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EXECUTIVE SUMMARY

A critical review of the Ahern & Hendryx ecological analysis of birth defects in mountaintop mining (MTM) areas revealed the following key issues:

Birth Defect Data

- The authors fail to fully recognize and account for the limitations in the US natality files

Mountaintop Mining Data

- The authors' use of an internet blog to assign mountaintop mining areas and to define the proxy measure of exposure does not meet the standard for epidemiological research.

Exposure Data

- There was no direct or indirect exposure measurement data for the MTM areas.
- The temporal association of exposure (MTM) to outcome (birth defect) an essential requirement for epidemiologic research (i.e., exposure must precede birth) could not be determined.

Data Analysis

- The authors did not include or analyze all known risk factors for birth defects.
- The authors did not adequately control for known confounders.

Findings

- The limitations inherent in the natality data in conjunction with the lack of specific and real-time data for MTM activities as well as valid and reliable data on confounding factors do not provide the quality or type of data required to support the conclusions made by the authors.

STUDY DESIGN

Retrospective, ecological

As stated on page 2 of their article, Ahern et al “conducted a retrospective, ecological analysis to determine whether mother’s residence during pregnancy in one of the three geographic areas (mountaintop mining county, other coal mining county, or non-mining county) was related to the rates of births with a congenital anomaly, before and after statistical control for other risks.” The retrospective ecological study employed by Ahern et al. is a hypothesis-generating study design in which the unit of analysis is a group or population rather than an individual. Exposure is measured with aggregate data for that population with assumptions about individual level exposure-effect often the goal. All ecological studies are potentially prone to the so-called “ecological fallacy,” a term used for the biases that may occur when the association that exists between variables at an aggregate level may not represent the true association that exists at an individual level. In other words, exposures and outcomes cannot be directly linked. The actual ‘exposure’ to ‘mountain top mining’ throughout a woman’s pregnancy cannot be determined for any individual in the study, either for those women who deliver babies with birth defects or for those women who deliver babies with no birth defects.

SOURCES OF DATA

Birth defect data

Birth defect data were obtained from the National Center for Health Statistics (NCHS) natality data files from 1996-2003. However, the natality files are available for the years 1968-2008. The rationale for limiting the study to this truncated time period, given the increase in MTM activity and the availability of more comprehensive natality files, is not discussed.

Limitations of natality data:

- The US natality files contain incomplete, invalid and unreliable data on important predictors of birth defects, particularly for tobacco and alcohol use, prenatal care, maternal risk factors, pregnancy complications, labor and delivery¹
- The authors assign exposure status based on mother’s county of residence at the time of delivery. However, they do not recognize that maternal residence at the time of delivery does not equate to mother’s residence during pregnancy, significantly impacting on the accuracy of the exposure assignment. Women with short-term residence in an MTM or a non-mining county at the time of delivery would be erroneously classified into a MTM or non-mining county

¹ Northam S, Knapp TR. The reliability and validity of birth certificates. J Obstet Gynecol Neonatal Nurs. 2006 Jan-Feb;35(1):3-12

- Socio-economic status is an important predictor of birth defects as noted by the authors, however, no socio-economic data, other than educational attainment are collected in the natality file substantially limiting the ability to measure this factor
- Congenital anomalies on birth certificates are rare events- a small change in the number of anomalies reported can result in a relatively large change in rates limiting their interpretation, particularly for county specific rates.

Exposure data

Data on coal mining was obtained from the Department of Energy, Energy Information Administration for 1996-2003 and from a map of surface mining areas in central Appalachia created from satellite imagery from 2009 as reported on an internet blog.² The authors do not provide sufficient source information or quantitative data for the selected counties for the reader to adequately critique their assignment of MTM to a county. Unnamed counties were classified as MTM regardless of the year(s) of operation, number or size of coal mining sites or whether the site was historical or active over the study period. The lack of annual data for MTM status and the inclusion of inactive mines significantly limit the reliability of this proxy measure.

