JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Coalition to End Childhood Lead Poisoning
Green & Healthy Homes Initiative

Lead Poisoning:

CDC's New Target for Prevention

Ana Navas-Acien, MD, PhD

Associate Professor

Environmental Health Sciences & Epidemiology

Outline

- Lead exposure: trends and current sources
- Health effects: children and adults
- Prevention strategies
    - CDC's new target for prevention

Acknowledgements

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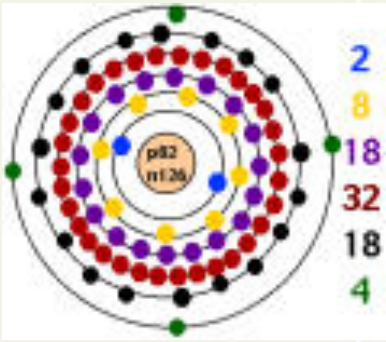
Lead

- Toxic metal – used since Ancient times
- Ubiquitous in the environment – human activities
  - Mining, smelting
  - Production of batteries, ammunition, metal products, medical, research and military equipment, ceramic glazes, paint
  - Gasoline additives – phased out in 1970s in US
- Lead is in air, food, drinking water, rivers, lakes, oceans, dust and soil



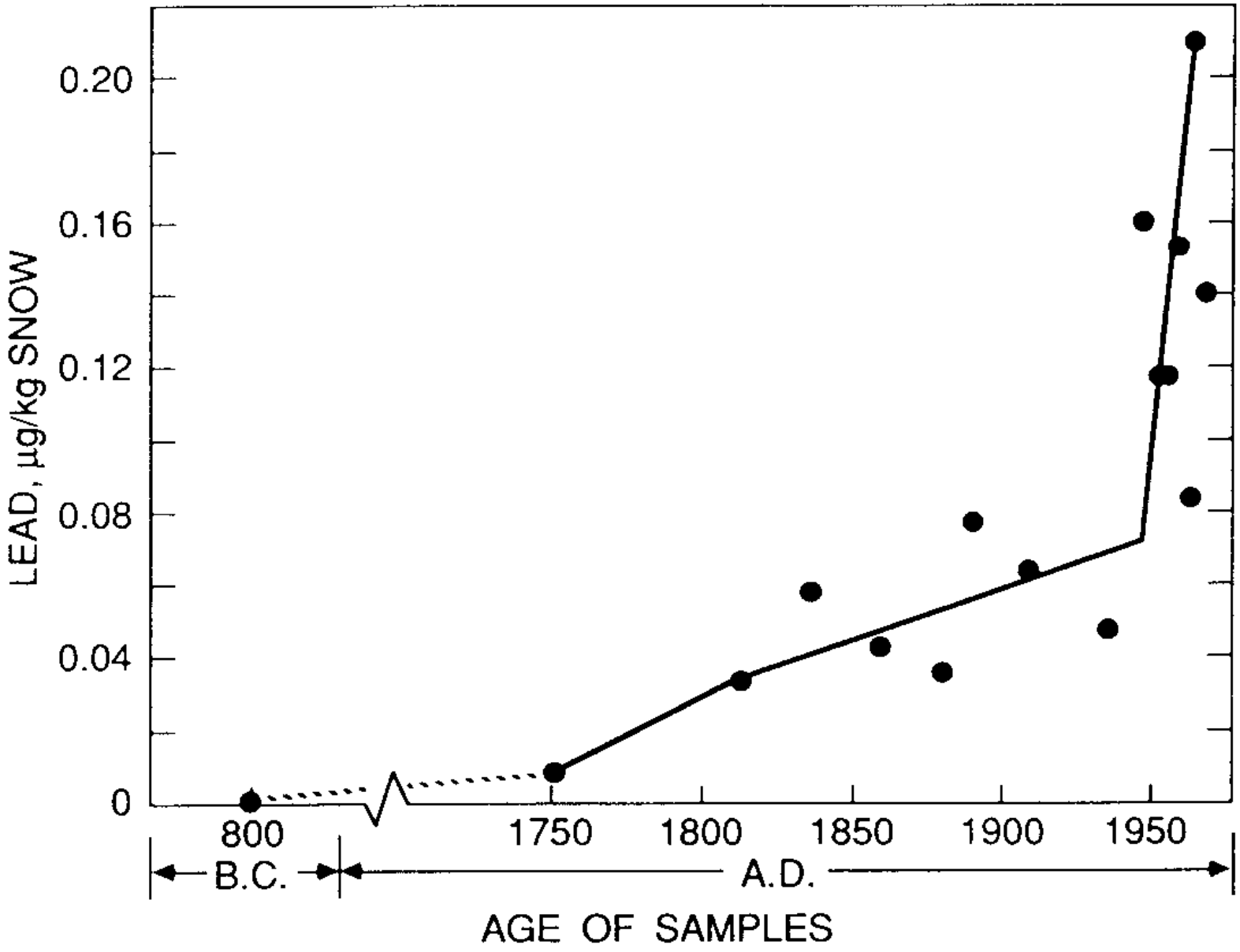


FIG. 2. Lead concentration, profile in snow strata of Northern Greenland (EPA, 1986).

Lippman. Environ Reseach 1990;51:1-24

The Decline in Blood Lead Levels in the United States

The National Health and Nutrition Examination Surveys (NHANES)

James L. Pirkle, MD, PhD; Debra J. Brody, MPH; Elaine W. Gunter; Rachel A. Kramer, ScD; Daniel C. Paschal, PhD; Katherine M. Flegal, PhD, MPH; Thomas D. Matte, MD, MPH

