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# Quantile regression in environmental health: Early life lead exposure and end-of-grade exams

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ABSTRACT

Conditional means regression, including ordinary least squares (OLS), provides an incomplete picture of exposure–response relationships particularly if the primary interest resides in the tail ends of the distribution of the outcome. Quantile regression (QR) offers an alternative methodological approach in which the influence of independent covariates on the outcome can be specified at any location along the distribution of the outcome. We implemented QR to examine heterogeneity in the influence of early childhood lead exposure on reading and math standardized fourth grade tests. In children from two urban school districts ($n=1{,}076$), lead exposure was associated with an 18.00 point decrease (95% CI: $-48.72$, $-3.32$) at the 10th quantile of reading scores, and a 7.50 point decrease (95% CI: $-15.58$, 2.07) at the 90th quantile. Wald tests indicated significant heterogeneity of the coefficients across the distribution of quantiles. Math scores did not show heterogeneity of coefficients, but there was a significant difference in the lead effect at the 10th ($\beta=-17.00$, 95% CI: $-32.13$, $-3.27$) versus 90th ($\beta=-4.50$, 95% CI: $-10.55$, 4.50) quantiles. Our results indicate that lead exposure has a greater effect for children in the lower tail of exam scores, a result that is masked by conditional means approaches.


## 1. Introduction

Epidemiological research often focuses on inference for high or low values in a population distribution, e.g. high body mass index, low birth weight, high blood pressure, or reduced lung function. However, the preponderance of statistical approaches in epidemiology employ conditional-mean modeling, such as ordinary least squares regression (OLS), which summarizes the relationship between the dependent variable and explanatory variables by describing the mean of the response for each fixed value of the predictors (Hao and Naiman, 2007). Conceptually, the primary limitation of conditional-mean modeling is that it cannot be easily extended to describe relationships for non-central locations, such as in the upper or lower tails of a distribution. Statistically, a main concern with conditional-means approaches is that these models provide an incomplete picture of the exposure-outcome function for regression models with heterogeneous variances. In many cases there may not be one, unique slope that effectively characterizes the changes across the probability distribution (Cade and Noon, 2003). In these instances, the assumptions for conditional-means models like ordinary least squares or other generalized linear model techniques are violated. Focusing primarily on changes in the mean effect may underestimate, overestimate, or fail to distinguish real changes in other locations of the distribution (Terrell et al., 1996; Cade et al., 1999; Cade and Noon, 2003).

Quantile regression, formalized by Koenker and Bassett (1978), can be considered a logical extension of linear regression. Rather than focusing on the change in the conditional mean of the dependent variable associated with a change in the explanatory variables, quantile regression models specify changes in the conditional quantile, or at any point along the distribution of the outcome (Hao and Naiman, 2007). Further, a set of equally spaced quantiles (e.g. every 5% of the population) can describe the shape of the distribution in addition to its central location (Hao and

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Naiman, 2007). Though quantile regression has been used extensively in the economics literature (Buchinsky, 1998; Eide and Showalter, 1998, 1999; Martins and Pereira, 2004; Machado and Mata, 2005), it is not a common analytic strategy in the epidemiologic literature (Beyerlein, 2014). We present an application of quantile regression to better understand the effect of early childhood lead exposure on elementary school end-of-grade examinations. We hypothesized that slope estimates obtained using ordinary least squares (OLS) methods would not fully describe the relationship between lead exposure and test scores at all points of the distribution of reading and math scores on a standardized end-of-grade exam. As socioeconomic status is considered to modify lead neurotoxicity (Bellinger, 2008), and is strongly associated with test scores (Duncan and Magnuson, 2005), we hypothesized that the effect of lead exposure on test scores would be greater for children scoring at lower quantiles, compared to children scoring at higher quantiles.

## 2. Method

### 2.1. Statistical approach

Quantile regression (QR) is a method for estimation of the functional relationships between outcomes and covariates at arbitrary quantiles of a conditional probability distribution (e.g. WKCE scores given gender, race, parental education). QR and linear regression can both be considered solutions to specific minimization problems. For example, OLS regression finds the center of the distribution (i.e. mean) by locating the point where the average squared deviance from data points of $Y$ is minimized, and means are then interpreted as predicted values for individuals (Hao and Naiman, 2007). The median has a similar minimizing property, but a distance of $Y$ to $m$ is measured in absolute terms ($|Y-m|$) rather than squared distance. QR uses a generalized absolute minimization procedure to estimate predicted values for individuals that are conditional not only on explanatory variables, but also on the location of that individual in the distribution of outcomes scores $Y$. This approach is particularly relevant if the relationship between outcome and explanatory variables varies across the distribution of $Y$, or if the distribution of unobserved variables varies across $Y$.

As an illustrative case, if the outcome variable $y$ represents exam score, and $x_1$ and $x_2$ represent gender and race, and $e$ represents the error term, a general linear model to describe the relation between $y$ and $x$ for each child $i$ can be written as

$$y_i = \beta_o + \beta_1 x_{i1} + \beta_2 x_{i2} + e_i$$

However, if unmeasured or unobserved confounding results in heterogeneity of exam scores across race and gender, then for every point $i$ in a distribution (e.g., 50% quantile, or the median), the outcome is not only conditioned on the values of the known parameters at that point in the distribution, but also the parameter estimates of the unknown or unmeasured covariates. Dividing the distribution of $Y$ into discrete quantiles $p$, the observed value for each individual $i$ at a specific quantile $p$ is captured by the conceptual expression

$$y_i = \beta_{p0} + \beta_{p1} x_{i1} + \beta_{p2} x_{i2} + (\gamma_{po} + \gamma_{p1} x_{i1} + \gamma_{p2} x_{i2}) XU_i$$

in which the effect of each known variable $X$ depends on both the quantile of the outcome, and also the distribution of unobserved variables $U$ scaled by the parameters $\gamma$ (Van Sickle et al., 2011). In other words, rather than a single summary statistic, QR provides parameter estimates for the outcome $y$ conditioned on covariates $X$ (both observed and unobserved) for every quantile specified ($p$). The estimates are considered to be semiparametric; the random error of the model has no parametric distributional form, though a parametric distribution is assumed for the deterministic part of the model (Cade and Noon, 2003).

### 2.2. Study population

The Wisconsin Children's Lead Levels and Educational Outcomes Project (CLLEO) is a collaborative study among the University of Wisconsin, the Wisconsin Childhood Lead Poisoning Prevention Program (WCLPPP), and the Wisconsin State Department of Public Instruction (DPI) to investigate the ongoing effects of early childhood lead exposure (Amato et al., 2012, 2013; Magzamen et al., 2013). The study protocol was approved by the University of Wisconsin Education Institutional Review Board. All parents/guardians signed informed consent documents prior to participation.

