron status (serum ferritin, total iron binding capacity). At month 4, the median increase from baseline BLLs in the treatment group was 57% of the increase for the control group (p=0.039), but this effect weakened after month 4 through the final 9th month of the trial. Because the effect did not last, cannot conclude that calcium glycerohosphate supplement prevented lead absorption.	10 children distributed evenly between groups has at least one urine sample with a ratio of urinary calcium to creatinine above the age-related norm; 2 had repeat elevated levels (one in each group); 1 in control group had elevated serum calcium level; 13 had low serum ferritin concentrations (5 control, 8 treatment).

Table 5. Nutrition Interventions

Author, Year	Nutritional Category	Population	N	Initial Blood Levels	Significant Results	Adverse Effects
Schell, 2004[91]	Calcium Ferritin Iron Protein Supplements Vitamin D Zinc	Mother/Infant pairs of low socioeconomic status in Albany County, NY from APILS (Albany pregnancy infancy lead study) 1992-1998	169	1.6-10 µg/dL at birth	By 6 months, mean BLLs significantly increased from birth to 2.3 µg/dL ($p<0.001$); none were $\geq$10 µg/dL. By 12 months, mean BLLs significantly increased from 6 months to 5.1 µg/dL ($p<0.001$) and 18% were $\geq$10 µg/dL. Observed significant inverse relationships between infant's 6 month lead level and intake of zinc ($p=0.003$), iron ($p=0.015$), and calcium ($p<0.001$). At 12 months, low iron intake continued to be associated with higher lead levels ($p=0.041$), although zinc and calcium did not. Protein had a paradoxal effect (associated with lower lead at 6 months ($p=0.001$), but higher lead at 12 months. Serum vitamin D and ferritin were not associated with lead levels, nor was vitamin supplement use.	ND
Schnell, 2003[92]	Calcium Ferritin Iron Supplements Vitamin D Zinc	Mother/Infant pairs of low socioeconomic status in Albany County, NY from APILS (Albany pregnancy infancy lead study) 1992-1998	220	1.58 µg/dL neonates	Mother's BLLs were strongly and positively related to neonates BLLs ($p<0.001$). For the anthropometric measures of maternal nutritional status, variables measuring gain in weight and arm circumference were negatively related to neonate BLLs ($p<0.001$). Dietary intakes in iron ($p=0.003$) and vitamin D ($p=0.038$) were negatively related to neonates BLLs. The effects of zinc varied substantially. Calcium was negatively related to BLLs before controlling for age, education index, etc. ($p=0.042$), but not after controlling for these variables. Serum ferritin, serum vitamin D, and supplements were not significantly related to BLLs of neonates. African American mothers and newborns have significantly higher BLLs than Caucasians ($p<0.001$), except in the 2nd trimester.	ND

Table 5. Nutrition Interventions

Author, Year	Nutritional Category	Population	N	Initial Blood Levels	Significant Results	Adverse Effects
Simon, 1999[98]	Ascorbic acid	Probability sample of US population from the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1994 without a history of lead poisoning. Adults and youths.	4,213 youths aged 6-16 and 15,365 adults aged ≥17	ND	22 (0.5%) youths had elevated BLLs. 57 (0.4%) adults had elevated BLLs. Serum ascorbic levels ranged from 0-170 µmol/L, with the mean for the youths 55 micro mol/L and mean for the adults 43 µmol/L. After controlling for the effects of age, race, sex, income level, and dietary energy, fat, calcium, iron, and zinc intake, youths in the highest serum ascorbic acid tertile had an 89% decreased prevalence of elevated BLLs compared with youths in the lowest serum ascorbic acid tertile (p=0.002). Adults in the highest 2 serum ascorbic acid tertiles had a 65% to 68% decreased prevalence of elevated BLLs compared with adults in the lowest serum ascorbic acide tertile (p=0.03). As a continuous predictor, serum ascorbic acid level was independently associated with decreased BLLs among adults (p<0.001), but not among youths.	ND
Zierold, 2004[99]	Many, not described	Data from Wisconsin Childhood Lead Poisoning Prevention Program from 1996-2000. Children ages 0-6.	111,196	Mean 5.29 µg/dL	For those in the Special Nutrition Program, mean BLLs declined over the 4 year time period from 7.89 µg/dL to 5.29 µg/dL. Average BLLs decline of 0.64 µg/dL per year. For the comparison group, mean BLLs declined over the 4 year time period from 5.51 µg/dL to 3.70 µg/dL. Average BLLs decline of 0.42 µg/dL per year. The difference between the groups was not statistically significant (p=0.25). African American children in the Special Nutrition Program BLLs had a significantly quicker decline compared with Caucasian children (p=0.03).	ND

