A Steepening Blood Lead/IQ Curve at Low Blood Lead Levels as Evidence for Confounding

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Three Objectives

- Put the recent results concerning the effectso of low level lead exposures in context and see if they appear credible.

- Review study design issues to look for sources of possible bias.

- Provide a few thoughts about where we should go from here.

Children with Low Blood Leads in Longitudinal Studies

	<7.5 ug/dL	<10 ug/dL
Rochester	69	103
Boston	13	41
Yugoslavia	11	46
Cincinnati	1	23
Other	9	31
TOTAL	103	244
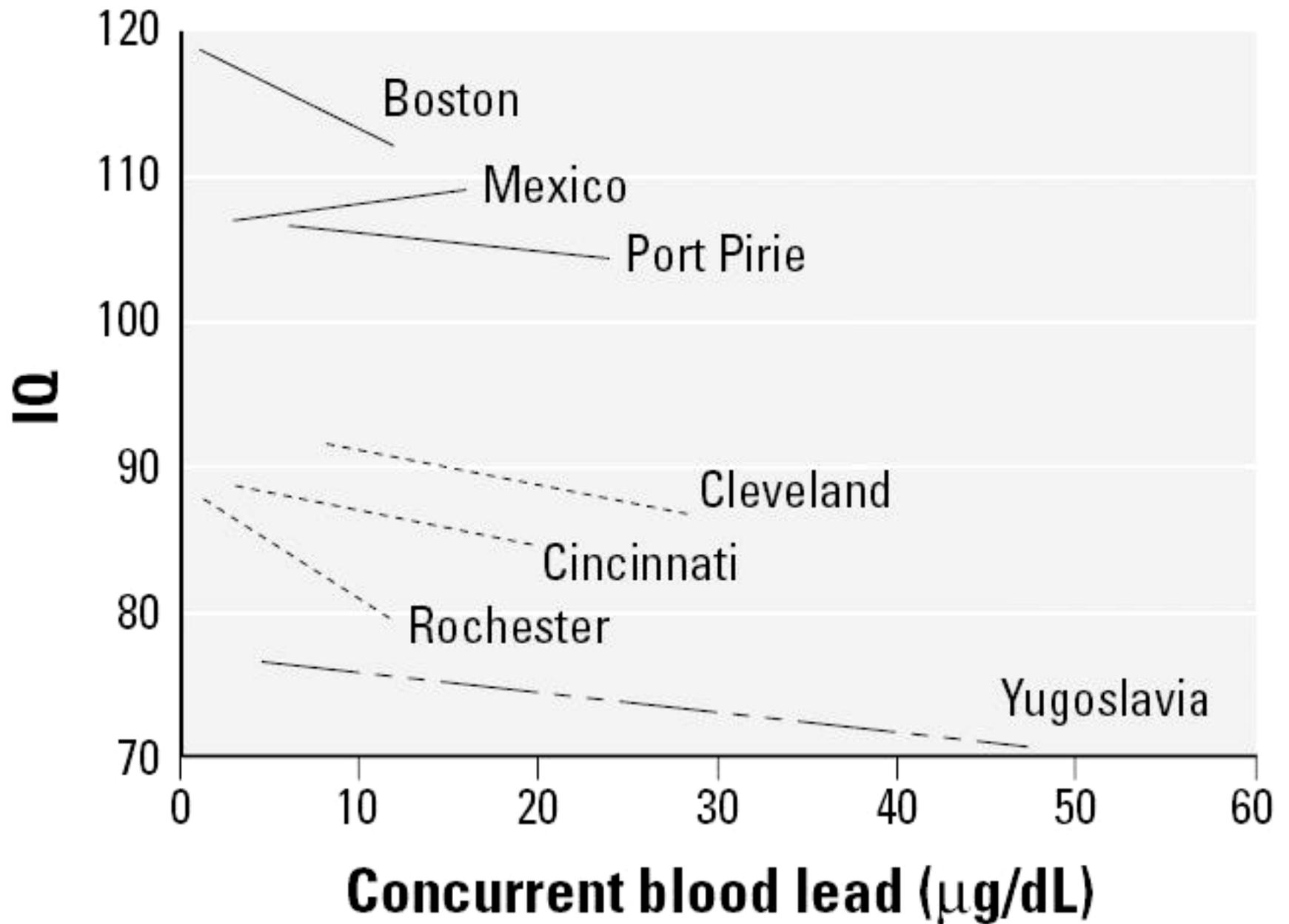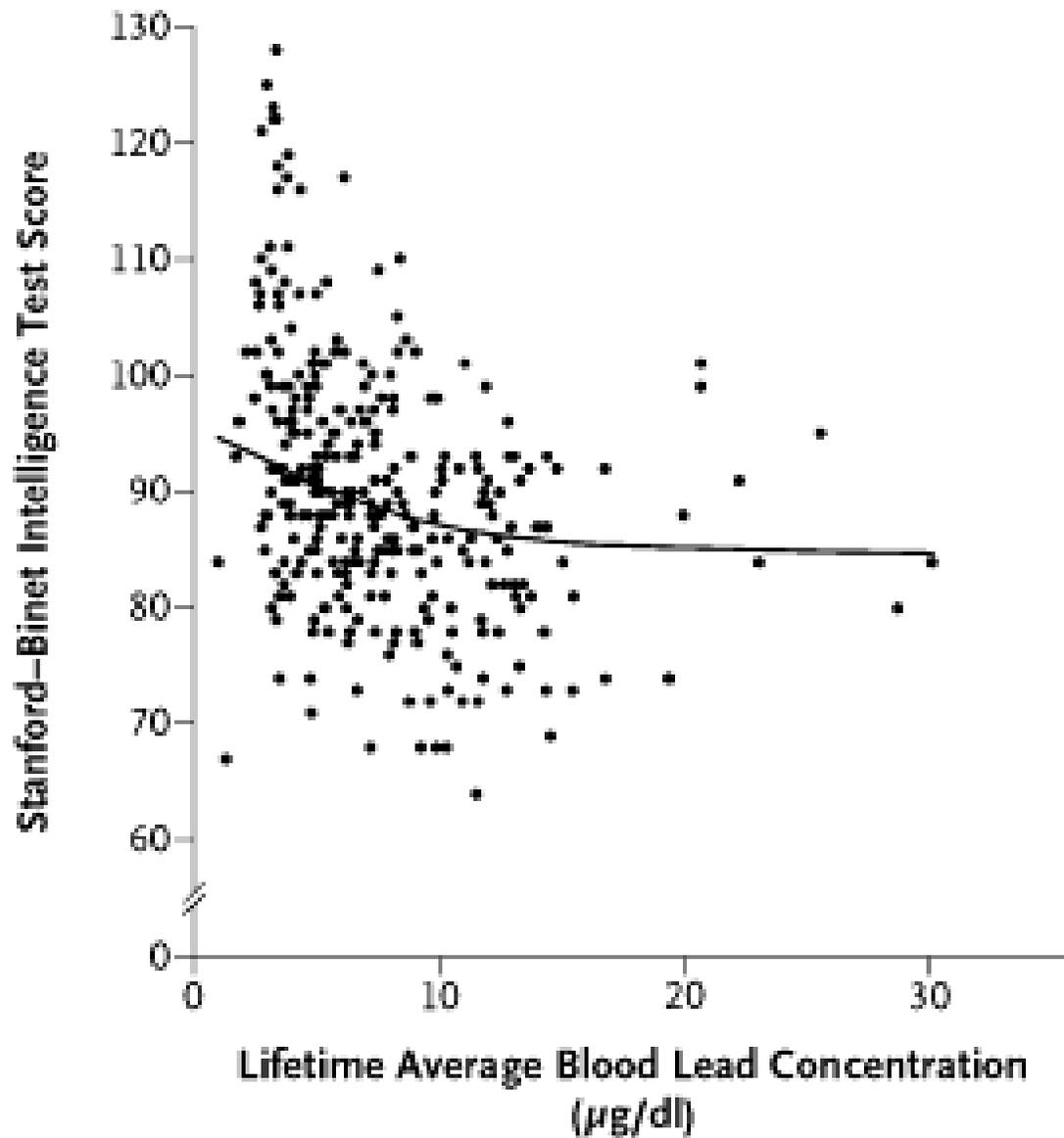
Adj. Decrease in IQ per 1 ug/dL Blood Lead (Age 3) – Canfield et al