The study design and sample recruitment strategies have been described elsewhere (Magzamen et al., 2013). Briefly, the Wisconsin Knowledge and Concepts Exam (WKCE) records from DPI were merged with early childhood blood lead level (BLL) data from WCLPPP to define the target population: 1) born between January 1, 1996 and December 31, 2000; 2) record of BLL $<5$ μg/dL (not exposed group) or between 10 μg/dL and 20 μg/dL (exposed group) before the child's third birthday; 3) confirmed by DPI to have taken a 4th grade WKCE and 4) Milwaukee or Racine address at time of BLL testing. Milwaukee and Racine are the 1st and 5th largest cities in Wisconsin, respectively, and are high-risk communities for lead exposure (Wisconsin Department of Health and Family Services, 2008). The exposure categories were defined to compare children with BLLs below the level of quantification at the time of their testing with children whose BLLs were elevated but not sufficiently elevated to receive state-mandated home remediation or education interventions. These exposure classifications were developed prior to the 2012 Centers for Disease Control (CDC) policy change which adopted a new reference value of 5 μg/dL for blood lead levels, but still have relevance for state and local interventions which do not necessarily begin at the CDC reference values.

### 2.3. Data

Survey packets were mailed to all parents/guardians of children who met eligibility criteria and for whom we could obtain current contact information (Magzamen et al., 2013). Current mailing addresses were obtained either from Racine Unified School District or with assistance from the University of Wisconsin Survey Center. Survey packets included an invitational letter, two consent forms to allow release of educational data from DPI to the study, and a four-page questionnaire on demographics, educational experiences, health information, and environmental exposures. Upon return of the completed survey and consent form, parents were mailed a $5 monetary incentive. With parental consent, DPI provided exam scores, classifications for disability, designation as an English Language Learner, record of an Individualized Education Plan (IEP) (a tailored educational program for students with a special education designation), and enrollment in the federal free/reduced price lunch program (FRLP).

### 2.4. Analysis

Scaled scores on the math and reading components of the 4th grade WKCE were the primary outcomes. As described in Section 2.2, the study sample was selected such that BLLs fell either below quantification or in an elevated range that was not sufficient to receive lead education and abatement. Due to this selection strategy, and for consistency with other project analyses, lead exposure was entered into the model as a binary variable that represented exposed and not exposed groups. Covariates included in the models were determined through the deletion/substitution/addition (D/S/A) algorithm, a cross-validated approach based on the L2 loss function for the prediction of multivariate outcomes (Sinisi and van der Laan, 2004), with several exceptions.

Though DPI record of disability and record of IEP were both related to reading and math scores, these factors may be on the causal pathway linking lead exposure and educational outcomes, and were not included in the analysis. In the prior analysis (Magzamen et al., 2013), gender and enrollment in the FRLP were significantly related to reading scores only. However, as these factors have important implications for both early childhood lead exposure (Meyer et al., 2003; Jones et al., 2009) as well as standardized exam performance (Hyde et al., 1990; Sirin, 2005), they were included as covariates for both the math and reading analyses. Other covariates included in the model were race, parent education, parent-rated child health, and DPI designation as an English Language Learner. Due to the relatively small percentage of parents/guardians with graduate level education ($<10\%$), parent education was dichotomized into $\leq$high school education and $>$high school education. With regard to parent-rated child health, results from our earlier analysis demonstrated that when “excellent health” was implemented as the reference value, all other categories for child health had negative associations of approximately equal magnitude with math (Magzamen et al., 2013). For this analysis, we sought to understand how an “excellent health” designation behaved across the distribution of test scores.

The first model included all main effect terms. Subsequent models assessed the presence of interactions; these models included all main effects from the first model as well as one term for the interaction to be tested. Five interactions were tested: race and exposure, gender and exposure, parent education and exposure, enrollment in the FRLP and exposure, parent-rated health and exposure. Interactions were tested individually, rather than simultaneously, to prevent spurious inferences due to small cell sizes.

Quantile regression models were estimated at 0.05 increments ($\tau$) from 0.05 to 0.95 using the quantreq command in SAS 9.2 (Cary, NC). Based on the size of the data set and the number of explanatory variables included in the analysis, the simplex method was used to calculate parameter estimates (Koenker and d'Orey, 1994) and confidence intervals were estimated using the rank score method (Kocherginsky et al., 2005). Wald tests were implemented to test for heteroscedasticity across the entire distribution of the quantiles. For comparison, OLS regressions including the same variables were also calculated. To illustrate potential differences in QR and OLS results, an additional Wald test was implemented to test potential differences between the lower tail to upper tail of the distribution of test scores.

## 3. Results

Fig. 1 presents the participant enrollment for the CLLEO project. A total of 1133 parents consented to participate, and allowed DPI

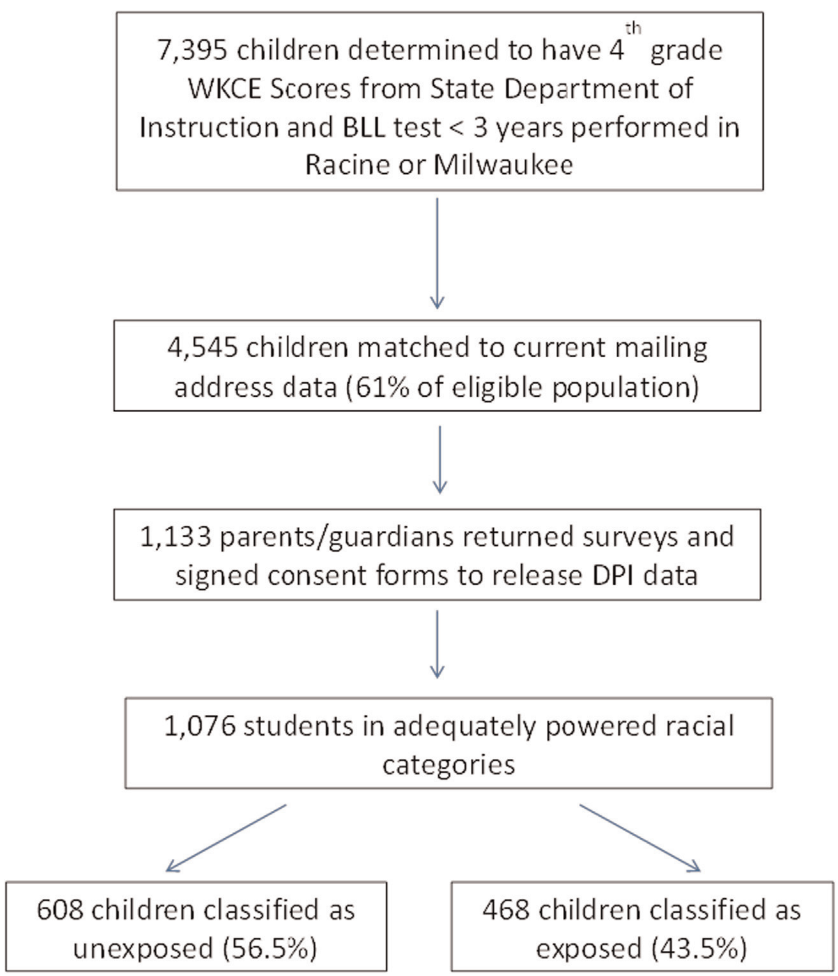


**Fig. 1.** Participant flow diagram for CLLEO QR analysis.

**Table 1**
Covariates of interest for survey population ($n$=1076), Wisconsin Children's Lead Levels and Educational Outcomes (CLLEO) Study.

