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Racial Disparities in Maternal Exposure to Ambient Air Pollution During Pregnancy and Prevalence of Congenital Heart Defects

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Abstract

Air pollution may be a potential cause of congenital heart defects (CHDs), but racial disparities in this association are unexplored. We conducted a statewide population-based cohort study using North Carolina birth data from 2003-2015 (N=1,225,285) to investigate the relationship between air pollution and CHDs (specifically pulmonary valve atresia/stenosis, Tetralogy of Fallot (TOF), and atrioventricular septal defect (AVSD)). Maternal exposure to particulate matter ≤ 2.5 micrometers in diameter (PM_{2.5}) and ozone during weeks 3-9 of pregnancy were estimated using the Environmental Protection Agency's Downscaler Model. Single- and co-pollutant log-binomial models were created for the entire population and stratified by race to investigate disparities.

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Positive associations between PM_{2.5} and CHDs were observed. An increasing concentration-response association was found for PM_{2.5} and TOF in adjusted, co-pollutant models (Quartile 4 prevalence ratio: 1.46; 95% CI: 1.06, 2.03). Differences in the effect of PM_{2.5} on CHD prevalence were seen in models stratified by race for Black and White individuals. Positive associations were also seen in adjusted, co-pollutant models of ozone and AVSD. Study results suggest that prenatal PM_{2.5} and ozone exposure may increase the prevalence of certain CHDs and that exposure may impact Black and White pregnancies differently. Study results suggest that prenatal PM_{2.5} and ozone exposure may increase the prevalence of certain CHDs. A consistent pattern of differences in association by race/ethnicity was not apparent..

Keywords

congenital heart defects; air pollution; pregnancy; racial disparities; birth defects

Birth defects are a leading cause of infant mortality in America^{1,2}. Although the causes of birth defects remain largely unknown, environmental factors are among the suspected causes. Epidemiologic studies suggest that air pollution may increase the risk of congenital heart defects (CHDs), which are the most common group of birth defects^{3,4}, but results are mixed^{5–17}. Epidemiologic studies have also shown racial disparities in exposure to air pollution, with Black people being disproportionately exposed to harmful air pollutants¹⁸. A higher proportion of Black people living near industrial facilities¹⁹, historical redlining²⁰, along with other components of structural racism can contribute to the racial disparities seen in air pollution exposure. Disparities in birth defect prevalence^{2,21} and survival²² also exist between babies of Black and White women. Babies of Black women have a higher prevalence of certain CHDs (i.e., Tetralogy of Fallot (TOF), atrioventricular septal defects (AVSDs), pulmonary valve atresia/stenosis), compared to White women^{2,21}. Infants born of Black women also have lower rates of survival when they are born with TOF or AVSD when compared to infants born of White women²².

Though racial disparities in exposure to air pollution and CHD prevalence have been described, previous studies have not presented racially-stratified effect estimates of the association between air pollution and CHDs. Previous studies of air pollution and CHDs often adjusted for race in their statistical models^{5,7–9,14,17,23,24}, but did not provide race-specific effect estimates, likely because of small sample sizes by race groupings due to the rareness of birth defects. Examination of differences in the association between pollution and CHDs in Black vs. White pregnancies may give insight into why racial disparities are seen in the prevalence of certain CHDs. It is possible that the typically higher air pollution exposure for Black women during pregnancy may contribute to increased prevalence of CHDs. Considering the increased chronic stress in Black populations²⁵, it is also possible that the physiological effects from air pollution exposure could compound with the adverse effects of chronic stress in the body, thereby increasing the prevalence of CHDs in Black pregnancies.

In this study, we used twelve years of North Carolina birth certificate data, linked to the statewide birth defects registry, and the Environmental Protection Agency's (EPA's)

Community Multiscale Air Quality Modeling System (CMAQ) to investigate the association between select criteria air pollutants and CHDs. Our primary objective was to investigate whether the association between air pollution and CHDs differs by race, specifically between offspring of Black and White women. We hypothesized that effects of structural racism, such as chronic stress and increased exposure to harmful pollutants, could increase the risk of adverse birth outcomes in Black individuals during pregnancy. Specifically, we hypothesized that the increased prevalence of CHDs in Black populations could be a result of one of two pathways: 1) structural racism causing increased air pollution exposure or 2) structural racism affecting how air pollution exposure influences health (i.e., chronic stress exacerbating the physiological effects of air pollution exposure).

Methods

North Carolina Birth & Congenital Malformations Data

The study population was identified via North Carolina birth certificate data, from 2003-2015, which were linked with the North Carolina Birth Defects Monitoring Program (BDMP) registry. The North Carolina BDMP is housed in the North Carolina Division of Public Health's State Center for Health Statistics and is a statewide, population-based surveillance program. BDMP field staff conduct active case ascertainment of birth defects diagnosed within the first year of life. The BDMP staff systematically review medical records throughout the state and incorporate data from administrative health databases (i.e., vital records, Medicaid claims, hospital discharge data, and others) to supplement case ascertainment. We focused our analysis on CHDs that were shown in previous literature to have a higher prevalence among babies born of non-Hispanic Black women compared with non-Hispanic White women: pulmonary valve atresia/stenosis, TOF, and AVSD^{2,21}. Infants with the aforementioned CHDs were compared with all other infants in the study population, including those who may have other types of birth defects.

Air Pollution Data

The ambient air pollution exposure data on particulate matter of 2.5 micrometers or less in diameter (PM_{2.5}) and ozone come from the Downscaler Model of the EPA CMAQ model. The CMAQ model incorporates meteorological, emission, and air pollution data together to give comprehensive estimates of ozone and particulates, as the model combines atmospheric science and air quality models²⁶. The Downscaler Model is a spatially-varying weighted model that takes data from CMAQ and smooths the output with weights that account for spatial and temporal differences. This allows for rigorous model predictions in geographical areas and on days in which data from a fixed-site pollution monitor may be missing or limited²⁷. Utilizing the Downscaler Model permits finer scale estimates of air pollution concentrations at the community level as the Downscaler Model creates averaged pollution estimates for each census tract²⁷. Daily pollution estimates of each census tract were approximated by assigning the model-estimated concentration at the centroid of the census tract to the entire census tract.

Air pollution exposure assignment for each pregnancy in the 2003-2015 North Carolina birth cohort was previously done by geocoding maternal addresses at delivery (found on

the birth certificate) and assigning daily exposure values of PM_{2.5} and ozone from the CMAQ Downscaler Model to each pregnancy^{28,29}. We were specifically interested in air pollution exposure during obstetric weeks 3-9 as this encompasses the critical window of susceptibility for CHDs. The exposure estimate for PM_{2.5} is a 7-week average of the daily 24-hour average exposure of PM_{2.5} (in micrograms per cubic meter (µg/m³)) during weeks 3-9 of pregnancy for the census tract containing the maternal address at date of birth. The exposure estimate for ozone is a 7-week average of the daily 8-hour maximum exposure of ozone (in parts per billion (ppb)) during weeks 3-9 of pregnancy for the census tract containing the maternal address at date of birth.