Limitations in exposure data:

- With no annual MTM data the temporal association of exposure (MTM) to outcome (birth defect) cannot be examined (i.e., exposure must precede birth)
- The lack of annual MTM county specific data prohibit direct examination of the impact of MTM on annual rates of birth defects
- The inclusion of non-active sites with no information on when MTM was operational is questionable and will overestimate MTM exposure and add to the potential for misclassification of births into the wrong exposure group.

STUDY METHODS

The following questions were considered when evaluating the ecological analysis of mountaintop mining (MTM) and birth defects reported by Ahern et al.

Did the investigators examine all known risk factors and important confounding variables (factors associated with both the exposure and outcome) that might explain the relationship reported between birth defects and giving birth in a county with MTM and have they been statistically adjusted for?

² <http://blog.skytruth.org/2009/12/measuring-mountaintop-removal-mining-in.html>

Several risk factors, such as maternal age and number of prenatal visits were re-coded by the authors from continuous variables into categorical variables without specifying a rationale for the categories. Assigning broad analysis categories for confounding variables that are measured on a continuous scale (e.g. mother's age (< 35, >=35 and prenatal care (<9 visits, >=9 visits) may lead to residual confounding.³ Additionally, the authors did not use the quantitative data collected on several risk factors such as number of cigarettes smoked per day, and number of alcoholic drinks per week, instead they categorized them broadly as alcohol consumption during pregnancy (yes/no) and cigarette smoking during pregnancy (yes/no). Again, this increased the likelihood that the confounding effects of these variables were not adequately adjusted for in the reported analyses.

Other risk factors and potential confounders associated with birth defects not analyzed include^{4,5}

- Plurality-multiple births (twins, triplets etc)
- Maternal weight
- Street drug use
- Infections during pregnancy
- Folic acid supplementation
- Socio-economic status

Were all the data analyzed?

Ahren et al. analyzed 1,889,071 live births between 1996-2003 in Kentucky, Tennessee, Virginia, and West Virginia. They omitted births with 'unknown' county of residence for the mother. We examined the natality files using CDC Wonder⁶ to determine the total number of births for the years 1996-2003 for these states and found 1,991,230 live births were recorded. The Ahren analysis omitted 102,159 births. This number is similar to the number of births analyzed for the 'non-mountaintop mining areas' (n=112,771) and 'mountaintop mining areas' (n=109,315). If births with 'unknown' county of residence were more likely to be in mining areas than non-mining areas, or vice-versa this would bias the results.

Was the analysis appropriate for the data collected?

- The authors used Poisson regression which is an appropriate analysis for rare events

³ Brenner H, Blettner M. Controlling for continuous confounders in epidemiologic research. *Epidemiology*. 1997 Jul;8(4):429-34.

⁴ <http://www.cdc.gov/ncbddd/birthdefects/facts.html>

⁵ Yang J, Carmichael SL, Canfield M, Song J, Shaw GM; National Birth Defects Prevention Study. Socioeconomic status in relation to selected birth defects in a large multicentered US case-control study. *Am J Epidemiol*. 2008 Jan 15;167(2):145-54.

⁶ <http://wonder.cdc.gov/Natality.html>

- The use of spatial analysis with such poor exposure data overall and without annual county-specific data on all aspects of MTM is problematic and precludes meaningful interpretation
- The lack of specificity for both the MTM measure and maternal residential history significantly limits the ability to analyze the impact of MTM on birth defects
- Table 5 presenting data from 1996-1999 and 2000-2003 indicating an increase in prevalence of several anomaly types does not consider that similar trends occurred in the general population⁷ irrespective of mining or MTM, resulting in over-interpretation of this analysis

Were birth defects analyzed appropriately?

