

Are Residents of Mountain-Top Mining Counties More Likely to Have Infants with Birth Defects? The West Virginia Experience

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Background: Pooled 1996 to 2003 birth certificate data for four central states in Appalachia indicated higher rates of infants with birth defects born to residents of counties with mountain-top mining (MTM) than born to residents of non-mining-counties (Ahern 2011). However, those analyses did not consider sources of uncertainty such as unbalanced distributions or quality of data. Quality issues have been a continuing problem with birth certificate analyses. We used 1990 to 2009 live birth certificate data for West Virginia to reassess this hypothesis. **Methods:** Forty-four hospitals contributed 98% of the MTM-county births and 95% of the non-mining-county births, of which six had more than 1000 births from both MTM and nonmining counties. Adjusted and stratified prevalence rate ratios (PRRs) were computed both by using Poisson regression and Mantel-Haenszel analysis. **Results:** Unbalanced distribution of hospital births was observed by mining groups. The prevalence rate of infants with reported birth defects, higher in MTM-counties (0.021) than in non-mining-counties (0.015), yielded a significant crude PRR (cPDR = 1.43; 95% confidence interval [CI] = 1.36–1.52) but a nonsignificant

hospital-adjusted PRR (adjPDR = 1.08; 95% CI = 0.97–1.20; $p = 0.16$) for the 44 hospitals. So did the six hospital data analysis ([cPDR = 2.39; 95% CI = 2.15–2.65] and [adjPDR = 1.01; 95% CI, 0.89–1.14; $p = 0.87$]).

Conclusion: No increased risk of birth defects was observed for births from MTM-counties after adjustment for, or stratification by, hospital of birth. These results have consistently demonstrated that the reported association between birth defect rates and MTM coal mining was a consequence of data heterogeneity. The data do not demonstrate evidence of a “Mountain-top Mining” effect on the prevalence of infants with reported birth defects in WV.

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Introduction

Birth defects are a leading threat to infant health in the United States. Every year birth defects affect approximately 130,000 newborns (NCBDDD, 2011) and account for 20% of infant deaths (Martin et al., 2005). The epidemiology of

birth defects is an evolving field that extends from dysmorphology, embryology, and pathology through to genetic susceptibility (Koury 1989). As Koury notes, “despite continuing inquiries into causes of human birth defects, the list of definite human teratogens remains short.”

Although the causes of most birth defect cases are unknown, identified causes of birth defects include chromosomal abnormalities (e.g., Down syndrome [Antonarakis et al., 2004]), genetic differences (e.g., Tay-Sachs disease [Myerowitz, 1997]), social exposures (e.g., alcohol [Warren and Foudin, 2001]), smoking (Hackshaw et al., 2011), specific medications (e.g., thalidomide [Rodin et al., 1962]), maternal diseases (e.g., diabetes mellitus [Correa et al., 2008]), micro-nutrient deficiencies (e.g., folic acid [Green, 2002]), environmental pollutants (e.g., methyl mercury [Choi et al., 1978; Hamada et al., 1993]), and occupational exposures (e.g., organic solvents [Gilboa et al., 2012]). A number of investigations have explored air pollution and water pollution as causes (Koren, 1994; Vrijheid et al., 2011).

We have been interested in whether birth defect data on birth certificates can reasonably be analyzed in environmental and occupational epidemiological research for 35 years (Lamm, 1979). Early concerns on the completeness and accuracy of reported information (e.g., observer bias [different reporters with no set criteria], nonconfirmed diagnoses, space limitations, and incomplete information) were already raised on the pre-1973 form (Mackeprang et al., 1972). While the section has

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undergone considerable revision in newly revised versions of the U.S. live birth certificate, these issues remain. Birth defects in stillbirths would not be recorded in this dataset.

Recently, Ahern et al. (2011) published an analysis of birth defect (congenital anomaly) data on the 1996 to 2003 live birth certificates for the four-state central Appalachian area (Kentucky, Tennessee, Virginia, and West Virginia) from which they concluded that residence in counties with mountain-top coal mining (MTM) activities was associated with an increased risk of infants with reported birth defects. MTM mining is believed to be hazardous to surface water, groundwater, and local air quality (Ghose, 2007; Palmer et al., 2010); however, neither the specific pollutants nor the route of administration have been demonstrated whereby MTM mining might be an independent risk factor for increased adverse health outcomes in the Appalachian area. By comparing to area residents of counties with no mining activity, Ahern et al. found significant increased crude prevalence rate ratios ($cPRR = 1.63$; 95% confidence interval [CI] = 1.54, 1.72) and adjusted PRRs ($adjPRR = 1.26$; 95% CI = 1.21, 1.32) for infants with birth defects for residents of counties with mountaintop mining activities.