Lead Measure	All Children N= 172	Those with Peak Blood Lead <10 ug/dL N= 101
Lifetime Mean	0.35	1.22
Concurrent at Age 3	0.31	1.36

Change in Mean Blood Lead in U.S. 1-5 Year Old Children
NHANES Data

YEAR	MEAN VENOUS BLOOD LEAD
1976-80 1988-91	15.0 ug/dL 3.6 ug/dL

Predicted Improvement in IQ in 3 Year-olds in 1980's Based on Data of Canfield

Pop Blood Lead Change: 15.0 → 3.6 ug/dL

15→10 @ 0.31 = 1.5 IQ Points

10→3.6 @ 1.36 = $\underline{8.7}$

10.2 IQ Points

NHANES III Analysis
Lanphear et al, 2000

- National sample of 4816 children aged 6-16 evaluated at one visit

- Venous blood lead collected

- Children completed several measures of psychological function and school achievement

Adj. Decrease in WRAT per 1 ug/dL Blood Lead (Ages 6-16),
Lanphear et al, NHANES III Data

Wide Range Achievement Test-Revised (Mean = 100 S.D. = 15)	All Children N= 4853	Those with Peak Blood Lead <7.5 ug/dL N= 4526
Reading Subtest	0.99	1.53
Arithmetic Subtest	0.70	1.06

Predicted Improvement in Reading in 9 Year-olds in 1980's Based on Cross Sectional Analysis of NHANES III Data
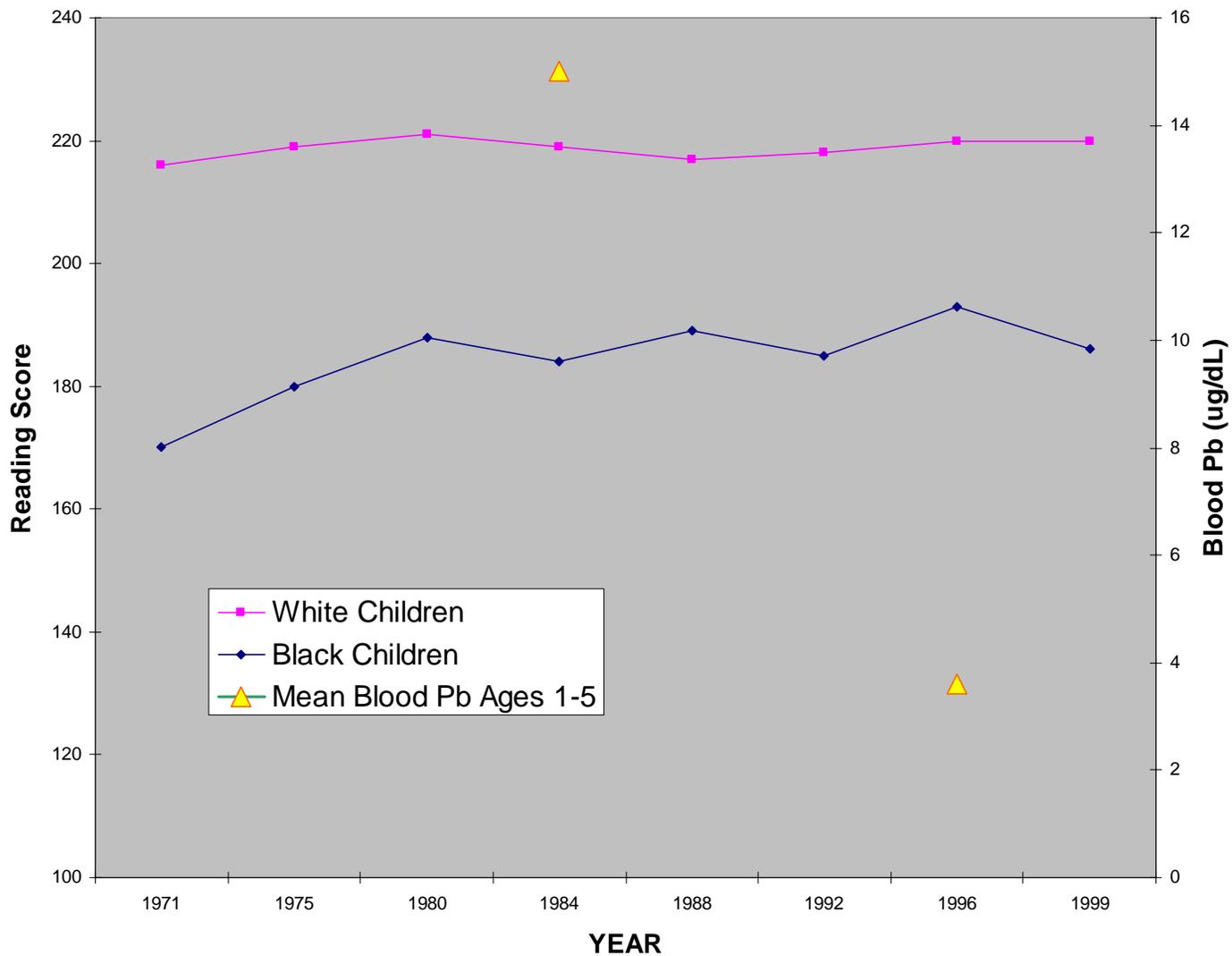
Pop Blood Lead Change: 15.0 → 3.6 ug/dL