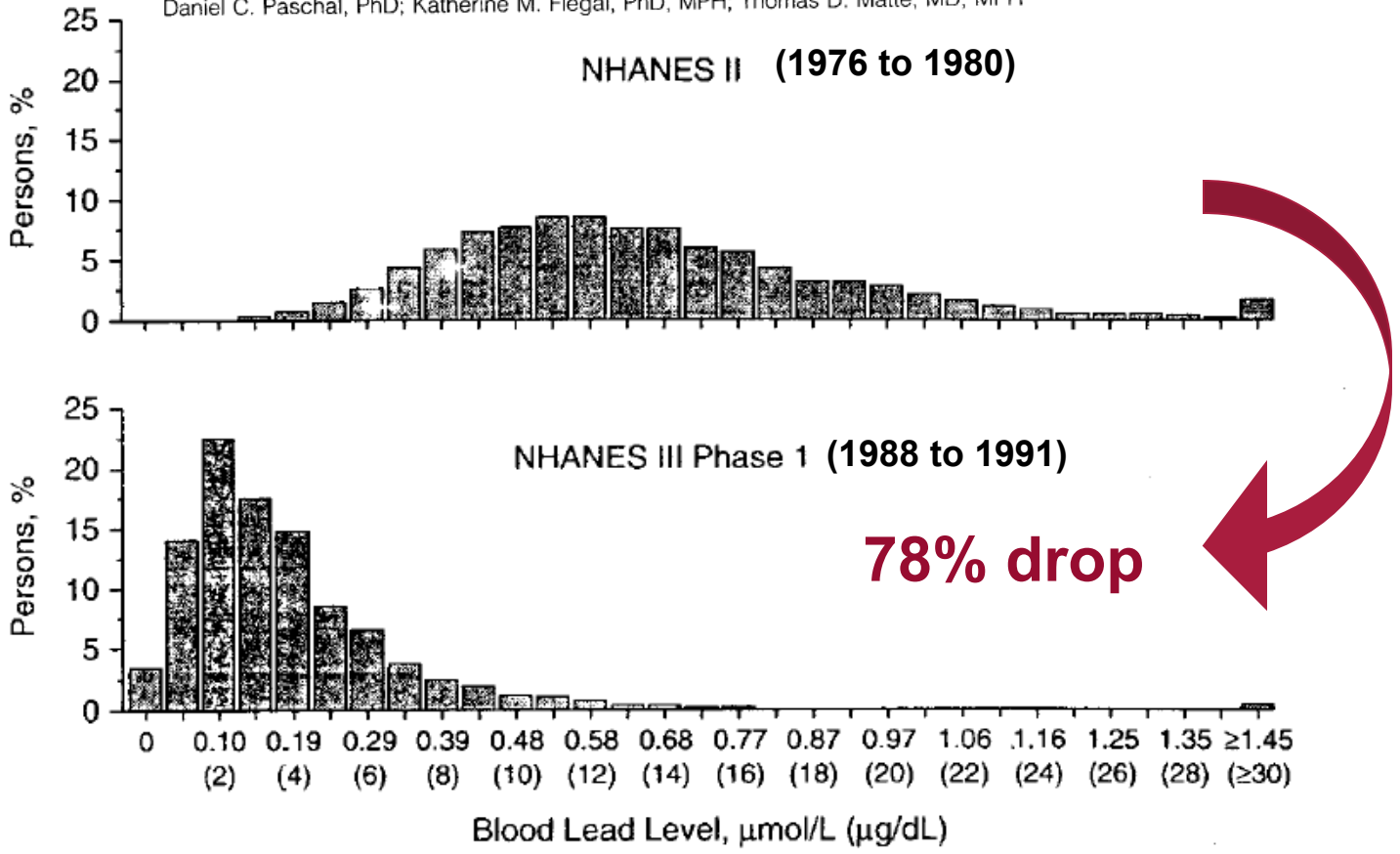


Fig 1.—Blood lead levels for persons aged 1 to 74 years: United States, second National Health and Nutrition Examination Survey (1976 to 1980, top) and phase 1 of the third National Health and Nutrition Examination Survey (1988 to 1991, bottom).

Children: reasons for increased susceptibility

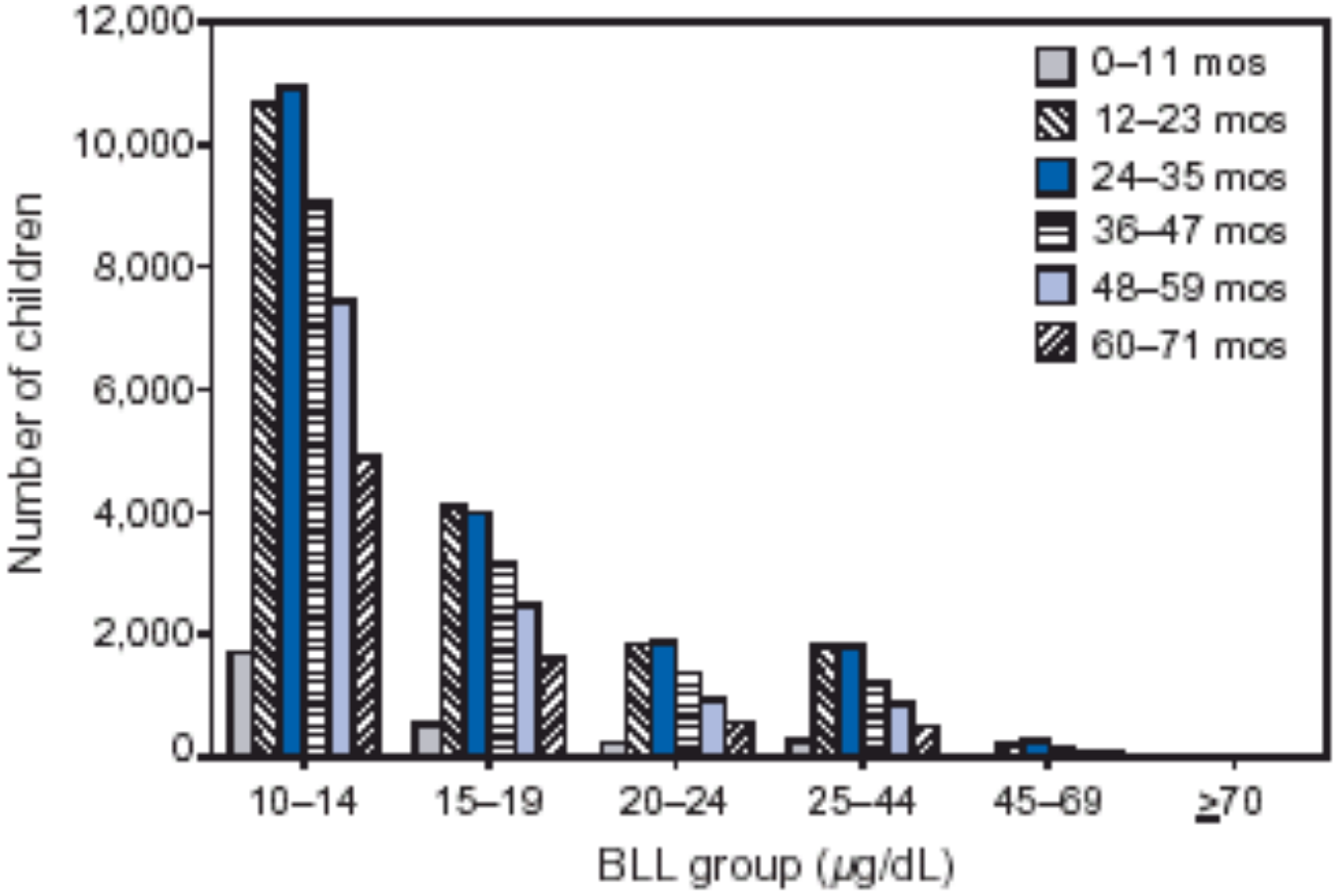
- **Disproportionately heavier exposures than adults:**
  - **Drink more water, eat more food and breathe more air per weight unit**
  - **Hand-to-mouth behavior**
  - **Play close to the ground**

- **Metabolic pathways, especially in fetal life and first months after birth, are immature**
  - **Metabolic, detoxification and excretion processes different from adults**
  - **Blood-brain barrier not fully developed**

Landrigan PJ. EHP 2004;112:257-265

Lead poisoning by age in US

FIGURE 3. Number of children with confirmed blood lead levels (BLLs) ≥10 µg/dL by program-relevant age group and BLL group — selected U.S. states, 2001



http://www.cdc.gov/mmwr/preview/mmwrhtml/ss5210a1.htm

Lead biomarkers – Blood vs. bone lead

	Bone (cortical, trabecular)	Whole blood
Half-life	Decades	~35 days
Reflect	Cumulative exposure	Recent external and internal exposure
Analysis	K X-ray fluorescence	AAS / ICPMS
Monitoring	No	Yes
Criterion	No	5 µg/dL children 40 µg/dL workers

AAS: atomic absorption spectometry / ICPMS: inductively coupled plasma mass spectometry
Other lead biomarkers not usually used (hair, toenails, urine, plasma, serum)