Abbreviations: BLL=Blood lead level; ND= Not described

Table 6. Summary of Nutrition Interventions

Studies	Ascorbic Acid	Calcium	Calories	Carbo-hydrates	Fat	Ferritin	Folate	Folate (serum)	Iron	Multiple, Not Described	Phos-phorus	Protein	Pyrido-xine	Supple-ments	Thiamine	Vitamin D	Zinc
Randomized Controlled Trials																	
Dalton 1997[88]	-	NS	-	-	-	-	-	-	NS	-	NS	-	-	-	-	-	-
Markowitz 2004[89]	-	NS	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sargent 1999[90]	-	NS	-	-	-	-	-	-	NS	-	NS	-	-	-	-	-	-
Prospective Cohort Studies																	
Gallicchio 2002[95]	N	-	P	N	P	-	-	-	-	-	-	-	-	-	-	-	-
Haynes, 2003[94]	-	N*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lanphear, 2002[93]	-	NS	-	-	-	-	-	-	N	-	-	-	-	-	-	-	-
Markowitz 1996[81]	-	-	-	-	-	-	-	-	NS	-	-	-	-	-	-	-	-
Schell 2003[92]	-	NS	-	-	-	NS	-	-	N	-	-	-	-	NS	-	N (dietary) NS (serum)	Varied
Schell 2004[91]	-	NS	-	-	-	NS	-	-	N	-	-	Varied	-	NS	-	NS (serum)	NS
Retrospective Cohort Study (with comparison group)																	
Zierold 2004[99]	-	-	-	-	-	-	-	-	-	NS	-	-	-	-	-	-	-
Cross Sectional Studies																	
Hammad 1996[97]	-	-	-	-	-	-	-	-	N	-	-	-	-	-	-	-	-
Lee, 2005[10]	-	-	-	-	-	-	P	N	P	-	-	-	P	-	N	-	-
Lucas 1996[96]	-	-	P	-	P	-	-	-	-	-	-	-	-	-	-	-	-
Simon 1999[98]	N	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Abbreviations: '-' = not evaluated; N = Negative/inverse relationship; NS = Not significant/no relationship; P = Positive relationship

*Calcium intake was inversely associated with children's blood lead level (p=0.03) in a multivariate model that included VDR Fok 1 genotype as an independent variable. No significant effect modification of calcium intake on blood lead by genotype was found (p=0.49). No significant association was observed when the polymorphism was not included (Lanphear, 2002[93]).

Table 7. Summary of Evidence

Key Question	Findings
CHILDREN	
KQ 1. Is there direct evidence that screening for lead results in improved health outcomes (i.e. cognitive changes, behavioral problems, learning disorders)?	There is no direct evidence from controlled studies of screening.
KQ 2. What is the prevalence of elevated lead in children?	The prevalence of blood lead >=10 µg/dL among children aged 1-5 years in the U.S. has declined from 9% in 1988-1991 to 1.6% 1999-2002.
Are there population-level risk factors that identify children at higher risk for elevated lead levels?	Population-level risk factors among children include age < 5 years; urban residence; low income; low parental educational attainment; pre-1950 housing; and recent immigration. Mean blood levels among African-American children remain significantly higher than Mexican American children and non-Hispanic whites.
KQ 3. Can screening tests accurately detect elevated blood lead levels?	Blood lead concentration is more sensitive and specific than free erythrocyte proptoporphyrin (EP) levels, but can be affected by environmental lead contamination and laboratory analytic variation. In one study of 47,230 suburban and rural children, 4.7% had an elevated EP level, while only 0.6% had elevated BLL. Capillary sampling has false-positive rates of 3-9%, and false-negative rates of 1-8%, compared with venous blood lead levels.
How accurate are questionnaires (or other tools) for risk factor assessment at various blood lead levels?	The sensitivity and specificity of questionnaires vary considerably with the prevalence of EBLL in the population surveyed and the cutoff BLL (10 vs. 15 µg/dL). One study found that rental status, lead-contaminated floor dust, and poor housing condition were associated with EBLL, suggesting that housing characteristics can be used to identify homes where a lead hazard may exist before or during occupancy.
What is the optimal frequency for screening?	Not addressed in this review.
What is the optimal frequency for repeat testing?	Not addressed in this review.
KQ 5. Do interventions for elevated lead levels result in improved health outcomes or lead levels?	We identified no evidence that treatment, lead abatement, or education improved neurocognitive outcome in asymptomatic children with mildly-moderately increased lead levels. In one trial of succimer there was no benefit or slight harm. Some interventions have small, inconsistent, or unsustained effects on lead levels in high-risk children.

Table 7. Summary of Evidence

Key Question	Findings
KQ 4, KQ 6. What are the adverse effects of screening and treatment?	See text.
KQ 7. What are cost effectiveness issues?	Not addressed in this review.
PREGNANT WOMEN	
KQ 1. Is there direct evidence that screening in asymptomatic pregnant women for lead results in improved health outcomes?	There is no direct evidence from controlled studies of screening that screening improves maternal hypertension, cognitive changes in offspring or perinatal outcomes.
KQ 2. What is the prevalence of elevated lead in pregnant women?	In 1992, two large surveys of low-income pregnant women found 0% and 6% with blood levels >15 µg/dL. A longitudinal study of pregnant women in Boston found that umbilical cord blood levels declined 82% between 1980 and 1990.
Are there population-level risk factors that identify pregnant women at higher risk for elevated lead levels (i.e., geography, racial/ethnicity, SES, age)?	Ethnic background, country of origin, and immigrant status of birth mothers have been shown to be associated with prenatal lead exposure in newborns. Cigarette smoking, maternal age, and alcohol intake have been found to increase umbilical cord blood lead levels.
KQ 3. Can screening tests accurately detect elevated blood lead levels?	See KQ 3. in Children, above.
How accurate are questionnaires (or other tools) for risk factor assessment at various blood lead levels?	We found one study of a 4-question prenatal survey developed by the CDC that had a sensitivity of 75.7%, and a negative predictive value of 93.1%.
What is the optimal frequency for screening? What is the optimal frequency for repeat testing?	Not addressed in this review.
KQ 5. Do interventions for elevated lead levels result in improved health outcomes?	We identified no evidence that treatment, lead abatement, or education improved neurocognitive outcome in asymptomatic children with mildly-moderately increased lead levels. In one trial of succimer there was no benefit or slight harm.