| Characteristic | Unexposed $n$ | Unexposed (%) | Exposed $n$ | Exposed (%) | $P$ | Avg reading score | $P$ | Avg math score | $P$ |
|---|---|---|---|---|---|---|---|---|---|
| *Total* | 608 | (56) | 468 | (43) | | 460.9 | | 452.0 | |
| **Gender** | | | | | | | | | |
| Male | 317 | (57) | 242 | (43) | | 455.2 | | 452.2 | |
| Female | 291 | (56) | 226 | (44) | 0.89 | 467.0 | 0.0002 | 451.8 | 0.86 |
| **Primary race** | | | | | | | | | |
| Black | 152 | (32) | 324 | (68) | | 437.6 | | 429.5 | |
| White | 456 | (76) | 144 | (24) | 0.0001 | 479.3 | 0.0001 | 469.7 | 0.0001 |
| **Parent education** | | | | | | | | | |
| ≤ 12 years | 182 | (43) | 244 | (57) | | 441.1 | | 435.5 | |
| > 12 years | 426 | (66) | 224 | (34) | 0.0001 | 473.8 | 0.0001 | 462.7 | 0.0001 |
| **Child's health rating** | | | | | | | | | |
| Excellent | 326 | (67) | 169 | (34) | | 477.1 | | 465.4 | |
| All other categories | 282 | (49) | 299 | (51) | 0.0001 | 446.9 | 0.0002 | 440.5 | 0.0001 |
| **ELL**[a] | | | | | | | | | |
| Yes | 53 | (66) | 27 | (34) | | 443.0 | | 436.2 | |
| No | 555 | (55) | 441 | (44) | 0.067 | 462.3 | 0.0022 | 453.2 | 0.0003 |
| **Free/reduced price lunch**[a] | | | | | | | | | |
| Yes | 280 | (43) | 366 | (57) | | 442.5 | | 434.8 | |
| No | 328 | (76) | 102 | (24) | 0.0001 | 488.5 | 0.0001 | 477.8 | 0.0001 |

[a] Data provided by Wisconsin Department of Public Instruction. All other covariate data were obtained from parent/guardian survey.

to release their child's 4th grade WKCE to the project staff. Of these students, 1117 (98.6%) had both reading and math WKCE scores available for analysis. Due to small numbers in several racial categories, we restricted analysis to children whose race/ethnicity was reported to be Black, White or Hispanic/Latino. Hispanic/Latino and White were collapsed into one racial category. No respondent reported both Black race and Hispanic/Latino ethnicity on the survey. The total sample for analysis included 1076 students, 95% of the enrolled participants.

The distributions of covariates by lead exposure category along with mean test scores by covariate are presented in Table 1. With regard to exposure, 43% ($n$=468) of children included in the analysis had a record of an elevated BLL before age three. Race, parent completion of high school, parent-rated child health (excellent vs. all other categories), and enrollment in the federal FRLP were all significantly related to exposure status. Over two-thirds of Black children in the sample were classified as lead exposed, while over 75% of White children had no record of an elevated BLL prior to age three.

### 3.1. Reading scores

The mean for the reading portion of the WKCE exam was 460.9 (SD: 54.2), and ranged from 280–604 (possible scores: 280–650) (Fig. 2). All covariates included in the analysis were significantly associated with mean scores for reading. The largest absolute difference in reading scores was for children enrolled in the FRLP compared to children who were not enrolled (46.0 points).

Results from the QR for reading scores are presented in Fig. 3. For each panel, the $x$-axis represents quantiles of the distribution of reading scores, and the $y$-axis represents the effect of that panel's covariate on reading scores for each quantile ($\beta_p$). The intercept panel can be interpreted as the estimate of the conditional quantile function of the WKCE reading scores distribution given all covariates set to zero (i.e. WKCE scores for children classified as not lead exposed, female, White, parents with > high school education, health status rated as other than excellent, English speaker, not in the FRLP) (Koenker and Hallock, 2001a, 2001b). All other panels illustrate the effect of one covariate with all other covariates held constant at the reference level. Using the lead exposed panel as an example, Wald tests indicated that students