We (Li et al., 2013) have previously published an analysis of the 1990 to 2009 live birth certificate data for the state of West Virginia, one of the four central Appalachian states, in which we found that reported rates of birth defects (congenital anomalies) varied markedly by hospital even within the same area. We choose now to examine the Ahern hypothesis using the West Virginia data and to assess the degree to which variation in reporting rates by specific hospitals may have affected the magnitude of the association they presented.

We had chosen to analyze the single-state data from West Virginia rather than the pooled data of the four central Appalachian states as Ahern et al. (2011) did for several data distribution reasons. The proportions of births to residents of MTM counties differed significantly across these four states—West Virginia (38%), Kentucky (9%), Tennessee (2%), and Virginia (1%). Similarly, the proportions of births to residents of nonmining counties varied markedly—West Virginia (34%), Kentucky (76%), Virginia (96%), and Tennessee (98%). As a result, the four-state analyses were more specifically a risk comparison between the MTM-mining counties of Kentucky and West Virginia and the nonmining counties of Tennessee and Virginia. The remaining births were to resident of counties with coal mining activities but not mountaintop mining.

West Virginia provided the most balanced distribution of counties, that is, 23 of the 55 West Virginia counties had been classified by Ahern et al. (2011) as having no mining activity, 18 as having only non-mountain-top coal mining activity (i.e., only underground mining), and 14 as having mountain-top coal mining (MTM) activity (i.e., also surface mining). West Virginia provided a similar number of counties and of live births for MTM counties and non-

mining counties. Therefore, we chose to conduct a within-state analysis (i.e., West Virginia) rather than a multi-state (i.e., Kentucky, Tennessee, Virginia, and West Virginia) analysis for testing the hypothesis presented in the study by Ahern et al.

We hypothesize that hospital of birth may bias the estimation and comparison of prevalence rates for birth defects by mining groups. We shall assess whether the prevalence rates for birth defects are explained by county of maternal residency (MTM or nonmining) or by hospital of birth. This gives us an opportunity to demonstrate how data quality issues, such as unbalanced distribution of live births among hospitals and observer bias, may be handled to bring clarity to findings and conclusions.

Material and Methods

We received the electronic birth certificate file of live births to residents of West Virginia during 1990 to 2009 from the West Virginia Department of Health in 2012. Of the 418,385 live birth certificates, birth defects (i.e., congenital anomalies) were reported for 7597 infants, for a prevalence rate of 0.018 (1.8%). The birth certificate file from the state, as opposed to that from the National Center for Health Statistics (NCHS), had the advantage of including the hospital of birth. Ahern used data from NCHS, while we used data from the state health department. The 1989 version of the U.S. birth certificate had been used throughout these two decades. The birth certificate has two parts of information. The first part asks about parental and infant background information, such as name, date of birth, place of birth, residence, ethnicity, and so on. The second part contains pregnancy-related questions, for example, prenatal care, pregnancy complications, obstetric procedures, etc. The last section on congenital anomalies collects birth defect information of child, which was the focus of this study. This section of the birth certificate is designed to have infants coded for either the presence or absence of any birth defect and then further for the presence of birth defects as either specified or non-specified ("other") by organ system.

The birth certificate uses the term "congenital anomalies of the child" and allows for recording of both specified and unspecified ("other") congenital anomalies. The term "congenital anomaly" is equivalent to the term "birth defect" and is used interchangeably (WHO, 2014). The specified birth defects on the birth certificate form are anencephaly, spina bifida/meningocele, hydrocephalus, microcephalus, heart malformations, rectal atresia/stenosis, tracheo-esophageal fistula/esophageal atresia, omphalocele/gastroschisis, malformed genitalia, renal agenesis, cleft lip/palate, polydactyly/syndactyly/adactyly, club foot, diaphragmatic hernia, and Down syndrome. The other or nonspecific birth defect categories are cited as other central nervous system, other circulatory/respiratory, other gastrointestinal, other

urogenital, other musculoskeletal/integumental, other chromosomal, and other.

The primary reported analysis of Ahern et al. (2011) was based on the proportion of live births for which any birth defect (congenital anomaly) was reported. Ahern further analyzed birth defect reports by organ system and for each of the specified birth defect and the unspecified "others." We and Ahern used the same birth defect entries, although we present 20 years (1990–2009) of experience and Ahern presented eight years (1996–2003). We here limit our analyses to the presence or absence of any birth defect or congenital anomaly, as we previously noticed marked misclassification of birth defects within the section on congenital anomalies. Thus, our analyses are of infants with birth defects rather than of the number of reported birth defects. Infants with more than one reported birth defect or congenital anomaly are reported only once. This is an analysis of the frequency of infants with reported birth defects or congenital anomaly rather than of the frequency of specific malformations.