Barbosa et al. EHP 2005;113:1669-74 Hu et al. EHP 2007;115:455-63

Lead related health effects

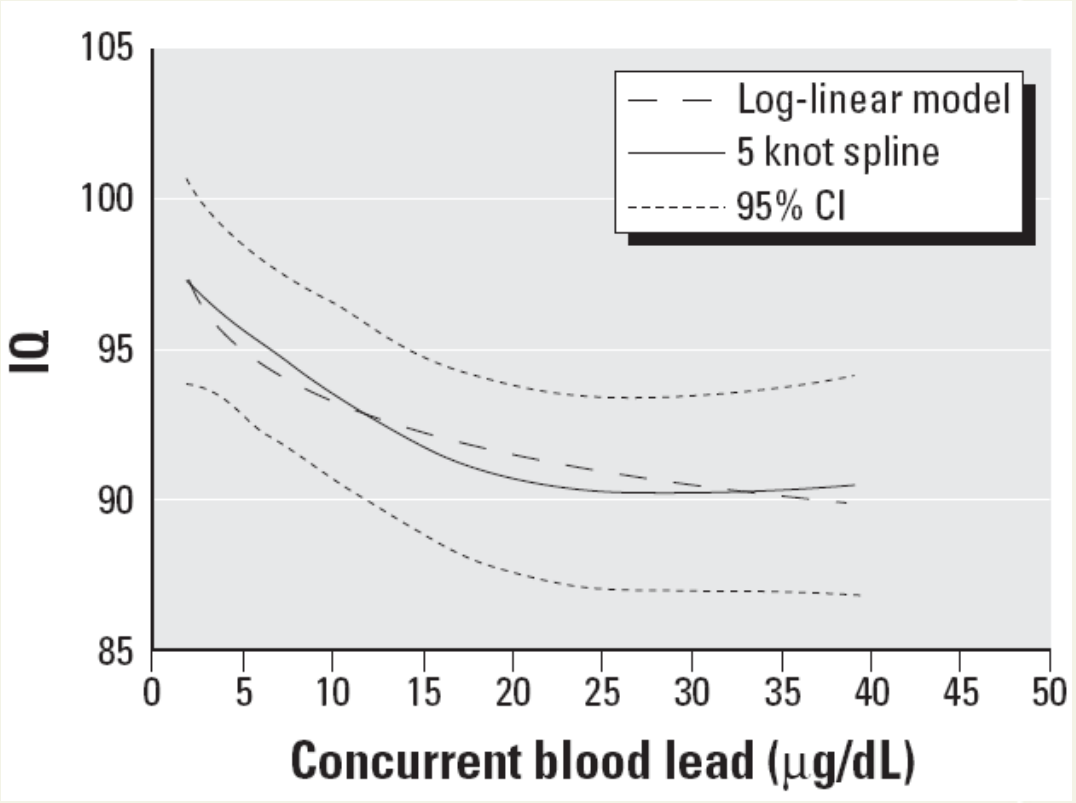
- Neurotoxic (children <5 µg/dL, 2 µg/dL adults)
- Nephrotoxic (<5 µg/dL)
- Immunotoxic (<10 µg/dL)
- Alters heme synthesis
- Alters bone and teeth metabolism
- Probable carcinogen (IARC, NTP)
- Cardiovascular outcomes:
  - Increased blood pressure and incidence of hypertension
  - Potential association with cardiovascular mortality and morbidity

EPA 2006 – Air Quality Criteria for Lead
http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158823

Blood lead and IQ in children – International pooled analysis

- **Estimated IQ decrements estimated with increases in blood lead from:**
- **2.4 to 10 µg/dL: 3.9**
- **10 to 20 µg/dL: 1.9**
- **20 to 30 µg/dL: 1.1**

→ Steepest declines were at blood lead levels <10 µg/dL



Lanphear BP, et al. Environ Health Perspect 2005;113:894-899

The weight of lead – Effects add up in adults

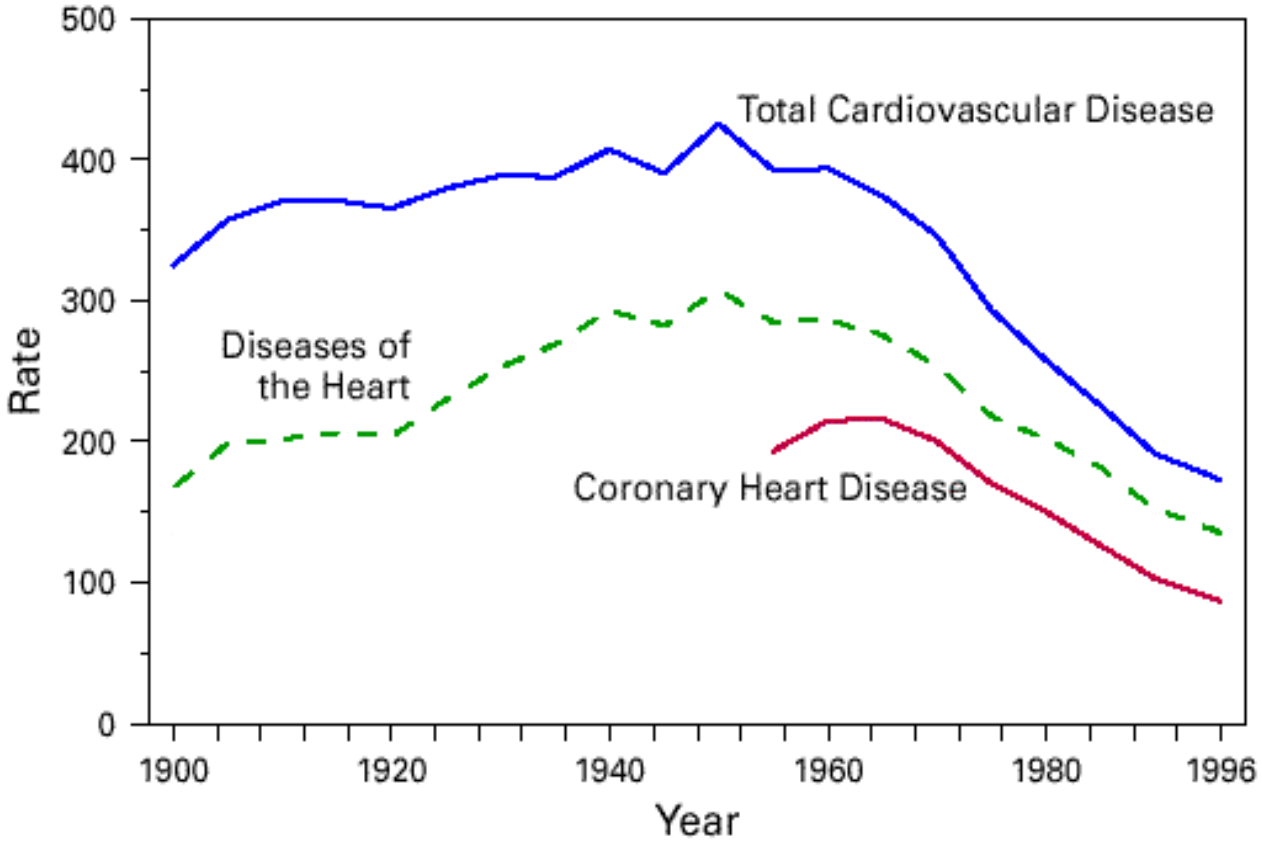
- Neurotoxic
- Nephrotoxic
- Immunotoxic
- Alters heme synthesis
- Alters bone and teeth metabolism
- Probable carcinogen (IARC, NTP)
- Cardiovascular outcomes

US EPA 2006 – Air Quality Criteria for Lead
http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158823

Source: Environ Health Perspect 2007;115:A30-36

Achievements in Public Health, 1900-1999: Decline in Deaths from Heart Disease and Stroke -- United States, 1900-1999 (MMWR 1999;48:649-656)

FIGURE 1. Age-adjusted death rates* for total cardiovascular disease, diseases of the heart, coronary heart disease, and stroke,† by year — United States, 1900–1996



*Per 100,000 population, standardized to the 1940 U.S. population.
†Diseases are classified according to *International Classification of Diseases* (ICD) codes in use when the deaths were reported. ICD classification revisions occurred in 1910, 1921, 1930, 1939, 1949, 1958, 1968, and 1979. Death rates before 1933 do not include all states. Comparability ratios were applied to rates for 1970 and 1975.

Research | Mini-Monograph

Lead Exposure and Cardiovascular Disease—A Systematic Review

Ana Navas-Acien,[1] Eliseo Guallar,[2,3] Ellen K. Silbergeld,[1] and Stephen J. Rothenberg[4,5]

Conclusions

- **Sufficient epidemiologic and mechanistic evidence to infer a causal effect of lead on blood pressure – no evidence of a threshold**
- **Suggestive but not sufficient epidemiologic evidence for clinical cardiovascular endpoints at blood lead < 5 µg/dL**
- **Suggestive but not sufficient epidemiologic evidence for cardiac function abnormalities: left ventricular hypertrophy and cardiac rhythm**

Environ Health Perspect 2007;115:472-482

Lead and blood pressure endpoints – Reviews and meta-analyses

Table 1. Reviews of the association between blood lead levels and blood pressure.