Exclusion Criteria

A total of 1,497,605 records of live-births were available for this research study. We applied several exclusion criteria (Supplementary Figure 1). We excluded 3,404 infants born with known chromosomal abnormalities to disentangle birth defects related to underlying chromosomal alterations from those that may be related to environmental factors. Additionally, we excluded pregnancies with critical windows occurring in 2002 because they were missing at least 1 week of pollution exposure data during weeks 3-9 of pregnancy (n=50,442). Our analytic dataset was also restricted to singleton births through excluding multiples (n=49,668). During the year of 2010, there were changes in reporting and data collection on the North Carolina birth certificate that resulted in the following missing covariates in our dataset for 2010 only: maternal education, maternal diabetes, and maternal smoking during pregnancy. The aforementioned missing covariates were identified as confounding variables in our research question³⁰⁻³⁴. Due to the potential to introduce bias, we excluded births occurring in 2010 (n=109,116). Furthermore, we excluded women with diabetes (occurring prior to or during pregnancy) (n=56,410)³³⁻³⁵. Lastly, we excluded births that were less than 500 grams in addition to births that were less than 20 weeks gestation or greater than 44 weeks gestation (n=3,280) due to the implausibility of these outliers in the data. After all exclusion criteria were applied, a total of 1,225,285 births remained for analyses.

Statistical Analysis

Log-binomial models were created to examine the association between selected criteria air pollutants (PM_{2.5} and ozone) and the CHDs of interest. PM_{2.5} and ozone exposures were examined as continuous and categorical variables for comparability with other epidemiologic studies. Log-binomial regression models estimated continuous exposure as a unit change equal to the interquartile range (IQR), where the IQR for PM_{2.5} and ozone are respectively 3.81 µg/m³ and 15.84 ppb. We examined various cut-points of PM_{2.5} exposure at and below the current EPA annual average standard of 12 µg/m³ as well. We created three dichotomous variables at different PM_{2.5} exposure levels to be examined in log-binomial models: 1) at or below 8 µg/m³ vs. greater than 8 µg/m³; 2) at or below 10 µg/m³ vs. greater than 10 µg/m³; 3) at or below 12 µg/m³ vs. greater than 12 µg/m³. We also created log-binomial models in which PM_{2.5} exposure greater than 10 µg/m³ and, separately, greater than 12 µg/m³ was compared to PM_{2.5} exposure that was at or below 8 µg/m³ in order to compare these cut-point groupings more directly.

Each CHD (coded dichotomously as yes/no) was examined with the aforementioned exposure groupings in unstratified and racially-stratified models. The stratified models were limited to non-Hispanic White and non-Hispanic Black individuals as our primary interest was to examine health disparities between these two race groups and because the CHDs examined in this study were shown in previous literature to be higher in non-Hispanic Black pregnancies. We created unadjusted single-pollutant models, adjusted single-pollutant models, and adjusted co-pollutant models. Confounding variables were identified *a priori* through a directed acyclic graph (DAG) (Supplementary Figure 2) and were included in adjusted models^{2,21,30–32,36}. Unstratified analyses included the following adjustment set: maternal smoking during pregnancy (yes/no), maternal age (<20yrs, 20–24yrs, 25–29yrs, 30–34yrs, ≥35yrs), maternal Medicaid status (yes/no), maternal education (less than high school, high school, more than high school), Social Vulnerability Index (SVI) (quartiles), and self-classified maternal race (non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander, American Indian, other/unknown). The inclusion and adjustment of race in our statistical models of the overall population is as a proxy of residual and unmeasured factors related to structural racism. Models stratified by race included the same adjustment set mentioned previously, but omitted race. The adjustment for maternal Medicaid status, maternal education, and SVI quartile assignment serve as proxies for SES.

The SVI³⁷, created by the Centers for Disease Control & Prevention and the Agency for Toxic Substances & Disease Registry, utilizes census data to approximate relative social vulnerability of census tracts throughout the USA³⁷. We used data from the state-level SVI for North Carolina where census tracts in North Carolina are compared within the state. The SVI assigns all census tracts an index score of vulnerability on a scale between 0 and 1, where 0 indicates the least vulnerable and 1 indicates the highest vulnerability³⁸. Additional details on the SVI and index assignment can be found in Supplementary Figure 3.

As a sensitivity analysis, we computed all aforementioned analyses for both isolated and multiple birth defect cases due to potential differences in etiology of isolated and multiple cases of CHDs. In our study, isolated birth defect cases were defined as having only the defect of interest (i.e., pulmonary valve atresia/stenosis, or TOF, or AVSD). Infants considered to have multiple birth defects in our analyses had one of the CHDs of interest and at least one additional birth defect of any kind. Due to potential differences in the etiology and severity of pulmonary valve atresia and pulmonary valve stenosis, we carried out sensitivity analyses of the previously mentioned analyses for the two defects separately. Prevalence ratios (PRs) with 95% confidence intervals (95% CI) were computed in all models. All analyses were carried out in SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Characteristics of the study population are shown in Table 1. Non-Hispanic White and non-Hispanic Black individuals make up 80% of the study population (Table 1). Women in the analysis were 27 years old on average, with non-Hispanic White women being slightly older than non-Hispanic Black women (Table 1). Most individuals had more than a high school education, did not smoke during pregnancy, and gave birth at 38.7 weeks gestation on

average (Table 1). Non-Hispanic White women had a lower average SVI than non-Hispanic Black women (0.43 vs. 0.62) and a slightly lower prevalence of all CHDs studied (Table 1).

Average prenatal exposure to PM_{2.5} and ozone in the overall study population did not differ by race group or between stratified and unstratified populations (Table 2); the average PM_{2.5} and ozone exposure during the critical window were respectively 11.7 µg/m³ and 41.9 ppb (Table 2). Average daily PM_{2.5} exposure in the study population, and in both non-Hispanic Black and non-Hispanic White subgroups, decreased gradually between 2003-2015 (Supplementary Figure 4). No consistent trend was seen in the exposure distribution of ozone between 2003-2015 (Supplementary Figure 5).

In the adjusted, co-pollutant, continuous exposure model of PM_{2.5} and pulmonary valve atresia/stenosis, a null association was observed (Table 3). Adjusted, co-pollutant models of PM_{2.5} quartiles suggest that exposure to PM_{2.5} increases the prevalence of pulmonary valve atresia/stenosis (Table 3). Individuals in the second quartile have the highest adjusted PR (aPR) of 1.21 (95% CI: 1.00, 1.46), though the aPR decreased in the higher exposure quartiles (Table 3). This pattern of association was stronger in non-Hispanic Black individuals than non-Hispanic White individuals (Table 4). In models of ozone and pulmonary valve atresia/stenosis, ozone exposure was unassociated with pulmonary valve atresia/stenosis prevalence (Tables 3 and 4). Due to small sample sizes of CHDs within strata of race, we reported results for isolated and multiples for the overall study population only. Associations with pulmonary valve atresia/stenosis did not differ greatly between isolated and multiple defect cases in the overall population (Supplementary Table 1). In results separately examining pulmonary valve atresia and pulmonary valve stenosis in the overall population, we observed positive effect estimates for both pollutants in pulmonary valve atresia models and near null estimates in most pulmonary valve stenosis models (Supplementary Tables 2 and 3). Due to the small sample size of pulmonary valve atresia, we were unable to examine isolated/multiple or racially-stratified groups of this CHD. Results for pulmonary valve stenosis did not differ greatly from results seen in the combined pulmonary valve atresia/stenosis analysis for racially stratified analyses and isolated/multiples analyses (Supplementary Tables 4 and 5).