Ahern et al. (2011) had classified counties as to whether they had MTM-mining activities, non-MTM-mining activities, or no mining activities. Individual records also included hospital of birth and maternal county of residence. We compared the birth defect rates of infants born with women who reside in counties with MTM-mining activities and women who reside in counties with no mining activities using in our analyses the Ahern classification.

The place of birth information was aggregated into 319 birth locations. Most were individual hospitals, although some were groups of hospitals, birthing centers, out-of-hospital births, or unspecified. Births to West Virginia residents were reported from 45 states and five foreign countries. Analyses were presented for all 319 birth locations, for the 44 hospitals with the most (greater than 1000) live births to West Virginia residents, and for the six hospitals that had at least 1000 live births from residents of MTM-mining counties in West Virginia and at least 1000 live births from residents of nonmining counties in West Virginia. The live birth count for each location was limited to births to residents of West Virginia, excluding births to nonresidents of West Virginia.

Analytic metrics were both prevalence rates (number of live born infants with birth defects divided by number of live born infants) for MTM and nonmining counties and their PRRs (prevalence rate for women resident in MTM-mining counties divided by prevalence rate for women resident in nonmining counties).

STATISTICAL ANALYSIS

Prevalence rates and PRRs were calculated for groups of hospitals. Rates for hospitals with many live births during the 20-year period 1990 to 2009 (at least 1000) were compared with those for hospitals with few births. Poisson regression analysis was conducted on the counts of live

births and the counts of live births with birth defects for each of the 44 hospitals and each of the two mining groups of maternal residency. Poisson regression models were fitted to examine the magnitude of the hospital effect and mining group effect on the birth defect rates. PRRs were calculated and described both adjusted for hospital and unadjusted.

Mining group-specific prevalence rates and PRRs were calculated for each of the six hospitals that had at least 1000 live births in each of the two mining groups and for all six hospitals combined and graphed. Averages for the six hospitals were calculated using arithmetic mean for counts and geometric means for rates where distributions were nonnormal. The numbers of live births for residents of each of the two mining groups were compared for each of the six hospitals. Mantel-Haenszel (M-H) analysis of the counts for the six hospitals was conducted to yield a stratified M-H adjPRR. The result was compared with the summary cPRR from the M-H analysis and the adjPRR from the Poisson analysis.

Calculations were made using Microsoft Excel. Statistical tests were performed using STATA (SE11) or OpenEpi. Statistical significance for the parameter coefficients was set as a two-tailed condition with $p < 0.05$. Mid- p values were used when generated; otherwise M-H summary chi-square p values were used.

Results

BIRTH DEFECT RATES BY MINING GROUP

The 1990 to 2009 West Virginia live birth registry contained birth certificate information for 294,985 live births to residents of either MTM-mining or nonmining counties in West Virginia. Birth defects (i.e., congenital anomalies) were reported for 5374 infants for a prevalence rate of 0.018 (1.8%). Ninety-one percent of the births to residents of West Virginia occurred within the state of West Virginia, 9% occurred in the neighboring states (Virginia, Maryland, Ohio, Kentucky, and Pennsylvania), and 0.1% occurred in an additional 39 states and five foreign countries. Births were initially identified by the county of maternal residence and by the hospital of birth. Births were subsequently aggregated for analysis into births to residents of the 14 West Virginia counties having mountain-top coal mining activity (MTM) and births to residents of the 23 West Virginia counties having no mining activities, as classified by Ahern et al. (2011).

The births to residents of MTM-mining counties numbered 155,382, and the births to residents of nonmining counties numbered 139,603. Birth defects were reported for 3297 of the births from the MTM-mining counties for a prevalence of 0.021 (2.1%) and for 2077 of the births from the nonmining counties for a prevalence of 0.015 (1.5%). The rates for the two groups of counties were significantly different with a significant PRR of 1.43 (95% CI = 1.36–1.52; $p < 0.001$) (Table 1).