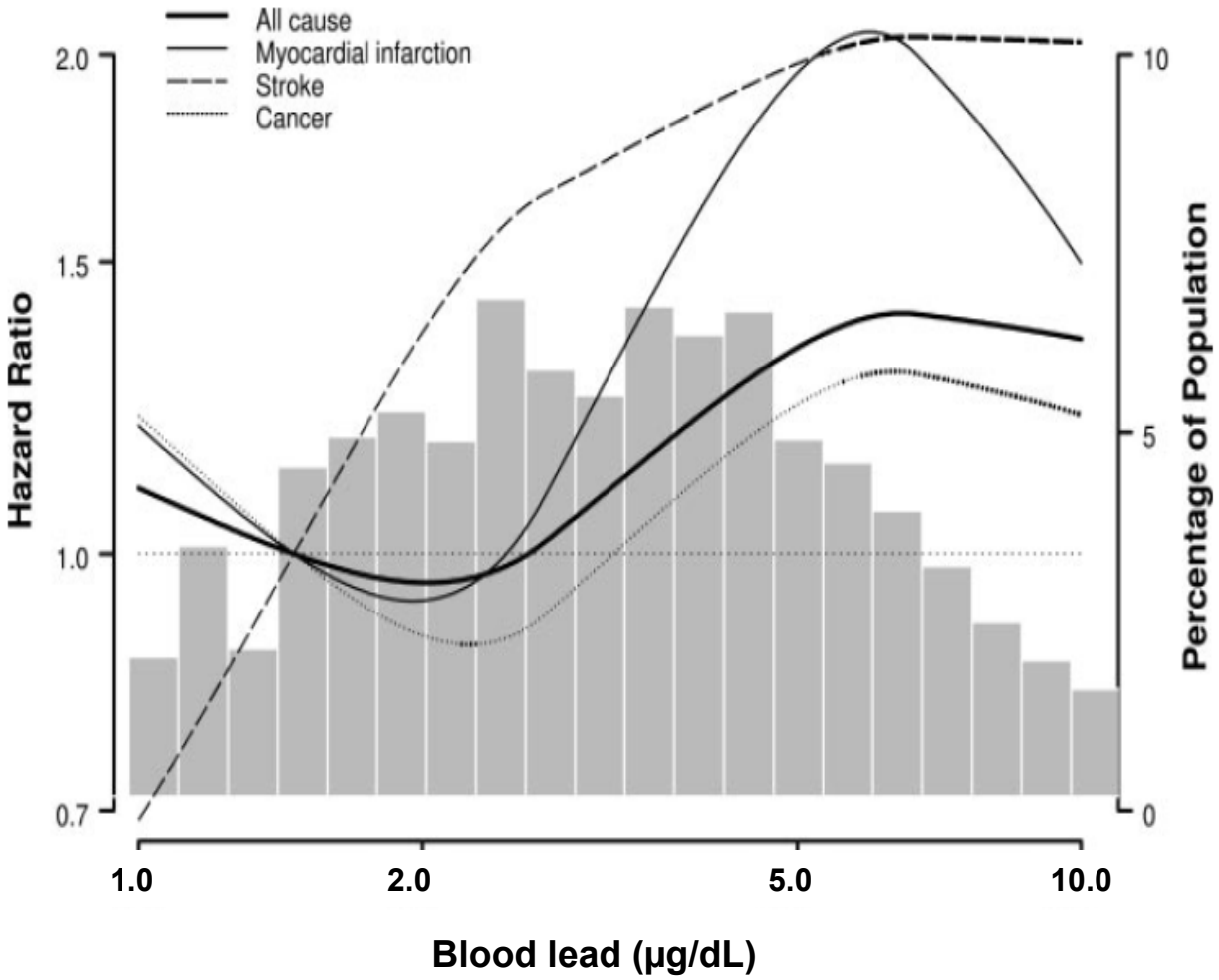
First author, year	Type[a]	No. of studies included	Year of publication of studies (range)	Language of literature search	Total no. of subjects	Age range of participants (years)	Comparison	Outcome	Pooled estimate [change in mmHg (95% CI)]	Median of estimates [change in mmHg (range)]	Conclusions as reported by authors
Sharp et al. 1987	Review	4	1982–1986	English, French	8,406	24–59	Per 2-fold ↑[b]	SBP	—	1.9 (0.7 to 2.3)	Evidence consistent with causation
Hertz-Picciotto and Croft 1993	Review	13	1980–1992	English	22,923	12–80	≠ for each study	SBP DBP Hypertension	— — —	2.0 (–5.9 to 8.0) 1.7 (–1.6 to 4.0) RR: 1.4 (1.2 to 1.7)	Evidence strongly supports causal association
Staessen et al. 1994, 1995	SR, MA	23	1980–1993	English, French, German	33,141	10–88	Per 2-fold ↑	SBP DBP	1.0 (0.4–1.6) 0.6 (0.2–1.0)	1.0 (–3.0 to 14.0) 1.0 (–2.0 to 13.0)	MA suggests a weak association
Schwartz 1995	SR, MA	15	1985–1993	English	NR Men only	18–76	Per 2-fold ↑[b]	SBP	1.25 (0.87–1.63)	1.45 (0.2 to 3.2)	MA consistent with causal association
ATSDR 1999	SR	24	1980–1996	No language restriction	NR	All ages	≠ for each study	SBP DBP Hypertension	— — —	NR NR NR	Suggestion of ↑ blood pressure, but evidence is inconclusive
Nawrot et al. 2002	SR, MA	31	1980–2001	English, French, German	58,518	10–90	Per 2-fold ↑	SBP DBP	1.0 (0.5–1.4) 0.6 (0.4–0.8)	1.0 (–5.0 to 14.0) 1.0 (–2.0 to 14.0)	MA suggests a weak association
U.S. EPA 2006	SR, MA	9 10	1990–2003	English	27,424 34,740	14–93	Per 2-fold ↑	SBP DBP	0.81 (0.46–1.16)[c] —	1.0 (–3.9 to 11) 1.0 (–1.3 to 7.3)	MA suggests an effect of blood lead on SBP

Abbreviations: ≠, different; ↑, increase; CI, confidence interval; DBP, diastolic blood pressure; MA, meta-analysis; NHANES, National Health and Nutrition Examination Survey; NR, not reported; RR, relative risk; SBP, systolic blood pressure; SR, systematic review; U.S. DHHS, U.S. Department of Health and Human Services; U.S. EPA, U.S. Environmental Protection Agency.
[a]Systematic review: a search strategy and criteria for manuscript selection are specified. Meta-analysis: a pooled analysis using meta-analysis techniques are presented. [b]In the study by Sharp et al. (1987), we divided by 3 the change per 15 µg/dL (equivalent to comparing 10 µg/dL vs. 5 µg/dL). The study by Schwartz et al. (1995) reports the change in mmHg comparing 10 µg/dL vs. 5 µg/dL. [c]Pooled estimate using an inverse variance weighted random-effects model (Egger et al. 2001) of two pooled estimates for linear and log-linear estimates, respectively.

Combined data from >30 original studies and ~60,000 participants consistently concluded that there is positive association between blood lead levels and blood pressure endpoints

Navas-Acien et al. Environ Health Perspect 2007;115:472-482

Lead and mortality – NHANES III Mortality Follow-up



N = 13,964

Follow-up 12 years

Figure 1. Multivariate adjusted relative hazard (left axis) of mortality associated with blood lead levels between 0.05 µmol/L (1 µg/dL) and 0.48 µmol/L (10 µg/dL). Histogram of blood lead levels is superimposed in the background and displayed on the right axis.

