Author's response to reviews

Title: Primary prevention of lead poisoning in children: A cross sectional study to evaluate state specific lead-based paint risk reduction laws in preventing lead poisoning in children

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Author's response to reviews: see over
Dear Dr. Aschengrau,

Thank you very much for your comments. They were extremely helpful as they helped to refine the message of this study. To aid in your review, we’ve sent both a track changes as well as a clean version of the document. We really appreciated your attention to detail and hope that our response adequately satisfies your concerns.

Response to comments from reviewer Ann Aschengrau

Major Compulsory Revisions

Comment 1: Provide more description about the selection of the two “exposed” and one “unexposed” comparison state. For example, it would be useful to know how many and which states do not currently have lead laws and how Mississippi was selected to represent them.

Response 1: At the time of this study, which was conducted between 2009-2012, of the 35 Childhood Lead Poisoning Prevention Programs (CLPPP) under cooperate agreement with the Centers for Disease Control and Prevention’s (CDC) Healthy Homes and Lead Poisoning and Prevention Program (HHLPPP), Mississippi was the only state that did not have either state or local legislation to prevent childhood lead poisoning, but had a high lead screening penetration rate among children <72 months old. Despite not having legislation to prevent lead poisoning, and having the highest poverty rate among children from birth to age 5 years, MS had annual
screening rates that was similar to other states that had lead legislation and had an annual elevated blood lead level (EBLL) rate similar to that of MA and lower than that of OH. From 1991 to 2012, CDC defined an EBLL as a BLL ≥10µg/dL. According to 2009 national estimates obtained from CDC’s Childhood Blood Lead Surveillance System (CBLS), the prevalence proportion of EBLL was ≤1% in all three states.

Despite profound socio-demographic differences noted in the three states, efforts were made, using census track data, to control for a priori, macro level variables that may have confounded the main effects association, addresses with subsequent cases of lead poisoning after identification of an index case. Pages 11 and 12 of the manuscript outline how both address as well as county level data was collected. Table 6 of the manuscript shows the specific address and county level data that was controlled for in the analysis. At the address level, these variables included year residence built (categorical variable: pre-1950’s vs. newer), building type (categorical variable: single vs. multi-unit) and building ownership (categorical variable: private, owner-occupied vs. other). County level data controlled for in the analysis, all of which were continuous variables, included % poverty in county, % CAPI in county, % households in county with high school graduates, % non-whites in county, % pre-1950’s homes in county and % rental in county.

Thus, while programmatic variables were used to examine the effectiveness of laws aimed at primary prevention of lead poisoning among young children, we tried where at all possible to control for those measured risk factors that may have created spurious associations, using all available data sources, including data from the United States census. Since the unit of analysis for this inquiry was addresses, socio-demographic risk factors that would confound the true associations at the address level were the primary focus for statistical adjustment.

Comment 2: The results section has too much emphasis on statistical significance. The magnitude of the odds ratio should be given greater emphasis.

Response 2: The odds ratio has been provided in the results section to show the magnitude of effect.

3. Stepwise regression uses the p value to determine which variables are confounders. Unfortunately, this practice can lead to erroneous conclusions. The change in the magnitude of the odds ratio (i.e. crude OR vs. adjusted OR) when potential confounders are controlled one at a time should be used instead. About a 10% difference is typically used as a cutoff for determining which variables need to be included in the final multivariate model.

Response 3: We did in fact include each covariate one at a time, to examine their individual effect on the main effects variable, address with subsequent cases of lead poisoning after identification of an index case. Table 6 presents the results of the adjusted main effects model which was obtained using stepwise regression, as well the effect estimate of each covariate when examined one at a time with the main effects model. The final model, which showed the main effect covariate being significant after controlling for each covariate, was obtained using
stepwise regression. The individual covariate estimates shown, were derived after each was examined one at a time with the main effects model.

**Comment 4:** It seems odd to compare dust sample from the three states because they were taken at different times (post-abatement for Massachusetts, pre- and post-abatement for Ohio, and pre-abatement for Mississippi). More explanation should be given regarding the utility of these comparisons. Also, given these differences, you should explore the impact of including the dust variables in the final multivariate model.