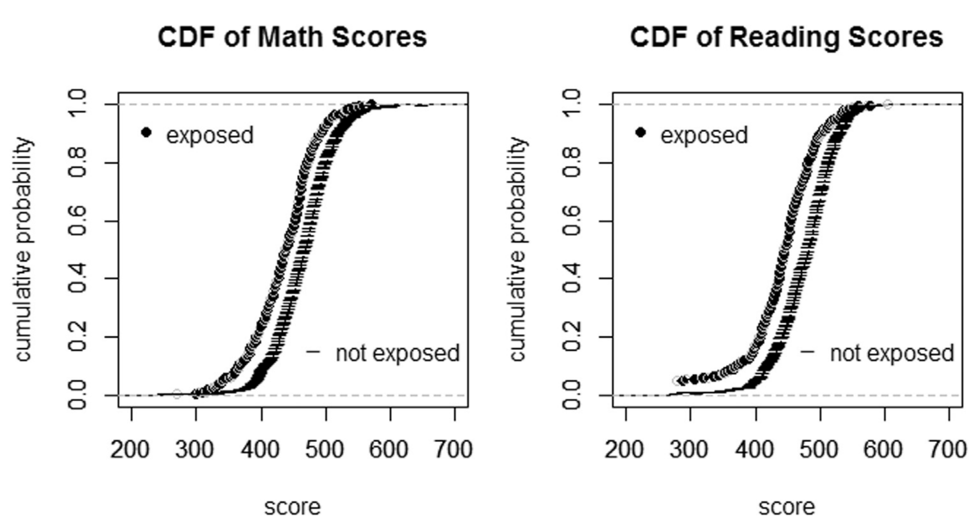


**Fig. 2.** Cumulative distribution functions for WKCE outcomes.

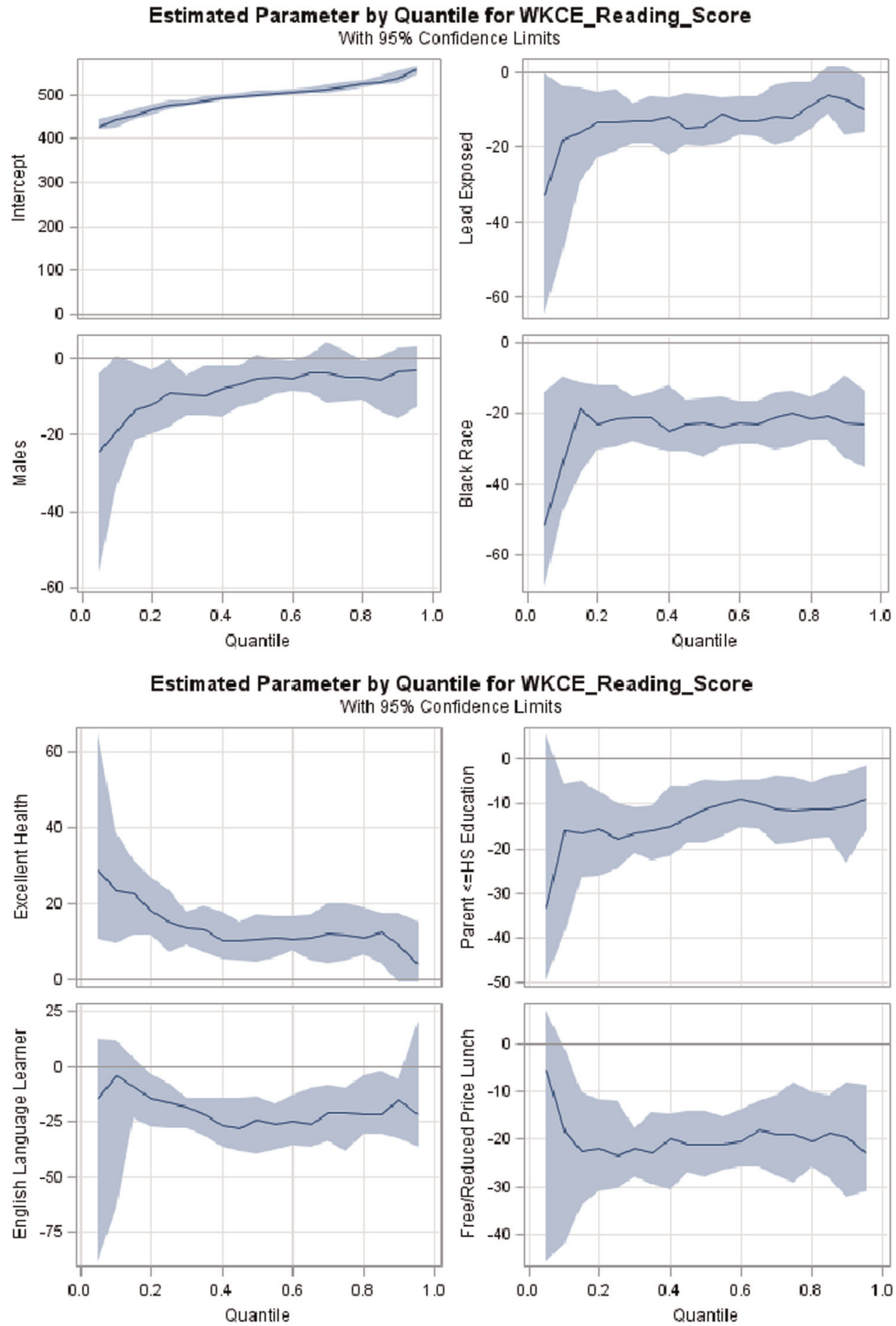


**Fig. 3.** Quantile plots for WKCE reading scores. The *x*-axis represents the location in the distribution (i.e. quantile) of the test scores; the *y*-axis represents the magnitude of the parameter estimates at each point of the outcome distribution for each covariate (holding all other covariates constant), with 0 representing the null value (i.e. no difference between covariate values at a given quantile in the distribution). The relation between the covariate and the outcome across the distribution of the outcome is represented by the black line; gray shaded area indicates 95% confidence interval.

classified as lead exposed had significantly lower scores compared to non-exposed children for each quantile, with the exceptions of the 0.10 quantile ($\chi^2=2.91$, $P=0.09$), the 0.85 quantile ($\chi^2=2.64$, $P=0.10$) and the 0.90 quantile ($\chi^2=2.73$, $P=0.10$). These data are also conveyed graphically in the panel where the upper band of the confidence interval crosses the null value indicator on the *y*-axis ($y=0$). The effect of race was significant at each quantile, while the effect of gender was inconsistent. Wide confidence intervals at the lower quantiles of the distribution for all covariates owe to a relatively large number of outliers at the lower range of the test scores. For example, approximately 6% ($n=28$) of Black students were classified as outliers at the lower tail of the reading score distribution, compared to only one observation as an outlier on that higher tail of the distribution; approximately 2% ($n=13$) of White students were outliers on the lower tail of the distribution, with one outlier on the high end of the distribution. The shapes of the distributions of quantile coefficients do not follow a single pattern for all variables. Instead, the extent to which each

**Table 2**
Effect estimates (95% CI) for ordinary least squares analysis and selected quantiles, WKCE reading scores.

| | OLS | | Quantile | | | | | | *P*-values for test of equality of coefficients across quantiles ($\chi^2$)[a] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\beta$ | 95% CI | 0.1 | 95% CI | 0.5 | 95% CI | 0.9 | 95% CI | Distribution | 0.10 and 0.90 |
| Lead exposed | −13.66 | −19.94, −7.37 | −18.00 | −48.72, −3.32 | −14.50 | −20.72, −5.61 | −7.50 | −15.58, 2.07 | 0.05 | 0.34 |
| Males | −9.56 | −15.04, −4.08 | −19.00 | −34.46, 0.20 | −5.50 | −11.85, 0.09 | −3.50 | −15.13, 2.42 | 0.64 | 0.07 |
| Black | −24.57 | −31.38, −17.76 | −33.50 | −47.62, −9.27 | −22.50 | −35.37, −16.56 | −22.50 | −32.61, −9.23 | 0.02 | 0.37 |
| Parent <HS ed | −14.45 | −20.48, −8.42 | −16.00 | −38.97, −5.81 | −11.00 | −19.13, −4.94 | −10.50 | −22.41, −2.56 | 0.27 | 0.63 |
| Excellent health | 15.22 | 9.52, 20.93 | 23.50 | 10.44, 39.47 | 10.50 | 4.75, 14.79 | 9.00 | 0.02, 17.39 | 0.37 | 0.10 |
| ELL | −20.09 | −31.38, −8.75 | −4.50 | −64.40, 11.40 | −24.50 | −36.34, −13.88 | −15.50 | −33.00, −6.09 | 0.50 | 0.46 |
| Free/reduced price lunch | −20.49 | −27.24, −13.75 | −18.50 | −35.24, −3.16 | −21.00 | −29.21, −14.34 | −19.50 | −32.19, −8.09 | 0.45 | 0.91 |

Effect estimates indicate points scored on the WKCE.

[a] Degrees of freedom for $\chi^2$ : distribution=18, comparison of tails=2.

covariate's effect varies over the distribution of reading scores depend on the specific covariate. However, all covariates had distinctly steeper slopes at the lower tails of the distribution than at the higher tails.

Table 2 presents parameter estimates and 95% confidence intervals for reading scores from the OLS regression, and from the QR at two quantiles: 0.10 and 0.90. In the OLS analysis, classification in the lead exposed group was associated with a mean 13.66 point decrease (95% CI: −19.94, −7.37) in reading scores compared to children in the non-exposed group (all other factors held constant). The largest covariate was Black race, which resulted in a mean 24.57 decrease in reading scores (95% CI: −31.38, −17.76) compared to White students. Alternatively, children classified by parents to be in excellent health scored, on average, 15.22 points higher (95% CI: 9.52, 20.93) compared to children in all other health status groups.