Menke A, et al. Circulation 2006;114:1388-94

Bone vs. blood lead and myocardial infarction – VA Normative Aging Study

Baseline 1991
$N_{CVD\text{-}free}$ = 837
Men 21-80 y, Boston

Follow-up
Dec 2001

83 fatal and nonfatal CHD events

Blood lead (AAS)
Patella, tibia lead (KXRF)
Questionnaire
Clinical exam
Laboratory

Clinical exams every 3 to 5 years

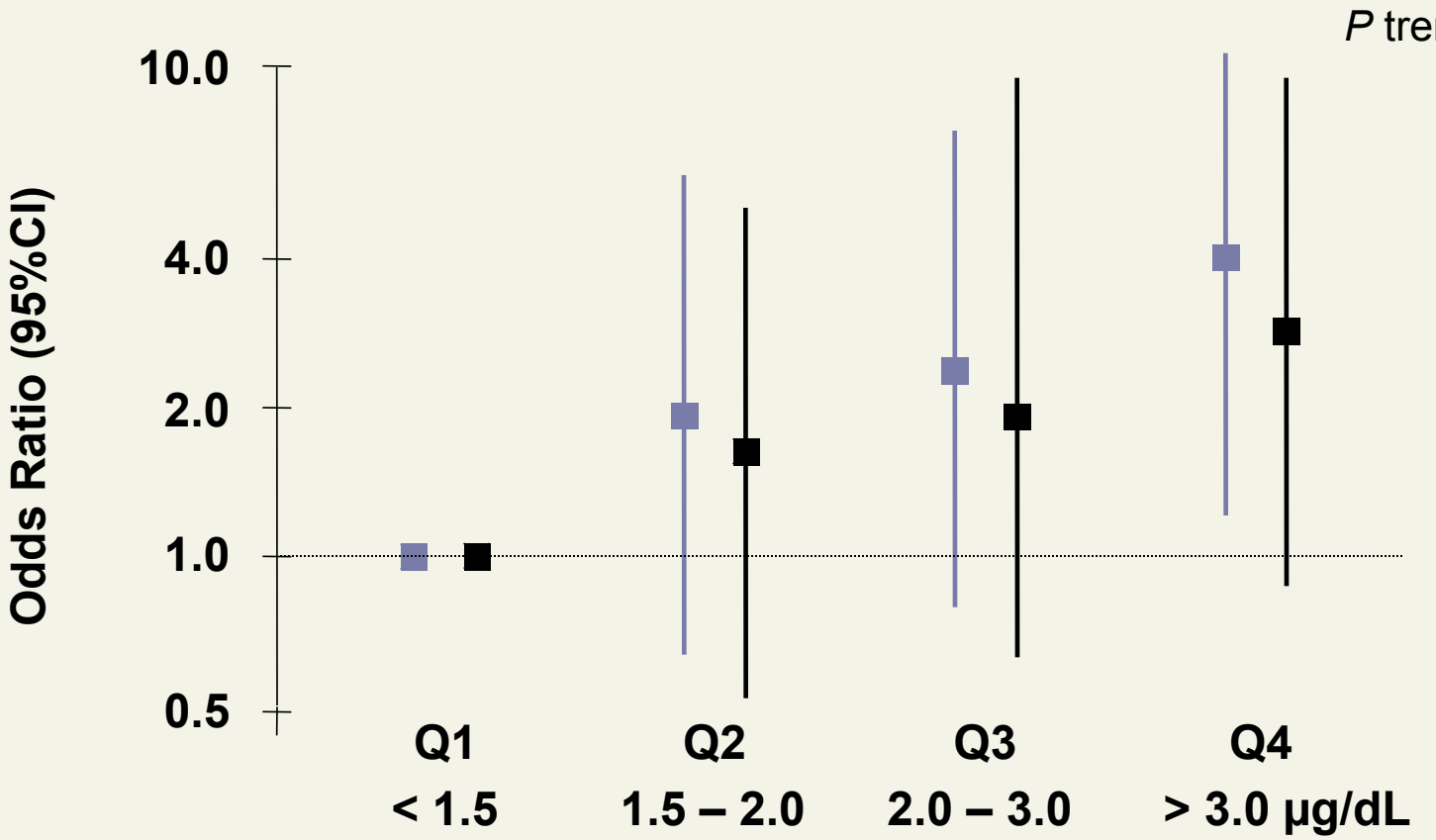
	HR_{crude}	95% CI	HR_{adj}	95% CI
Blood lead (per log µg/dL)	**1.40**	**0.99 – 1.98**	**1.45**	**1.01 – 2.06**
Patella lead (per log µg/g)	**3.27**	**1.41 – 7.58**	**2.64**	**1.09 – 6.37**
Tibia lead (per log µg/g)	**2.76**	**0.94 – 8.12**	**1.84**	**0.57 – 5.90**

Adjusted for age, race, HDL-cholesterol
No change in estimates when smoking, BMI, alcohol, blood pressure, family history of hypertension and total serum cholesterol were added to the model

AAS: atomic absorption spectrometry
KXRF: K X-ray fluorescence

Jain et al. Environ Health Perspect. Epub Feb 6 2007

Blood Lead and Peripheral Arterial Disease – NHANES 1999-2000



- Adjusted for age, sex, race, education, body mass index, alcohol intake, hypertension, diabetes, hypercholesterolemia, glomerular filtration rate and C-reactive protein
- Further adjusted for smoking status (never/former/current) and serum cotinine

Navas-Acien et al. Circulation 2004; 109:3196-201

Public health implications of lead related cardiovascular disease

Sufficient evidence to infer a causal association with elevated blood pressure with no evidence of a threshold

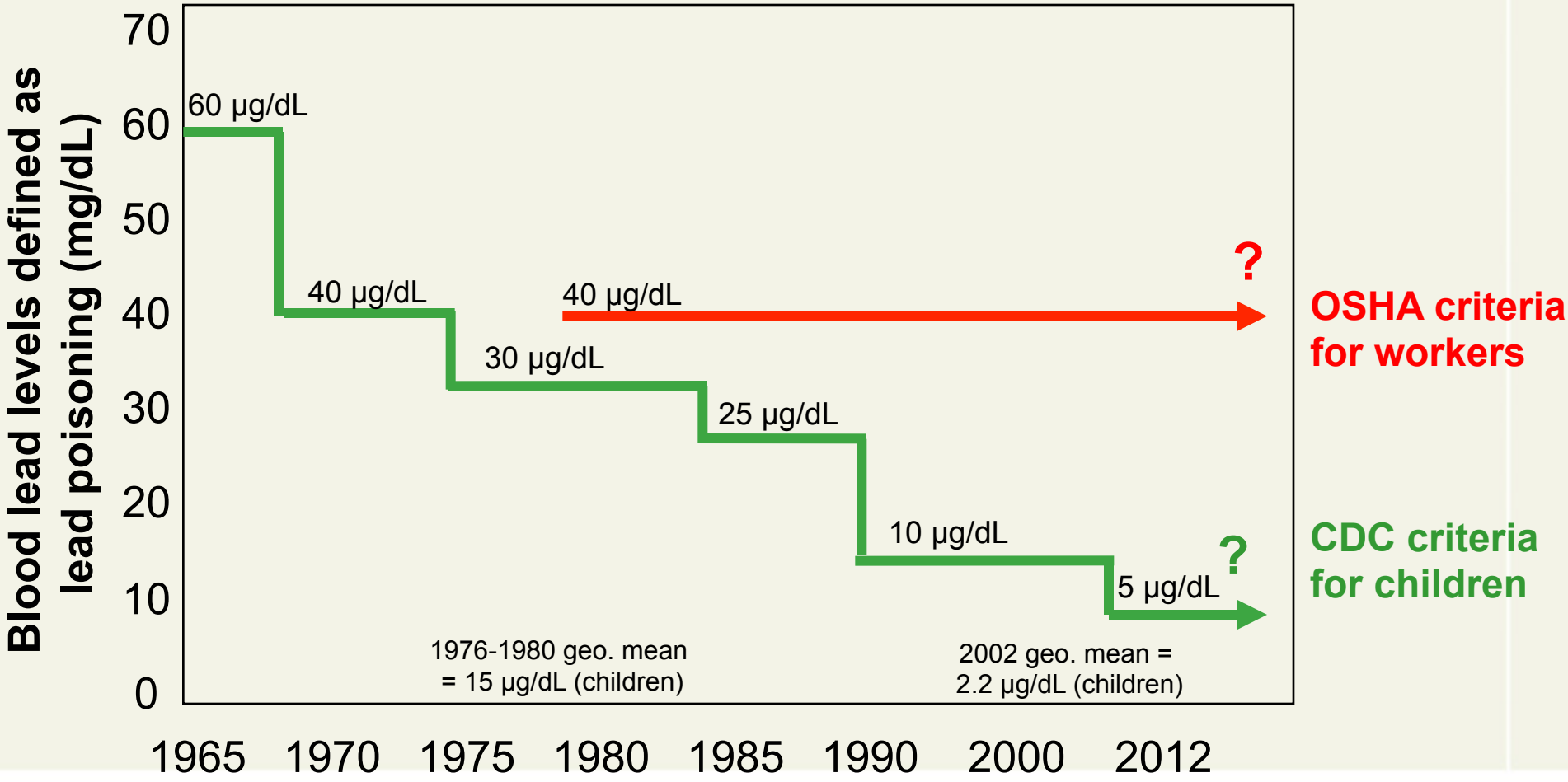
Suggestive evidence for other cardiovascular endpoints at blood lead levels < 5 µg/dL