Results from the adjusted, co-pollutant, continuous exposure model of PM_{2.5} and TOF suggest a positive association, with an aPR of 1.12 (0.96, 1.30) per IQR of PM_{2.5}, though the confidence interval included the null (Table 5). In adjusted, co-pollutant PM_{2.5} categorical exposure models with TOF, there was a positive, increasing concentration-response trend between PM_{2.5} and TOF (Quartile 4 aPR: 1.46; 95% CI: 1.06, 2.03) (Table 5). In threshold models examining PM_{2.5} cut-points and TOF, the 10 µg/m³ and 12 µg/m³ groupings showed positive associations between TOF and PM_{2.5}, with positive associations observed among those exposed to more than 10 µg/m³ (aPR: 1.32; 95% CI: 1.05, 1.67) or more than 12 µg/m³ (aPR: 1.30; 95% CI: 1.03, 1.64) (Table 5). Differences were seen in racially stratified models of PM_{2.5} and TOF, with infants of non-Hispanic White individuals generally having higher effect estimates (Table 6). There was no clear pattern of association for ozone and TOF; results in adjusted, co-pollutant continuous models generally had a null association while results in quartile models had positive/negative associations, though imprecise. Associations

between PM_{2.5} and TOF were stronger among cases with multiple defects than cases with only TOF (Supplementary Table 6).

Adjusted, co-pollutant continuous exposure models for PM_{2.5} and AVSD generally showed a null association. AVSD models with categorical exposure for both PM_{2.5} and ozone suggested a positive association for quartile 2, but a decreasing concentration-response trend from quartile 2 to quartile 4 (Tables 7 and 8). Prevalence ratios in adjusted, categorical models for PM_{2.5} and ozone in the unstratified population were respectively 1.39 (95% CI: 0.99, 1.96) and 1.50 (95% CI: 1.05, 2.14) in quartile 2 (Table 7). In the adjusted, co-pollutant continuous exposure model examining ozone and AVSD, a positive association was seen, though the confidence interval was wide and included the null. The pattern of association between PM_{2.5} and AVSDs was not present in racially-stratified models, though elevated aPRs (with CIs containing the null) were observed in categorical models. The association between ozone and AVSDs seen in racially-stratified models did not differ between non-Hispanic White and non-Hispanic Black pregnancies. The sample size of isolated cases of AVSD was too small to make comparisons between cases of isolated and multiple defects (Supplementary Table 7).

Discussion

Summary of Principal Findings

In our study, we observed that maternal exposure to PM_{2.5} and ozone during the critical window of fetal heart development may be associated with an increase in prevalence of pulmonary valve atresia/stenosis, TOF, and AVSD. We observed a positive concentration-response gradient between PM_{2.5} and TOF. We observed no clear concentration-response gradients between PM_{2.5} and pulmonary valve atresia/stenosis or PM_{2.5} and AVSDs. The strongest association within ozone models was observed between ozone and AVSDs. Racially-stratified results suggest that air pollution exposure may be impacting non-Hispanic Black and non-Hispanic White pregnancies differently. Specifically, we observed stronger effect estimates at lower air pollution exposures levels in non-Hispanic Black pregnancies for pulmonary valve atresia/stenosis and lower effect estimates for TOF in non-Hispanic Black pregnancies.

Previous Literature

Our study is the first, to our knowledge, to investigate and present racial differences in associations between selected criteria air pollutants and CHDs. One previous study by Ritz et al., which examined 185 cases of pulmonary valve atresia/stenosis in relation to hourly ozone exposure²³, mentioned stratifying by race in their study, but did not present findings as authors noted that the number of cases in the strata were too small to be informative. In contrast, we examined 854 cases of pulmonary valve atresia/stenosis in relation to daily 8-hour maximum ozone concentrations from the EPA CMAQ Downscaler model. While no studies have presented racially-stratified effect estimates in the association between maternal exposure to selected criteria air pollutants (PM_{2.5} and ozone) during pregnancy and selected CHDs (pulmonary valve atresia/stenosis, TOF, AVSDs), our overall findings within the unstratified analyses are also generally consistent with the previous epidemiologic literature.

While few studies examined the relationship between TOF and our pollutants of interest in stratified isolated vs. multiple birth defect analyses, our study examined ozone exposure during pregnancy in infants who have TOF in conjunction with other birth defects. The few previous epidemiologic studies that studied the relationship between maternal ozone exposure during pregnancy and AVSDs have generally found null or negative results^{5,7,17}. However, our study observed a positive association between maternal ozone exposure and AVSDs. The one study that found negative associations between maternal ozone exposure and AVSDs had a very small AVSD case count (n=14)⁵. In our overall analyses using quartiles models, we observed adjusted prevalence ratios ranging from 1.14 to 1.50, with the highest prevalence ratio of 1.50 in quartile 2.

Potential Relationship between Structural Racism, Air Pollution and Birth Defects

Though we did not observe clear evidence of a stronger association between the air pollutants and all CHDs in our study for non-Hispanic Black individuals, we believe that some differences seen by race could result from effects of structural racism. Structural racism can generally be described as ideologies, processes, and systems embedded in society that reinforce racial and ethnic inequities^{25,39}. As a result of embedded racism within societal structures, minority populations, particularly non-Hispanic Black people in the United States, often live in areas with higher exposure to air pollution^{18,25,40}, have higher amounts of chronic stress, and poorer health outcomes²⁵. Effects of structural racism, such as a higher exposure to air pollutants and chronic levels of toxic stress, can contribute to effects such as increased oxidative stress, inflammation, and cell death within the body⁴¹; these physiological effects can in turn lead to adverse health outcomes.

In our study, we observed that non-Hispanic Black people generally had similar exposures to PM_{2.5} and ozone during pregnancy compared to non-Hispanic White people. Results that we observed in our study are then likely not due to air pollution exposure differences but may rather be a result a different pathway, such as chronic stress exacerbating physiological effects of air pollution during pregnancy. Further investigation on what impact structural racism may have on birth outcomes in non-Hispanic Black individuals during pregnancy is warranted.

Study Strengths and Limitations

Among the strengths present in our study are comprehensive exposure assessment, recent data, large sample size for birth defect groups, and also a diverse study population that is well suited for studying racial disparities. Moreover, we are the first study that has presented racially-stratified estimates for the relationship between air pollution and selected heart defects. Many studies simply adjust for race in their models and may also be underpowered to examine differences in effect estimates by race. As disparities have been shown to exist in air pollution exposure and birth defect prevalence, examining race-specific effect estimates is important in understanding if racial differences are present in the effect of air pollution on birth defects.

The use of EPA's CMAQ Downscaler Model to estimate exposure allows for estimation of air pollution in areas that do not have pollution monitors and on days in which data on air

pollution levels is missing. In addition, the Downscaler Model has high spatial and temporal resolution and provides exposure data at the census tract level, allowing estimates within both urban and rural areas of North Carolina.