For QR, the magnitude of the parameter for lead exposure varied based on the location of the quantile in the distribution. The negative association of lead exposure with reading score was greater in magnitude at the lower tail of the distribution than at the upper tail. For example, for students who scored at the 0.10 quantile of the reading portion of the WKCE lead was associated with an 18.00 point decrease in exam score (95% CI: −48.72, −3.32), while at the 0.90 quantile of reading scores lead exposure was associated with a 7.50 decrease in exam score (95% CI: −15.58, 2.07). The parameter estimate for the 0.5 quantile was −14.50 (95% CI: −20.72, −5.61), which represents the median regression value. In this case, it closely approximates the OLS regression estimate, which represents the mean regression value. Tests for equality of coefficients across quantiles (i.e. heteroscedasticity) demonstrated significant differences for the effect of lead exposure across the entire distribution of reading scores ($\chi^2$=29.16, $P$=0.05), but did not show significant pairwise differences from the 0.10 quantile to the 0.90 quantile.

Black race was associated with a 33.50 point lower reading score at the 0.1 quantile (95% CI: −47.62, −9.27), an effect that was similar across the 0.5 and 0.9 quantiles. Race showed significant heteroscedasticity across the entire distribution of quantiles ($\chi^2$=32.47, $p$=0.02), but a significant pairwise difference was not found between the 0.10 quantile and the 0.90 quantile. Designation as an English Language Learner was associated with a 24.00 point lower reading score at the 0.50 quantile (95% CI: −36.34, −13.88), but only a 4.5 point lower score at the 0.10 quantile. For students who were classified as being in excellent health, both the OLS and the QR showed a strong positive effect on test scores. However, in the QR analysis the magnitude of the parameter was attenuated somewhat as the quantile of reading score increased. At the 0.10 quantile, excellent health was associated with a 23.50 point increase in reading scores (95% CI: 10.44, 39.47); at the 0.9 quantile it was associated with a 9.00 increase in reading scores (95% CI: 0.36, 17.76). However, heteroscedasticity in the effect of excellent health was not significant.

Of the five interaction terms tested, three terms were significantly associated with reading scores at several quantiles (Fig. 4). Values associated with these figures can be found in Table 3. For example, considering the interaction between lead exposure and parent education, at the 0.10 quantile, children exposed to lead and a parent with less than a high school education scored 47.00 points lower (95% CI: −91.46, −8.78) on the exam compared to students for whom only one of those covariates was true. For the interaction of participation in the free/reduced price lunch program × lead exposure, the 95% confidence interval of the OLS estimate included zero (−14.85, 95% CI: −27.29, 2.41). However, at the 0.90 quantile, children exposed to lead and enrolled in the FRLP scored 21.00 points lower (95% CI: −42.15, −12.92) compared to either children not enrolled in the FRLP, or children not exposed to lead. For the parent education X lead exposure interaction, the OLS estimate of −9.91 (95% CI: −1.62, 21.45) obscures the magnitude and direction of the effect at all points in the distribution of reading scores. QR reveals a much larger effect of −47.00 in the lower tail (95% CI: −91.46, −8.78), but no interaction effect at points higher in the distribution. The 95% confidence intervals of interaction terms for gender × lead exposure and race × lead exposure included zero in the OLS analysis, and all quantiles specified in the QR.

### 3.2. Math scores

The mean math score on the WKCE was 451.9 (SD: 24.0) and ranged from 280–650 (Fig. 2.) All covariates were significantly associated with math mean test score with the exception of gender. The largest absolute difference in math scores was by racial designation (40.2 points).

Fig. 5 shows the QR results for the WKCE math scores by covariate, with all other covariates held constant. Effect estimates for math using OLS and QR for select quantiles are presented in Table 4, similar to the presentation in Table 2 for reading. In the OLS analysis for math, lead exposure, conditional on all other covariates in the model, was significantly related to a nine point decrease in test score (95% CI: −14.84, −3.05). In the QR analysis,