Table 7. Summary of Evidence

Key Question	Findings
KQ 4, KQ 6. What are the adverse effects of screening and treatment?	See text.
KQ 7. What are cost effectiveness issues?	Not addressed in this review.

Appendix 1. Key Questions and Critical Key Questions

Members of the USPSTF and AHRQ identified an analytic framework (Figure 1) and key questions (KQs) for updating the USPSTF guidelines for lead screening.

Key Questions for *Children* Were Stated as Follows:

- KQ 1: Is there direct evidence that screening for lead results in improved health outcomes (i.e. cognitive changes, behavioral problems, learning disorders)?
- KQ 2: What is the prevalence of elevated lead in children? Are there population-level risk factors that identify children at higher risk for elevated lead levels (i.e. geography, race/ethnicity, socioeconomic status, age)?
- KQ 3: Can screening tests accurately detect elevated blood lead levels? What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels? What is the optimal frequency for screening? What is the optimal frequency for repeat testing?
- KQ 4: What are the adverse effects of screening?
- KQ 5: Do interventions (i.e. counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?
- KQ 6: What are the adverse effects of interventions?
- KQ 7: What are cost effectiveness issues?

Key Questions for *Pregnant Women* were Stated as Follows:

- KQ 1: Is there direct evidence that screening in asymptomatic pregnant women for lead results in improved health outcomes (i.e. cognitive changes in offspring, perinatal outcomes including birth weight/preterm delivery etc, maternal blood pressure)?
- KQ 2: What is the prevalence of elevated lead in asymptomatic pregnant women? Are there population-level risk factors that identify pregnant women at higher risk for elevated lead levels (i.e. geography, racial/ethnicity, SES, age)?
- KQ 3: Can screening tests accurately detect elevated blood lead levels? What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?
- KQ 4: What are the adverse effects of screening?
- KQ 5: Do interventions (i.e. counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?
- KQ 6: What are the adverse effects of the interventions?
- KQ 7: What are cost effectiveness issues?

Members of the USPSTF and AHRQ identified KQs 1 and 5 for children and pregnant women as critical key questions. For these critical key questions, we used USPSTF methods to systematically abstract information about the design, results, and internal validity of each study, and included only those studies we rated fair-quality or better.[2] We conducted a selected review of the literature that addressed KQs 2, 3, 4, and 6. The cost-effectiveness of screening would be examined only in the presence of

adequate evidence of intervention efficacy. We did not examine KQ 7 because of the lack of evidence of improved clinical outcomes for KQ 5. We reviewed the populations of asymptomatic children and pregnant women separately.

Appendix 2. Criteria for Grading the Quality of Individual Studies

The Methods Work Group for the Third U.S. Preventive Services Task Force (USPSTF) developed a set of criteria to evaluate the quality of individual studies. At its September 1999 quarterly meetings, the USPSTF accepted the criteria and definitions of quality categories relating to internal validity.

Presented below are a set of minimal criteria for each study design and a general definition of three categories — "good," "fair," and "poor." 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 major limitations. "Poor" studies have at least one major limitation.

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.

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.

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 followup or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- 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 (followup at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; 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 in followup; 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.

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
- Appropriate 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 (>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 of very narrow selected spectrum of patients.

Appendix 3. Detail on Prevalence and Risk

What is the Prevalence of Elevated Lead in Children?

The prevalence of elevated blood lead levels in the US continues to decline sharply, due primarily to marked reductions in lead in gasoline, air, dietary sources, and residential paint.[4] In a 1999-2002 national survey of children aged 1-5 years, 1.6% had blood lead levels ≥10 µg/dL, compared to 9% in a similar survey in 1988-1991.[5] Although the nationwide prevalence of elevated blood lead levels among children ages 1-5 years declined dramatically from 1991-94 through 1999-2002, the prevalence still varies substantially among different communities and populations, and an estimated 310,000 children remain at risk for exposure to harmful levels of lead.[4]

What is the Prevalence of Elevated Lead in Asymptomatic Pregnant Women?