In addition to the high-quality exposure data used, our study represents the most recent birth cohort among the US-based studies that have examined pulmonary valve atresia/stenosis, TOF, and AVSD in relation to ozone and PM_{2.5}. While the most recent US-based study spans 2000-2009, our study includes births from 2003-2009 and 2011-2015, allowing for a longer study time period as well as 5 years of more recent data. Furthermore, our study has the largest number of pulmonary valve atresia/stenosis cases to be examined in relation to ozone and PM_{2.5}. While individual birth defects are rare, the number of pulmonary valve atresia/stenosis cases in our study is 854, whereas the largest case count from similar, previous literature⁹ is 436. With nearly double the cases of pulmonary valve atresia/stenosis, our study has higher statistical power to examine the relation between this CHD and pollutants of interest, especially in racially-stratified analyses. Additionally, the source of our birth defect data is robust as it comes from the North Carolina BDMP, which used active case ascertainment.

Our study also has a number of limitations. We estimated air pollution exposure during weeks 3-9 of pregnancy, the CHD critical window, based on the maternal address on the birth certificate. In cases where pregnant individuals move out of the census tract that they were living in between the first trimester of pregnancy and when they gave birth, there is potential for exposure misclassification due to residential address change. However, we believe the chance for misclassification is moderately low based on a previous study⁴² that observed that most pregnant individuals move within the same exposure region, thereby maintaining nearly the same level of air pollution exposure upon moving. The use of the birth certificate for covariate data on maternal smoking, education, and diabetes status is also a limitation. There is also potential for residual, unmeasured confounding in our study. While we utilized race as a proxy for structural racism, there may be additional unmeasured confounders related to structural racism. There may also be residual confounding due to unmeasured spatially-varying factors (e.g., other air pollutants, lack of green spaces, etc.) that could potentially be associated with CHDs.

Conclusions and Future Directions

In conclusion, results from our study suggest that PM_{2.5} exposure during early pregnancy may be associated with an increased prevalence of pulmonary valve atresia/stenosis, TOF, and AVSD. While aPRs were greater than one, we found an increasing, concentration-response trend in models with TOF and PM_{2.5} but no clear concentration-response trend in categorical models with PM_{2.5} and the other two CHDs. Ozone exposure during early pregnancy was also shown to increase the prevalence of AVSDs in our study. We found that in models stratified by race, non-Hispanic Black and non-Hispanic White pregnancies may be impacted differently by air pollution when it comes to CHD prevalence.

Our findings are also consistent with previous literature that show air pollution to have differing impacts on various subtypes of CHDs^{5,7-9,16}. Additional studies are needed to confirm findings from our study. We recommend that future studies avoid grouping CHDs

when evaluating the impact of air pollution as differing etiologies of CHDs may contribute to varying associations seen between CHDs and pollutants. We also recommend future epidemiologic studies estimate effects within race subgroups, when sample size permits, to improve understanding of observed racial disparities in these outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement:

Air pollution data used to assign exposure are publicly available and may be accessed here at <https://www.epa.gov/hesc/rsig-related-downloadable-data-files>. Study population data were provided by the North Carolina Birth Defects Monitoring Program, State Center for Health Statistics. Because data from the North Carolina Birth Defects Monitoring Program contain personally identifiable information, these data cannot be released publicly. The Birth Defects Monitoring Program provides data about birth defects in North Carolina to researchers, health care providers, public health program planners, community organizations, and interested citizens. Inquires can be directed to <https://schs.dph.ncdhhs.gov/units/bdmp/contacts.htm>.

Abbreviations:

aPR	adjusted prevalence ratio
ATSDR	Agency for Toxic Substances and Disease Registry
AVSD	atrioventricular septal defect
BDMP	Birth Defects Monitoring Program
CDC	Centers for Disease Prevention and Control
CHD	congenital heart defect
CMAQ	Community Multiscale Air Quality Modeling System
DAG	directed acyclic graph
EPA	Environmental Protection Agency
IQR	interquartile range

PM2.5	Particulate matter less than or equal to 2.5 micrometers in diameter
PR	prevalence ratio
SES	socioeconomic status
SVI	Social Vulnerability Index
TOF	Tetralogy of Fallot
95% CI	95% confidence interval

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Table 1:

Characteristics of the North Carolina study population (years: 2003 – 2009 & 2011 – 2015).

	Overall Population N=1,225,285 n (%)	Non-Hispanic White N=699,422 n (%)	Non-Hispanic Black N=282,010 n (%)
Maternal Age in Years [Median/Mean (SD), Range]	27.0 / 27.1 (6.0), 10-55	28.0 / 28.0 (5.8), 12-55	24.0 / 25.4 (6.0), 11-51
Missing	14 (<0.01)	7 (<0.01)	3 (<0.01)
Maternal Age			
<20 years	125,515 (10)	52,809 (8)	44,928 (16)
20-24 years	324,081 (26)	160,682 (23)	97,035 (34)
25-29 years	341,248 (28)	201,594 (29)	70,355 (25)
30-34 years	282,095 (23)	184,958 (26)	44,323 (16)
>= 35 years	152,332 (12)	99,372 (14)	25,366 (9)
Missing	14 (<0.01)	7 (<0.01)	3 (<0.01)
Maternal Medicaid Status at Delivery			
Yes	609,350 (50)	250,871 (36)	203,552 (72)
No	615,935 (50)	448,551 (64)	78,458 (28)
Missing	0	0	0
Maternal Smoking During Pregnancy			
Yes	130,716 (11)	95,932 (14)	27,904 (10)
No	1,091,989 (89)	601,852 (86)	253,383 (90)
Missing	2,580 (0.21)	1,638 (0.23)	723 (0.26)
Maternal Race			
Non-Hispanic White	699,422 (57)	699,422 (100)	0
Non-Hispanic Black	282,010 (23)	0	282,010 (100)
Hispanic	186,204 (15)	0	0
Asian/Pacific Islander	40,887 (3)	0	0
American Indian	14,679 (1)	0	0
Other/Unknown	2,083 (0.17)	0	0
Missing	0	0	0
Infant Sex			
Male	626,959 (51)	359,399 (51)	143,179 (51)