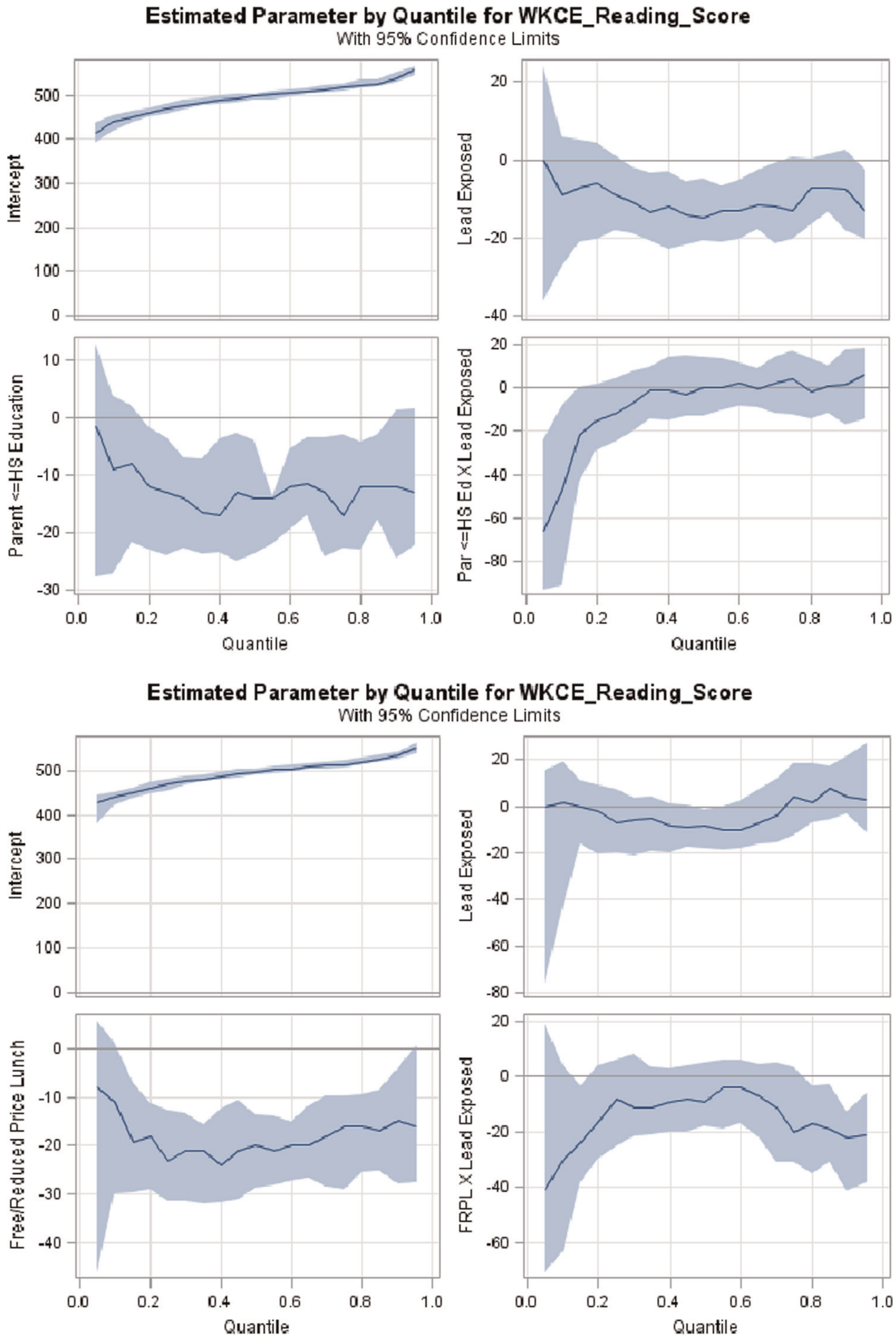


**Fig. 4.** Quantile plots for interaction terms, WKCE reading scores.

the effect of lead exposure on math scores followed a similar pattern to that of the reading scores, with a larger effect at the 0.10 quantile ($\beta = 17.00$, 95% CI: 32.12, $-3.27$) compared to the 0.90 quantile ($\beta = -4.50$, 95% CI: $-10.55$, 4.50). The Wald test indicated that these two coefficients were significantly different as shown in Table 4, although overall heteroscedasticity was not. Lower scores were associated with Black race throughout the distribution of scores, though the effect of race was attenuated at higher quantiles of the distribution. As observed with reading scores, both QR and OLS showed a robust positive effect of excellent health on math scores, and in the QR analysis the coefficients did not show heterogeneity. No other covariates demonstrated significant differences in coefficients across the quantile distribution, or for the selected set of quantiles compared. None of the five interaction terms tested were significantly associated with math scores, either for OLS or QR (data not shown.)

## 4. Discussion

The analyses presented here yield three major findings. First, we found that early childhood lead exposure has heterogeneous

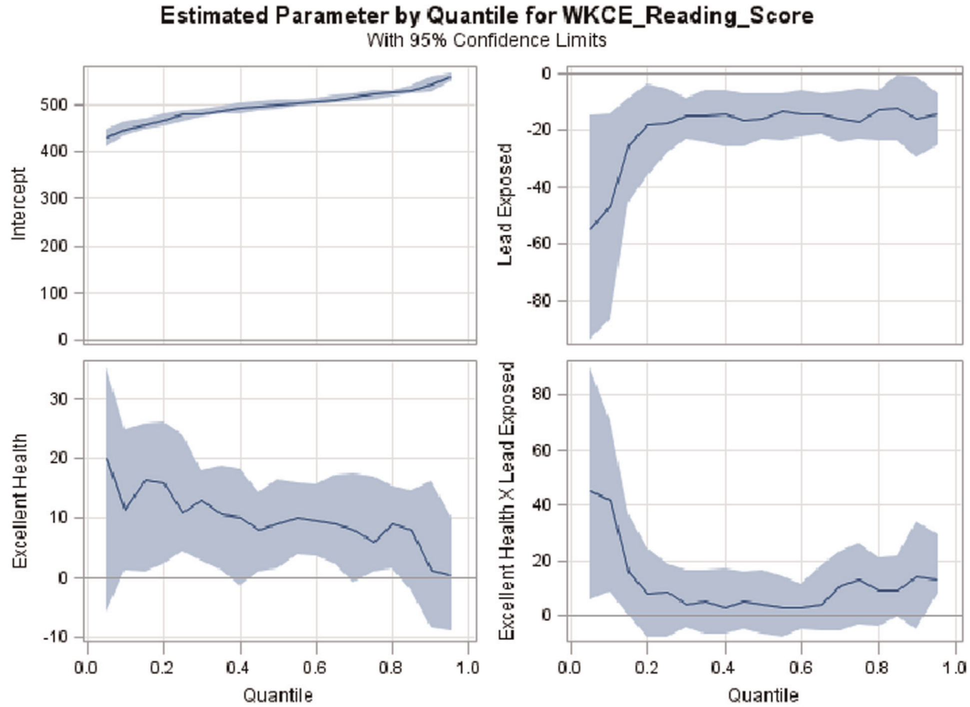


**Fig. 4.** (*continued*)

effects across the distribution of standardized end-of-grade exam scores. Second, the results showed an interaction of lead exposure and parent education such that lead exposure combined with low parental education was strongly associated with reduced reading test scores at lower quantiles, but had little interactive effect on other children. Third, the positive effect on test scores of child excellent health was relatively uniform across quantiles for both reading and math, but interacted with lead exposure at the low quantiles of reading scores. We discuss each of these findings in turn.

First, the quantile regression showed heterogeneity of coefficients for lead exposure such that stronger effects of lead exposure

**Table 3**
Effect estimates (95% CI) for interactions terms and selected quantiles, WKCE reading scores.

| | OLS | | Quantile | | | | | | *P*-values for tests of equality of coefficient (interaction term) ($\chi^2_{df}=18$) |
|---|---|---|---|---|---|---|---|---|---|
| | $\beta$ | 95% CI | 0.1 | 95% CI | 0.5 | 95% CI | 0.9 | 95% CI | |
| **Reading** | | | | | | | | | |
| Lead exposure | −9.42 | −17.40, −1.44 | −9.00 | −27.36, 5.91 | −15.00 | −20.93, −4.78 | −7.50 | −18.05, 2.42 | |
| Parent <HS ed | −9.54 | −17.84, −1.25 | −9.00 | −27.28, 3.69 | −14.00 | −24.69, −4.87 | −12.00 | −24.21, 1.39 | |
| Interaction | −9.91 | −1.62, 21.45 | **−47.00** | **−91.46, −8.78** | 0.00 | −11.81, 12.11 | 1.50 | −17.27, 17.16 | 0.04 |
| Lead exposure | −3.80 | −6.56, 14.17 | 2.00 | −25.17, 19.14 | −8.00 | −17.95, 0.21 | 3.00 | −3.37, 21.84 | |
| Free/reduced price lunch | −15.39 | −23.36, 7.42 | −11.00 | −31.20, 1.17 | −20.00 | −28.59, −16.24 | −15.00 | −27.80, −3.87 | |
| Interaction | −14.85 | −27.29, −2.41 | −30.00 | −63.50, 4.61 | −9.00 | −18.01, 5.02 | **−21.00** | **−42.15, −12.92** | 0.45 |
| Lead exposure | −10.46 | −18.86, −2.05 | −13.50 | −33.53, 5.77 | −15.00 | −21.09, −1.04 | −4.33 | −19.40, 5.12 | |
| Males | −6.84 | −14.09, 0.40 | −13.50 | −27.78, 7.32 | −5.00 | −13.76, 0.83 | 0.00 | −15.18, 8.96 | |
| Interaction | −6.31 | −17.32, 4.70 | −29.50 | −80.84, 12.51 | −0.00 | −13.68, 11.84 | −4.67 | −17.92, 11.88 | 0.34 |
| Lead exposure | −11.21 | −19.88, −2.53 | −13.00 | −49.54, 1.94 | −12.00 | −22.53, −1.40 | −2.00 | −12.08, 10.62 | |
| Black race | −22.28 | −31.09, −13.49 | −23.00 | −45.51, −3.17 | −22.00 | −32.91, −14.10 | −15.50 | −30.30, 2.03 | |
| Interaction | −5.03 | −17.29, 7.23 | −19.00 | −47.18, 11.86 | −3.00 | −17.49, 11.92 | −15.00 | −26.88, 5.94 | 0.78 |
| Lead exposure | −19.25 | −27.18, −11.30 | −46.50 | −86.63, −14.38 | −16.00 | −22.85, −7.02 | −15.66 | −29.47, −1.01 | |
| Excellent health | 9.79 | 2.40, −17.20 | 11.50 | 1.26, 24.74 | 9.00 | 1.41, 16.27 | 1.33 | −8.44, 16.08 | |
| Interaction | 12.92 | 1.65, 24.20 | **41.50** | **8.77, 70.34** | 4.00 | −6.46, 16.34 | 14.33 | −5.14, 34.11 | 0.34 |