TABLE 1. 1990–2009 Births, Birth Defects, Prevalence Rates, and Prevalence Rate Ratios (Unadjusted and Hospital-Adjusted) for West Virginia Residents of MTM-mining and Nonmining Counties

Hospitals	MTM-mining live births	MTM-mining with birth defect	Prevalence in MTM-mining	Nonmining live births	Nonmining with birth defect	Prevalence in nonmining	Crude PRR	95% CI	p-value	Adjusted PRR	95% CI	p-value
All sites	155,382	3,297	0.021	139,603	2,077	0.015	1.43	(1.36-1.52)	<0.001	[Non-convergent]		
44 Hosps ^c	152,540	3,235	0.021	132,732	1,972	0.015	1.43	(1.35-1.51)	<0.001	1.08 ^a (0.97-1.20)	0.16	
6 Hosps ^d	119,058	2,768	0.023	41,918	408	0.010	2.39	(2.15-2.65)	<0.001	1.01 ^b (0.89-1.14)	0.87	
Hosp 04	53,595	211	0.004	11,900	68	0.006	0.69	(0.52-0.90)	0.01			
Hosp 07	2,366	26	0.011	5,460	67	0.012	0.90	(0.57-1.41)	0.64			
Hosp 14	10,529	128	0.012	2,353	26	0.011	1.10	(0.72-1.67)	0.67			
Hosp 21	8,431	125	0.015	1,259	17	0.014	1.10	(0.66-1.82)	0.73			
Hosp 22	31,039	2,155	0.069	1,137	71	0.062	1.11	(0.88-1.40)	0.36			
Hosp 26	13,098 	123	0.009	19,809	159	0.008	1.17	(0.93-1.48)	0.19			

Mountain-top mining (MTM) mining / Non-mining.

^aPoisson regression.

^bMantel-Haenszel analysis.

^cHospitals with greater than 1,000 live births in MTM-mining and Non-mining counties, combined

^dHospitals with greater than 1,000 live births in MTM-mining and Non-mining counties, separately

The locations of birth were aggregated as 319 locations, which included hospitals, birthing centers, and out-of-hospital births. This included births in West Virginia, births in neighboring states, and births elsewhere. Most locations reported few births, with 275 having fewer than 1000 births to West Virginia residents over the 20-year period (i.e., < 50 births per year). The Poisson regression analysis by hospital of birth did not converge.

UNADJUSTED AND ADJUSTED PRRS IN SUB-SAMPLE OF HOSPITALS
 Analysis was then performed using the data from the 44 hospitals that had more than 1000 live births to West Virginia residents during the 20-year period which provided stability to their prevalence rates (Table 1). The 44 hospitals accounted for 98% of all infants born to a resident of the MTM-mining counties in West Virginia (152,540/155,382) and 98% of those born with birth defects (3235/3297). The 44 hospitals accounted for 95% of all infants who were born to residents of the nonmining counties in West Virginia (132,732/139,603) and 95% of those born with birth defects (1972/2077). Of the 152,540 born to residents of the MTM-mining counties of West Virginia, birth defects were recorded for 3235, or 2.1%, for a prevalence of 0.021. Of the 132,732 born to residents of the nonmining counties of West Virginia, birth defects were recorded for 1972, or 1.8%, for a prevalence of 0.015.

The birth defect prevalence rates for residents of MTM-mining counties were compared with those for residents of nonmining counties as PRRs using both unadjusted and hospital-adjusted Poisson regression analysis.

The model converged when based on the data for the 44 hospitals. Both the cPRR and the adjPRR are shown in Table 1.

The unadjusted Poisson analysis demonstrated a significantly ($p < 0.001$) higher birth defect prevalence rate among residents of MTM-mining counties than among residents of nonmining counties with a cPRR of 1.43 (95% CI, 1.35-1.51). However, when the Poisson analysis was adjusted for hospital, the adjPRR was no longer statistically significant ($p = 0.16$) with the adjPRR of 1.08 (95% CI, 0.97-1.20). Adjustment by hospital alone had accounted for more than 80% of the excess rate seen in the unadjusted analysis.

The Poisson regression analysis has demonstrated hospital of birth to be a bias in the analysis of birth defect prevalence by mining group of residence. The absence of hospital of birth as a co-variate had biased the association metric. While this conclusion may be globally true for births aggregated into the two sets of counties (i.e., ecological analysis), it does not necessarily follow that the same is true within individual hospitals, (i.e., in a within-hospital analysis).