	Overall Population N=1,225,285 n (%)	Non-Hispanic White N=699,422 n (%)	Non-Hispanic Black N=282,010 n (%)
Gestational Age in Weeks [Median/Mean (SD), Range]			
Female	598,318 (49)	340,021 (49)	138,827 (49)
Missing	8 (<0.01)	2 (<0.01)	4 (<0.01)
Preterm Birth (<37 weeks gestation)			
Missing	0	0	0
Maternal Education			
Less than high school	246,121 (20)	73,296 (11)	57,056 (20)
High school	317,552 (26)	163,478 (23)	96,197 (34)
More than high school	658,599 (54)	461,369 (66)	128,129 (46)
Missing	3,013 (0.25)	1,279 (0.18)	628 (0.22)
Birthweight in Grams [Median/Mean (SD), Range]			
3,333.0 / 3,302.3 (570.6), 500-6209		3,402.0 / 3,377.9 (553.0), 500-6209	3,160.0 / 3,114.2 (600.8), 500-6170
Birthweight for preterm births [median/mean (SD), range]	2,438.0 / 2,335.8 (719.2), 500-6160	2,523.0 / 2,437.2 (692.9), 500-5812	2,268.0 / 2,147.4 (734.1), 500-5648
Birthweight for term births [median/mean (SD), range]	3,374.0 / 3,389.7 (465.0), 510-6209	3,445.0 / 3,453.9 (463.2), 520-6209	3,232.0 / 3,239.1 (449.1), 652-6170
Missing	0	0	0
Social Vulnerability Index			
Overall percentile [Median/Mean (SD), range]	0.50 / 0.50 (0.29), 0-1	0.42 / 0.43 (0.27), 0-1	0.66 / 0.62 (0.28), 0-1
Missing	14 (<0.01)	5 (<0.01)	3 (<0.01)
Social Vulnerability Index Quartiles			
Quartile 1 (percentile of 0 – 0.26)	306,631 (25)	218,467 (31)	40,614 (14)
Quartile 2 (percentile of 0.26 – 0.50)	306,110 (25)	196,036 (28)	55,852 (20)
Quartile 3 (percentile of 0.50 – 0.74)	306,517 (25)	176,008 (25)	69,476 (25)
Quartile 4 (percentile of 0.74 – 1)	306,013 (25)	108,906 (16)	116,065 (41)
Missing	14 (<0.01)	5 (<0.01)	3 (<0.01)
Birth Defect Prevalence [cases per 10,000 births]			
Pulmonary valve atresia/stenosis	6.97	6.25	8.55
Tetralogy of Fallot	3.05	2.77	4.01
Atrioventricular septal defect	2.17	1.93	2.94
Missing	0	0	0
Cut-points for PM_{2.5}			
At or below 8µg/m ³	92,379 (8)	56,849 (8)	20,232 (7)

	Overall Population N=1,225,285 n (%)	Non-Hispanic White N=699,422 n (%)	Non-Hispanic Black N=282,010 n (%)
Above 8µg/m ³	1,132,906 (92)	642,573 (92)	261,778 (93)
Missing	0	0	0
At or below 10µg/m ³	413,243 (34)	244,196 (35)	92,366 (33)
Above 10µg/m ³	812,042 (66)	455,226 (65)	189,644 (67)
Missing	0	0	0
At or below 12µg/m ³	760,387 (62)	438,588 (63)	174,743 (62)
Above 12µg/m ³	464,898 (38)	260,834 (37)	107,267 (38)
Missing	0	0	0

Notes: Overall population is the entire study population and includes the following racial groupings in our dataset: non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander, American Indian, and other/unknown. For Social Vulnerability Index percentiles, 0 is the least vulnerable and 1 is the most vulnerable.

Abbreviations: US EPA = United States of America Environmental Protection Agency; PM_{2.5} = particulate matter less than 2.5 micrometers in diameter.

Table 2:
Distribution of average air pollution exposure during weeks 3 – 9 of pregnancy in study population.

	Overall Population			Non-Hispanic White			Non-Hispanic Black		
	Percentile	Mean (SD)	Range	Percentile	Mean (SD)	Range	Percentile	Mean (SD)	Range
	50 (25, 75)			50 (25, 75)			50 (25, 75)		
PM _{2.5}	11.2 (9.4, 13.2)	11.7 (3.1)	4.4 – 29.4	11.1 (9.3, 13.1)	11.6 (3.2)	4.4 – 29.0	11.2 (9.4, 13.2)	11.7 (3.1)	4.9 – 26.7
Ozone	41.9 (33.6, 49.5)	41.9 (9.7)	22.4 – 74.4	41.9 (34.0, 49.4)	42.0 (9.6)	22.5 – 74.4	41.9 (33.0, 49.6)	41.8 (9.9)	22.4 – 74.2

Note: There is no missing exposure data as exposure data during weeks 3 – 9 of pregnancy was one of the inclusion criteria for this study. The sample sizes for each of the above groups are as follows: overall population: N = 1,225,285; non-Hispanic White strata: N = 699,422; non-Hispanic Black strata: N = 282,010. Overall population is the entire study population and includes the following racial groupings in our dataset: non-Hispanic White, non-Hispanic Black, Hispanic, Asian/Pacific Islander, American Indian, and other/unknown. The units of measurement for PM_{2.5} and ozone respectively are µg/m³ and ppb.

Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter.

Table 3:

Unadjusted and adjusted prevalence ratios (PR) in the association between pulmonary valve atresia/stenosis and air pollution (PM_{2.5} and ozone) in overall population.

Pulmonary Valve Atresia/Stenosis					
		Unadjusted Single Pollutant Model		Adjusted Single Pollutant Model	
		n _{cases}	PR _{unadj} (95% CI)	n _{cases}	PR _{adj} (95% CI)
PM_{2.5}					
IQR		854	0.98 (0.91, 1.07)	849	1.00 (0.92, 1.09)
Quartile 1		200	reference	199	reference
Quartile 2		240	1.20 (0.99, 1.45)	238	1.21 (1.00, 1.46)
Quartile 3		210	1.05 (0.87, 1.28)	209	1.08 (0.89, 1.31)
Quartile 4		204	1.02 (0.84, 1.24)	203	1.06 (0.87, 1.29)
≤ 8µg/m ³		66	reference	66	reference
> 8µg/m ³		788	0.97 (0.76, 1.25)	783	0.99 (0.77, 1.28)
> 10µg/m ³		575	0.99 (0.77, 1.28)	572	1.00 (0.77, 1.30)
> 12µg/m ³		300	0.90 (0.69, 1.18)	298	0.86 (0.64, 1.14)
≤ 10µg/m ³		279	reference	277	reference
> 10µg/m ³		575	1.05 (0.91, 1.21)	572	1.09 (0.94, 1.26)
≤ 12µg/m ³		554	reference	551	reference
> 12µg/m ³		300	0.89 (0.77, 1.02)	298	0.89 (0.76, 1.05)
Ozone					
IQR		854	0.98 (0.88, 1.10)	849	0.98 (0.86, 1.12)
Quartile 1		215	reference	213	reference
Quartile 2		205	0.95 (0.79, 1.16)	202	0.94 (0.78, 1.15)
Quartile 3		229	1.06 (0.88, 1.28)	229	1.06 (0.88, 1.28)
Quartile 4		205	0.95 (0.79, 1.15)	205	0.94 (0.75, 1.18)

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, categorical Social Vulnerability Index, and maternal race. In the co-pollutant model, the adjustment set includes the other pollutant. The co-pollutant model includes the continuous IQR form of the other pollutant.

Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.

Table 4:

Unadjusted and adjusted prevalence ratios (PR) in the association between pulmonary valve atresia/stenosis and air pollution (PM_{2.5} and ozone) in Non-Hispanic White and Non-Hispanic Black populations in North Carolina.