- **Lower the current OSHA / WHO safety standards for blood lead in workers (40 µg/dL)**
- **Establishment of a criterion for elevated blood lead levels in adults**
- **Include hypertensive and cardiovascular effects of lead in risk assessment and in economic analyses of the impact of lead exposure**
- **Develop regulations and public health interventions to prevent and reduce lead exposure in adults needed**

Adult Lead Exposure: Time for Change

Brian S. Schwartz[1,2] and Howard Hu[3]

[1]Departments of Environmental Health Sciences and Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [2]Department of Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland, USA; [3]Department of Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan, USA



Lead poisoning prevention programs

- Surveillance
- Secondary prevention
  - Case management children blood lead levels over a certain level
  - Identify most important sources related to this level of exposure: Housing age, lead paint-hazards, drinking water sources, industrial sources, other
- Primary prevention
  - Identification of most common sources, plot distribution
  - Target prevention strategies to reduce exposure of at-risk populations
  - Enact laws to require actions to protect children from exposure to hazards (housing standards)
- Secondhand smoke not considered by most programs

CDC's new lead poisoning recommendations

1. Eliminates "level of concern"
2. Establishes a childhood BLL reference value based on 97.5th percentile of the population BLL in US children ages 1-5 [now 5µg/dL] to:
    a. Identify children
    b. Identify environments with lead hazards
3. To develop and implement a national primary prevention strategy to ensure no US children live in or spend significant time in homes, buildings, other environments exposed to lead hazards

CDC's new lead poisoning recommendations

4. **Clinicians** serve as a reliable source of information on lead hazards, taking primary role in educating families about prevention
    a. Environmental assessments prior to BLL screening
5. **Clinicians** notify family and monitor health status of children with confirmed BLL ≥5µg/dL
    a. until environmental investigation/remediation complete
6. Where no mandatory reporting, **clinicians** to
    a. ensure reporting of all BLLs at or above reference value to local/state health and housing agencies
    b. collaborate with agencies to provide appropriate services and resources to children/families

CDC's new lead poisoning recommendations

7. **Education** on **primary prevention** in homes and child-occupied facilities to eliminate hazards before children are exposed.
    a. Targets families, providers, advocates, public officials
8. Develop **primary prevention infrastructure**:
    a. Encourage data sharing between health and housing
    b. Develop and enforce preventive lead-safe housing standards for rental and owner occupied properties
    c. ID funding for lead hazard remediation
    d. Provide families with information so they can protect their children from home environment hazards

CDC's new lead poisoning recommendations

9. Work with elected officials, health, housing and code enforcement agencies to ensure adoption of a suite of **primary prevention policies** to protect children from lead exposure in their homes.
10. Adopt **primary prevention strategies** to reduce environmental exposures in soil, dust, paint and water before children are exposed

a. Emphasize environmental assessment to ID and remediate lead hazards before children's BLLs are at/above reference value

CDC's new lead poisoning recommendations

11. **Multi-family housing**: if lead hazards trigger actions in any unit, apply the same actions to all similar but untested units in the complex unless risk assessment shows no hazards are present
12. Encourage **health outcomes research** focused on interventions that can maintain child BLLs below reference value
13. **Research priorities**:
    a. improve use of screening data,
    b. develop point-of-care analyzers,
    c. improve knowledge of epigenetic mechanisms of lead action

Recommendations - Summary

Major shift to primary prevention
- Federal
- State
- Local
- Private providers
- Families

No level that can be thought to be “safe”

Unacceptable to wait until children reach a specific BLL to “qualify” for lead-safe housing

Secondhand Tobacco Smoke: A Source of Lead Exposure in US Children and Adolescents

Andria Apostolou, PhD, MPH, Esther Garcia-Esquinas, MD, MPH, Jeffrey J. Fadrowski, MD, MHS, Pat McLain, RN, DrPH, MPH, Virginia M. Weaver, MD, MPH, and Ana Navas-Acien, MD, PhD

Objectives. We evaluated the relationship between secondhand tobacco smoke (SHS) exposure and blood lead levels in US children and adolescents.

Methods. We analyzed data from 6830 participants aged 3–19 years in the National Health and Nutrition Examination Survey (1999–2004) who were not active smokers and for whom SHS exposure information and blood lead measurements were available.