Effect estimates indicate points scored on the WKCE. Interactions were tested in separate models, which included all main effect terms and the single interaction term being tested.

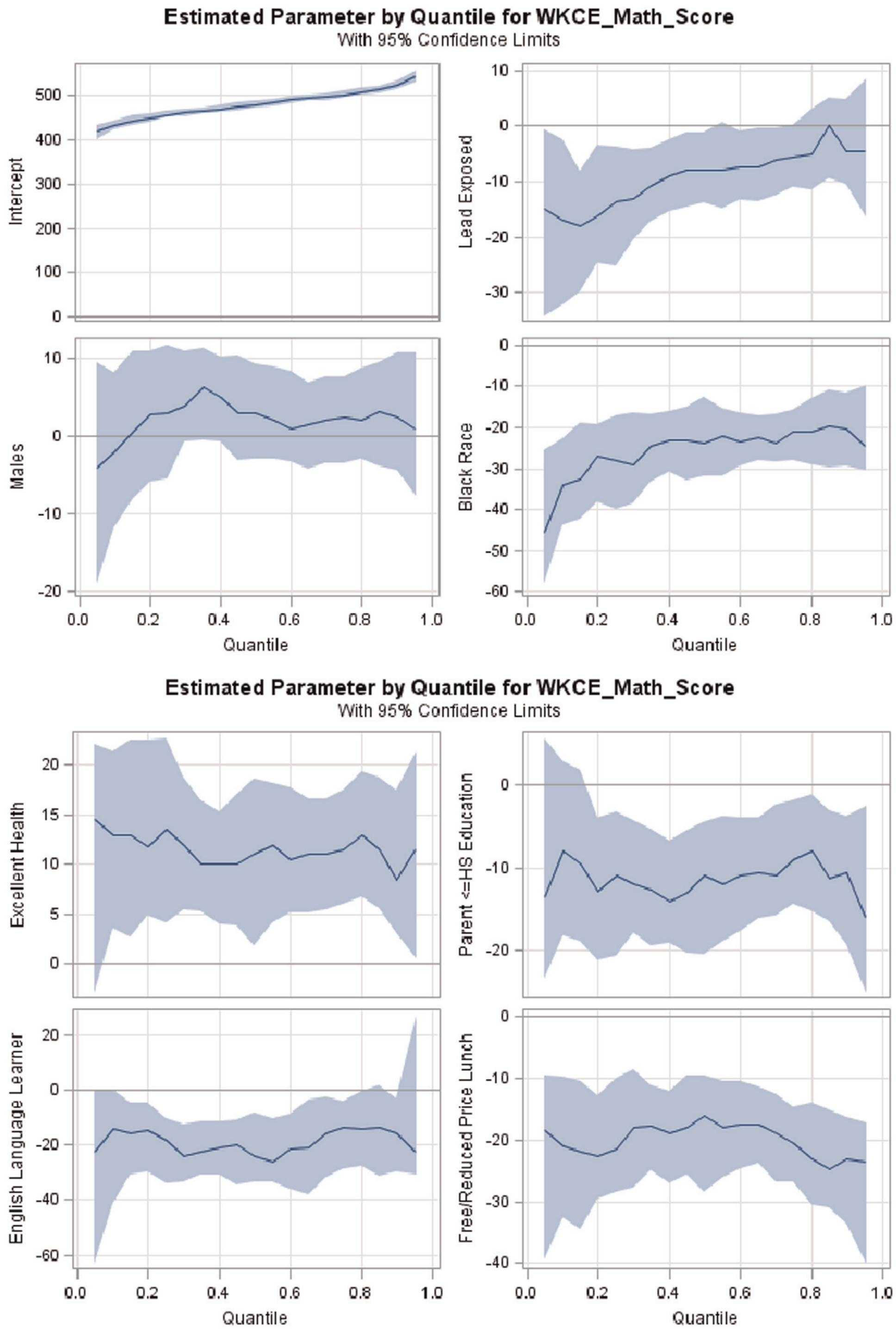


**Fig. 5.** Quantile plots for WKCE math scores.

were observed at the lower quantiles of performance. The shape of the coefficient distribution across reading and math is similar. The Wald tests showed overall heterogeneity of coefficients for reading, while for math there was a significantly stronger negative effect of lead exposure at the 10th quantile than at the 90th quantile. Though lead exposure has been consistently related to cognitive functioning as measured by IQ tests (Bellinger et al., 1992; Canfield et al., 2003; Lanphear et al., 2005; Surkan et al., 2007; Jusko et al., 2008), and more recently as measured by standardized school achievement scores (Miranda et al., 2007, 2009; Zahran et al., 2009; Zhang et al., 2013), the present study adds to the literature by demonstrating that lead exposure has stronger effects for children who perform in the lower quantiles compared to the upper quantiles, after including a robust set of covariates in the model. This finding is not evident in the OLS, but it is consistent with other literature showing that children with poor academic performance are likely to have multiple life risks, and therefore are also likely to be more sensitive to an additional risk such as lead exposure (Sameroff et al., 1987).

Second, the QR showed a lead exposure $\times$ parent education interaction in the lower quantiles of the reading scores. Children with both lead exposure and parent education less than high school showed a deficit of $-47.00$ at the 0.10 quantile, compared to children with one or none of those characteristics. This