Pulmonary Valve Atresia/Stenosis										
Non-Hispanic White						Non-Hispanic Black				
Unadjusted Single Pollutant Model			Adjusted Single Pollutant Model			Unadjusted Single Pollutant Model			Adjusted Single Pollutant Model	
n _{CASES}	PR _{unadj} (95% CI)	n _{CASES}	PR _{adj} (95% CI)	n _{CASES}	PR _{adj} (95% CI)	n _{CASES}	PR _{adj} (95% CI)	n _{CASES}	PR _{adj} (95% CI)	Adjusted Co-pollutant Model PR _{adj} (95% CI)
PM_{2.5}										
IQR	437	0.98 (0.88, 1.10)	434	1.01 (0.90, 1.13)	1.04 (0.90, 1.19)	241	0.91 (0.77, 1.07)	240	0.92 (0.78, 1.08)	0.94 (0.78, 1.14)
Quartile 1	109	reference	109	reference	reference	49	reference	49	reference	reference
Quartile 2	121	1.15 (0.89, 1.49)	120	1.16 (0.89, 1.50)	1.16 (0.89, 1.50)	76	1.50 (1.05, 2.15)	75	1.48 (1.04, 2.13)	1.48 (1.04, 2.13)
Quartile 3	99	0.97 (0.74, 1.28)	98	1.01 (0.77, 1.33)	1.02 (0.77, 1.34)	68	1.31 (0.91, 1.89)	68	1.33 (0.92, 1.93)	1.33 (0.92, 1.93)
Quartile 4	108	1.04 (0.80, 1.36)	107	1.11 (0.84, 1.45)	1.17 (0.86, 1.58)	48	0.96 (0.64, 1.42)	48	0.98 (0.65, 1.46)	0.99 (0.64, 1.55)
≤ 8µg/m ³	42	reference	42	reference	reference	15	reference	15	reference	reference
> 8µg/m ³	395	0.83 (0.61, 1.14)	392	0.87 (0.63, 1.19)	0.87 (0.63, 1.20)	226	1.16 (0.69, 1.96)	225	1.18 (0.70, 1.99)	1.20 (0.71, 2.02)
> 10µg/m ³	289	0.86 (0.62, 1.19)	286	0.90 (0.65, 1.24)	0.91 (0.65, 1.26)	166	1.18 (0.70, 2.00)	166	1.20 (0.71, 2.05)	1.23 (0.72, 2.09)
> 12µg/m ³	150	0.78 (0.55, 1.10)	148	0.85 (0.60, 1.20)	0.78 (0.54, 1.14)	83	1.04 (0.60, 1.81)	83	1.04 (0.60, 1.82)	1.09 (0.61, 1.94)
≤ 10µg/m ³	148	reference	148	reference	reference	75	reference	74	reference	reference
> 10µg/m ³	289	1.05 (0.86, 1.28)	286	1.09 (0.89, 1.33)	1.11 (0.90, 1.36)	166	1.08 (0.82, 1.42)	166	1.11 (0.84, 1.47)	1.16 (0.87, 1.54)
≤ 12µg/m ³	287	reference	286	reference	reference	158	reference	157	reference	reference
> 12µg/m ³	150	0.88 (0.72, 1.07)	148	0.91 (0.75, 1.11)	0.92 (0.73, 1.15)	83	0.86 (0.66, 1.12)	83	0.88 (0.67, 1.15)	0.91 (0.68, 1.23)
Ozone										
IQR	437	0.96 (0.82, 1.12)	434	0.96 (0.82, 1.13)	0.94 (0.78, 1.13)	241	0.90 (0.73, 1.10)	240	0.90 (0.74, 1.11)	0.94 (0.74, 1.19)
Quartile 1	104	reference	103	reference	reference	67	reference	66	reference	reference
Quartile 2	112	0.99 (0.76, 1.29)	110	0.94 (0.72, 1.24)	0.95 (0.72, 1.25)	57	0.98 (0.69, 1.39)	57	0.99 (0.69, 1.41)	0.99 (0.69, 1.41)
Quartile 3	120	1.08 (0.83, 1.41)	120	1.05 (0.81, 1.37)	1.05 (0.80, 1.36)	68	1.10 (0.78, 1.54)	68	1.11 (0.79, 1.56)	1.11 (0.79, 1.56)
Quartile 4	101	0.94 (0.71, 1.23)	101	0.93 (0.71, 1.23)	0.90 (0.65, 1.23)	49	0.77 (0.53, 1.11)	49	0.78 (0.54, 1.13)	0.78 (0.51, 1.21)

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, and categorical Social Vulnerability Index. In the co-pollutant model, the adjustment set includes the other pollutant. The unadjusted model is a single pollutant model. The co-pollutant model includes the continuous IQR form of the other pollutant. There n for the adjusted single pollutant model and the adjusted co-pollutant model are exactly the same (also having, the same observations in both

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models). Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.

Table 5:

Unadjusted and adjusted prevalence ratios (PR) in the association between Tetralogy of Fallot and air pollution (PM_{2.5} and ozone) in overall population.

		Tetralogy of Fallot					
		Unadjusted Single Pollutant Model		Adjusted Single Pollutant Model		Adjusted Co-pollutant Model	
		n _{cases}	PR _{unadj} (95% CI)	n _{cases}	PR _{adj} (95% CI)	n _{cases}	PR _{adj} (95% CI)
PM_{2.5}							
	IQR	374	1.05 (0.93, 1.18)	370	1.08 (0.95, 1.22)	370	1.12 (0.96, 1.30)
	Quartile 1	84	reference	84	reference	84	reference
	Quartile 2	84	1.00 (0.74, 1.35)	82	0.99 (0.73, 1.34)	82	0.99 (0.73, 1.34)
	Quartile 3	101	1.20 (0.90, 1.61)	99	1.23 (0.92, 1.65)	99	1.24 (0.93, 1.67)
	Quartile 4	105	1.25 (0.94, 1.66)	105	1.32 (0.99, 1.77)	105	1.46 (1.06, 2.03)
	≤ 8µg/m ³	27	reference	27	reference	27	reference
	> 8µg/m ³	347	1.05 (0.71, 1.55)	343	1.07 (0.72, 1.58)	343	1.07 (0.72, 1.58)
	> 10µg/m ³	266	1.12 (0.75, 1.67)	263	1.14 (0.77, 1.71)	263	1.15 (0.77, 1.72)
	> 12µg/m ³	156	1.15 (0.76, 1.73)	155	1.20 (0.80, 1.82)	155	1.22 (0.79, 1.87)
	≤ 10µg/m ³	108	reference	107	reference	107	reference
	> 10µg/m ³	266	1.25 (1.00, 1.57)	263	1.30 (1.04, 1.63)	263	1.32 (1.05, 1.67)
	≤ 12µg/m ³	218	reference	215	reference	215	reference
	> 12µg/m ³	156	1.17 (0.95, 1.44)	155	1.23 (1.00, 1.51)	155	1.30 (1.03, 1.64)
Ozone							
	IQR	374	0.98 (0.83, 1.16)	370	0.99 (0.84, 1.17)	370	0.92 (0.75, 1.11)
	Quartile 1	95	reference	92	reference	92	reference
	Quartile 2	98	1.03 (0.78, 1.37)	98	1.06 (0.80, 1.41)	98	1.07 (0.81, 1.43)
	Quartile 3	79	0.83 (0.62, 1.12)	79	0.85 (0.63, 1.15)	79	0.84 (0.62, 1.14)
	Quartile 4	102	1.07 (0.81, 1.42)	101	1.10 (0.83, 1.46)	101	1.02 (0.73, 1.42)

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, categorical Social Vulnerability Index, and maternal race. In the co-pollutant model, the adjustment set includes the other pollutant. The co-pollutant model includes the continuous IQR form of the other pollutant.

Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.

Table 6:

Unadjusted and adjusted prevalence ratios (PR) in the association between Tetralogy of Fallot and air pollution (PM_{2.5} and ozone) in Non-Hispanic White and Non-Hispanic Black populations.

Tetralogy of Fallot											
Non-Hispanic White						Non-Hispanic Black					
Unadjusted Single Pollutant Model			Adjusted Single Pollutant Model		Adjusted Co-pollutant Model		Unadjusted Single Pollutant Model		Adjusted Single Pollutant Model		Adjusted Co-pollutant Model
	n _{cases}	PR _{unadj} (95% CI)	n _{cases}	PR _{adj} (95% CI)	PR _{adj} (95% CI)	n _{cases}	PR _{adj} (95% CI)	n _{cases}	PR _{adj} (95% CI)	PR _{adj} (95% CI)	
PM _{2.5}											
IQR	194	1.08 (0.91, 1.27)	191	1.10 (0.93, 1.30)	1.11 (0.91, 1.36)	113	0.86 (0.68, 1.10)	112	0.88 (0.69, 1.13)	0.90 (0.67, 1.19)	
Quartile 1	42	reference	42	reference	reference	31	reference	31	reference	reference	
Quartile 2	50	1.23 (0.82, 1.86)	48	1.19 (0.79, 1.80)	1.19 (0.78, 1.80)	19	0.59 (0.33, 1.05)	19	0.61 (0.34, 1.08)	0.61 (0.34, 1.08)	
Quartile 3	43	1.10 (0.72, 1.68)	42	1.10 (0.71, 1.68)	1.11 (0.72, 1.70)	41	1.25 (0.78, 1.99)	40	1.27 (0.79, 2.04)	1.28 (0.80, 2.06)	
Quartile 4	59	1.48 (1.00, 2.20)	59	1.53 (1.02, 2.28)	1.65 (1.05, 2.59)	22	0.69 (0.40, 1.19)	22	0.74 (0.42, 1.28)	0.77 (0.42, 1.43)	
≤ 8µg/m ³	13	reference	13	reference	reference	13	reference	13	reference	reference	
> 8µg/m ³	181	1.23 (0.70, 2.16)	178	1.23 (0.70, 2.16)	1.22 (0.69, 2.14)	100	0.59 (0.33, 1.06)	99	0.61 (0.34, 1.09)	0.62 (0.34, 1.10)	
> 10µg/m ³	139	1.34 (0.76, 2.36)	137	1.34 (0.75, 2.37)	1.31 (0.74, 2.34)	74	0.61 (0.34, 1.09)	73	0.61 (0.34, 1.11)	0.62 (0.34, 1.14)	
> 12µg/m ³	80	1.34 (0.75, 2.41)	80	1.35 (0.75, 2.45)	1.25 (0.67, 2.33)	42	0.61 (0.33, 1.13)	41	0.61 (0.32, 1.15)	0.61 (0.31, 1.19)	
≤ 10µg/m ³	55	reference	54	reference	reference	39	reference	39	reference	reference	
> 10µg/m ³	139	1.36 (0.99, 1.85)	137	1.39 (1.01, 1.91)	1.39 (1.00, 1.93)	74	0.92 (0.63, 1.36)	73	0.95 (0.64, 1.41)	0.98 (0.66, 1.47)	
≤ 12µg/m ³	114	reference	111	reference	reference	71	reference	71	reference	reference	
> 12µg/m ³	80	1.18 (0.89, 1.57)	80	1.24 (0.93, 1.66)	1.26 (0.91, 1.74)	42	0.96 (0.66, 1.41)	41	0.98 (0.66, 1.44)	1.05 (0.68, 1.62)	
Ozone											
IQR	194	1.05 (0.83, 1.32)	191	1.06 (0.84, 1.34)	0.98 (0.74, 1.29)	113	0.88 (0.66, 1.19)	112	0.90 (0.67, 1.21)	0.96 (0.68, 1.37)	
Quartile 1	46	reference	44	reference	reference	31	reference	30	reference	reference	
Quartile 2	49	0.98 (0.66, 1.47)	49	1.01 (0.67, 1.51)	1.01 (0.67, 1.52)	31	1.15 (0.70, 1.89)	31	1.18 (0.71, 1.95)	1.16 (0.70, 1.92)	
Quartile 3	41	0.84 (0.55, 1.28)	41	0.86 (0.56, 1.32)	0.86 (0.56, 1.31)	26	0.91 (0.54, 1.53)	26	0.93 (0.55, 1.57)	0.94 (0.55, 1.58)	
Quartile 4	58	1.22 (0.83, 1.79)	57	1.24 (0.84, 1.84)	1.20 (0.76, 1.90)	25	0.85 (0.50, 1.44)	25	0.89 (0.52, 1.50)	0.99 (0.53, 1.84)	

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, and categorical Social Vulnerability Index. In the co-pollutant model, the adjustment set includes the other pollutant. The unadjusted model is a single pollutant model. The co-pollutant model includes the continuous IQR form of the other pollutant. There n for the adjusted single pollutant model and the adjusted co-pollutant model are exactly the same (also having, the same observations in both

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models). Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.

Table 7:

Unadjusted and adjusted prevalence ratios (PR) in the association between atrioventricular septal defects and air pollution (PM_{2.5} and ozone) in overall population.

Atrioventricular Septal Defect						
		Unadjusted Single Pollutant Model		Adjusted Single Pollutant Model		Adjusted Co-pollutant Model
		n _{cases}	PR _{unadj} (95% CI)	n _{cases}	PR _{adj} (95% CI)	n _{cases} PR _{adj} (95% CI)
PM_{2.5}						
IQR		266	1.01 (0.87, 1.16)	264	1.02 (0.88, 1.18)	264 0.98 (0.82, 1.16)
Quartile 1		58	reference	57	reference	57 reference
Quartile 2		79	1.36 (0.97, 1.91)	79	1.39 (0.99, 1.96)	79 1.39 (0.99, 1.96)
Quartile 3		66	1.14 (0.80, 1.62)	65	1.15 (0.81, 1.65)	65 1.13 (0.79, 1.62)
Quartile 4		63	1.09 (0.76, 1.55)	63	1.12 (0.78, 1.61)	63 0.99 (0.66, 1.49)
≤ 8µg/m ³		26	reference	25	reference	25 reference
> 8µg/m ³		240	0.75 (0.50, 1.13)	239	0.79 (0.52, 1.20)	239 0.78 (0.51, 1.18)
> 10µg/m ³		179	0.78 (0.52, 1.18)	178	0.83 (0.55, 1.27)	178 0.81 (0.53, 1.24)
> 12µg/m ³		96	0.73 (0.48, 1.13)	96	0.77 (0.49, 1.20)	96 0.70 (0.43, 1.13)
≤ 10µg/m ³		87	reference	86	reference	86 reference
> 10µg/m ³		179	1.05 (0.81, 1.35)	178	1.06 (0.82, 1.38)	178 1.03 (0.79, 1.35)
≤ 12µg/m ³		170	reference	168	reference	168 reference
> 12µg/m ³		96	0.92 (0.72, 1.19)	96	0.95 (0.73, 1.22)	96 0.87 (0.65, 1.16)
Ozone						
IQR		266	1.11 (0.91, 1.35)	264	1.10 (0.90, 1.34)	264 1.12 (0.88, 1.42)
Quartile 1		52	reference	52	reference	52 reference
Quartile 2		77	1.48 (1.04, 2.11)	77	1.48 (1.04, 2.11)	77 1.50 (1.05, 2.14)
Quartile 3		72	1.38 (0.97, 1.98)	71	1.35 (0.95, 1.94)	71 1.34 (0.94, 1.92)
Quartile 4		65	1.25 (0.87, 1.80)	64	1.23 (0.85, 1.77)	64 1.14 (0.75, 1.73)