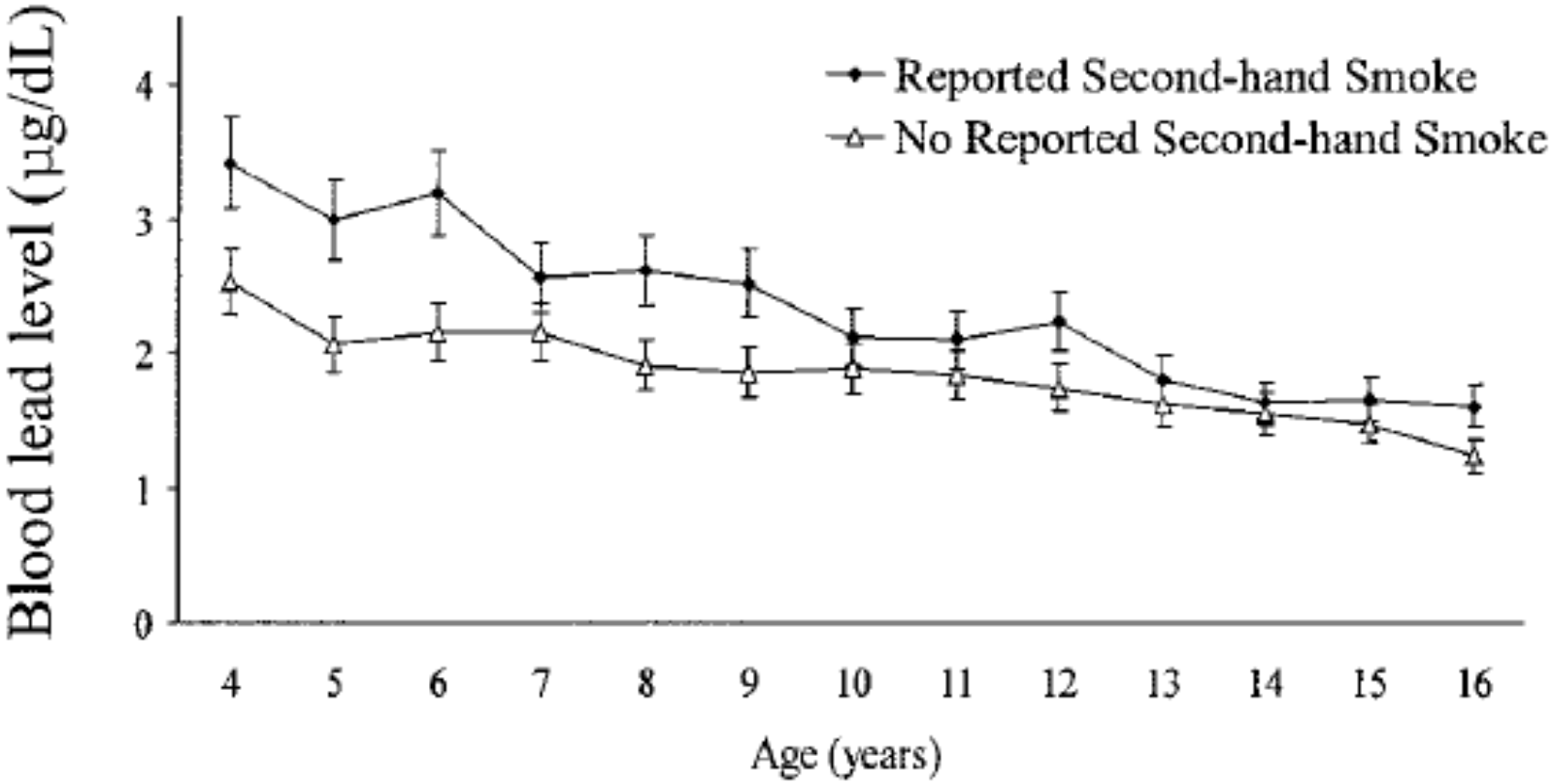
Results. After multivariable adjustment, participants in the highest quartile of serum cotinine (≥0.44 μg/L) had 28% (95% confidence interval = 21%, 36%) higher blood lead levels than had those in the lowest quartile (<0.03 μg/L). Similarly, blood lead levels were 14% and 24% higher in children who lived with 1 or with 2 or more smokers, respectively, than they were in children living with no smokers. Among participants for whom lead dust information was available, the associations between SHS and blood lead levels were similar before and after adjustment for lead dust concentrations.

Conclusions. SHS may contribute to increased blood lead levels in US children. Lead dust does not appear to mediate this association, suggesting inhalation as a major pathway of exposure. Eliminating SHS exposure could reduce lead exposure in children. (*Am J Public Health.* 2012;102:714–722. doi: 10.2105/AJPH.2011.300161)

Secondhand tobacco smoke (SHS) remains a major source of indoor air pollution worldwide,[1–3] causing major health effects in children, including sudden infant death syndrome, lower respiratory tract infections, reduced lung growth,[1] and behavioral problems.[4–6] In the United States, around 1 in 5 children aged 3 to 11 years live with at least 1 individual who smokes.[1,7] Globally, the burden of SHS exposure during childhood is even higher.[3,8] Lead, a major neurocognitive and kidney toxicant for children at relatively low levels,[9] is a tobacco constituent that is measured in mainstream smoke (exhaled by the smoker) and sidestream smoke (from the burning cigarette), including the gas phase.[10–13] During the period 1988 to 1994, US children exposed to SHS showed increased blood lead levels.[14]

National and local childhood lead poisoning prevention programs identify and follow children

SHS and Lead in NHANES III



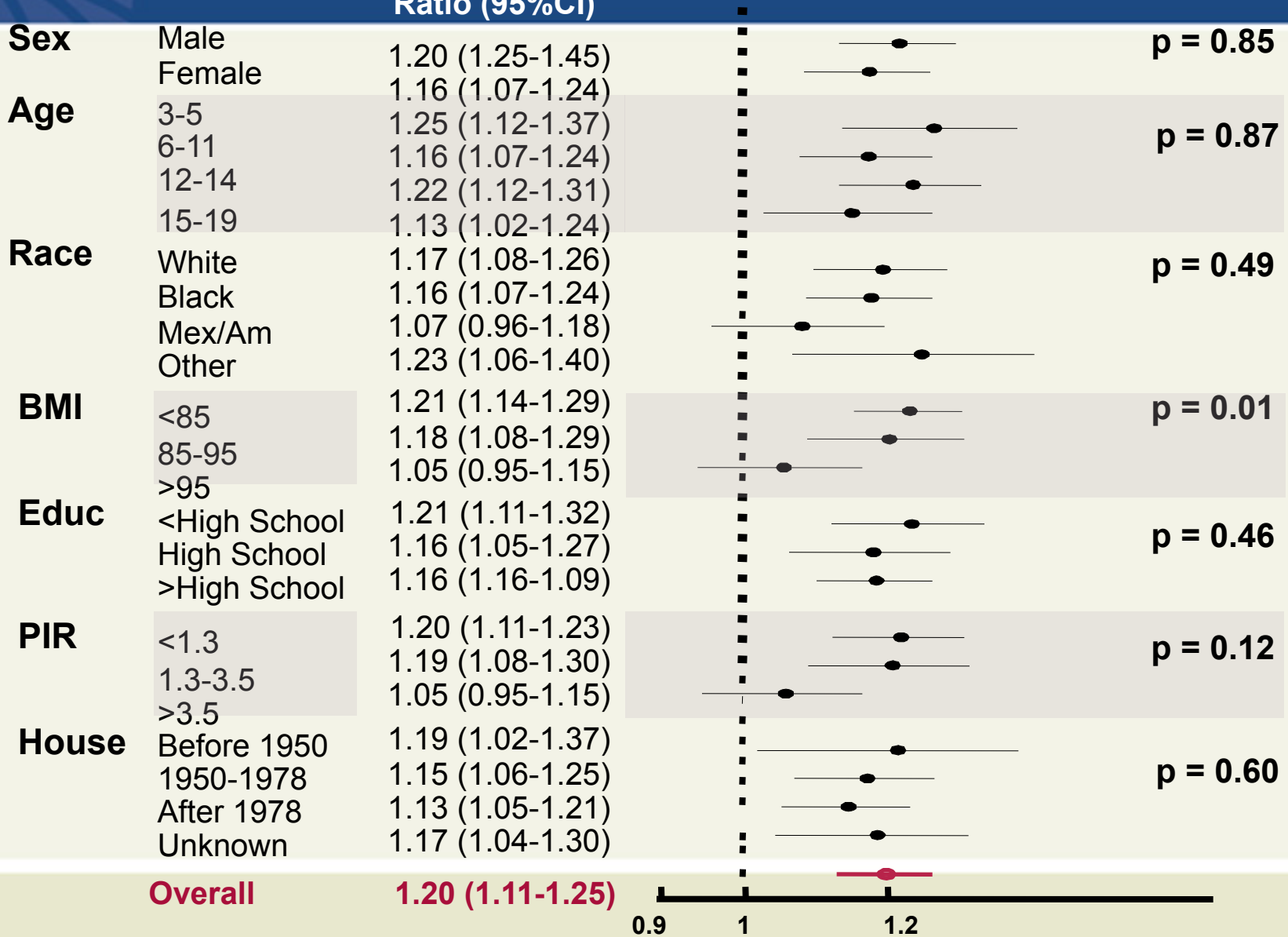
Points: geometric mean; vertical bars: 95% CI

Mannino et al. Epidemiology 2003;14:719-727

Ratio (95% CI) of geometric mean of blood lead by SHS exposure in NHANES 1999-2004