Predicted Change in WRAT Reading Score

15→7.5 @ 0.99 = 7.4
7.5→3.6 @ 1.53 = 6.0
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13.4 Points on WRAT

NAES Reading Scores at Age 9 and Mean Blood Pb at Ages 1-5

Sources of Possible Bias

- All studies relating blood lead to neurodevelopment of children are observational and could be biased by differences between highly exposed and less exposed children.

- Although many factors are taken into account, it is impossible to be sure that this eliminates all important differences

Stronger Blood Pb – IQ Relationship at <10ug/dL Suggests Reverse Causality

- Surprising finding obviously not widely predicted when level of concern was set at 10 ug/dL

- Exactly what one would predict under a scenario where children with less IQ potential had

  more hand-to-mouth activity, or

  more opportunity to ingest non-foods

Thought Experiment (1)

- Suppose, for a moment, an association between slow development and ingestion, or poor parenting and ingestion opportunity that is independent of any lead effect.

- Suppose further a comparison of two groups of children, one with more ingestion and lower IQ potential and the other with less ingestion and higher IQ potential. Let's say the IQ difference between the two groups is 3 points.

Thought Experiment (2)

Then:

- In a high lead environment children with low potential or poor parenting will have substantially higher blood leads than other children because the extra ingestion will include a lot of lead. To illustrate, let's say 9 ug/dL.

- In low lead environments the blood lead difference between the same two groups of children will be slight. Let's say 3 ug/dL.

Thought Experiment (3)

Then:

- In a high lead environment we have 3 IQ points associated with a blood lead difference of 9 ug/dL which is 0.33 IQ points per 1 ug/dL blood lead.

- In a low lead environment we have 3 IQ points associated with a blood lead difference of 3 ug/dL which is 1.00 IQ points per 1 ug/dL blood lead.