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, categorical Social Vulnerability Index, and maternal race. In the co-pollutant model, the adjustment set includes the other pollutant. The co-pollutant model includes the continuous IQR form of the other pollutant.

Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.

Table 8:

Unadjusted and adjusted prevalence ratios (PR) in the association between atrioventricular septal defects and air pollution (PM_{2.5} and ozone) in Non-Hispanic White and Non-Hispanic Black populations.

	Atrioventricular Septal Defect									
	Non-Hispanic White					Non-Hispanic Black				
	Unadjusted Single Pollutant Model	PR _{unadj} (95% CI)	n _{CASES}	Adjusted Single Pollutant Model	PR _{adj} (95% CI)	Adjusted Co-pollutant Model	PR _{adj} (95% CI)	n _{CASES}	Unadjusted Single Pollutant Model	PR _{adj} (95% CI)
PM_{2.5}										
IQR	135	0.95 (0.77, 1.17)	134	0.97 (0.79, 1.20)	0.97 (0.76, 1.24)	reference	0.90 (0.68, 1.19)	83	0.93 (0.70, 1.23)	0.89 (0.65, 1.24)
Quartile 1	33	reference	32	reference	reference	reference	reference	20	reference	reference
Quartile 2	43	1.35 (0.86, 2.12)	43	1.41 (0.89, 2.23)	1.41 (0.89, 2.23)	1.41 (0.89, 2.23)	1.11 (0.61, 2.03)	23	1.14 (0.62, 2.07)	1.14 (0.63, 2.08)
Quartile 3	28	0.91 (0.55, 1.50)	28	0.96 (0.57, 1.59)	0.95 (0.57, 1.59)	0.95 (0.57, 1.59)	1.13 (0.63, 2.05)	24	1.19 (0.66, 2.16)	1.17 (0.64, 2.12)
Quartile 4	31	0.99 (0.61, 1.61)	31	1.05 (0.64, 1.73)	1.02 (0.58, 1.79)	1.02 (0.58, 1.79)	0.78 (0.40, 1.50)	16	0.83 (0.43, 1.62)	0.74 (0.35, 1.55)
≤ 8µg/m ³	16	reference	15	reference	reference	reference	reference	10	reference	reference
> 8µg/m ³	119	0.66 (0.39, 1.11)	119	0.72 (0.42, 1.24)	0.72 (0.42, 1.24)	0.72 (0.42, 1.24)	0.56 (0.29, 1.09)	73	0.59 (0.31, 1.15)	0.59 (0.30, 1.15)
> 10µg/m ³	88	0.69 (0.40, 1.17)	88	0.77 (0.44, 1.34)	0.78 (0.45, 1.36)	0.78 (0.45, 1.36)	0.58 (0.29, 1.13)	54	0.61 (0.31, 1.20)	0.59 (0.30, 1.18)
> 12µg/m ³	45	0.61 (0.35, 1.08)	45	0.67 (0.37, 1.21)	0.63 (0.33, 1.20)	0.63 (0.33, 1.20)	0.53 (0.26, 1.09)	28	0.55 (0.26, 1.15)	0.53 (0.24, 1.17)
≤ 10µg/m ³	47	reference	46	reference	reference	reference	reference	29	reference	reference
> 10µg/m ³	88	1.00 (0.70, 1.43)	88	1.05 (0.73, 1.50)	1.06 (0.73, 1.53)	1.06 (0.73, 1.53)	0.91 (0.58, 1.42)	54	0.95 (0.60, 1.50)	0.94 (0.59, 1.51)
≤ 12µg/m ³	90	reference	89	reference	reference	reference	reference	55	reference	reference
> 12µg/m ³	45	0.84 (0.59, 1.20)	45	0.86 (0.60, 1.24)	0.84 (0.56, 1.26)	0.84 (0.56, 1.26)	0.83 (0.53, 1.31)	28	0.87 (0.55, 1.37)	0.82 (0.49, 1.38)
Ozone										
IQR	135	1.00 (0.75, 1.32)	134	0.99 (0.75, 1.31)	1.01 (0.73, 1.41)	1.01 (0.73, 1.41)	1.02 (0.72, 1.43)	83	1.02 (0.72, 1.44)	1.10 (0.73, 1.67)
Quartile 1	27	reference	27	reference	reference	reference	reference	19	reference	reference
Quartile 2	41	1.40 (0.86, 2.27)	41	1.37 (0.84, 2.23)	1.38 (0.84, 2.25)	1.38 (0.84, 2.25)	1.51 (0.83, 2.75)	25	1.48 (0.82, 2.69)	1.48 (0.82, 2.70)
Quartile 3	37	1.29 (0.78, 2.11)	36	1.22 (0.74, 2.02)	1.22 (0.74, 2.01)	1.22 (0.74, 2.01)	1.20 (0.64, 2.23)	21	1.17 (0.63, 2.18)	1.17 (0.63, 2.18)
Quartile 4	30	1.07 (0.64, 1.80)	30	1.06 (0.63, 1.79)	1.03 (0.57, 1.86)	1.03 (0.57, 1.86)	1.00 (0.52, 1.90)	18	1.00 (0.53, 1.91)	0.99 (0.47, 2.11)

Notes: The IQR for PM_{2.5} is 3.81. The IQR for ozone is 15.84. Adjusted models include the following covariates: maternal smoking, categorical maternal age, maternal Medicaid status at delivery, maternal education, and categorical Social Vulnerability Index. In the co-pollutant model, the adjustment set includes the other pollutant. The unadjusted model is a single pollutant model. The co-pollutant model includes the continuous IQR form of the other pollutant. There n for the adjusted single pollutant model and the adjusted co-pollutant model are exactly the same (also having, the same observations in both

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models). Abbreviations: PM_{2.5} = particulate matter less than 2.5 micrometers in diameter; IQR = interquartile range; n_{cases} = the number of birth defect cases; PR_{unadj} = unadjusted prevalence ratio; PR_{adj} = adjusted prevalence ratio; 95% CI = 95% confidence interval.