Blood lead levels and blood umbilical cord lead levels are frequently used to assess both the mother's and fetus's level of lead exposure and risk. In 1992, two large surveys of low-income pregnant women found 0% and 6%[1] with blood lead levels >15 µg/dL. A study of all women who enrolled in prenatal clinics in Mahoning County, Ohio, from 1990 to1992 found that 13% of prenatal patients had blood lead levels ≥ 10 µg/dL, with 1% having blood lead levels greater than 15 µg/dL.[6]

Population mean blood lead levels in women of childbearing age and pregnant women have fallen over the past two decades. Although it was estimated in 1990 that 4.4 million women of childbearing age, and over 400,000 pregnant women, had blood lead levels of >10 µg/dl,[7] a longitudinal study of pregnant women in Boston demonstrated that

umbilical cord blood lead levels declined 82% between 1980 and 1990.[8] A recent study of 1109 infants in Quebec, Canada, found a mean cord blood lead of 1.5 µg/dL (0.076 µmol/l; 95% CI = 0.074, 0.079).[9] and in a recent review of NHANES data of 4394 women of child-bearing age, the GM blood lead level was 1.78 µg/dL.[10]

Are there Population-level Risk Factors that Identify Children at Higher Risk for Elevated Lead Levels (i.e. geography, race/ethnicity, socioeconomic status, age)?

The highest geometric mean blood lead levels (GM blood lead levels) in the U.S. occur in children aged 1-5 years (GM 1.9 µg/dL) and in adults $\geq$ 60 years of age (GM 2.2 µg/dL), with the lowest in youth aged 6-19 years (GM 1.1 µg/dL).[4] Children under five are at greater risk for elevated blood lead levels and lead toxicity because of increased hand to mouth activity, increased lead absorption from the gastrointestinal tract, and the greater vulnerability of a developing central nervous system.[11] Geometric mean levels are significantly higher in males than in females except among children aged 1-5 years.[4]

Correlates of higher blood lead levels at all ages include minority race/ethnicity, urban residence, low income, low educational attainment, older (pre-1950) housing, and recent immigration.[4, 12-16] These factors are associated with increased exposure to important lead sources, including dilapidated housing containing lead-based paint, lead-soldered pipes, household lead dust, and lead in dust and soil from heavy traffic and industry.[1, 17] There have been major reductions in the number of US homes with lead-based paint from the estimated 64 million in 1990, but approximately 24 million housing units still contain substantial lead hazards, with 1.2 million of these units occupied by low-income families with young children.[4, 18]

Less frequent sources of household lead exposure include contaminated clothing or materials brought home by workers in lead-using industries, lead-using home businesses or hobbies, lead-based paint and dust contamination in pre-1978 housing that is undergoing remodeling or renovation,[16] dietary intake from lead-contaminated consumer products, drinking water, and lead-based pottery, and traditional ethnic remedies.[4, 19-22]

Geometric mean blood lead levels among African-American children (2.8 µg/dL) remain significantly higher than Mexican-American children (1.9 µg/dL) and non-Hispanic whites (1.8 µg/dL). Even among low income families, however, GM blood lead levels declined significantly from 1991-1994 (3.7 µg/dL) to 1999-2002 (2.5 µg/dL).[4]

A woman of childbearing age with a high blood lead level risks transmitting lead to her unborn child.[23] Ethnic background, country of origin, and immigrant status of birth mothers, pica behavior, as well as lifestyle and work patterns of pregnant women and age have shown to be associated with prenatal lead exposure in newborns. Multivariate analyses of pregnant women in Quebec, Canada revealed that both cigarette smoking (15% increase) and alcohol intake (17% increase) make significant and independent contributions to cord blood lead concentrations.[24] In a survey of 10 Quebec hospitals, umbilical cord blood samples were obtained from 1109 newborns. Although blood lead levels were considered low, a statistically significant relationship was observed between maternal age, and smoking during pregnancy, in cord blood lead concentrations.[9]

One hundred and fifty nine mother-infant pairs from a cohort of women receiving prenatal care in Pittsburgh, PA provided blood samples at delivery for lead determination.

Alcohol use was associated with relatively greater cord blood lead compared with maternal Blood lead. No association was found with cord blood lead or maternal blood lead with smoking, physical exertion, or calcium consumption.[25]

A recent study in NYC of pregnant women in their 3rd trimester with an incident blood lead level (blood lead levels) of 20 µg/dL or greater showed they had newborns with a median incident blood lead level of 12 µg/dL. In addition, maternal blood lead levels were directly associated with gestational age and pica behavior. These cases were more than twice as likely to be foreign-born women.[26]

Neurotoxic Effects of Lead Exposure in Children

High levels of lead can produce serious central and peripheral neurological complications, including acute encephalopathy which can result in coma, death or long-term impairment.[1, 27, 28] Prospective cohort studies across several child populations have suggested that a rise in blood lead from 10 to 20 µg/dL is associated with a likely decrement of 2-3 points (reported range -6 to +1) in intelligence test scores (IQ).[1] The variety of test instruments that have been used, and differences in adjustment for important covariates, make direct comparison of these studies difficult but a consistent negative effect on intellectual development is reported.