- The numbers are arbitrary, but they illustrate how the bias might operate.
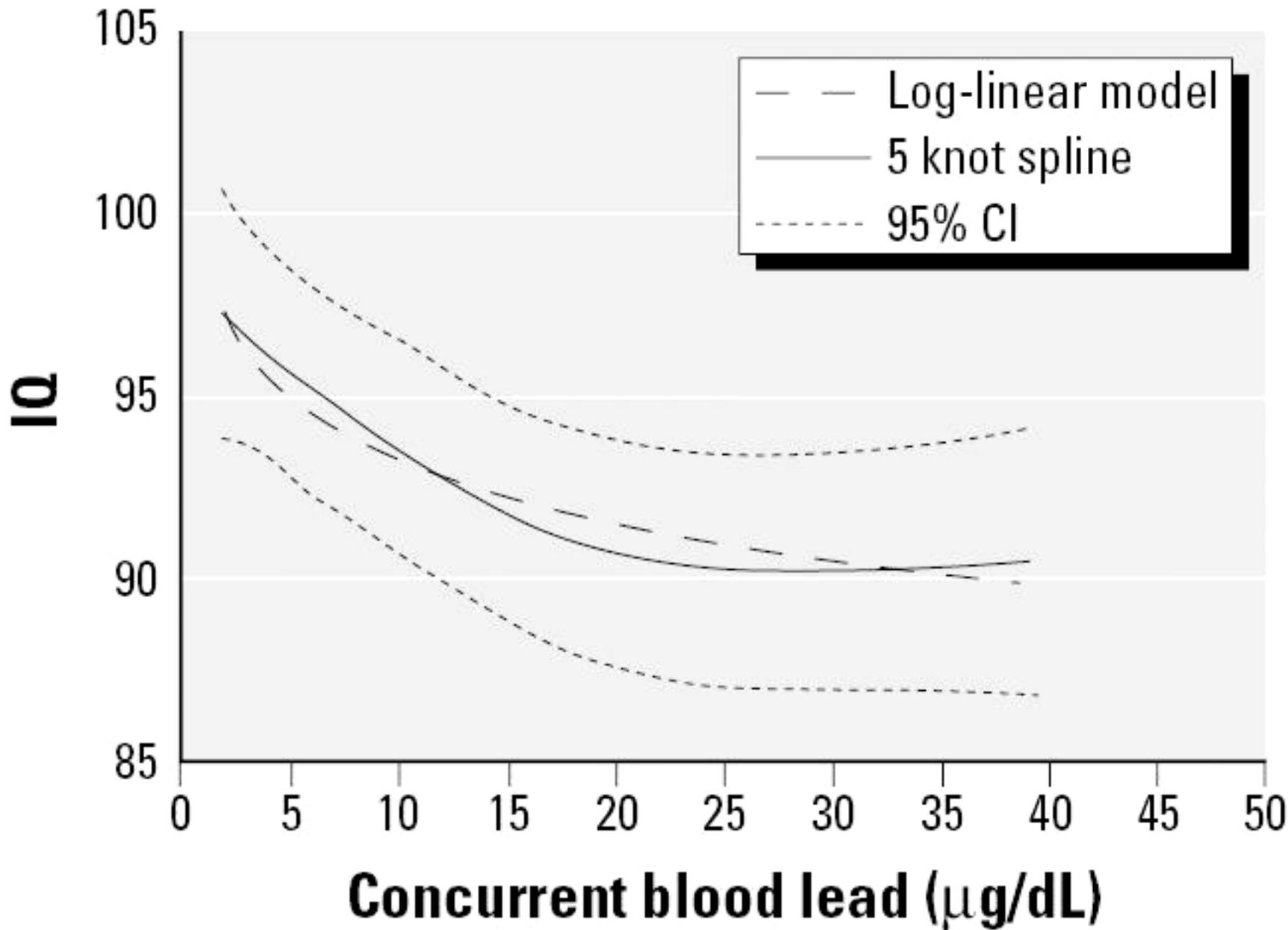
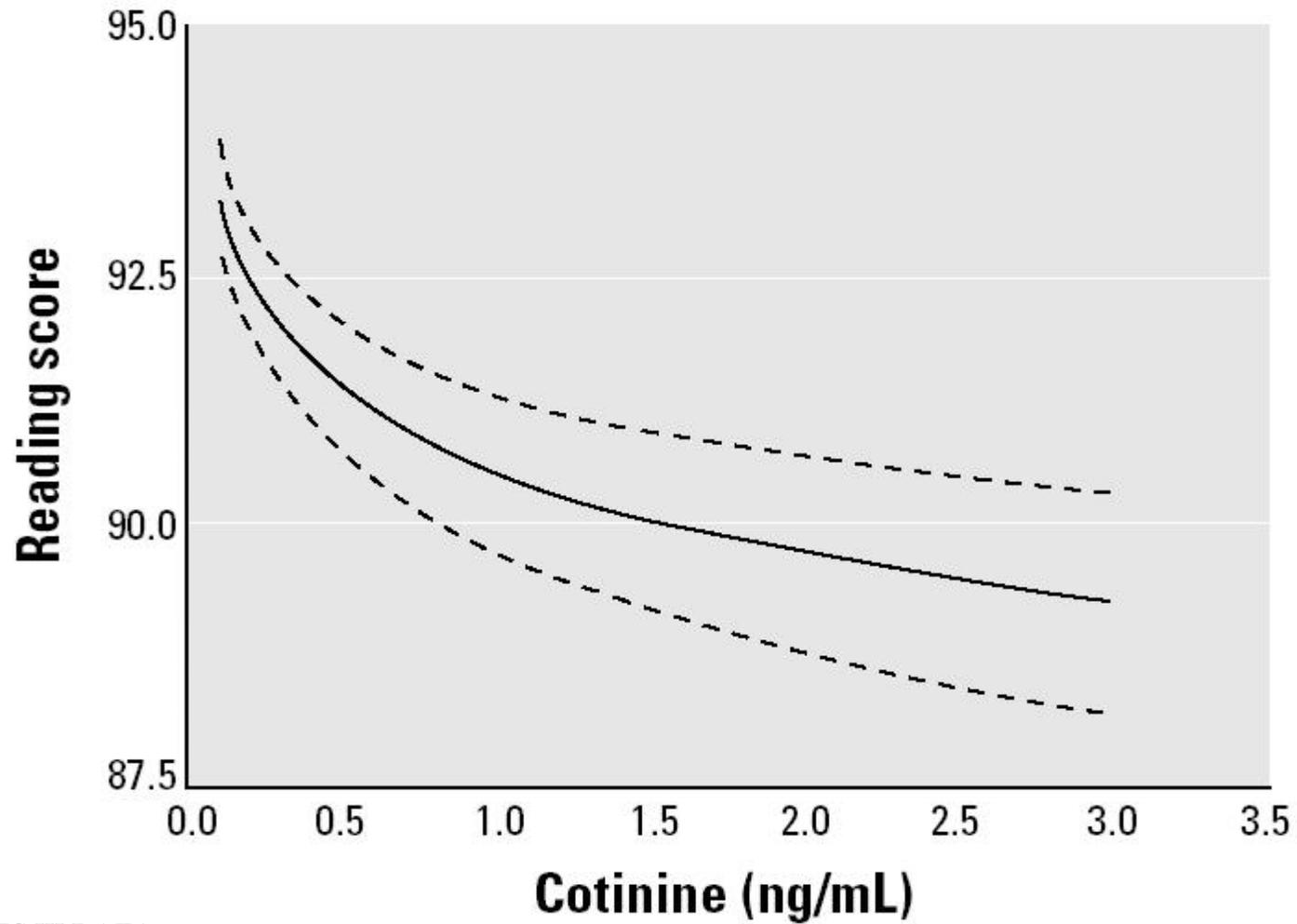Lanphear et al, 2005

Summary

- The IQ-blood lead slopes reported in the recent low level studies appear too steep to be entirely credible.

- The steepening of the the blood lead – IQ curve at low blood lead levels suggests possible reverse causality.

- However, these considerations to not rule out an IQ effect at low blood lead levels.

- New studies with designs that separate lead intake from pica are needed to rule out the type of reverse causality posited earlier.

Where Can We Go from Here

- More observational studies are likely to be subject to the same biases as the ones recently reported. They may never provide a basis for deciding when blood leads are low enough.

- Observational studies of different designs might be helpful.

- A randomized primary prevention trial appears to be the best way to clarify these issues.

End

Environmental Tobacco Smoke and Reading Scores

NHANES III DATA