HOSPITAL-SPECIFIC BIRTH DEFECT RATES BY MINING GROUP

To assess the comparison of birth defect prevalence rates within hospitals and across mining groups, we sought those hospitals that had at least 1000 live births from both the residents of the MTM-mining counties and the nonmining counties. Six West Virginia hospitals met the criteria of having at least 1000 live births from residents of the MTM-mining counties and as well as at least 1000 live births from

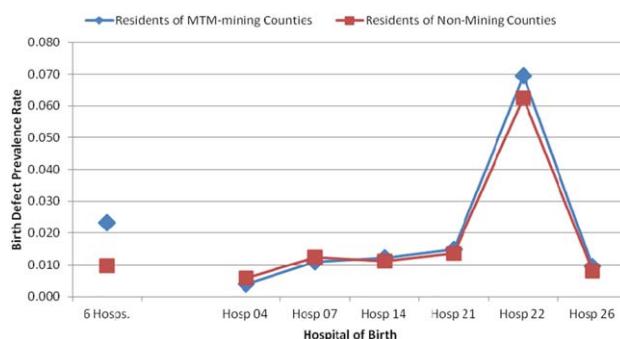


FIGURE 1. Comparison of birth defect rates by maternal residence in mountain-top mining and nonmining counties for hospitals with ≥ 1000 live births in each group (WV, 1990–2009).

residents of the nonmining counties (Table 1). These six hospitals accounted for 77% of the live births from residents of the MTM-mining counties ($119,058/155,382 = 77\%$) and 30% of the live births from residents of the nonmining counties ($41,918/139,603 = 30\%$). The number of live births per hospital averaged approximately 20,000 per hospital with a range of 2366 to 53,595 for residents of MTM-mining counties and approximately 7000 per hospital with a range of 1137 to 19,809 for residents of nonmining counties. Overall, the six hospitals together had nearly three times as many births (2.8) from residents of MTM-mining counties as from residents of nonmining counties. Four of the six hospitals had more births from MTM-mining counties than from nonmining counties with Hospital 22 having greater than 25 times as many births from MTM-mining counties than from nonmining counties. Two of the hospitals (Hospitals 07 and 26) had fewer births from MTM-mining counties than from nonmining counties, approximately half as many.

Hospital 22 had proportionally more births for residents from MTM-mining counties than did the other hospitals. The six hospitals accounted for 84% of live births with reported birth defects for the residents of the MTM-mining counties ($2768/3297 = 84\%$) and for 20% of live births with reported birth defects for the residents of the nonmining counties ($408/2077 = 20\%$). The number of live births with reported birth defects per hospital averaged approximately 461 per hospital with a range of 26 to 2155 for residents of MTM-mining counties and approximately 70 per hospital with a range of 26 to 159 for residents of the nonmining counties. Hospital 22 accounted for 2155 of the 2768 live births with reported birth defects for residents of the MTM-mining counties (78%) but only for 71 of the 408 live births with reported birth defects for residents of the nonmining counties (17%).

Table 1 gives the birth defect prevalence rates for the six hospitals combined and individually for the MTM-

mining county residents and for the nonmining county residents. Overall, the prevalence for the six hospitals combined is 0.023 (or 2.3%) with a 17-fold range of 0.004 to 0.069 and an average of 0.020 for residents of MTM-mining counties and is 0.010 (or 1.0%) with a 10-fold range from 0.006 to 0.062 and an average of 0.19 for residents of nonmining counties.

The birth defect PRR is significantly ($p < 0.001$) elevated with a PRR of 2.39 (95% CI, 2.15–2.65) for the data from the six hospitals combined. However, for the six hospitals individually, the PRRs range from 0.69 to 1.17 with an average of 1.01. None of them is significantly elevated, and one of them (Hospital 04) is significantly ($p = 0.01$) depressed with a PRR of 0.69 (95% CI, 0.52–0.90).

The birth defect prevalence rates for MTM-mining county residents and for nonmining county residents for the combined data from all six birth hospitals and at each of the six birth hospitals individually are demonstrated in Figure 1. Each hospital may be considered to be a separate observer or reporter of birth defects and those with sufficient numbers of live births in each group may be used to assess the hypothesis.

The pair of values at the left of the graph, which present the analysis for the combined data from the six hospitals, indicate that the prevalence rate for residents of the MTM-mining counties (prevalence rate = 0.023 [95% CI, 0.022–0.024]) is significantly greater than that for residents of nonmining counties (prevalence rate = 0.010; 95% CI, 0.009–0.011). In contrast, for each of the six hospitals, the birth defect prevalence rates for residents of the MTM-mining counties and for residents of the nonmining counties are quite similar, showing no differences in the rates for the individual hospitals when stratified by mining status of the county of residence. This visually demonstrates the effect of bias by hospital of birth, as the difference observed in the pooled data is not seen in the hospital-stratified data.

The existence of unbalanced distribution of hospital births by mining groups is dealt with in Table 1, where M-H stratified analysis approaches the same question. The PRRs approximate 1.0 for five of the hospitals (range of 0.90–1.17). The PRR of 0.69 at Hospital 04 is significantly lower than 1.0.