	N (%)	+Age, sex, race, country born, BMI, survey yr	+Household education, income	+Year home construction
Cotinine (µg/L)				
≤ 0.03	1,538 (25%)	1.00 (ref)	1.00 (ref)	1.00 (ref)
0.03–0.07	1,876 (25%)	1.10 (1.04-1.16)	1.09 (1.031.15)	1.08 (1.02-1.15)
0.08–0.44	1,804 (25%)	1.26 (1.21-1.32)	1.19 (1.14-1.24)	1.17 (1.12-1.23)
≥ 0.44	1,612 (25%)	1.47 (1.40-1.55)	1.30 (1.23-1.37)	1.28 (1.21-1.35)
p-value for trend		<0.001	<0.001	<0.001
Smokers at home				
0	5,484 (78%)	1.00 (ref)	1.00 (ref)	1.00 (ref)
1	929 (14%)	1.26 (1.18-1.33)	1.16 (1.08-1.23)	1.14 (1.07-1.22)
≥ 2	417 (8%)	1.39 (1.32-1.47)	1.25 (1.17-1.33)	1.24 (1.16-1.33)
p-value for trend		<0.001	<0.001	<0.001

Ratio of blood lead levels: Smokers at home vs. no smokers

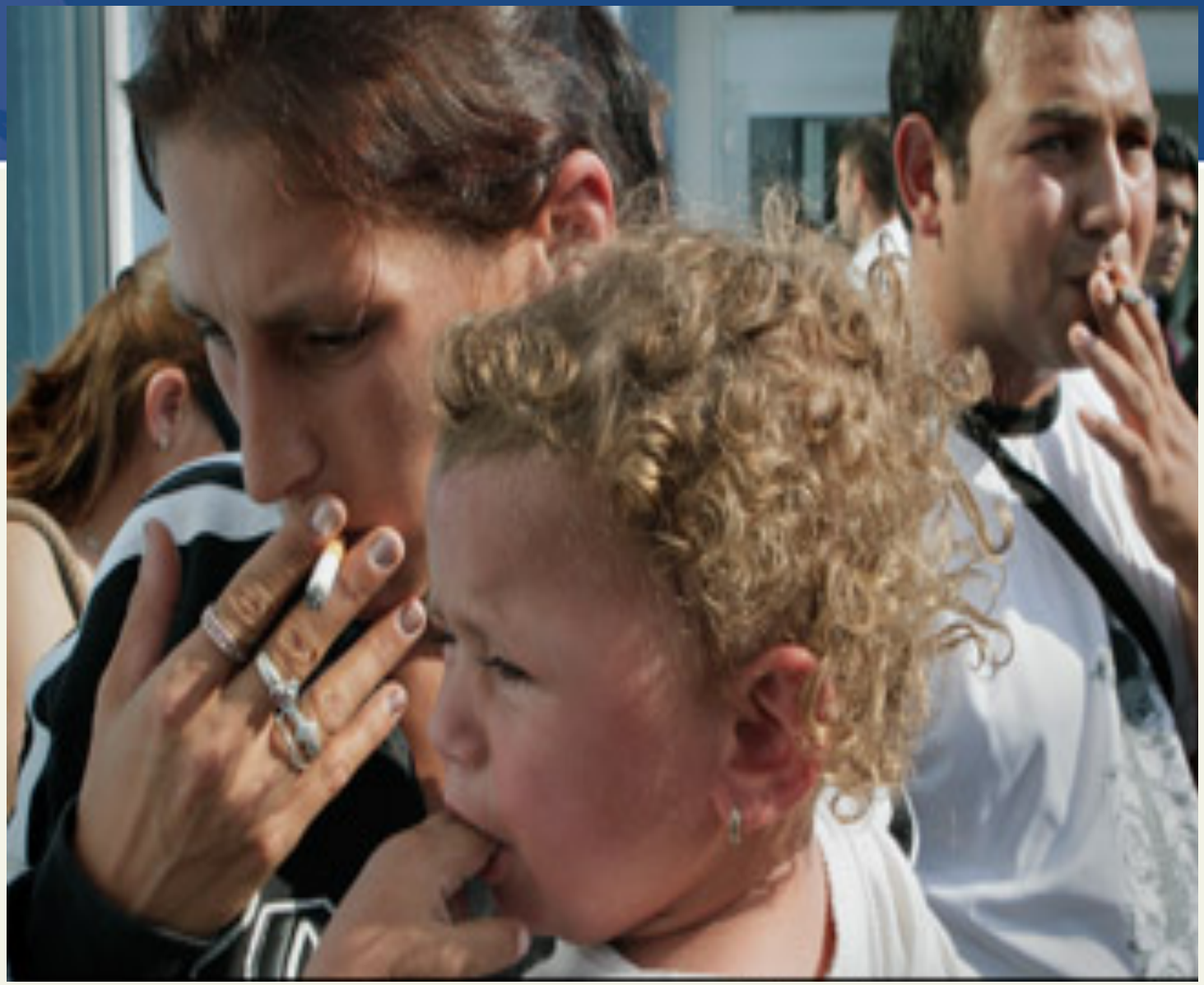


Sub-analysis: Children 3-5 years of age with house dust data

	N (%)	All adjustment variables	+ Window lead dust	+ Floor lead dust	+ Window and floor lead dust
Cotinine (µg/dL)					
≤ 0.03	133 (17)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
0.03–0.07	189 (24)	1.01 (0.88-1.14)	1.00 (0.87-1.13)	1.00 (0.87-1.14)	1.00 (0.87-1.13)
0.08–0.44	236 (30)	1.14 (1.02-1.25)	1.13 (1.02-1.25)	1.13 (1.01-1.24)	1.12 (1.01-1.24)
≥ 0.44	233 (29)	1.31 (1.21-1.42)	1.31 (1.19-1.42)	1.31 (1.20-1.41)	1.30 (1.19-1.41)
p-value for trend		<0.001	<0.001	<0.001	<0.001
N^0 smokers at home					
0	623 (78)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
≥1	168 (22)	1.17 (1.04-1.30)	1.17 (1.04-1.30)	1.17 (1.04-1.30)	1.17 (1.04-1.30)

TABLE 3—Lead Dust in the Homes of Children Aged 3–5 Years: National Health and Nutrition Examination Survey, United States, 1999–2004

	No. (Weighted %)	Lead Dust on Window, μg/sq ft, Median (IQR)	Lead Dust on Floor, μg/sq ft, Median (IQR)
Total sample	791 (100)	4.9 (2.2–18.7)	0.46 (0.24–0.93)
Child's blood lead level, μg/dL			
≤0.8	72 (13)	2.8 (1.6–4.8)	0.28 (0.17–0.46)
0.9–1.1	98 (15)	2.4 (1.6–5.9)	0.35 (0.19–0.53)
1.2–1.7	184 (27)	4.6 (2.4–12.2)	0.39 (0.23–0.67)
≥1.8	437 (45)	8.9 (2.8–37.7)	0.70 (0.36–1.56)
Child's serum cotinine level, μg/L			
≤0.03	133 (20)	2.9 (1.8–6.3)	0.33 (0.16–0.52)
0.031–0.074	189 (21)	3.3 (2.0–15.8)	0.50 (0.26–0.82)
0.075–0.44	236 (31)	5.4 (2.1–22.3)	0.45 (0.24–0.90)
≥0.441	233 (28)	7.9 (3.0–29.2)	0.66 (0.27–1.23)
Smoking at home			
No	623 (79)	4.3 (2.0–13.1)	0.41 (0.23–0.80)
Yes	168 (21)	12.3 (3.0–34.9)	0.67 (0.28–1.24)



Picture taken from El País (spanish newspaper) 2010-08-19

Implications for Public Health

- Eliminating SHS exposure in children could lower lead exposure and reduce adverse lead-related health effects
- Lead poisoning prevention programs should systematically evaluate smoking at home (no. smokers, smoking bans)
- Lead poisoning prevention programs can borrow strategies from SHS prevention programs (explaining benefits of smoke-free homes and cessation counseling)
- Smoke-free programs can incorporate lead prevention as an argument to implement tobacco control initiatives, particularly in disadvantaged communities at increased risk of both lead and SHS exposure