Significant associations have been demonstrated between umbilical blood lead levels and neurodevelopmental testing at two years of age although the association was not significant at later ages. Blood lead levels at two years of age, however, were associated with neurocognitive performance at 10 years of age.[11] A recent analysis of school-aged children demonstrated a stronger cross-sectional inverse association of IQ

with contemporary blood lead levels (mean BLL = 8 mcg/dL at age 7 years) than with baseline blood levels (mean BLL = 26 mcg/dL at 24 months old) suggesting an ongoing adverse effect of lead on cognitive performance among school-aged children.[29]

Prior cross-sectional studies[1] consistently reported small, inverse associations between blood or tooth lead and reaction (attentional) performance, but studies evaluating the effect of mildly elevated lead levels on other measures of neurodevelopmental function (e.g., behavior, learning disorders, auditory function) produced inconclusive results. These outcomes have been less thoroughly evaluated than IQ, and more recent studies bolster an association between childhood lead exposure and disorders of attention and learning, and aggressive and delinquent behavior.[11, 27, 30, 31]

A growing number of human epidemiology studies have reported associations between neurotoxic effects and blood lead levels once thought to be harmless. Several recent studies have demonstrated an inverse relationship between historical blood lead levels and subsequent measures of intellectual and cognitive performance at blood lead levels of < 10 µg/dL. The shape of the dose response curve at levels below 10 µg/dL is uncertain although data suggests that lead associated cognitive changes may be greater with incremental changes in blood lead levels in this range.[11, 27, 31-35] A recent meta-analysis of seven prospective international cohort studies found evidence of deficits on standard IQ testing among children with maximal blood lead levels <7.5 mcg/dL. A decline of 6.2 IQ points (95% CI, 3.8-8.6) was observed as blood lead levels increased from 1 to 10 µg/dL.[36]

Lead associated effects on neurobehavioral functioning must be considered relative to other important covariates such as socioeconomic status, home and parenting

environment, and genetic factors.[32] The contribution of childhood lead exposure to the observed variance in cognitive ability (IQ testing) is believed to be in the range of 1-4%, while social and caregiving factors may be responsible for 40% or more.[30, 32] Blood lead levels, however, appear to be associated with a substantial proportion of the known, modifiable variance in children's cognitive ability and incur a substantial social and economic burden among those affected and on the nation.[37, 38]

Reproductive Effects of Lead Exposure

The effects of high blood lead levels on reproductive outcomes have been well described.[1] High paternal blood lead levels (>40 µg/dL or prolonged levels greater than 25 µg/dL) are associated with impaired fertility, spontaneous abortion, and fetal growth abnormalities (preterm deliver and low birth weight). Maternal blood lead levels as low as 10 µg/dL have been associated with pregnancy hypertension, spontaneous abortion, and neurobehavioral effects in offspring. Studies evaluating potential associations between parental lead exposure and congenital malformations in offspring have not demonstrated consistent patterns of defects or magnitude of risk, and often lack biological indices of exposure at developmentally significant times.[3]

The Mexico City Prospective Lead Study examined the association of maternal prenatal blood lead level during pregnancy (range 7.5-9.0 µg/dl [0.36-0.43 µmol/l]) and child postnatal blood lead level (range of median blood lead level from birth to 48 months 7.0-10.0 µg/dl [0.34-0.48 µmol/l]) with head circumference in a sample of Latino immigrants living in Los Angeles. Multiple regression modeling showed significant negative associations ($p<0.05$, two-tailed) between 6-month head circumference and 36-

week maternal blood lead level, and 36-month head circumference and 12-month blood lead level but these were the only significant associations among the over fifty assessed in this study.[39]

In 272 mother-infant pairs, tibia bone lead was the only lead biomarker clearly related to birth weight (other significant birth weight predictors included maternal nutritional status, parity, education, gestational age, and smoking during pregnancy). Findings suggest that bone lead might be a better biomarker of lead body burden than blood lead.[40]

Neurodevelopmental and Cognitive Measures and Lead Effects

Recent observational studies (prospective cohort and cross-sectional) provide limited, preliminary data that prenatal blood lead levels may be associated with neurodevelopmental delay or impairment. Study design and measurement issues, however, limit interpretation of these studies.

A prospective study of 103 African American neonates with low-level (<5 µg/dL) parental lead exposure included a battery of 16 neonatal behavioral assessments at 1 to 2 days after birth. No differences were found in 15 of the 16 domains studied, with neonates in the higher exposure group receiving lower scores on the hand-to-mouth motor activity than did those infants in the lower exposure group ($P< 0.05$).[41] A sample of 79 African-American infants with low-level prenatal parent lead exposure were given the Fagan test of Infant Intelligence (FTII) battery at 7 months of age.[42] Excluding all but infants with scores in the 5th and 95th percentiles of the FTII (n=5 in both groups) revealed that subjects rated at high risk for impairment on the FTII (lower 5th percentile)

were 6 times more likely to be in the highest maternal blood lead level quartile (P< .004). Infants scoring in the lower 15th percentile on FTII score (n=12), were 2 times more likely to be in the high maternal blood lead level quartile, though significance dropped to P<0.056.[42] The difference between the mean blood lead levels in the infants with lowest and highest FTII scores (5th and 95th percentiles) was very small, however (0.44 vs. 0.94 mcg/dL). Recent evidence suggests that children may demonstrate differences in evoked visual and auditory potentials associated with increased levels of prenatal lead exposure.[43, 44]

Other Adverse Effects of Lead Exposure

Higher levels of blood lead (>40 µg/dL) exert detrimental effects on neurological, cardiovascular, renal, and hepatic function.[1] Subclinical effects on renal function can be observed at lower levels of exposure and children may be more vulnerable.[45, 46]