In contrast, while the cPRR for the combined data from the six hospitals calculates to be a highly statistically significant ratio of 2.39 (95% CI, 2.15–2.65; $p < 0.001$), the M-H adjPRR in which the data are stratified by hospital calculates to be a nonsignificant ratio of 1.01 (95% CI, 0.89–1.14; $p = 0.87$), which is indistinguishable from 1.0. This analysis demonstrates that the nonstratified analysis of the data has been markedly biased by hospital. Thus, the stratified M-H analysis has provided a robust with-in hospital check on the global hospital-adjusted Poisson analysis.

The PRR estimates were quite similar with adjPRR = 1.08 (95% CI, 0.97–1.20; $p = 0.16$) in the Poisson analysis

and 1.01 (95% CI, 0.89–1.14; $p = 0.87$) in the M-H analysis. Both analyses yield a PRR close to 1.0 with a symmetrically distributed 95% confidence interval. Thus, the adjPRR is essentially 1.0, whether adjusted globally in the Poisson analysis or stratified by hospital in the M-H analysis.

Discussion

Passive birth defect surveillance systems began development in the United States in the 1970s. Thirty-five years ago, Lamm (1979) published a comparison of reporting frequencies for specific birth defects in two national birth defect surveillance systems: NCHS (1974) birth certificate data for all states and the Centers for Disease Control (1974) hospital discharge data for hospitals that collaborated in the Birth Defects Monitoring Program. He observed that the reported birth defect frequencies from the birth certificates were approximately half those from the hospital discharge reports. Nonetheless, he suggested that despite the underreporting the temporal and geographic distribution of the data might make feasible the testing of occupational and environmental hypotheses of birth defects etiology. This study is a demonstration of that, showing the strengths and weaknesses in the data.

Ahern et al. (2011) had hypothesized a higher birth defect rate among births to residents of MTM-mining counties than to residents of non-mining counties and demonstrated this significantly in both their unadjusted and adjusted Poisson analyses of the combined 1996 to 2003 birth certificate files of the states of Kentucky, Tennessee, Virginia, and West Virginia that they had obtained from the National Center for Health Statistics. The Ahern analyses had been adjusted for several demographic and socio-economic covariates (mother's age ≥ 35 , years of education, smoking during pregnancy, drinking during pregnancy, African American race, Native American race, Hispanic ethnicity, infant sex, low prenatal care, diabetes co-morbidity, and residence in a metropolitan area). Their adjustments reduced the four-state PRR from 1.62 (95% CI, 1.54–1.72) to 1.26 (95% CI, 1.21–1.32). However, their analyses were not adjusted for either state of residence or hospital of birth.

Significant bias may be present when birth defects rates are compared without taking into account factors related to variations in the reporting of birth defects on birth certificates. Boulet et al. (2011) examined the sensitivity of birth certificate reports of birth defects in Atlanta (1995–2005) by comparing the birth certificate derived rates with the rates derived in their active surveillance system for birth defects, the Metropolitan Atlanta Congenital Malformation Program. They indicated that the active surveillance rates were approximately four times greater than those from the birth certificates and concluded that "The underreporting of birth defects on birth certificates

is influenced by socio-demographic and hospital characteristics. Interpretation of birth defects prevalence estimates derived from birth certificate reports should take these issues into account." Therefore, our analysis has taken hospital into account in its adjPRR analyses.

Our 1990 to 2009 dataset was restricted to a single state for which we were able to obtain information on hospital of birth as a covariate. We did find a higher birth defect rate for the births to residents of the MTM-mining counties of West Virginia (0.021) than for the births to residents of the nonmining counties of West Virginia (0.015) with a statistically significant birth defect PRR ($PRR = 1.43$ [95% CI, 1.35–1.51]; $p < 0.001$) in our Poisson analysis that was not adjusted for hospital of birth. However, in contrast, we did not find the birth defect PRR to be statistically significant in our hospital-adjusted Poisson analysis ($PRR = 1.08$ [95% CI, 0.97–1.20]; $p = 0.16$).

As the Ahern et al. (2011) analyses were limited to the 1996 to 2003 time period, we replicated our analysis of the West Virginia data set, using the same time period of 1996 to 2003 and then adjusting by hospital of birth. Our unadjusted Poisson analysis for the 1996 to 2003 data yielded a significant risk estimate ($PRR = 1.31$ [95% CI, 1.20–1.43]; $p < 0.001$) that was similar to that of Ahern (adjPRR = 1.25 [95% CI, 1.21–1.32]; $p < 0.001$). However, our hospital-adjusted Poisson analysis for the 1996 to 2003 data yielded a nonsignificant risk estimate ($PRR = 1.10$ [95% CI, 0.96–1.31]; $p = 0.27$) which was similar to our findings for 1990 to 2009. Furthermore, we analyzed for the adjPRRs for birth defects reported for the various organ systems and for "other" birth defects and found them to be nonsignificant ($p > 0.05$) with a range of 0.88 to 1.58. We did not further adjust by the demographic and socio-economic covariates.