**Table 4**
Effect estimates (95% CI) for ordinary least squares analysis and selected quantiles, WKCE math scores.

| | OLS | | Quantile | | | | | | *P*-values for tests of equality of coefficients across quantiles ($\chi^2$)[a] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $\beta$ | 95% CI | 0.1 | 95% CI | 0.5 | 95% CI | 0.9 | 95% CI | Distribution | 0.10 and 0.90 |
| Lead exposed | −8.94 | −14.84, −3.05 | −17.00 | −32.13, −3.27 | −8.00 | −15.24, −0.36 | −4.50 | −10.55, 4.50 | 0.46 | 0.05 |
| Males | 2.05 | −3.09, 7.19 | −2.00 | −11.34, 7.38 | 3.00 | 0.25, 9.30 | 2.50 | −5.86, 12.39 | 0.91 | 0.43 |
| Black | −26.29 | −32.68, −19.90 | −34.00 | −44.00, −21.63 | −24.00 | −32.64, −12.32 | −20.50 | −29.27, −11.44 | 0.27 | 0.05 |
| Parent <HS ed | −11.31 | −16.95, −5.66 | −8.00 | −17.69, 2.63 | −11.00 | −20.44, −3.25 | −10.50 | −20.70, −3.29 | 0.43 | 0.68 |
| Excellent health | 12.01 | 6.66, 17.35 | 13.00 | 3.57, 21.73 | 11.00 | 3.02, 18.60 | 8.50 | 3.08, 17.66 | 0.96 | 0.44 |
| ELL | −18.83 | −29.41, −8.26 | −14.00 | −41.85, −0.70 | −24.00 | −33.82, −7.61 | −15.50 | −29.66, −2.21 | 0.43 | 0.92 |
| Free/reduced price lunch | −20.28 | −26.81, −14.16 | −21.00 | −32.62, −9.34 | −16.00 | −27.74, −9.40 | −23.00 | −32.94, −15.87 | 0.87 | 0.77 |

Effect estimates indicate points scored on the WKCE.

[a] Degrees of freedom for $\chi^2$ : distribution=18, comparisons of tails=2.

interaction was not evident at other quantiles, nor in the OLS analysis. This finding is consistent with previous literature which has observed that children at 'social disadvantage' show stronger effects of lead exposure (Winneke and Kraemer, 1984).

Third, a new finding here is the protective effect of "parent rated excellent health" in both the OLS and the QR analyses, and an interaction of health status × lead exposure at the 0.10 quantile. Our search of the literature revealed little on the association of general child health with school outcomes, beyond literature on children with specific disabilities or special health care needs. In a representative nationwide sample of children without special health care needs, 13% were rated by their parents as in less than optimal health; those children also had worse school outcomes on four measures: repeating a school grade, problem reports from school, lack of school engagement, and many missed school days, after adjusting for covariates including child gender, age, race/ethnicity, family structure, household income, and health insurance status during interview, and season of interview (Reuben and Pastor, 2013). While that study did not have an academic performance measure other than repeating a grade, the findings are consistent with those reported here. The interaction of health status × lead exposure in the QR approach of the present study showed that a parent rating of 'excellent health' had an especially protective effect on reading scores for lead exposed children performing at the lower quantiles.

Among all covariates investigated in this study, health status was unique in having a positive relationship with outcomes among this population of children. This unforseen result may be related to the fact that lead can affect both cognitive and immune function differentially when it occurs at different points in development (see Dietert et al. (2004) for a review). Future research should seek to verify this finding, and investigate the mechanism by which "parent rated excellent health" exerts its protective effect.

One previous study (Miranda et al., 2009) has used QR to investigate the association between early childhood lead exposure and performance on 4th grade end-of-grade exams. In a large sample of 4th grade students in North Carolina (>57,000) lead exposure was associated with a larger decrease in reading scores at the lower end of the distribution compared to other quantiles of the distribution, similar to the current results (Miranda et al., 2009). Covariates included in both studies were similar (race, gender, parental education, and enrollment in the federal FRLP). However, while the North Carolina analysis included the effects of FRLP and parental education via quantile regression, race was implemented in OLS but not QR. The CLLEO study demonstrated significant differences in the effect of race across the quantiles of reading scores, as well as a significant difference between the 10th and 90th quantiles of math test scores. Our results show a larger deficit for Black students at the lower quantiles. Because the North Carolina study did not include race in their QR analyses, this effect was not evident. Further, interaction effects were not observed in the North Carolina analysis, while the present study found significant interactions at some quantiles for lead exposure × parental education, lead exposure × parent-rated child health, and lead exposure × participation in the FRLP. The other difference between the two studies is that the parent survey data available through CLLEO provided the opportunity to investigate the effect of child health status, which had a large protective effect as discussed above.

Quantile regression has not yet been widely implemented in the epidemiologic literature, though it has been used for certain topics such as birth weight (Wehby et al., 2009; Verropoulou and Tsimbos, 2013) and childhood obesity (Beyerlein et al., 2008, 2008, 2011; Fenske et al., 2013; Mitchell et al., 2013, Riedel et al., 2013) where extreme values are of primary research interest. For these topics QR has been quite fruitful. For example, in a re-analysis of natality data from the National Center for Health Statistics, Koenker and Hallock (2001a, 2001b) demonstrated that Black children in the 5th quantile of birth weight weighed approximately one-third kg less compared to White children at the same quantile; the difference was reduced to approximately 160 g at the 95th quantile (Koenker and Hallock, 2001a, 2001b). QR has also been used to investigate the role of environmental exposures (prenatal lead exposure, tobacco exposure, and their interaction) on birthweight, and found significant differences in the interaction term across the distribution from the 10th to 50th quantiles (Burgette et al., 2011).

The analyses of the present study have several limitations. First, the magnitude of the effect estimates from this analysis may not be readily applied to other states because each state in the U.S. develops its own standardized school performance tests. Second, because of the longitudinal prospective nature of the data (lead test before age 3, participants relocated after 4th grade tests), address matching was successful for 61% of the targeted sample, and the response rate to the mailed survey was approximately 25%. In addition to the relatively low prevalence of early childhood blood lead testing (Wisconsin Department of Health and Family Services, 2008), results may not be generalizable to a larger population. However, earlier studies demonstrated good agreement between effect estimates derived using administrative data provided by the Milwaukee Public Schools and the survey data collected directly from parents (Magzamen et al., 2013). Third, though recent lead exposure studies have sought to demonstrate the deleterious effects of lead below the 1991 CDC threshold (Lanphear et al., 2005, Miranda et al., 2007, 2009), our exposure groups were defined specifically to address a population who, at study conception, were designated with elevated exposure status, but were not guaranteed access to remediation resources or lead exposure education because of a gap in policy. Our exposure definition precludes extrapolation of our study to lead exposures at or below the current CDC reference value elevated exposure ($\geq 5$ μg/dL). Finally, given the size of the study sample, the number of covariates and quantiles included in the model may have resulted in wide confidence intervals that contributed to the limited number of significant differences. Specifically, the data-driven approach to covariate selection and dichotomization of parental education and parent-rated child health) suggest that the present findings should be interpreted cautiously.

Despite these limitations, the present study demonstrates the utility of quantile regression in epidemiology for revealing important effects that are missed by OLS. Complicated forms of heterogeneous response distributions should be expected in observational studies where OLS is unlikely to capture or adequately measure all important covariates (Cade and Noon, 2003). This issue is not unique to lead exposure and school outcomes, but extends to many areas of epidemiology. Furthermore, where exposure variables may affect the slope and variance of an outcome variable, understanding those relationships can have important implications for clinical and public health policy. In the present study, our data point to the important conclusion that the most vulnerable children, those performing at lowest quantiles, are likely to suffer the most from lead exposure and the combined risks of lead and poverty indicators.

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## Human subjects Institutional Review Board

The protocol for this study was approved by the University of Wisconsin–Madison Education Research Institutional Review Board.

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