**Response 5:** Since the unit of analysis was the address, we felt it pertinent to have measures of dust lead levels within the analysis. While abatement was not mandatory for MS, it was for MA and OH. The best effort was made to control for dust lead level since dust lead level is associated with the addresses and is causally related to development of subsequent cases.

**Comment 5:** More description (particularly results) should be given for the only prior study (reference 14) that examined the effectiveness of state lead laws.

**Response 5:** Document updated to provide more description.

**Comment 6:** Residual confounding by individual-level characteristics should be given more emphasis in the discussion section.

**Response 6:** The discussion has been updated to note this. We did however want to note that since the address was the unit of analysis, we did not control for characteristic of the child. If we were analyzing data at the child level, then we would have had to control for the child’s age, gender and race/ethnicity. However, our inquiry focused on the likelihood of an address having a subsequent case of lead poisoning after identification of an index case.

**Minor Essential Revision**

**Comment 1:** Methods/Design and Data Sources (page 6): Randomization is not the same as random selection. This sentence should read “Random selection occurred in a three-step process.”

**Response 1:** The document has been updated to reflect this change in wording.

We look forward to hearing from you soon.

With Best Regards,

*Chinaro Kennedy*
Chinaro Kennedy, DrPH, MPH
Principal Investigator

Enc:
Dear Dr. Braun,

Thank you very much for your comments. They were extremely helpful as they helped to refine the message of this study. To aid in your review, we’ve sent both a track changes as well as a clean version of the document. We really appreciated your attention to detail and hope that our response adequately satisfies your concerns.

Response to comments from reviewer Joseph Braun

Major Compulsory Revisions

Comment 1: The justification for using MS as a control state seems somewhat arbitrary. Are there other states that meet the criteria set forth by the authors (i.e., no lead laws)? This is especially problematic given the ecological nature of the exposure in this study (state lead laws) and the fact that there are profound differences in the features of the states being compared.

Response 1: At the time of this study, which was conducted between 2009-2012, of the 35 Childhood Lead Poisoning Prevention Programs (CLPPP) under cooperate agreement with the Centers for Disease Control and Prevention’s (CDC) Healthy Homes and Lead Poisoning and Prevention Program (HHLPPP), Mississippi was the only state that did not have either state or local legislation to prevent childhood lead poisoning, but had a high lead screening penetration
rate among children <72 months old. Despite not having legislation to prevent lead poisoning, and having the highest poverty rate among children from birth to age 5 years, MS had annual screening rates that was similar to other states that had lead legislation and had an annual elevated blood lead level (EBLL) rate similar to that of MA and lower than that of OH. From 1991 to 2012, CDC defined an EBLL as a BLL ≥10µg/dL. According to 2009 national estimates obtained from CDC’s Childhood Blood Lead Surveillance System (CBLS), the prevalence proportion of EBLL was ≤1% in all three states.

Despite profound socio-demographic differences noted in the three states, efforts were made, using census track data, to control for a priori, macro level variables that may have confounded the main effects association, addresses with subsequent cases of lead poisoning after identification of an index case. Pages 11 and 12 of the manuscript outline how both address as well as county level data was collected. Table 6 of the manuscript shows the specific address and county level data that was controlled for in the analysis. At the address level, these variables included year residence built (categorical variable: pre-1950’s vs. newer), building type (categorical variable: single vs. multi-unit) and building ownership (categorical variable: private, owner-occupied vs. other). County level data controlled for in the analysis, all of which were continuous variables, included % poverty in county, % CAPI in county, % households in county with high school graduates, % non-whites in county, % pre-1950’s homes in county and % rental in county.

Thus, while programmatic variables were used to examine the effectiveness of laws aimed at primary prevention of lead poisoning among young children, we tried where at all possible to control for those measured risk factors that may have created spurious associations, using all available data sources, including data from the United States census. Since the unit of analysis for this inquiry was addresses, socio-demographic risk factors that would confound the true associations at the address level were the primary focus for statistical adjustment.