Our previous analyses of the birth defects reported on the West Virginia birth certificate had indicated that reported rates of birth defects varied widely by hospital of birth (Li et al., 2013) and that the temporal and geographic distribution of birth defect rates were markedly affected by one outlier hospital (Zhou et al., 2012). Analysis of the descriptions of birth defects reported on the birth certificates revealed that a large proportion of the observations reported as birth defects (or congenital anomalies) were actually observations of nonmalformations or of neonatal conditions (Li et al., 2013). For example, heart murmur was reported as an "other" congenital anomaly of the circulatory/respiratory system, and reflux was reported as an "other" congenital anomaly of the gastrointestinal system. The inclusion of reports of neonatal conditions as birth defects (congenital anomalies) had increased the apparent overall birth defect prevalence rate for the state from 1.1 per 100 live births to 1.8 per 100 live births.

Our analyses, including Poisson analyses and M-H analyses, have demonstrated that the birth defect rates for

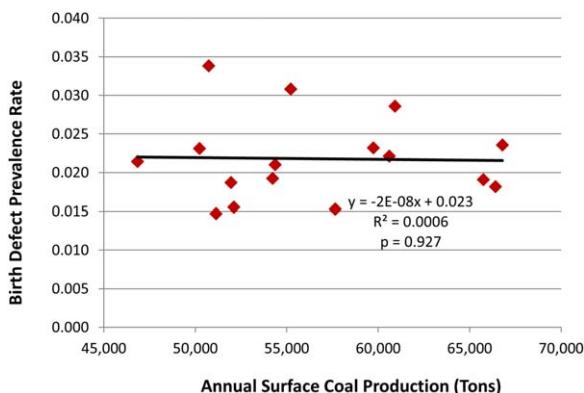


FIGURE 2. Birth defect prevalence rates (1994–2009) reported for residents of MTM-mining counties in West Virginia by annual surface coal production (tons).

births to mothers who reside in a MTM-mining county or in a nonmining county have been biased by the hospital of birth. The discrepancy between the pooled analyses and hospital-stratified analyses lies in the unbalanced distribution of hospital births by mining groups. While the six hospitals on average had approximately three times as many births from residents of MTM-mining counties as from residents of nonmining counties, Hospital 22 had nearly 27 times as many births from MTM-mining counties as from nonmining counties. Graphic analyses have shown that within hospitals the reported birth defect rates for residents of MTM-mining counties and for residents of nonmining counties were quite similar but that there was considerable between-hospital variation. The consistent results of our analyses do not support the hypothesis of a “Mountain-top Mining” effect on the prevalence of reported birth defects in the West Virginia data. In addition, the birth defects rates observed may reflect not only nonmalformation observations but also genetic and chromosomal abnormalities that may be unrelated to MTM or other exposures.

The reporting from Hospital 22 had a marked effect on the distribution of reported birth defects for the state. The proportion of its births to residents of MTM-mining counties compared with nonmining counties is approximately nine times greater than for the other hospitals, and the reported birth defect prevalence rate from Hospital 22 was more than six times that of the other hospitals (Fig. 1). Hospital 22 accounted for a greater proportion of the births to residents of the MTM-mining counties (26%) at these six hospitals than it does for the births to residents of the nonmining counties (2.7%). The probable explanation for the marked influence of Hospital 22 is that reported rate for neonatal conditions as birth defects (i.e., congenital anomalies) for Hospital 22 was 17 times that of the rest of the state (Li et al., 2013). Comparison between Hospital 22 and other WV hospitals as well as a more

extensive discussion of the prevalence rates estimated using live birth certificate data have been presented elsewhere (Li et al., 2013).

While Ahern et al. (2011) had reported a temporal correlation with tons of mountain-top coal mining production and birth defects, our analysis did not find this (Fig. 2). We found no association between annual mountaintop-mining production and rates of reported birth defects for the mountaintop-mining counties for either the Ahern eight year period ($p = 0.79$) or for our 20-year period ($p = 0.93$).