In a cohort of women in their third trimester, immigrant women were more likely to have elevated blood lead levels and elevated blood pressures, compared to non-immigrant women. An association between elevated blood level and blood pressure was significant only in the immigrant group.[47] Past lead exposure was associated with hypertension and elevated blood pressure during pregnancy. Bone lead concentration, however, was not shown to be related to hypertension or elevated blood lead in pregnancy.[48]

Among 110 women in their 3rd trimester, gestational hypertension cases showed significantly higher blood lead levels than normotensives, and blood lead was significantly related to blood pressure, even after correcting for the body mass indices

and age. The lead:ionized-calcium ratio showed a stronger association with blood pressure, than lead alone.[49] A cross-sectional study of 39 pregnant women in the third trimester of pregnancy compared red blood cell (RBC) levels of lead (Pb) and blood pressure. The study population included 20 women with normal pregnancies, 15 with mild hypertension, and 4 with severe hypertension and preeclampsia. Preeclamptic pregnancies were more likely to have an elevated RBC Pb. Rank correlation showed a significant effect of RBC Pb level on blood pressure.[50]

Appendix 4. Detail on Residential Lead Hazard Control on Blood Lead Levels

Although newer residential hazard control methods can effectively reduce exposure to lead paint and lead-contaminated dust,[1] compared to older strategies that often increased lead exposure during the intervention, these newer techniques can still result in an elevation of blood lead in a subset of children immediately following lead control interventions (Tables 3 and 4). In an evaluation of HUD-sponsored lead control interventions among fourteen state and local governments, 81 of 869 children (9.3%) had an elevation of $\geq$ 5 µg/dL. Risk factors associated with post-intervention increases were the number of exterior paint deteriorations, the educational level of the female parent or caregiver, and younger age of the child.[69]

Before 1996, retrospective cohort studies, case series, and uncontrolled experiments suggested a modest decline (4-10 µg/dL) in mean blood lead levels in children with initial blood lead levels $\geq$ 25 µg/dL. More recent studies of newer lead-based paint hazard control techniques that included an untreated comparison group, however, found more modest beneficial effects[70, 71] or no effects.[72, 73]

A meta-analysis of four randomized controlled trials conducted in 1996-2000 found that interventions had no effect on mean blood levels (-0.62 µg/dL, 95% CI -1.55 to 0.32), but there were significant reductions in the proportion of children who had blood lead concentrations exceeding 15 µg/dL (6% vs. 14%, p=0.008) and 20 µg/dL (2% vs. 6%, p=0.024) in the intervention group compared with controls.[74]

Two of these four trials evaluated dust control and two evaluated providing education and equipment to families. The earlier of the two trials of dust control (1998)

evaluated one-time professional dust control and window-sill-paint sealing in homes of children aged four or younger, with mean blood lead of 16.9 µg/dL.[72] There were similar reductions in blood levels in the intervention and control groups (-6.2 vs. -5.9 µg/dL) six months after abatement. In the second randomized trial (1999), conducted in Jersey City, N.J., investigators recruited children aged 6 to 36 months who had lead paint in the home. Families (n=113) were randomized to a lead exposure reduction group or to an accident prevention control group. In the lead exposure reduction group, staff members visited the home every two weeks and spent about two hours cleaning up dust. After one year, there was a small but statistically significant difference in blood lead change between intervention and control groups, adjusted for baseline lead levels (-2.1 vs. +0.1 µg/dL, $p<0.05$).[70]

A follow-up study in urban children participating in the TLC trial examined the effects of a second professional lead dust cleaning of homes 18 months after an initial cleaning and therapy commencement .[75] All homes in the Philadelphia site (n=165) of the TLC trial were offered a second professional cleaning. Participation in the follow-up intervention was voluntary rather than randomized. The mean BLL at study initiation was 26 µg/dL. The mean BLL was 15.7 µg/dL at the second cleaning visit, but six months later there was no difference in blood lead levels between children whose homes were cleaned (n=73) and those whose homes were not cleaned (n=86). The report did not stratify results by the original treatment assignment of the subjects (chelation vs. placebo), so the effects of the combined interventions cannot be compared with an untreated group.

A 2003 retrospective cohort study identified children listed in the New York City child blood lead registry and compared blood levels before and 10-14 months after remediation with those of a control group that did not have remediation.[73] Mean blood levels declined significantly from 24.3 µg/dL to 12.3 µg/dL at follow-up, regardless of remediation. After adjusting for confounders, the remediation effect was 11% (p=ns). Race was identified as the only confounding factor, and white and Asian children had an adjusted mean follow-up blood lead level 30% lower than African American children ($p<0.01$). The effect of remediation appeared to be stronger in younger children (10 - <36 months) than in older children (36-72 months.) Another retrospective cohort study that evaluated in-home counseling, combined with professional lead paint remediation, compared lead levels in children aged six months to six years with mean blood lead of 28.8 µg/dL with similar children who did not receive the intervention.[71] Follow-up blood lead was measured on average 69 days after abatement, 172 days after the initial sample. After adjusting for season and age of the child, the treatment group blood lead decreased 6.0 µg/dL from 28.8 to 22.8, and the effect of treatment was significant ($p<0.05$). The comparison group mean blood lead decreased 1.6 µg/dL from 31.1 to 29.5 (p=ns).