Comment 2: Related to this point is the concern for ecological confounding. Differences in the rate of blood lead screening may be driving the relationship observed in this study. In fact, this is suggested by Table 2, which shows that the rate of screening was higher in MA compared to OH or MS. Thus, the observed relationship may not be related to the state laws, but the presence of more aggressive screening that is better at detecting children at-risk for EBLs. The potential for confounding related to temporal changes in housing characteristics, sociodemographics, and neighborhoods is a potential concern with this type of data. The authors briefly mention changes in housing stock over time on Page 18, but could adjust for the time elapsed between the index and subsequent case in their statistical models. Other confounders worth considering would be individual level characteristics that are associated with lead poisoning, including child sex, age, and race/ethnicity.

Response 2: Since our analysis focused on the identification of addresses with subsequent cases of lead poisoning after an index case was recorded, the rate of blood lead screening would most likely not play a role in the findings. In all three states we identified addresses at which an index case of lead poisoning was found; thus, our starting point for this inquiry was addresses with an
identified index case. We therefore aimed to falsify the hypothesis that, the likelihood of seeing subsequent case at addresses in which an index case was found, in Massachusetts (MS) and Ohio (OH) will be lower than in Mississippi (MS). The primary aim was to determine whether the proportion of addresses with subsequent cases of lead poisoning recorded after identification of an index case, was lower in the lead law states, MA and OH, compared to MS.

While blood lead screening is a very important component to case identification, the main effects inquiry used address as the unit of analysis. In fact, MA had the lowest number of addresses with children with lead poisoning, despite having a two-fold increased screening rate. MS on the other hand had the largest number of addresses identified with children with lead poisoning and had a lower screening rate than MA. Given this, the rate of blood lead screening between the three states may have therefore been perfunctory to the main effects inquiry at hand.

The identification of subsequent cases followed a specific algorithm. A subsequent case was identified not less than 24 months after identification of the index case and could not have been a case at any other address. This algorithm adjusted for time differences between identification of the index case and development of subsequent cases, as well as adjusted for time needed for remediation and re-habitation.

Regarding potential for confounding related to housing characteristics, socio-demographics and neighborhoods, census track information using county level data was presented in Table 6 and were among covariates used in adjusting the main effects model. Since address was the unit of analysis, macro-level demographic information, assessed at the county level, including % of non-whites living in the county, % in county living in poverty, % household in county with high school graduates, % pre-1950 homes in county, % rentals in county and % in county requiring assistance in completing the census interview (% CAPI) were used to control for county level characteristics that may affect the probability that an address would have a subsequent case after identification of an index case. That notwithstanding, the limitation section within the discussion was updated to show possible residual confounding by individual level risk factors such as child sex, age and race/ethnicity.

Comment 3: Did the authors consider examining continuous blood lead levels of children who lived in houses after remediation by state to see if interventions may be effective at reducing blood lead levels among children who do not meet the programmatic definition of lead poisoned? Furthermore, is it possible to see if more children have blood Pb’s greater than CDC’s current EBL definition of 5 #g/dL in MS compared to OH/MA? In addition, the different programmatic definitions used to identify the index case should be noted in the discussion.

Response 3: The main effects inquiry was to, starting at the address level, determine the likelihood of identifying subsequent cases of lead poisoning after identification of an index case in the lead law states, MA and OH, compared to the comparison state MS. The legal limit to trigger an environmental investigation, mandating remediation at the residence in both MA and OH is set at specific blood lead trigger levels of $\geq 25\mu g/dL$ and $\geq 15\mu g/dL$ respectively. Therefore, remediation would not be mandated at blood lead levels lower than the trigger level.
and information on the effectiveness of remediation at trigger levels lower than the action level would not have been available. In addition, at the time of this inquiry, the current CDC blood lead level requiring public health action of 5µg/dL was not being used; at the time of this inquiry in 2009, CDC’s definition of EBLL was ≥ 10µg/dL. Therefore, due to limited resources, most programmatic action requiring environmental investigation occurred at specific programmatic trigger levels. Limited resources precluded environmental investigation of BLL falling below program specific trigger level. Today, this is a more pressing issue where funds to programs nationally have been cut drastically.

Comment 4: The authors should clearly articulate in the manuscript and abstract that the unit of study is the state, and that comparisons are being made among a set of children who are living in homes that were previously occupied by a child who had an EBL.

Response 4: The unit of analysis is actually the individual addresses across the three states. The abstract and manuscript has been revised to clearly show this.