Grouping birth defects by organ system is a quick and easy way to organize the data, however data grouped this way limits meaningful interpretation and analysis. For example, in the urogenital system, missing a kidney is not the same as a bladder or urethra problem. Collapsing these groups across severity and clinical significance will artificially inflate some of the reported findings. Additionally, putting birth defects into groups that are inconsistent with respect to mechanism of action and fetal development is inappropriate for the purposes of assessing risk with outcome.

Were alternative explanations for the association between MTM and birth defects considered by the investigators?

The central Appalachian population, as the authors indicate is generally socioeconomically disadvantaged and more likely to smoke and be less educated which impact on maternal and infant health. The author's assertion in the discussion that birth defect rates remained elevated

⁷ NCHS. 2005. Births: Final data for 2003. National Vital Statistics Reports 54(2). http://www.cdc.gov/nchs/data/nvsr/nvsr54/nvsr54_02.pdf; NCHS. 2003. Births: Final data for 2002. National Vital Statistics Reports 52(10). http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_10.pdf NCHS. 2002a. Births: Final data for 2001. National Vital Statistics Reports 51(2). http://www.cdc.gov/nchs/data/nvsr/nvsr51/nvsr51_02.pdf. NCHS. 2002b. Births: Final data for 2000. National Vital Statistics Reports 50(5). http://www.cdc.gov/nchs/data/nvsr/nvsr50/nvsr50_05.pdf NCHS. 2001. Births: Final data for 1999. National Vital Statistics Reports 49(1). http://www.cdc.gov/nchs/data/nvsr/nvsr49/nvsr49_01.pdf. NCHS. 2000. Births: Final data for 1998. National Vital Statistics Reports 48(3). http://www.cdc.gov/nchs/data/nvsr/nvsr48/nvs48_03.pdf NCHS. 1999. Births: Final data for 1997. National Vital Statistics Reports 47(18). http://www.cdc.gov/nchs/data/nvsr/nvsr47/nvs47_18.pdf

after accounting for socioeconomic risks is a gross overstatement given the lack of socioeconomic data in the natality file.⁸

Data on known risk factors for birth defects are available from statewide surveys conducted annually by the Center for Disease Control and Prevention.^{9,10,11} These data indicate higher rates of several important risk factors for birth defects statewide in West Virginia, Tennessee and Kentucky. County specific analyses suggest higher prevalence of selected risk factors for birth defects in counties with MTM. These data were not considered in the present analysis.

Is the identified ecological relationship between MTM and birth defects biologically plausible and consistent with what is already known about birth defects at the individual level?

- The authors acknowledge that they do not have the data to examine the biological mechanism by which MTM would result in birth defects
- The reported elevations across all organ systems is unusual and inconsistent with reproductive toxicology

Did the investigators interpret the data with appropriate caveats?

- The authors did acknowledge in general terms the limitations of their study (Section 4.2).

Did the investigators acknowledge the possibility of an ecological fallacy?

- The authors did acknowledge that county of residence does not equate to individual level of exposure.

CONCLUSIONS

Data on residential history for birth mothers is essential and analysis should have been restricted to those women who resided in one county throughout their pregnancy to avoid misclassifying women into the wrong exposure group. The use of an internet blog as the sole source of information to define the proxy measure of exposure does not meet the standard for epidemiological research. The limitations inherent in the natality data in conjunction with the lack of specific and real-time data for MTM activities as well as valid and reliable data on confounding factors do not provide the quality or type of data required to support the conclusions made by the authors.

⁸ Socioeconomic Status in Health Research: One Size Does Not Fit All. Paula A. Braveman, Catherine Cubbin, Susan Egarter, Sekai Chideya, Kristen S. Marchi, Marilyn Metzler, Samuel Posner. JAMA. 2005;294(22):2879-2888.

⁹ <http://www.wvdhhr.org/bph/hsc/pubs/BRFSS/2003/default.htm>

¹⁰ <http://chfs.ky.gov/NR/rdonlyres/F6C0EE67-F23F-4685-9D4A-AF37FA5930B0/0/2001report.pdf>

¹¹ <http://health.state.tn.us/statistics/brfss.htm>