In a retrospective study that measured blood lead levels in children whose homes were abated from 1987 to 1990, before and after abatement policies in Massachusetts became more stringent in 1988, the mean blood lead decreased from 26.0 µg/dL at baseline to 21.2 µg/dL ($p<0.001$) measured between two weeks to six months post abatement. Reductions were only seen, however, among children whose baseline blood lead levels were greater than 20 µg/dL. This study found no meaningful change in pre- to post abatement levels by calendar year of intervention.[76] The effect of different housing

policies on the risk of subsequent lead exposure in homes where a child with elevated blood lead resided in the past was demonstrated in adjacent geographic regions of two northeastern states. Approximately eight years later, the risk of identifying at least one child with an elevated blood lead level ($\geq$ 10 µg/dL) was four times greater in the state with less stringent housing-based lead poisoning prevention policies.[77]

A study of 1212 HUD dwellings that received interior treatment for lead hazard control in thirteen states from 1994 to 1998 reported a mean 2.8 µg/dL reduction in children's (n=240) blood lead levels at 12 months post-intervention, from a median level of 10 µg/dL at baseline.[78] The effect of treatment in these studies was not compared with an untreated population. Another study of HUD dwellings in four Massachusetts communities found a significantly larger decline in blood lead levels between 1993 and 2002 among children in treated homes than in untreated homes, matching on pre-intervention BLL. Children's BLLs decreased from 7.07 and 6.62 µg/dL to 3.59 and 4.28 in the treated and untreated homes respectively (p=0.015). The study adjusted for time and seasonality to account for the downward trend in BLLs observed among children in the general Massachusetts population, from 5.9 µg/dL in 1994 to 3.2 µg/dL in 2002.[79]

These trials highlight the difficulties of lead-paint hazard control as a method to reduce lead exposure. Poor, inner-city families tend to move frequently, so that treating the current residence may have limited long-term benefit to the individual child, although benefit accrues to subsequent children moving into that residence. In the Jersey City, N.J. study, for example, approximately 30% of the randomized families moved during the 12-month follow-up period.[70] Residential lead-paint hazard control can be costly and labor-intensive, limiting the availability of intervention, especially in poor communities.[1]

Recontamination by nearby lead sources, including soil lead, may occur after lead-paint hazard control efforts in a dwelling[1, 80] These limitations demonstrate the need for effective comprehensive individual interventions, as well as community-based interventions, to reduce household lead exposure. Unfortunately, available data about programs that employ multiple interventions are sparse.[69, 81]

Appendix 5. Detail on Effect of Counseling and Education Interventions on Blood Lead levels

There have been no controlled studies to evaluate whether counseling families to perform cleaning would be as effective in reducing blood lead levels as professional cleaning. Two randomized controlled trials that administered counseling alone,[82] or with the provision of cleaning supplies,[83] found no significant effects of the intervention on children's blood lead levels. A retrospective cohort study of children with blood lead of 20-24 µg/dL found that a one-time in-home educational visit was associated with a greater reduction in blood lead after six months, compared with households that did not receive an educational visit (-4.2 µg/dL vs. -1.2 µg/dL, $p<0.001$).[84]

Appendix 6. Detail on the Effect of Soil Abatement on Blood Lead Levels

Results of the U.S. Environmental Protection Agency's Three City Urban Soil Lead Abatement Demonstration Project suggest that substantial declines in soil lead cause only modest or no reduction in mildly-elevated blood lead concentrations.[1, 80, 85, 86] The small effect is due at least in part to rapid recontamination with dust lead in households undergoing soil abatement. Cross-sectional surveys before and after soil abatement in the vicinity of a former smelting and milling operation observed a statistically significant reduction in blood lead levels among children aged 6 to 36 months who had not been exposed to lead-contaminated yards in early childhood. A significant reduction was not seen in children aged 36 to72 months.[87]

Appendix 7. Detail on Nutritional Interventions on Blood Lead Levels

Three RCTs[88-90] and three prospective cohort studies[91-93] did not find a significant correlation between calcium and blood lead levels, although one prospective cohort study[94] found an inverse association. Fat and caloric intakes were positively associated with blood levels in a prospective cohort study[95] and a cross-sectional study.[96] Carbohydrates had an inverse association according to a prospective cohort study.[95] Two prospective cohort studies[91, 92] found that ferritin is not significantly related to blood lead levels. One cross-sectional study[10] found a positive association with folate and a negative association with serum folate. Iron has not been shown to have a effect on blood lead levels in two RCTs[88, 90] and one prospective cohort study,[81] although three prospective cohort studies[91-93] and one cross-sectional study[97] reveal a negative association, while one cross-sectional study shows a positive association.[10] Two RCTs[88, 90] found no correlation between blood lead levels and phosphorus. One cross-sectional study found a positive association between blood lead levels and pyridoxine.[10] Protein had a paradoxical effect in one prospective cohort study, significantly associating with low lead levels at six months, but then higher lead levels at 12 months.[91] Two prospective cohort studies showed no relationship between supplement use and blood lead levels.[91, 92] One cross-sectional study found a negative association between blood lead levels and thiamine.[10] Vitamin C is inversely related with blood lead levels according to a prospective cohort study.[95] Vitamin C has also been inversely associated with blood lead levels in a cross-sectional study,[98] Dietary vitamin D is also inversely related to blood lead levels according to a prospective cohort study,[92] whereas serum vitamin D has not been

correlated with blood lead levels in two prospective cohort studies.[91, 92] Two prospective cohort studies yielded different results concerning zinc, showing no association to blood lead levels,[91] and conflicting results.[92]

Despite the significant relationships between nutrients and children's blood lead levels in the epidemiological studies described above, it is noticeable that none of the RCTs found significant correlations.[88-90] Similarly, a 2004 retrospective cohort study, using data from the Wisconsin Childhood Lead Poisoning Prevention Program in children aged 0-6 compared children's blood levels enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children from 1996 to 2000 with children not enrolled in the nutrition program did not find any significant differences between the two groups.[99] Other cohort studies reveal significant association with calories, carbohydrates, fat, iron, vitamin C and vitamin D,[81, 91-95] whereas the cross-sectional studies demonstrate significant associations with ascorbic acid, calories, fat, folate, serum folate, iron, pyridoxine, and thiamine[10, 96-98] Adverse effects were reported in two of the fourteen studies; both are RCTs. A calcium study using a 1800 µg/dL[89] dosage reported abdominal pain in both the treatment and control groups. A calcium glycerophosphate-supplemented infant formula study reported elevated ratios of urinary calcium to creatinine and low concentrations of serum ferritin, but these effects also occurred in both the treatment and placebo groups.[90] None of the other studies reported adverse effects.

A recent review, however, concluded that experimental studies in animals and observational studies of humans provide evidence that calcium supplementation during the second half of pregnancy may reduce prenatal lead exposure by reducing mobilization of lead from bone.[3]

Appendix 8. Recommendations of Other Groups

The CDC updated its lead screening recommendations in 1997 in response to evidence of inadequate screening of children at high risk, and to concerns regarding appropriate use of limited resources in low prevalence communities. The revised CDC guidelines provided state public health entities with authority and guidance to develop state and local policies for childhood lead screening. The CDC recommended universal screening in communities without data regarding the prevalence of elevated blood lead levels adequate for local policy development, and in communities where $\geq$ 27% of the housing was built before 1950. Screening of all children receiving Medicaid, Supplemental Food Program for Women, Infants and Children (WIC) or other governmental assistance, and in populations where $\geq$ 12% of children ages one-two years have elevated blood lead levels was also recommended. Targeted screening is recommended for all other children based on individual risk assessment.[19] This approach is also supported by the American College of Preventive Medicine.[100]

In 1998, the American Academy of Pediatrics recommended that pediatricians: (1) provide anticipatory guidance to parents of all infants and children regarding potential risk factors and specific prevention strategies tailored for the family and community, (2) in conjunction with public health authorities, develop and use community-specific risk assessment questionnaires to guide targeted screening in communities where universal screening is not appropriate, (3) provide lead screening at age 9-12 months and consider again at approximately 24 months following state health department guidelines utilizing individualized targeted or universal screening as recommended, (4) assess possible lead exposure periodically between six months and six years of age using community-specific

risk assessment questionnaires. Blood lead testing should be considered in children with a history of abuse, neglect, or conditions associated with increased lead exposure, and (5) actively participate in state and local lead poisoning prevention activities. Recommendations by the AAP regarding the urgency and extent of follow-up differ slightly from those of the CDC and depend on the risk classification and on confirmed venous blood lead levels.[101] The 1998 Recommendation was recently updated to include recent data regarding the prevalence and adverse effects of lead exposure, and to provide recommendations for pediatricians and government policymakers.[102]

The American Academy of Family Physicians (AAFP) recommends lead screening at 12 months of age in infants who have the following risk factors: residence in a community with a high or undefined prevalence of lead levels requiring intervention, residence in or frequent visits to a home built before 1950 that has dilapidated paint or has recently undergone or is undergoing renovation or remodeling, close contact to a person who has an elevated blood lead level, residence near a lead industry or heavy traffic, residence with a person whose hobby or job involves lead exposure, use of lead-based pottery, or use of traditional remedies that contain lead.[103]

Medicaid's Early and Periodic Screening, Diagnostic, and Treatment Program requires that all children be considered at risk and must be screened for lead poisoning. CMS requires that all children receive a screening blood lead test at 12 months and 24 months of age. Children between the ages of 36 months and 72 months of age must receive a screening blood lead test if they have not been previously screened for lead poisoning. At this time, states may not adopt a statewide plan for screening children for lead poisoning that does not require lead screening for all Medicaid-eligible children.[4, 104]

Studies of provider behavior before and after the 1997 Revision of the CDC Recommendations demonstrate that blood lead screening and follow-up of children is often inadequate.[105, 106]

Recently, the CDC Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) reaffirmed its support for state and local decision-making based on local data and conditions regarding the appropriate lead screening recommendations. The ACCLPP also acknowledged the limitations of screening and other forms of secondary prevention, and advocated a increased local and national focus on housing-based primary prevention of lead exposure.[21]

No national organizations currently recommend screening pregnant women for elevated lead levels. Some state organizations have developed local policies regarding lead screening. In 1995, the New York State Department of Health and American College of Obstetricians and Gynecologists District II developed lead poisoning prevention guidelines that mandate anticipatory guidance for pregnant women, risk assessment, and risk reduction counseling and childhood lead poisoning prevention education.[107]

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