In toto, we find in the West Virginia data that the apparent increased risk of reported birth defects for residents of MTM-mining counties compared with that for residents of nonmining counties was a consequence of bias by hospital of birth and that residence in a MTM-mining county was not an independent determinant of the risk of reported birth defects.

STRENGTHS AND LIMITATIONS

Strengths. This present study has evaluated the rates of birth defects by mining status of county of maternal residence and by hospital of birth using the West Virginia birth certificate data for the years 1990 to 2009. Our study has the following strengths: (1) large sample size: a total of 418,385 live births to West Virginia residents provide us sufficient statistical power to test our hypotheses using various statistical methods; (2) within-state analysis rather than a between-state analysis: our primary exploration showed that among the four states of the central Appalachian area, West Virginia birth certificate data had the most balanced distribution of counties from the three mining groups, i.e., non-mining group, non-MTM mining group, and MTM-mining group; (3) analysis of rates by hospital: previous studies have found significant variation in practices of reporting birth defects by hospital (Li et al., 2013; Northam and Knapp, 2003). Compared with other research (Ahern et al., 2011); we were able to take the hospital effect into account when examining the association between birth defect prevalence rates and residence in MTM-mining counties.

Data source limitations. Passive birth defect surveillance systems developed in the United States in the 1970 to 1980s and presented with published analyses of NCHS data based on birth defect data reported on birth certificates from most of the United States and of Centers for Disease Control data from the Birth Defect Monitoring Program based on birth defect data from hospital discharges that represented approximately one-third of U.S. births. However, concerns have been frequently expressed by researchers (Kirby, 1997, 2001, 2013) that the birth certificate data remain too unreliable and that statistical analyses based on these data should not be published.

Ascertainment biases are inherent, as the analysis is limited to information on live birth certificates. The information on these certificates may also include genetic or

chromosomal diseases in addition to nonmalformations. Malformations in those whose pregnancy ended in stillbirth or in elective termination following prenatal screening would not be included. The rates in these groups are likely to be greater than in live births, although the numbers would be fewer. These analyses have not considered factors such as smoking, diabetes, or hypertension.

The twenty-first century methodology for birth defect surveillance in the United States has matured with the development of birth defect registries at the state level. The case ascertainment and case validation in these registries, while variable, can exceed those from passive surveillance systems. The reporting frequencies in these registries are considerably greater than the birth certificate-based frequencies. Birth defect registries do exist in the states studied by Ahern (Kentucky, Tennessee, Virginia, and West Virginia) but are not generally available as a public use dataset.

Other limitations. Neither our study nor Ahern's study included any hypotheses of specific pollutants or of biological mechanisms whereby environmental impairments from MTM-mining might lead to birth defects. There are no exposure data for either of these two studies as well. So far, no studies have provided evidence on the specific pollutants or route of administration by MTM mining that might be an independent risk factor for increased adverse health outcomes in the Appalachian area. Borak et al. (2012) assessed the predictive value of coal mining for mortality rates across the Appalachian region based on publicly available databases for 2000 to 2004. They found that age-adjusted all-cause mortality was independently correlated with several variables, including poverty rate, household income, education, obesity, gender, race, etc., but not independently related to coal mining. They concluded that instead of coal mining itself, huge economic and cultural disadvantages negatively influenced the health of Appalachian residents, especially those in the coal-mining areas of Central Appalachia where the four states of the Ahern et al. study were located.

CONCLUSIONS

This present study analyzed the 1990 to 2009 live birth data for West Virginia to examine the Ahern hypothesis that higher birth defect rates occurred in MTM-mining areas. In contrast to the other central Appalachian states (i.e., Kentucky, Tennessee, and Virginia), the West Virginia dataset provided a balanced distribution of counties among the mining groups. Unadjusted analysis of the West Virginia data supported the hypothesis. However, when the effect of data heterogeneity (i.e., unbalanced distribution of live births reported by hospitals) was controlled for in the analysis, no significant association was detected between proportion of live births with reported birth defects and residence in counties with mountaintop coal mining. Bias by hospital of birth was not a method-dependent finding, as it

was demonstrated in both Poisson adjusted and M-H stratified analyses.

This study provides an example of a problem in the pooling of heterogeneous data from different sources. The data from the six hospitals that had sufficient data individually to test the hypothesis supported the hypothesis in an aggregate analysis but did not in the analysis of the hospitals individually. What was found to be "true" in the ecological analysis was found to be "false" in the individual analyses, an example of an ecological fallacy.

We conclude that neither the 20-year analyses nor the 8-year analyses of the West Virginia birth certificate data provide evidence supporting the Ahern hypothesis. Whether evidence supporting the Ahern hypothesis resides in the data of the other three states remains to be determined.

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