Comment 5: The dust Pb measurements don’t seem relevant to the manuscript and distract from the main findings. Furthermore, given that they were collected at different times relative to the abatement, they aren’t very comparable.

Response 5: Since the unit of analysis was the address, we felt it pertinent to have measures of dust lead loading within the analysis. While abatement was not mandatory for MS, it was for MA and OH. The best effort was made to control for dust lead loading since the measurement of the dust lead level differed by address, given the variability of its measurement by state, and dust lead is causally related to development of lead poisoning, which is inherent to the detection of subsequent cases. By adjusting for dust lead level, we minimized any effect this variable would have had on the main effects association, likelihood of identifying a subsequent case after identification of an index case, in addresses in lead laws states compared to the state without lead laws.

Comment 6: Page 18-Is it really a good thing that these neighborhoods are being gentrified? This drives people out of these neighborhoods and increases the cost of living for the remaining residents.

Response 6: This inquiry did not address gentrification and its importance. Instead, the findings were aimed at showing the importance of laws aimed at preventing lead poisoning among young children. Due to changing demographics, many inner city neighborhoods are seeing a change in population structure where once those traditionally known to be affected by exposure to lead based paint mainly included low income families living in lead contaminated dwellings; now we see a shift. Today, many of those dwellings are being purchased and renovated by more affluent families. There is evidence that many home renovations, occurring among middle income families, have resulted in the inadvertent lead poisoning among their young children. Lead poisoning is no longer an issue that only affects the poor but has now become an issue for many middle income families.
Minor Essential Revisions

Comment 1: Abstract: Please define the threshold(s) used to designate EBLL. Also, please state the sample size and years/place of study.

Response 1: Abstract updated.

Comment 2: The power calculations are unnecessary since it sounds like they were done post hoc. If they were done before the study was conducted, then the authors need to define the OR that they had sufficient power to detect.

Response 2: The power calculation sentence has been deleted.

Comment 3: The authors mention “target number” throughout the manuscript. I suggest defining this or changing the term to something less “jargon-y”.

Response 3: We did not find this term in the text when a word search was performed.

Comment 4: Page 11-I suggest changing “Summary Level 050” to something that sounds less like jargon.

Response 4: It is the official term used by the 2000 United States census to designate county level data.

Comment 5: Did the authors conduct analysis of MA vs. MS and OH vs. MS to see if the results were driven by one state?

Response 5: Yes, we did conduct said analysis and the results were similar to what we found when both states were combined.

Comment 6: Table 3 seems unnecessary since it is related to one covariate.

Response 6: Table 3 outlines the specific county level codes used to segment and define urbanicity.

Comment 7: Could Table 2 be merged with Table 4?

Response 7: Two different types of information are being presented in Tables 2 and 4. Whereas Table 2 presents state level demographic information, to show comparability, table 4 presents demographic information on the addresses.

Comment 8: I suggest dropping Table 5 since these data are not directly relevant to the manuscript’s primary question.
Response 8: Table 8 provides information on the mean window sill and floor dust lead loading in addresses within each state. Since the address was the unit of analysis, adjusting for dust lead loading is important since we know the results can affect true associations.

Comment 9: Table 6 is confusing. It is not clear what the sample size numbers refer to. Is this the N in the model or the n with that characteristic? Are the presented beta coefficients from a single model or different models with each term run one-at-a-time? The term ‘Slope Parameters’ could be confusing. I suggest the following
a. Clearly designate the variables included in the final model.
b. Change “slope parameters” to effect estimates and only present the OR and its 95% CI for all the variables.
c. Include the OR for the effect estimate of OH/MA vs. MS.
d. Specify which covariates are modeled as continuous variables.

Response 9: Table 6 has been updated to reflect suggestions A to D.

Comment 10: Figure 1 could be dropped if the OR for the state effect estimate is presented in Table 6.

Response 10: Figure 1 was requested by an independent reviewer who suggested a graphic display for those not comfortable reading results from the table.

We look forward to hearing from you soon. Please don’t hesitate to contact us if you have any additional concerns.

With Best Regards,

Chinaro Kennedy

Chinaro Kennedy, DrPH, MPH

Enc: