Association of Prenatal Exposure to Air Pollutants with Select Birth Defects Using the Case-Cohort Approach

by

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Abstract

Background: Annually, 3-5% of infants are born with birth defects in the United States. In New York State (NYS), air pollution, specifically ozone (O_3) and fine particulate matter ($PM_{2.5}$), is detectable at levels that affect human health. Air pollution is associated with poor birth outcomes and contains components that are suspected to cause oxidative stress, which is one mechanism by which birth defects are formed.

Methods: This study investigated the relationship between the development of select birth defects (oral clefts, craniosynostosis, and clubfoot) in singleton live births in NYS between 2002 and 2015 and weekly peak and average concentrations of O_3 and $PM_{2.5}$ at the mother's residence using modeled air pollution data and single-pollutant distributed lag logistic models. The second analysis incorporated green space at various buffers using the National Land Cover Database (NLCD). The third analysis explored multi-pollutant models.

Results: O_3 most greatly affected risk of clubfoot around conception in the single- and multi-pollutant models. $PM_{2.5}$ most greatly affected risk of clubfoot around weeks 3, 8, and 12 of pregnancy in the single- and multi-pollutant models. O_3 most greatly affected risk of cleft lip with or without cleft palate around conception in the single- and multi-pollutant models. $PM_{2.5}$ most greatly affected risk of cleft lip with or without cleft palate just after conception in the single-pollutant model and week 12 of pregnancy in the multi-pollutant model. O_3 most greatly affected risk of cleft palate around conception in the single- and multi-pollutant models. $PM_{2.5}$ most greatly affected risk of cleft palate in month 2 of pregnancy in the single- and multi-pollutant models. Including green space slightly altered the effect of O_3. O_3 most greatly affected risk of craniosynostosis around weeks 7-8 of pregnancy in the single- and multi-pollutant models. $PM_{2.5}$ most greatly affected risk of cleft palate around conception in the single- and multi-pollutant models. Green space slightly altered the effect of $PM_{2.5}$.

Conclusion: O_3 and $PM_{2.5}$ affected the risk of all birth defects evaluated. In multi-pollutant models, these effects were altered for clubfoot, cleft lip with or without cleft palate, and craniosynostosis. Including green space altered these effects for cleft palate.

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1. Background

The causes of birth defects are not well understood. Birth defects vary in how strongly genetics contributes to their rates. An estimated 30%-40% of birth defects have known causes related to genetics, environment, and maternal health.[1,2] The rest are not well understood and are believed to have multiple causes that interrelate.[2]

Several studies have suggested possible causes for birth defects besides genetics. Proposed demographic factors for birth defects include maternal and paternal age,[3] maternal race, ethnicity,[3,4] and education,[5] and infant sex and parity.[6] Behavioral factors include maternal and paternal smoking and maternal alcohol and folate use. Other maternal health characteristics include obesity and diabetes.[5,7–9] Maternal socio-economic status (SES) is also associated with birth defects.[3,4,10]

Air pollution may be a risk factor for development of birth defects in the fetus, notably the three birth defects explored in this study. The connection between birth defects and maternal smoking is well documented. Given this connection, and similarities between cigarette smoke and some forms of air pollution, notably $PM_{2.5}$, a possible link between air pollution, this study explored the association between maternal exposure to $PM_{2.5}$ and O_3 during the first trimester of pregnancy and risk of infants being born with clubfoot, oral clefts, or craniosynostosis. It examined the three following aims using statewide time-varying data for the exposures and statewide surveillance data for the outcomes.

1.1 Specific Aims

Air pollution may be a risk factor for development of oral clefts, clubfoot, and craniosynostosis in the fetus. This study explored the association between maternal exposure to $PM_{2.5}$ and O_3 during the first trimester of pregnancy and examined these three aims using statewide time-varying data for the exposures and statewide surveillance data for the outcomes.

1. To assess the association between the exposures of $PM_{2.5}$ and O_3 at different time periods and the outcomes of clubfoot, craniosynostosis, cleft palate, and cleft lip with or without cleft

palate from 2002 to 2015 in NYS outside New York City (NYC).

2. To assess whether green space has an interactive effect on the relationship between the time-varying exposures of $PM_{2.5}$ and O_3 and the outcomes of clubfoot, craniosynostosis, cleft palate, and cleft lip with or without cleft palate from 2002 to 2015 in NYS outside NYC.
3. To assess whether time-varying exposures of $PM_{2.5}$ and O_3 have an interactive effect on their relationship with the outcomes of clubfoot, craniosynostosis, cleft palate, and cleft lip with or without cleft palate from 2002 to 2015 in NYS outside NYC.

1.2 Birth defects

Birth defects are structural abnormalities that develop in the fetus during pregnancy. They can affect any part of the fetus's body.[11] Since the development of birth defects differs, scientists believe they have different teratogenic mechanisms and should be studied separately.[12] The three birth defects that will be investigated in this study include clubfoot, oral clefts, and craniosynostosis, which are among the more common birth defects in NYS, with over 100 cases of each defect annually.[13] They are all included in this study because they are posited to be susceptible to similar routes of exposure, as described in subsubsection 1.2.4.1 Biological mechanisms for birth defect formation. In addition, they can all be diagnosed prenatally.[14–16]

1.2.1 Clubfoot

Clubfoot is a deformation of the foot that occurs in about five of every 10,000 NYS births.[13] Clubfoot is slightly more common in male infants than in female infants. It is one of the most common birth defects and 80% of cases are isolated, or idiopathic.[17] In the NYS Congenital Malformations Registry (CMR), an estimated 95% of clubfoot cases are talipes equinovarus, in which the foot is twisted inward like a hand.[18] Between one fourth and one half of idiopathic clubfoot cases have a family history of clubfoot.[17] Treatment includes manipulating and immobilizing the foot by stages or, in extreme cases, surgery. Risk factors for clubfoot include parity,[6] maternal education, obesity, and diabetes, but not maternal age.[5] Because family history is so strongly associated with clubfoot, most causal research has focused on genetics. The main environmental factor in clubfoot research is smoking, for which there is evidence of an association.[19–21] Very little published research could be located for clubfoot and air pollution; only one study was identified for coarse particulate matter (PM_{10}).[22]

1.2.2 Oral clefts

Oral clefts include cleft lip (about 2 per 10,000 NYS births), cleft palate (about 5 per 10,000 NYS births), and cleft lip with cleft palate (about 5 per 10,000 NYS births).[13] Cleft palate is more prevalent among female infants, while cleft lip alone or with cleft palate is more common among male infants.[13] Cleft lip occurs when the cells on each side of the head do not fuse fully before birth and cleft palate occurs when the palate of the mouth does not fuse fully before birth.[23] Studies often separate oral clefts into two groups, cleft palate alone and cleft lip with or without cleft palate, under the hypothesis that the causes of of cleft lip and cleft palate are different. An estimated 80% of oral cleft cases are not syndromic.[24] Treatment is surgery. Risk factors include maternal and paternal age[25], race, smoking[26], alcohol, and obesity[9]. Research on oral clefts and air pollution has shown mixed results, with more research showing associations with cleft palate than with cleft lip with or without cleft palate.[10,22,27–41]

1.2.3 Craniosynostosis

Craniosynostosis is a common birth defect, occurring in about 4 of every 10,000 births in NYS.[13] Craniosynostosis is about twice as common in male infants as in female infants.[13] In craniosynostosis, two or more skull plates fuse prematurely, limiting the brain's ability to grow properly and distorting the skull as other sutures stretch to compensate.[42] An estimated 85% of cases are isolated, involving only one suture.[43] An estimated 8% of cases are syndromic or familial.[44] Infants born with craniosynostosis can be treated with surgery.[44] Research suggests that craniosynostosis is associated with maternal smoking.[45,46] Research on craniosynostosis and air pollution has shown mixed results.[10,38,47]

1.2.4 Gestational age and critical windows

Critical windows are the weeks during pregnancy when the parts of the body affected by each defect develop. Each of the birth defects of interest has a slightly different critical window. The central nervous system develops around week 3, followed by craniofacial structures. The mouth and jaw develop approximately weeks 4 to 9 from neural crest cells, with palatial shelves developing a week later in females than in males.[48] The skull develops approximately weeks 4 to 12 from neural crest cells. The limbs and feet develop approximately weeks 4 to 12, with the footplates developing in week 6 and rotating in week 7.[48]

1.2.4.1 Biological mechanisms for birth defect formation

The fetus is most at risk for each birth defect during its critical window, when environmental insults can most easily disrupt normal development.[48] For the three birth defects under consideration, the critical windows all occur in the first trimester of pregnancy, sometime during weeks 3 to 12. All three birth defects can be partially explained by heredity.[5,49,50] The greatest risk for clubfoot occurs during limb development, between week 4, when limb buds appear, and week 12, when limb bones begin to ossify.[48] Incorrect cell signalling or cell death due to reduced oxygen may also be linked to abnormal limb development.

The greatest risk for oral clefts occurs during development of the face and mandible in weeks 3 to 9.[48] If cell signalling is disrupted so that neural crest cells receive the message to die prematurely, then there will not be sufficient neural crest cells to form the full face, which will result in oral clefts. Premature cell death is also believed to be caused by an imbalance of reactive oxygen species (ROS) and antioxidants. An imbalance between ROS and antioxidants can occur either because there is an increase in ROS creation or there is a decrease in antioxidant creation. This imbalance is representative of oxidative stress, in which the body is unable to remove harmful chemicals and oxygen by-products become reactive, damaging the fetus' deoxyribonucleic acid (DNA), lipids, and proteins.[51]

The greatest risk for craniosynostosis occurs during development of the skull in weeks 4 to 12. Craniosynostosis occurs when skull plates ossify or fuse prematurely.[42] This is believed to occur when neural crest cells fail to differentiate properly due to incorrect signalling. Incorrect signalling can be caused by an excess of reactive oxygen species (ROS) beyond what the cell's antioxidants can handle.

1.2.4.2 General risk factor epidemiology

Established risk factors for one or more of the three birth defects under consideration include demographic, behavioral, and maternal health characteristics, as well as genetics. Demographic factors include maternal and paternal age,[3] maternal race, ethnicity,[3,4] and education,[5] and infant sex and parity.[6] Behavioral characteristics include maternal and paternal smoking and maternal alcohol and folate use. Maternal health characteristics include obesity and diabetes[5,7], notably for orofacial clefts.[8,9] Maternal SES is also associated with these birth defects.[3,4,10]

All three birth defects have an increased risk of developing if the mother smokes.[10,41,52–55] The mechanism by which inhaled chemicals would cause oxidative stress is still undetermined. One theory is that components of cigarette smoke disrupt the ability of the placenta to transmit oxygen and nutrients. The reduced oxygen atmosphere triggers an increase in both mitochondrial DNA and ROS, which damages the mitochondria over time.[56] A related theory suggests that extreme oxidative stress causes the blood vessels in the placenta to develop too quickly, which introduces the fetus to a high oxygen environment prematurely, and with it the risk of cellular damage from ROS.[57] Normally, the fetus grows in a low-oxygen environment in the first trimester, shifting gradually to a higher oxygen environment in the second trimester.

Many components of cigarette smoke, such as benzene and chromium VI[58], are also found in particulate matter and in ambient air[59]. Some of these components are believed to cause epigenetic changes in the developing fetus. Pregnant women exposed to higher concentrations of air pollution show more markers of DNA damage that are associated with oxidative stress than pregnant women exposed to lower concentrations of air pollution.[60]

The proposed mechanism is that air pollution contains chemicals that lead to an increase of ROS beyond what antioxidants can handle. These ROS are necessary to cell functioning, but when they go unchecked, they interact with lipids and proteins, damaging the molecules and disrupting natural signaling processes. Because smoking is associated with the three birth defects of interest, air pollution, which contains many of the same components as cigarette smoke, could also be a causative factor. Cigarette smoke contains chemicals that are believed to increase the concentration of ROS in cells, triggering oxidative stress.[10,41,52,54]

One fourth to one half of clubfoot cases are estimated to be genetic. Several genes have been identified that may increase risk of developing clubfoot.[17] Many cases are hypothesized to be caused by interaction between genetics and the environment.[5] One of the most studied environmental factors in relation to clubfoot is maternal smoking. A study in Atlanta found an odds ratio (OR) of 6.52 for infants with family history of clubfoot and an OR of 1.34 for infants whose mothers smoked.[61] They found an OR of 20.30 for infants with both family history of clubfoot and mothers who smoked, which supports the hypothesis that many clubfoot cases can be explained by gene-environment interactions.

Alcohol is also a trigger of oxidative stress. Alcohol increases the concentration of superoxide (H_2O_2) in the cell. H_2O_2 is a ROS. Alcohol has also been shown to increase markers of lipid damage in cells, leading to neural crest disruption.[57] Research on maternal alcohol consumption and oral clefts has shown mixed results.[10,54]

1.2.5 Data sources for Birth Defects

Some birth defects may be difficult to diagnose objectively, but the birth defects of interest are all well defined in the CMR. All three can be identified by ultrasound[14,15,62] and are easily recognizable at birth. The CMR captures an estimated 71% of all births with birth defects, including 90% of all births with oral clefts.[63]

The CMR is a database of all birth defects among children under one year old in NYS. It is maintained by the NYS Department of Health (DOH)[64] and is linked to NYS Vital Records.[65] The CMR classifies cases using British Pediatric Association (BPA) codes[66], which provide more detailed diagnoses for birth defects than International Classification of Diseases (ICD) codes. Since the datasets are linked and all variables except BPA codes and malformation narratives come from Vital Records, they will be described together. An evaluation of the CMR concluded that the CMR captures most cases and has an accuracy of about 80% of reports.[67] Because the birth defects of interest are easily recognizable and since that evaluation, several cases in the CMR have been reviewed for accuracy, including clubfoot, accuracy should be higher now.

The CMR is a surveillance registry to which hospitals and doctor's offices submit all new cases of congenital malformations[68]. CMR staff follow up on unclear and missing information, de-duplicate records, and assign appropriate BPA codes. Because the CMR relies on doctors to correctly diagnose and report their patients, some level of underreporting is likely, so additional cases are identified using corresponding ICD codes in the NYS Statewide Planning and Research Cooperative System (SPARCS).

NYS Vital Records includes all births registered in NYS excluding NYC and NYC Vital Records includes all births registered in NYC. In an assessment of NYS vital records validity, sensitivity for tobacco and alcohol use was over 80%, with specificity over 90%.[69] The authors generally found NYS birth certificate data to be accurate.

1.3 Exposures

Several exposures are associated with health outcomes, including air pollution and green space. Air pollution refers to particles suspended in the air and inhaled. Green space refers to open land with grass, trees, or other vegetation, such as parks and gardens.

1.3.1 Air Pollution

Air pollution is a composite of chemicals suspended in the air that, when inhaled, can cause damage to human health. Two types of air pollution are ground-level O_3 gas and particulate matter

(PM), which is a mixture of pollutants. PM is produced by combustion from industry, car exhaust, wood burning, and other forms of combustion and continues to be an issue in NYS, especially in urban areas. Ozone is produced by chemical reactions in the air between PM and nitrogen oxides (NO_x).

PM and O_3 are being studied in relation to birth defects because they are prevalent in NYS, with exposures averaging $11.2\frac{\mu g}{m^3}$ for $PM_{2.5}$ and 38ppb for O_3.[39] Both exposures have been linked to asthma[70,71] and other health outcomes and have been studied as possible causal factors in the development of birth outcomes and birth defects.

Particulate Matter

PM is a mixture of solid, liquid, and gaseous particles that range in size up to 10 micrometers in diameter.[72] These particles include metals, acids, and organic and inorganic compounds. PM tends to be localized and the composition of PM varies from locality to locality. PM is released by combustion from many sources, including industries, vehicles, wood burning (either as agricultural waste or to heat homes), and cigarette smoking. It comprises haze and smog.

PM has been associated with lung damage due to inhaled particles.[73] This can cause and exacerbate respiratory ailments such as asthma. PM has also been associated with cardiopulmonary issues, heart attacks, and diabetes and with both short-term and long-term PM exposure. PM has been strongly associated with respiratory issues and poor lung function in young children and infants, as well as adverse birth outcomes. PM has been associated with health effects several days after exposure.

PM is generally measured in the form of PM_{10}, $PM_{2.5}$, and ultrafine particulate matter ($PM_{0.1}$). The numbers correspond to the maximum diameter of the particles in micrometers. As particles decrease in size, they become easier to inhale and therefore more likely to damage the lungs. $PM_{2.5}$ measurements are most readily available in NYS.

While PM as a whole may vary little seasonally, the concentrations of components that make up PM may change over the course of the year. For polycyclic aromatic compounds (PAHs), for example, lighter molecules tend to be gaseous and predominate in summer months while heavier molecules tend to exist as particulates and predominate in winter months.[74]

Ozone

O_3 is an air pollutant that is created when light and heat from the sun cause volatile organic compounds (VOCs) and NO_x in the atmosphere to chemically react.[75] NO_x and VOCs can be emitted by industries, vehicle exhaust, and other forms of combustion as well as vapors from gasoline and solvents.[76]

O_3 located in the stratosphere is beneficial to humans, since it blocks solar radiation, but O_3 close to the earth's surface can damage human health. Ground level O_3 is caused when VOCs and nitrogen oxides (NO_x) in PM react with sunlight. Ozone tends to be higher in the summer than in the winter, with spikes on hot, sunny days, which are ideal for the chemical reactions that produce O_3.

O_3 is associated with respiratory and cardiovascular health.[73] Short-term increased exposure to O_3 has been linked to asthma mortality, heart attacks, and hospitalization due to asthma and coronary obstructive pulmonary disease (COPD). Repeated exposure to increased O_3 has been associated with cardiopulmonary mortality. Some studies have linked O_3 to decreased lung function, cognitive effects, and preterm birth.[73]

1.3.2 Data sources for Air Pollution

Monitoring station data

The Environmental Protection Agency (EPA) maintains the Ambient Monitoring Archive (AMA).[77] They collect data from all states, including the NYS Department of Environmental Conservation (DEC), which maintains over 50 widely scattered air monitoring stations, most of which are located near urban areas and nearly half of which are located in NYC. Monitoring stations vary by years of operation, frequency data of collection (usually every 3 days), which of the 197 pollutants they measure, and monitoring station altitude, making direct analysis of the raw data difficult. Of the monitoring stations maintained by the NYS DEC, 30 monitor O_3 and 52 monitor $PM_{2.5}$.[78]

In most cases, the monitoring stations do not consider specific exposure sources, elevation, or meteorological data. This can complicate exposure assignment, which is generally limited to ground-level buffer areas around the monitoring stations, thereby excluding a lot of potential cases.

With few monitors along NYS' borders with Pennsylvania and New England and distances up to 70 miles between monitoring stations, a study in NYS would need to incorporate monitoring station data from neighboring states. However, the EPA warns that exposure estimates between states may not be comparable due to differences in equipment used, frequency of measures, and state regulations.

Traffic data

The NYS Department of Transportation (DOT) maintains annual estimates of average daily traffic.[79] The NYS DOT data provide statewide annual means of measured or estimated traffic density (annual average daily traffic), from which relative air pollutant exposure can be estimated. They monitor major roads a few days each year, so their estimates may not be applicable outside the season they were collected. They may not monitor minor roads at all and which roads are monitored may vary from year to year.

As with monitoring station data, traffic studies generally rely on buffers 150 to 300 meters from major roads.[47] However, they may ignore other sources of $PM_{2.5}$. The composition of $PM_{2.5}$ on roadways can vary depending on the type of traffic and the concentration of $PM_{2.5}$ may be misclassified if a section of road experiences a lot of stop-and-go traffic.

Satellite data

One type of satellite data is aerosol optical depth (AOD), which refers to measurements of the opacity of airborne particles between orbiting satellites and the earth's surface. AOD data are collected by several satellites maintained by the National Aeronautics and Space Administration (NASA). These satellites vary in how quickly they circumnavigate the earth and in their spatial resolution, but all cover the entire planet. AOD data have been used to estimate ground-level air pollution.

Raw satellite data is difficult to work with for several reasons. It may contain gaps due to cloud cover. It measures the entire column of air between the satellite and the earth, so raw values are unlikely to match ground-level measurements. It does not provide information on the components of the air pollution. Satellite data are generally incorporated into models that include land surface and meteorology instead of being used in their raw form for health studies.

Strengths of AOD data include that it is available globally and measures are available for any given area at least every few weeks. AOD data, when angled relative to the earth's surface, can provide some information to estimate ground-level PM exposure.

Modeled data

The EPA maintains several datasets that provide modeled estimates of air pollution nationwide. Most of these datasets are based on the Community Multi-scale Air Quality (CMAQ) model[80], which is a complex atmospheric chemistry and air transport model that incorporates meteorology, land use, atmospheric chemistry and several types of pollution sources. Some models also incorporate AOD data. This allows for reasonable estimates of exposure for the entire area, but because they are estimates, inferences cannot be drawn based on specific levels of exposure. Instead, studies use modeled data to estimate health effects in areas of higher versus lower exposure. The CMAQ model can be calibrated to provide estimates of individual airborne chemicals, like benzene or cadmium, or combinations of chemicals, like PAHs or various sizes of PM.

The datasets produced using CMAQ vary in chemicals available and temporal frequency. The National-Scale Air Toxics Assessment (NATA)[81] contains estimates for over 100 individual chemicals, but only provides annual estimates every three or six years. The Downscaler model[82,83] provides daily estimates over a span of fifteen years, but contains only O_3 and combined $PM_{2.5}$. Both models recalibrate their estimates using monitoring station data where available. Datasets also vary by spatial resolution from 1km to 12km square grids or census tracts. All modeled estimates are subject to error.

1.3.3 Green Space

Studies on the relationship between trees and air pollution have found that trees reduce various types of air pollution by either absorbing them (for example, CO_2) or by trapping them in their leaves (for example, $PM_{2.5}$).[84,85] While trees and shrubs have been shown to remove O_3 and $PM_{2.5}$ from the air, published research on the relationship between grasses and air pollution could not be located. Many studies have found positive health benefits from proximity to green space, but have not differentiated whether the green space was trees or other plants. A recent literature review on air pollution and green space[85] noted a few studies on trees' ability to remove various air pollutants from the air, including PM and O_3, and stated the need for more research on the connection between green space and air pollution. Another review published more recently found mixed results when assessing the relationship between green space and air pollution, notably for O_3.[86] Green space has been linked to several health outcomes, including cancer[87], asthma[86], and infant health[88].

1.3.4 Data sources for green space

There are several datasets that measure land type, vegetation, and tree canopies. Many of these could be used to estimate the presence and amount of green space in an area. Two of the more common datasets are described below.

Normalized Difference Vegetation Index

The Normalized Difference Vegetation Index (NDVI) is a dataset that measures surface vegetation. It is collected by NASA's Moderate Resolution Imaging Spectroradiometer (MODIS) satellite approximately every 16 days.[89] The NDVI data are provided in 30m square grids, with each color representing a different measure of vegetation density. This dataset provides the amount of green space in each grid, but does not differentiate between types of green space.

One study measured the relationship between green space and birthweight in two US cities using the NDVI.[90] The researchers created buffers of varying sizes around each residence and calculated the percentage of tree cover and green space in each buffer, averaged over one year after removing snow, cloud cover, and other visual disturbances. They found only the closest (50m) buffers for green space and tree cover remained significant after controlling for SES and other factors.

Another study measured the relationship between green space and NVDI in Ottawa, Canada.[91] The researchers found that $PM_{2.5}$ and $PM_{0.1}$ were both inversely associated with green space in fall and winter, but not in summer.

National Land Cover Database

The NLCD is released every five years.[92,93] It is a grid of 16 different colors of pixels that cover the United States. Each pixel represents a 30m square area. The NLCD data are categorized to differentiate built environment from natural environment. The pixel colors represent 16 land use types, such as green space (forest, wetlands, or pasture), level of development (low to high intensity), or other characteristic, such as water or barren land. Cells that contain predominantly trees can be identified in this dataset. While the NLCD is produced every few years, it benefits from modeling at very small areas that is only possible by collecting data over a period of time.

One study investigated the relationship between birthweight and green space using the NLCD.[94] They collapsed the 16 categories into three categories and created 250 meter buffers around each birth, then calculated the proportion of pixels in each category that fell in the buffer for each birth. They found a positive correlation between birthweight and green space. They also identified the need for further research on the association among green space, air pollution, and birth outcomes.

1.4 Epidemiology

The studies in this section were identified in EBSCOhost using the keywords “oral clefts”, “clubfoot”, “talipes equinovarus”, and “craniosynostosis” for the outcomes and “pm2.5”, “particulate matter”, “ozone”, and “air pollution” for the exposures. Many studies have found significant relationships between birth defects and air pollution and many studies have not. Of the birth defects of interest, results have been mixed for oral clefts and craniosynostosis. The only research study located that evaluated the relationship between clubfoot and air pollution did not find a significant relationship.

Studies were included in Table 1.1 if they contained distinct exposures of $PM_{2.5}$, PM_{10}, or O_3 and distinct outcomes cleft lip with or without cleft palate, cleft palate, oral clefts combined, or craniosynostosis. Most of these studies were case-control.

1.4.1 Clubfoot and air pollution

No published studies were identified on clubfoot and $PM_{2.5}$ or O_3. One study assessed PM_{10} and clubfoot by calculating monthly kriged averages.[22] The results were not significant. As stated in subsection 1.2.1 Clubfoot, many of the components of cigarette smoke are also found in $PM_{2.5}$, so the same teratogenic mechanism of oxidative stress that applies for cigarette smoking may also apply for higher levels of $PM_{2.5}$.

1.4.2 Oral clefts and air pollution

Several studies explored the relationship between oral clefts and air pollution. Table 1.1 includes three studies that used monitoring station measures of PM, five studies that used monitoring station measures of PM and O_3, three studies that used modeled PM estimates, and four studies that used modeled PM and O_3 estimates.

Two studies that used monitoring station PM measurements averaged measurements over the entire critical window. One study assigned averages of monitoring stations within 10km.[34] The other study assigned average measurements of any monitoring stations within the census tract.[36] Neither study found significant associations between PM and oral clefts. The third study used monthly averages of kriged exposures for the first three months of pregnancy.[22] This study found significant associations between PM_{10} and cleft palate alone in the first month (RR = 1.09; 95% confidence interval (CI) = 1.01-1.17) and between PM_{10} and cleft lip with or without cleft palate in the second month (RR = 1.05; 95% CI = 1.01-1.08).

Of the five studies that used monitoring station measurements for PM and O_3, four averaged measurements over the entire critical window. The fifth study used monthly averages over the first trimester to introduce some temporality.[31] Two studies used distance weighted estimates to assign exposure based on how far the residence or neighborhood was from the monitoring station.[31,47] The other three studies assigned the nearest monitoring station value, though one study excluded residences more than 40km from the nearest monitoring station. One study found an OR of 0.69 (95% CI = 0.50-0.93) for cleft palate given a $4\frac{\mu g}{m^3}$ increase in PM_{10}.[30] Another study found increased odds of cleft lip and palate with a 10ppb increase of O_3 for the first and second months of pregnancy.[31] The other three studies found no significant association between oral clefts and either PM or O_3.

Of the three studies that investigated the relationship between oral clefts and modeled data to estimate PM, one used annual PM values and two averaged PM values over the entire critical window. In one study, cases were assigned the average exposure in the census ward of the residence at birth. The other two studies assigned exposure based on grid values for the residence at birth. None found significance.

Of the four studies that investigated the relationship between oral clefts and modeled PM and O_3, three studies averaged exposure over the entire critical window, one averaged over the first trimester, and one also averaged over the three months prior to conception. Three studies assigned the grid estimate of exposure at the residence of birth and one study assigned exposure based on the average exposure for the entire hospital referral area. One study found an OR of 0.90 (95% CI = 0.82-0.99) for combined oral clefts given a $5\frac{\mu g}{m^3}$ change in $PM_{2.5}$.[38] One study found an OR of 1.43 (95% CI = 1.11-1.86) for cleft palate given a $10\frac{\mu g}{m^3}$ increase in $PM_{2.5}$.[39] The third study to find significance found an adjusted OR of 1.74 (95% CI = 1.15-2.64) for cleft palate and $PM_{2.5}$ during the critical window and of 1.72 (95% CI = 1.12-2.66) for cleft palate and PM_{10} in the three months prior to conception.[40]

1.4.3 Craniosynostosis and air pollution

Two studies explored the relationship between craniosynostosis and both PM and O_3. One study used inverse distance weighting of monitoring station data and included births within 5km of the monitoring stations.[47] They analyzed quartiles of exposure. They found no association between craniosynostosis and either O_3 or $PM_{2.5}$. Their study averaged exposure measures over the first two months of pregnancy, which reduces variation in exposure values and limits how closely exposures can be linked to different points during the critical window.

The other study used modeled PM and O_3 measures based on CMAQ.[38] The modeled data allowed use of births from the entire state, but exposure was averaged over the entire first trimester. They analyzed exposure as continuous values and found an adjusted OR of 0.78 (95% CI 0.64-0.96) for a $5\frac{\mu g}{m^3}$ increase in $PM_{2.5}$ in a multi-pollutant model and could not explain why higher odds of craniosynostosis would be associated with lower $PM_{2.5}$. They also found an adjusted OR of 1.38 (95% CI 1.11-1.72) for a 13.3ppb increase in O_3.

1.5 Summary

All studies used average values for their exposures. Most averaged over the critical window period, around 3 to 10 weeks, and some averaged by month or over the entire first trimester. Only one study looked at exposure prior to pregnancy. Since a few studies also had small study areas, this could reduce variation in the exposure and complicate detection of significant variations. All studies used residence at birth to assign exposure. For most studies, residential and daily mobility while pregnant was unavailable.

The studies used a variety of covariates, the most common of which were maternal age, race, ethnicity, education, and smoking. All of these except maternal age are associated with SES, which is associated with air pollution, and three (maternal age, race, and smoking) are associated with birth defects.

This dissertation used the NYS CMR and NYS Vital Records data. Vital Records data contained residence at birth, which was used as the exposure source, as other studies have done. Vital Records data also contained the covariates listed in the previous paragraph, as well as date of birth and estimated gestational age in days.

This dissertation addressed the weaknesses in past research in two ways. First, it covered the entire NYS outside of NYC for a period of fifteen years, which allowed for a wide variation of $PM_{2.5}$ and O_3 measures. Second, it used weekly mean and peak exposures beginning before birth to capture exposure in greater detail and allow for a possible lagged response to the exposures.

This dissertation aimed to fill part of the gap in knowledge by exploring the relationship between birth defects and maternal exposure to ambient air pollution in NYS. Because most studies lack time varying exposure, may use imprecise gestational age, and/or are not state-wide, this dissertation could provide valuable insight into the connection between birth defects and air pollution. This dissertation addressed temporality and variation in exposure by using weekly modeled measurements instead of averages over the trimester, month, or critical window. This dissertation used estimated date of conception to determine the critical window instead of the month and used point-level maternal residence addresses, so exposure could be assigned to the modeled grids rather than to county or tract averages.

Tables

Table 1.1: A summary of epidemiological studies that have examined exposure to PM and O_3 and select birth defects

Author, Year	**Design, Population**	**Study size**	**Exposure**	**Outcome**	**Methods**	**Findings**	**Covariates**
Dolk et al, 2010	ecologic, birth defects registries (UK), 1991-1999	759993 births in 1474 wards	PM10 annual value	CP, CLP	assigned rate per ward from grid values	Non-significant	maternal age
Gasca-Sanchez et al, 2019	ecological	333 cases	PM_{10}	CLP	assigned monthly means of daily kriging values from monitoring stations	spatial association between CLP and PM10	NA
Gilboa et al, 2005	case-control, birth defects registry (TX), 1997-2000	7381 case, 4580 control	week 5-10 average, PM_{10}, O_3	CP, CLP	assigned nearest monitoring station, no max distance	Non-significant	maternal alcohol, age, education, race, parity, ethnicity, prenatal care, season, smoking
Girguis et al,2016	case-control, birth defects registry (MA), 2001-2008	726 case, 7816 control	week 6-12 average, $PM_{2.5}$	CP, CLP	assigned modeled 4km grid value	Non-significant	maternal age, language, race/ethnicity, plurality, education, insurance, smoking, prenatal care, alcohol, marital status
Hansen et al, 2009	case-control, birth defects registry (Australia), 1998-2004	302 case, 1510 control?	week 3-8 average, PM_{10}, O_3	CP, CLP	assigned nearest monitoring station to tract centroid, no max distance	PM_{10} + CP 4 $\frac{\mu g}{m^3}$ change: OR 0.69 (0.50-0.93)	infant sex
Huang et al, 2021	case-control, birth defects registry (China), 2019	635 case, 31914 control	$PM_{2.5}$, PM_{10}, O_3	CP, CLP, CF with other CM combined	assigned means of kriging values from monitoring stations	PM_{10} OR 2nd month 1.14 (1.12-2.43), 3rd month 1.51 (1.13-2.03)	maternal age, education, parity, infant sex, birth weight, residence, other air pollutants

Table 1.1: A summary of epidemiological studies that have examined exposure to PM and O_3 and select birth defects *(continued)*

Author, Year	**Design, Population**	**Study size**	**Exposure**	**Outcome**	**Methods**	**Findings**	**Covariates**
Hwang et al, 2008	case-control, birth defects registry (Taiwan), 2001-2003	653 case, 6530 control	monthly average for 1st 3 months, PM_{10}, O_3	CP, CLP	assigned neighborhood level distance-weighted monitoring station value	CLP + O_3 10ppb change: month1 aOR 1.17 (1.01-1.36), month2 aOR 1.22 (CI 1.03-1.46)	maternal age, gestational age, population density, conception season, plurality
Marshall et al, 2010	case-control, birth defects registry (NJ), 1998-2003	414 + 303 case, 12925 control	week 5-10 average, days > 90th pctile, O_3, $PM_{2.5}$, PM_{10}	CP, CLP	assigned monitoring station value up to 40km	Non-significant	maternal age, race, ethnicity, smoking, alcohol, conception season
Padula et al, 2013a	case-control, NBDPS and CHAPS, 1997-2005	874 case, 849 control	month 1-2 average, $PM_{2.5}$, O_3	CS	assigned value from inverse square distance weighting	Non-significant	maternal race, ethnicity, nativity, education, parity, smoking, birthyear, infant sex
Padula et al, 2013b	case-control, NBDPS and CHAPS, 1997-2006	806 case, 849 control	month 1-2 average, $PM_{2.5}$, O_3	CP, CLP	assigned interpolated distance value up to 50km	Non-significant	maternal age, parity, smoking, year, infant sex
Rankin et al, 2009	case-control, birth defects registry (UK), 1985-1990	195 case, 11816 control	1st trimester average, PM_4	CP, CLP	assigned average of all stations within 10km	Non-significant	birthweight, infant sex, deprivation (SES)
Ritz et al, 2002	case-control, birth defects registry (CA), 1987-1993	876 case, 10649 control	PM_{10}, O_3	CP, CLP	assigned monthly estimates based on monitoring station data	Non-significant	birth decade, maternal age, race, education, prenatal care, conception season, parity, single vs multiple birth
Schembari et al, 2014	case-control, birth defects registry (Spain), 1994-2006	2247 case, 2991 control	week 3-8 average, $PM_{2.5}$, PM_{10}	CP, CLP (non-chromo-somal)	assigned ESCAPE model value	Non-significant	maternal smoking, education, age, conception season, birthyear

Table 1.1: A summary of epidemiological studies that have examined exposure to PM and O_3 and select birth defects *(continued)*

Author, Year	**Design, Population**	**Study size**	**Exposure**	**Outcome**	**Methods**	**Findings**	**Covariates**
Tanner et al, 2015	case-control, birth defects registry (FL), 2000-2009	2361 case, 1.7m control	CL 3-8 week, CP 5-12 week, CLP 3-12 week average, $PM_{2.5}$	CP, CLP	assigned average of census tract monitoring stations	Non-significant	maternal nativity, age, race/ethnicity, parity, education, smoking, marital status, block group median income, infant sex, year
Vinikoor-Imler et al, 2013	case-control, birth defects registry (NC), 2003-2005	395 case, 322574 control	week 3-8 average, $PM_{2.5}$, O_3	CP, CLP	assigned average of Downscaler grid	Non-significant	maternal age, education, parity, race/ethnicity, smoking, marital status, prenatal care, urbanicity, month
Vinikoor-Imler et al, 2015	case-control, birth defects registry (TX), NBDPS, 2002-2006	21k case, 1.4m control	1st trimester average, PM2.5, O_3	CP, CLP, CS	assigned average of Downscaler grid	$PM_{2.5}$ + combined oral clefts $5\frac{\mu g}{m^3}$ change OR 0.90 (0.82-0.99); $PM_{2.5}$ + CS $5\frac{\mu g}{m^3}$ change aOR 0.78 (0.64-0.96); O_3 + CS 13.3ppb change OR 1.28 (1.04-1.58)	prenatal care, parity, maternal age, education, race/ethnicity, urbanicity
Wang et al, 2018	case-control	1525 case, 747k control	monthly average for 1st 3 months, PM_{10}	CP, CLP, CF	assigned monthly means of daily kriging values from monitoring stations	PM10 + CP (month1 RR = 1.086; CI: 1.013-1.165); PM10 + CLP (month2 RR = 1.046; CI: 1.013-1.080)	temperature, humidity
Zhou et al, 2017	case-control, NBDPS, 2001-2007	all case, all birth	week 5-10 average, $PM_{2.5}$, O_3	CP, CLP	assigned average of Downscaler grid	$PM_{2.5}$ + CP $10\frac{\mu g}{m^3}$ increase OR 1.43 (1.11-1.86)	infant sex, maternal race, ethnicity, smoking, age, education, parity
Zhu et al, 2015a	case-control, study population (MD), 2002-2008	222 case, 188k control	3-month preconception + week 3-8 average, $PM_{2.5}$, PM_{10}, O_3	CP, CLP	assigned average CMAQ value for hospital referral area	PM_{10} + CP_{pre} (aOR 1.72; CI: 1.12-2.66); $PM_{2.5}$ + CP_{wk3-8} (aOR 1.74; CI: 1.15-2.64)	maternal age, parity, race/ethnicity, marital status, insurance, BMI, season, smoking, alcohol, diabetes
Baldacci et al, 2018	systematic review	NA	$PM_{2.5}$, PM_{10}, O_3	CP, CLP, CS	NA	Non-significant	NA

Table 1.1: A summary of epidemiological studies that have examined exposure to PM and O_3 and select birth defects *(continued)*

Author, Year	**Design, Population**	**Study size**	**Exposure**	**Outcome**	**Methods**	**Findings**	**Covariates**
Rao et al, 2016	systematic review	NA	PM_{10}, O_3	CP, CLP	pooled 5 studies for PM_{10}, 4 studies for O_3	O_3 + CLP OR 1.08 (1.01-1.16)	NA
Ravindra et al, 2021	systematic review	NA	PM_{10}	CP, CLP, CS	pooled 6 studies for PM_{10} and oral clefts	OR = 0.87 (0.79<96>0.93)	NA

Note:

Abbreviations: CP=cleft palate; CLP=cleft lip with or without cleft palate; CS=craniosynostosis; CF=clubfoot

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2. Individual Air Pollutants and Risk of Birth Defects

2.1 Background

Birth defects affect 3-5% of infants in the United States annually.[1] In NYS, they result in 20% of deaths among infants between one month and one year old[2] and babies born with birth defects are ten times more likely to die before they are a year old than babies without birth defects.[3] Roughly 125,000 children are born in Upstate New York each year. Of these, approximately 6000 children are diagnosed with birth defects before age 3.[4]

To date, approximately 30%-40% of birth defects have known causes related to genetics, environment, and maternal health.[5,6] The rest are not well understood and are believed to have multiple causes that interrelate.[6] Birth defects vary in how strongly genetics contributes to their rates.

Air quality is an ongoing concern in NYS. One study reported that the NYS population-weighted average of exposure to $PM_{2.5}$ was $11.2\frac{\mu g}{m^3}$ and to O_3 was 38ppb.[7] Poor air quality has been linked to asthma, cardiovascular diseases, cancer, and low birthweight in NYS. In urban areas, traffic, industry, and commercial waste add to air pollution. In rural areas, burning agricultural waste and using wood-burning stoves to heat homes add to air pollution.

The connection between birth defects and maternal smoking via oxidative stress is well documented.[8–13] Many components of cigarette smoke, such as benzene and chromium VI[14], are also found in PM and in ambient air.[15] Some of these components are believed to cause epigenetic changes in the developing fetus. Pregnant women exposed to higher concentrations of air pollution show more markers of DNA damage that are associated with oxidative stress than pregnant women exposed to lower concentrations of air pollution.[16] Given similarities between cigarette smoke and some forms of air pollution, notably $PM_{2.5}$, a possible link between air pollution and birth defects was explored.

The three birth defects investigated in this study include clubfoot, oral clefts, and craniosynostosis, which are among the more common birth defects in NYS, with over 100 cases born with each birth defect annually.[3] They were selected because they are posited to be susceptible to oxidative stress caused by similar routes of exposure. All three birth defects have an increased risk of developing if the mother smokes[8–13] and can be diagnosed prenatally.[17–19]

Air pollution may be a risk factor for development of oral clefts, clubfoot, and craniosynostosis in the fetus. Results of research have been inconclusive.[11,12] Studies have not been directly comparable, however. They vary in whether they use monitored or modeled pollution data, size of the study area and availability of pollution data throughout the study area, and frequency of pollution measurements.

This study explored the association between maternal exposure to $PM_{2.5}$ and O_3 during the first trimester of pregnancy using statewide time-varying data for the exposures and a statewide dataset for the outcomes from 2002 to 2015 in NYS. It used a case-cohort design with logistic regression to determine the relationship between select measures of air pollution and select birth defects.

2.2 Methods

2.2.1 Study population

The study population was identified through NYS Vital Records, a registry of all births in NYS, and included all live births in NYS outside NYC, with residence addresses in NYS, that were conceived between February 1, 2002 and December 31, 2015. This time frame allowed for one month of exposure prior to the earliest estimated conception date and three months of exposure (until the end of the critical window) following the latest estimated gestation date. The conception date was assigned the last menstrual period if available and within one year of the birth date; otherwise, clinical age of gestation at birth was subtracted from the birth date. Births were geocoded at street level to the mother's residence at birth. If they could not be geocoded, they were assigned to the centroid of the mother's residence Zone Improvement Plan (ZIP) code. Births were excluded if they had invalid NYS ZIP codes (170 births), had maternal residence outside NYS (9,949 births), or were missing gestational age at birth or date of last menstrual period (77 births), as missing these fields made linking to environmental data impossible.

Controls were selected at random from all births in the study population. For each case group, three controls per case were selected, matched on year of birth. Controls were not limited to non-cases. Cases were selected by identifying the infants with the relevant birth defects in the NYS CMR.[4] The CMR and Vital Records[20] are linked, so all case-level variables except BPA codes[21] and malformation narratives came from Vital Records.

Cases were classified as shown in Table 2.1 and included infants with clubfoot, oral cleft (lip and/or palate), or craniosynostosis. Craniosynostosis, clubfoot, and cleft palate alone were distinct groups. Cleft lip occurs when the cells on each side of the head do not fuse fully before birth and cleft palate occurs when the palate of the mouth does not fuse fully before birth.[22] This study separated oral clefts into two groups, cleft palate alone and cleft lip with or without cleft palate, as the causes of cleft lip and cleft palate may have different biological mechanisms and are often evaluated separately in birth defects studies. This study combined cleft lip and palate with cleft lip alone, consistent with other studies.

In all, 472 cases were excluded from the four case groups because they had various genetic syndromes in addition to the birth defects of interest as their causes may be genetic rather than environmental. Cases with the following syndromes were excluded based on narrative descriptions and additional diagnosis codes: Antley-Bixler, Apert, Beals-Hecht, Beckwith-Wiedemann, Birk-Barel, Bohring-Opitz, Carey-Fineman-Ziter, Carpenter, CHARGE, Cornelia De Lange, Cri du Chat, Crouzon, DiGeorges, Ehlers-Danlos, Ellis-Van Creveld, Escobar, Fanconi, Femoral Facial, Fragile X, Freeman-Sheldon, Fryns, Gardner-Silengo-Wachtel, Hay-Wells, Jacobsen, Joubert, Kabuki, Kallmann, Kenny-Caffey, Larsen, Loeys-Dietz, Marfan, Meckel-Gruber, Miller-Dieker, Moebius, Nager, Noonan, Oral-Facial-Digital, Otopalatodigital, Pena-Shokeir, Peters-plus, Pfeiffer, Pierre-Marie-Bamberger, Reiters, Roberts, Rubenstein-Taybi, Smith-Lemli-Opitz, Stickler, Treacher-Collins, Turner, Van der Woude, Velo-Cardio-Facial, William, Wolf-Hirschhorn, Zellweger, and various deletion syndromes. Trisomies, which include Down, Edwards, and Patau syndromes, were also excluded.

2.2.2 Exposure assessment

This study used the Downscaler air pollution model[23,24] developed by the EPA to estimate daily hazardous air pollutant (HAP) exposure for the years 2002-2016. The Downscaler dataset provides modeled daily estimates of average $PM_{2.5}$ and maximum O_3 exposure for someone at ground level averaged over census tracts throughout NYS. This model is based on the CMAQ model[25], which is a complex air transport model that incorporates meteorology, land use, atmospheric chemistry and several types of pollution sources. This allows for reasonable estimates of exposure for the entire area. Downscaler recalibrates the CMAQ estimates using air monitoring station data. Weekly average and peak measures of modeled $PM_{2.5}$ and O_3 were calculated from four weeks prior to pregnancy until week 12 of gestation, inclusive. $PM_{2.5}$ and O_3 exposure were calculated from the modeled estimates of $PM_{2.5}$ and O_3, respectively, in the census tract where the residence at birth was geocoded.

2.2.3 Statistical analysis

This study used data from the years 2002-2016 to model each air pollutant and birth defect pair individually. The exposure times covered from 4 weeks prior to conception until 12 weeks after conception. Mother's birth residence was geocoded and if it could not be geocoded, the zip code centroid was used. Air pollutant measures ($PM_{2.5}$ and O_3), census measures (median household income), and RUCA scores were assigned to each birth based on the census tract of the mother's residence. Location data were spatially joined in ArcGIS.[26]

Descriptive analyses were run on all variables to check for missing data, outliers, and coding issues. Each variable to be considered for analysis was evaluated separately. Missing data and impossible values were assessed and were not imputed. Univariate analyses for categorical variables included frequencies and proportions. Categorical variables included infant's sex, mother's race, mother's ethnicity, mother's pre-pregnancy diabetes, mother's smoking, mother's alcohol use, mother's education level, Rural-Urban Commuting Area (RUCA) score, infant's cleft palate, infant's cleft lip and/or palate, infant's craniosynostosis, infant's clubfoot, infant's year of conception, infant's month of conception, and whether the mother's residence was geocoded or assigned the zip code centroid. Univariate analyses for continuous variables included summary statistics, such as mean, mode, median, range, interquartile range, and variance. Data transformations, such as log scale, were considered and rejected. Some continuous variables were categorized into ranges. Numeric variables include mother's body-mass index (BMI), $PM_{2.5}$ and O_3 peaks and means for each week from one month before conception to three months after conception, median household income, and mother's age.

Bivariate analyses were performed among all variables. Chi-square tests were run for categorical variables, t-tests to compare dichotomous and continuous variables, and correlation tests for continuous variables. Several variables measured components of SES, including mother's race, mother's education level, and median household income. Where two of these covariates were closely correlated, only one was chosen based on which one is more closely associated with the exposures and outcomes.

Logistic regression models were used to calculate adjusted risk ratio (RR)s and 95% CIs for each birth defect group and air pollutant measure. Models were adjusted for the following covariates from birth certificate data: mother's education level, mother's smoking, and season of conception, and median tract-level income from the US Census.[27]

The multivariate analysis contained several components. First, a series of distributed lag logistic models were run from the R package dlnm[28] for each birth defect group and combination of O_3 and $PM_{2.5}$. These models have been used previously to study birth outcomes.[29] Since an estimate of reasonable lag was not available, but people can experience both chronic and acute (same day) effects of inhaling $PM_{2.5}$, this study used several possible lag times ranging from one month before estimated conception to estimated end of first trimester, each one week apart.

For clarity the lag weeks were as follows, all calculated from estimated conception date. For the first run, lag 0 was the last week of the first trimester (week 12) of pregnancy, lag 12 was the week of conception, and lag 16 was the week one month before conception. For the second run for the other three case groups, lag 0 was the last week of the second month (week 8) of pregnancy, lag 8 was the week of conception, and lag 12 was the week one month before conception. The first run was intended to capture any association in the first trimester. The second run was intended to focus on the second month of pregnancy, when cranial features develop.

This approach allowed modeling of the change in values from week to week, any possible effect of exposure a few weeks prior to the critical window of weeks 3 to 12 of pregnancy, and the week during that time that shows the strongest association with each outcome.[30] Running the models using weekly peaks as well as weekly averages captured spikes in exposure effect that would be smoothed out by only averaging. One set of models contained means for O_3 or $PM_{2.5}$; the other set contained peaks for O_3 or $PM_{2.5}$.

Models were run twice. The first time, the basic exposure-outcome models were run to check Akaike information criterion (AIC) values and residuals with best fit lines to determine the settings for each cross-basis. Settings considered included the shapes of linear, polynomial, or natural splines for the relationship between exposure and outcome at lag 0 and for the relationship between exposure and outcome for the matrix containing the remaining lags. For polynomial and natural splines settings, degrees ranged from 2 to 8 and knots ranged from 3 to 8, respectively. The basic model had this structure:

$$logit(RR_{bd}) = \beta_0 + \sum (\alpha_j Air)$$

- $\alpha_j Air$ = series of betas for each week of estimates for each air pollutant ($PM_{2.5}$ or O_3)
- bd = birth defect (cleft lip with or without cleft palate, cleft palate, craniosynostosis, or club-foot)

For all cross-basis analyses, a linear relationship between exposure and outcome at lag 0 (end of the first trimester in the four-month evaluation and eight week of pregnancy in the three-month evaluation) resulted in the best combinations of lower AIC values and more horizontal fitted lines on the residual plots, so this setting was used for all cross-basis objects. The relationship between exposure and outcome for the matrix containing the remaining lags varied depending on the air pollutant and birth defect, but in general, linear relationships and polynomial relationships using two to four degrees gave the best results. Final selected settings are shown in Table 2.2.

After the cross-basis settings were selected, the full covariate models were run with these settings to determine critical weeks. For diagnostic models, the cross-prediction object was centered on the overall first quartile value for the air pollutant measure and the prediction plot was centered two standard deviations from the mean for the air pollutant measure, which was considered the upper bound of typical values.

The full models were based on a directed acyclic graph developed a priori of the relationship between air pollution and birth defects, shown in Figure 2.1.[31] Season of conception was included since the mother may have spent more time indoors in colder months and some components of $PM_{2.5}$ increase in colder weather while others decrease, and the $PM_{2.5}$ estimates alone would not be sufficient to capture that variation. Seasons of conception were coded as “winter” (December to February), “spring” (March to May), “summer” (June to August), and “autumn” (September to November). Maternal education level was coded as “some high school” (did not complete high school), “high school graduate” (completed high school, but no further education past high school), “some college” (education past high school, but no college degree), “college graduate” (college degree, but no further education), and “advanced education” (any education past a college degree). Smoking was coded as “yes” (ever smoked during pregnancy) or “no” (never smoked during pregnancy). Tract-level median household income was included as a proxy for socio-economic status and was coded as “low” (lowest quartile), “medium low” (second quartile), “medium high” (third quartile), and “high” (highest quartile). Four models were run for each birth defect group: $PM_{2.5}$ or O_3, with either mean or peak values. The full lagged model looked like this:

$$logit(RR_{bd}) = \beta_0 + \sum(\alpha_j Air) + \beta_1 Education + \beta_2 Season + \beta_3 Smoking + \beta_4 Income$$

- $\alpha_j Air$ = series of betas for each week of estimates for each air pollutant ($PM_{2.5}$ or O_3)
- bd = birth defect (clubfoot, cleft lip with or without cleft palate, cleft palate, or craniosynostosis)

The final model contained all weeks of exposure without regard to significance. All analyses were completed in R.[32]

2.2.4 Sensitivity analysis

Smoking while pregnant is under-reported in NYS[33], so sensitivity analysis was performed to identify whether that under-reporting was likely to influence study results. The sensitivity analysis was a thought experiment due to the strong association between most of the birth defects and maternal smoking.

Roughly 95% of clubfoot cases in the NYS CMR are talipes equinovarus, but which 95% is not available. Sensitivity analysis was performed to identify the likelihood that misclassifying clubfoot may influence study results using the EValue[34] package in R. This package models potential bias due to unmeasured confounders based on estimated prevalence of those confounders.

Sensitivity analysis was performed for geocodability for two reasons: (1) urban areas are more likely to be geocoded in NYS than rural areas and (2) residences geocoded to the ZIP code centroid, especially in rural areas where the ZIP code area may be large, could be assigned to the wrong census tract and therefore assigned the wrong exposure. The sensitivity analysis was performed by rerunning the model with only cases geocoded at street level and comparing the resulting model estimates and confidence intervals to the full-data models.

2.3 Results

2.3.1 Descriptive analysis

Per Table 2.4, non-cases included 18,153 births that were conceived between February 1, 2002 and December 31, 2015 and born to mothers living in NYS outside NYC across all four study groups. Cases included 2,423 births with clubfoot, 952 births with cleft palate, 1,281 births with cleft lip with or without cleft palate, and 931 births with craniosynostosis after excluding genetic syndromes. Across all controls, 78.9% of mothers reported white race and 84.5% of mothers reported non-Hispanic ethnicity. Among the case groups, 82.5%-84.4% of mothers reported white race and 84.1%-87.4% of mothers reported non-Hispanic ethnicity. Across all controls, 15.4% of mothers reported smoking while pregnant; among cases, 18.6%-22.3% of mothers reported smoking while pregnant. Across all controls, 61.2% of mothers reported education above high school; among cases, 52.3%-61.5% of mothers reported education above high school. Across all controls, 28.7% of mothers reported ages between 30 and 34; among cases, 25.1%-30.0% of mothers reported ages between 30 and 34.

Exposures were assigned to all cases and controls throughout the study period based on census tract of mother's residence and estimated week of conception. As shown in Table 2.3, the mean weekly O_3 mean concentration was 37.2ppb for all controls and 36.1 to 37.6ppb for the case groups. The mean weekly O_3 peak concentration was 48.3ppb for all controls and 46.7 to 48.9ppb for the case groups. The mean weekly $PM_{2.5}$ mean concentration was $10.0\frac{\mu g}{m^3}$ for all controls and 9.8 to $10.1\frac{\mu g}{m^3}$ for the case groups. The mean weekly $PM_{2.5}$ peak concentration was $16.8\frac{\mu g}{m^3}$ for all controls and 16.3 to $17.0\frac{\mu g}{m^3}$ for the case groups.

2.3.2 Multivariate Analysis

As shown in Table 2.5, the cumulative effect of air pollution was not associated with any of the birth defects studied during the time period of one month prior to conception through the end of the third month of pregnancy. In general, the effect of O_3 on the risk of developing the birth defect was at or above an RR of 1.0 for clubfoot and cleft palate and below 1.0 for cleft lip with or without cleft palate and craniosynostosis. The effect of $PM_{2.5}$ on the risk of developing the birth defect was lower than for O_3 for all birth defects except craniosynostosis, for which the RR was around 1.0, just above the RR for O_3. These patterns held true in both the 12-week and 16-week evaluations.

Clubfoot

In the 12- and 16-week evaluations, the effects of a 10ppb increase on weekly O_3 concentrations on risk of clubfoot were similar between mean O_3 and peak O_3. The effects of both were highest prior to conception and decreased linearly as the pregnancy progressed to the end of the evaluations.

In the 12-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase in weekly $PM_{2.5}$ mean concentration on clubfoot was slightly curved with the highest effect in week 8 of pregnancy. In the 16-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase in weekly $PM_{2.5}$ mean concentration on clubfoot was slightly curved with the highest effect in weeks 11 to 12 of pregnancy. In the 12-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase in weekly $PM_{2.5}$ peak concentration on clubfoot was curved with the highest effect in weeks 2 to 3 of pregnancy. In the 16-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase in weekly $PM_{2.5}$ mean concentration on clubfoot was curved with the highest effect in weeks 6 to 8 of pregnancy. See Table 2.6 and Figure 2.2 for full results.

Cleft lip with or without cleft palate

In the 12- and 16-week evaluations, the effects of a 10ppb increase of weekly O_3 concentrations on the risk of cleft lip with or without cleft palate were similar between mean O_3 and peak O_3. The effects of both were significantly higher at $\alpha < 0.05$ in the weeks just before to just after conception. In the 12- and 16-week evaluations, the effects of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ mean concentration on the risk of cleft lip with or without cleft palate were consistently below the RR of 1.0 for all weeks. In the 12-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ peak concentration was curved with the highest effects in weeks 1 to 3 of pregnancy. In the 16-week evaluation, the effects of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ peak concentration was consistently below the RR of 1.0 for all weeks. See Table 2.7 and Figure 2.3 for full results.

Cleft palate

In the 12-week evaluation, the effect of a 10ppb increase of weekly O_3 mean concentration on the risk of cleft palate was consistently at the RR of 1.0 for all weeks. In the 16-week evaluation, the effect of a 10ppb increase of weekly O_3 mean concentration was highest in the weeks just before to just after conception. In the 12- and 16-week evaluations, the effects of a 10ppb increase of weekly O_3 peak concentrations on the risk of cleft palate were similar. The effects of both were higher in the weeks just before to just after conception. In the 12-week evaluation, the effects of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ concentration on the risk of cleft palate were similar between mean

$PM_{2.5}$ and peak $PM_{2.5}$. The effects of both were highest in week 8 of pregnancy. In the 16-week evaluation, the effects of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ concentration on the risk of cleft palate were similar between mean $PM_{2.5}$ and peak $PM_{2.5}$. The effects of both were highest in weeks 4 to 7 of pregnancy. See Table 2.8 and Figure 2.4 for full results.

Craniosynostosis

In the 12-week evaluation, the effects of a 10ppb increase on weekly O_3 concentrations on risk of craniosynostosis were similar between mean O_3 and peak O_3. The effects of both were highest in the weeks just before to just after conception. In the 16-week evaluation, the effect of a 10ppb increase of weekly O_3 mean concentration was highest in weeks 8 to 9 of pregnancy and the effect of a 10ppb increase of weekly O_3 peak concentration was highest in weeks 2 to 5 of pregnancy. In the 12-week evaluation, the effects of a $10\frac{\mu g}{m^3}$ increase on weekly $PM_{2.5}$ concentrations on risk of craniosynostosis were similar between mean $PM_{2.5}$ and peak $PM_{2.5}$. The effects of both were highest in the weeks just before to just after conception. In the 16-week evaluation, the effect of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ mean concentration was significantly higher at $\alpha < 0.05$ around the week of conception and the effect of a $10\frac{\mu g}{m^3}$ increase of weekly $PM_{2.5}$ peak concentration was highest around the week of conception. See Table 2.9 and Figure 2.5 for full results.

2.3.3 Sensitivity analysis

For three of the study groups, clubfoot, cleft palate, and cleft lip with or without cleft palate, maternal smoking during pregnancy was significantly associated with the birth defect of interest. From descriptive analyses, the percent of mothers whose infants were born with these birth defects and who smoked during pregnancy ranged from 20% to 22%, while the percent of mothers among the combined control groups who smoked during pregnancy was 15%. While under-reporting of maternal smoking on birth certificates has been documented in NYS, this difference between cases and controls would likely still exist even if maternal smoking was accurately reported. The roughly 1% of records missing maternal smoking would not have impacted the significance.

To check if misclassification of clubfoot would have an appreciable impact, the R package EValue[34] was used. Tests for clubfoot against all four pollutant measures were non-significant, suggesting that any misclassification would not appreciably impact model results. To check if misclassification of exposure due to failure to geocode would have an appreciable impact, 507 records that could only be geocoded at ZIP code level were removed and the models were run with the remaining records. In comparing the pairs of models, all estimates for the model with centroids removed fell inside the respective confidence intervals for the paired model without centroids removed, suggesting that any misclassification would not appreciably impact model results.

2.4 Discussion

2.4.1 Cumulative effect

This study proposed that a relationship exists between select measures of air pollution and select birth defects. Results varied by evaluation (three- or four-month), case group, and air pollution measure. Overall, there were no strong cumulative associations between air pollution and birth defects in any of the evaluations.

Research on the association between birth defects and air pollution is inconclusive. Most studies have used monitoring station data and most have used means or single weighted estimates to represent exposure over periods ranging from one to three months. Consistent with most research, risk ratios for the full time period were not significant, likely because development of birth defects is time-dependent, so the longer the time period under consideration, the more likely the effect is to be diluted. These results suggest that looking at discrete time periods may show stronger effects than looking at broader, more general time periods. Of the 18 studies reviewed, 7 found significant relationships between at least one of the birth defects we studied and $PM_{2.5}$ or O_3.

In this study, while we found no cumulative associations, air pollutant exposures for some individual weeks were associated with one or more of the birth defects of interest. Only one of the studies we reviewed evaluated any birth defects by week.[35] That study reviewed oral clefts and modeled CMAQ exposures. In general, O_3 had the highest effects on the risk of each birth defects around conception and $PM_{2.5}$ had the highest effects on the risk of each birth defect during the birth defects' critical windows of pregnancy.

2.4.2 Clubfoot

Weekly O_3 mean and peak concentrations had the highest effect on risk of infants being born with clubfoot before conception, well before the limbs start to form. Weekly $PM_{2.5}$ mean and peak concentrations in two evaluations had the highest effects during the critical window, when the limbs are forming, weekly $PM_{2.5}$ mean concentration in the 16-week evaluation had the highest effect just after the limbs finish forming, and weekly $PM_{2.5}$ peak concentration in the 12-week evaluation had the highest effect just before the limbs start forming. While clubfoot can form later in pregnancy due to awkward positioning in the womb, notably for multiple birth pregnancies, there is not a clear mechanism linking air pollution to awkward positioning.

Only one previous study of clubfoot and either PM or O_3 was identified and its results were non-significant.[36] However, that study averaged the entire first trimester and used a model based on monitoring station data. Averaging may have diluted any effect and modeling may have resulted in misclassification if monitoring stations were far apart and other air pollution sources were not considered. Another study combined clubfoot with several other birth defects and found associations with monitoring station monthly PM_{10} mean concentrations.[37] However, the extent to which clubfoot contributed to those associations is unknown.

2.4.3 Cleft lip with or without cleft palate

Weekly O_3 mean and peak concentrations had the highest effect on risk of infants being born with cleft lip with or without cleft palate around conception, well before the mandible starts to form, and all results were significant. Weekly $PM_{2.5}$ peak concentration in the 12- week evaluation had the highest effect in early pregnancy, just before the mandible starts to form. The remaining $PM_{2.5}$ measures had no effect on risk of cleft lip with or without cleft palate in their evaluations.

Of 16 prior studies of cleft lip with or without cleft palate and O_3 or PM that we reviewed, 11 used monitoring station data and 5 used modeled data. All of the studies averaged exposures over time periods of a month or more. None of the studies using modeled data reported significant findings. Two of the studies using monitoring station data reported significant findings. The only study to report a significant association with O_3 reported it for months 1 and 2 of pregnancy.[38] While our study found a higher effect of O_3 on risk before conception, a second, less high and non-significant, effect was sometimes present for a few weeks later in the pregnancy, depending on the model, consistent with this study.

Consistent with our findings, no studies found any associations with PM before conception. No studies found and associations in month 1 of pregnancy and one study found a strong association with PM_{10} in month 2 of pregnancy.[36] This makes sense, since the mandible forms in weeks 3 to 8 of pregnancy, a time period that roughly corresponds with month 2 of pregnancy. No prior studies reported PM associations during month 3 of pregnancy, but one study that combined all oral clefts together reported an association with $PM_{2.5}$ for the full first trimester.[39]

2.4.4 Cleft palate

Weekly O_3 mean and peak concentrations had the highest effect on risk of infants being born with cleft palate around conception in two evaluations, well before the palatine shelves start to form; in the other two evaluations, they had no effect or the effect was highest at week 12 of pregnancy, after the palatine shelves have finished forming. Weekly $PM_{2.5}$ mean and peak concentrations had the highest effect during the critical window when the palatine shelves are forming.

Of 16 prior studies of cleft lip with or without cleft palate and O_3 or PM that we reviewed, 11 used monitoring station data and 5 used modeled data. All of the studies except one averaged exposures over time periods of a month or more. None reported significance with O_3, which is not consistent with our findings.

Of the four studies that reported significance with $PM_{2.5}$, two used modeled data and two used monitoring station data. The two studies that used monitoring station data reported significant associations with PM_{10} averaged over the first month of pregnancy[36] and averaged over weeks 3 to 8 of pregnancy[40]. While the first month of pregnancy is not consistent with our findings, all weeks with strong effects of $PM_{2.5}$ in our study fall between weeks 3 and 8 of pregnancy. One of the studies that reported significance with modeled PM data used Downscaler, as we did, and the other used CMAQ, the model on which Downscaler is based. The study using Downscaler reported significance with $PM_{2.5}$ during the combined period of week 5 to 10 of pregnancy[7], which is consistent with our findings. The study using CMAQ reported significance with PM over several time periods, including with PM_{10} in the three-month period prior to conception and with $PM_{2.5}$ during the combined period from week 3 to 8 of pregnancy and during each individual week from week 3 to week 5 of pregnancy[41], which is earlier in the pregnancy than our findings.

2.4.5 Craniosynostosis

Weekly O_3 mean and peak concentrations in the 12-week evaluation had the highest effect on risk of infants being born with cleft palate around conception, well before the cranium starts to form. In the 16-week evaluations, weekly O_3 mean concentration had the highest effect at the end of the critical window and weekly O_3 peak concentration had the highest effect at the beginning of the critical window. Weekly $PM_{2.5}$ mean and peak concentrations in the 12-week and 16-week evaluations had the highest effects around conception, well before the cranium starts to form.

Only two studies have evaluated the association between craniosynostosis and air pollution. The study that averaged distance-weighted monitoring station measures over the first two months found no association with either $PM_{2.5}$ or O_3.[42] The study that averaged Downscaler estimates over the full first trimester found associations with both $PM_{2.5}$ and O_3.[39] As our study found high effects of both $PM_{2.5}$ and O_3 at conception and of O_3 around the critical window, this is somewhat consistent with our findings.

2.4.6 Strengths and limitations

Strengths of this study included that birth defect cases covered fourteen years and most of NYS. Birth defects studied are well-diagnosed, so case misclassification is unlikely, and a sensitivity analysis of the one birth defect known to have misclassification issues was not significant. Air pollutant exposure was available daily and residential information was available at point level for most births, allowing greater granularity both temporally and spatially than many currently published studies.

Limitations of this study include possible exposure misclassification that is presumed to be non-differential, which would bias results toward the null. Air pollutant exposures were assigned based on the mother's geocoded residence at birth, but no information was available regarding the mother's activity patterns, including how much time she spent at that residence during her pregnancy, so we cannot assess if assigned exposures are an accurate reflection of actual exposures. However, a sensitivity test of geocoding results showed no issues when ungeocoded births were assigned to ZIP code centroids and research suggests that mothers who move during pregnancy tend to move to areas with similar levels of air pollution.[43] In NYS, smoking is known to be under-reported on birth certificates[33], but even with presumed non-differential under-reporting, mothers of cases reported smoking more frequently than mothers of controls. Income is based on median census tract income, but the mother's household may have an income much higher or lower than the median in her census tract of residence, which could bias results toward the null.

2.5 Conclusion

In conclusion, evaluating the relationship between birth defects and air pollutants over long time periods washes out any effect. O_3 showed delayed effects for all birth defects studied given exposure before and around conception. $PM_{2.5}$ showed effects given exposure during the critical period for three of the birth defects and O_3 showed effects given exposure during the critical period for craniosynostosis. Future studies should focus on shorter time periods, especially around the time of conception and during the birth defects' critical periods. This study is the first of which the authors are aware to evaluate peak values and more studies should evaluate this method and these findings. Overall, the mother's exposure to air pollutants during the entire period from one month before pregnancy to the end of the first trimester increases her fetus' risk of developing birth defects, so reducing the mother's exposure should be a focus of health policy work.

Tables

Table 2.1: Relevant codes for birth defect categories used in the study

Birth Defects	ICD-9-CM Codes	CDC/BPA Codes	ICD-10-CM Codes
Clubfoot	754.51, 754.70	754.50, 754.73	Q66.0, Q66.89
Cleft lip with cleft palate	749.2	749.20-749.29	Q37.0-Q37.9
Cleft lip alone (without cleft palate)	749.1	749.10-749.19	Q36.0-Q36.9
Cleft palate alone (without cleft lip)	749	749.00-749.09	Q35.1-Q35.9
Craniosynostosis	No specific code	756.00-756.03	Q75.0

Abbreviations:

BPA = British Pediatric Association; CDC = Centers for Disease Control and Prevention; CM = Clinical Modification; ICD = International Classification of Diseases

Table 2.2: Cross-basis settings for distributed lag logistic regression models

		12-week models		16-week models	
Pollutant	**Measure**	**Setting**	**RR**	**Setting**	**RR**
Clubfoot					
Ozone	mean	poly4	0.05	poly4	0.10
	peak	poly4	0.06	poly3	0.00
$PM_{2.5}$	mean	lin	0.10	lin	0.66
	peak	poly2	0.24	lin	0.84
Cleft lip with or without cleft palate					
Ozone	mean	lin	0.02	poly4	0.07
	peak	poly4	0.06	poly3	0.06
$PM_{2.5}$	mean	lin	0.03	poly2	0.06
	peak	lin	0.08	poly2	0.04
Cleft Palate					
Ozone	mean	poly3	0.01	poly4	0.00
	peak	poly4	0.05	poly2	0.08
$PM_{2.5}$	mean	poly2	0.02	poly4	0.05
	peak	poly4	0.02	poly3	0.85
Craniosynostosis					
Ozone	mean	poly2	0.91	lin	0.05
	peak	lin	0.07	lin	0.05
$PM_{2.5}$	mean	poly2	0.12	poly2	0.56
	peak	poly2	0.08	poly3	0.04

Note:
Settings are for the unadjusted models. Setting refers to the relationship between exposure and outcome for the matrix containing the lag weeks.

Table 2.3: Means and ranges of air pollutants by case group, week of conception, New York State outside New York City, 2002 to 2015

	Controls (n=18,153)		Clubfoot (n=2423)		Cleft lip w/wo cleft palate (n=1281)		Cleft palate (n=952)		Craniosynostosis (n=931)	
Pollutant	**mean**	**(range)**	**mean**	**(range)**	**mean**	**(range)**	**mean**	**(range)**	**mean**	**(range)**
Ozone mean	37.2	(8.6-92.9)	37.3	(12.7-80.9)	36.1	(9.3-93.6)	37.6	(12.3-80.1)	36.9	(9.7-71.8)
Ozone peak	48.3	(15.8-125.8)	48.5	(18-117.6)	46.7	(17.8-125.1)	48.9	(19.2-110.1)	47.7	(21.7-96.5)
PM2.5 mean	10.0	(1.9-36.2)	9.9	(3.3-35.2)	9.8	(3.2-32.3)	10.1	(2.7-34.5)	9.8	(3.6-27.3)
PM2.5 peak	16.8	(3.4-80.5)	16.6	(4.8-77.7)	16.4	(4.6-60.1)	17.0	(4.1-75)	16.3	(4.6-56.6)

Note:

Ozone was measured in ppb and $PM_{2.5}$ was measured in $\mu g/m^3$.

Table 2.4: Distribution of maternal and infant characteristics by case status, New York State outside New York City, 2002 to 2015

	Controls (n=18,153)		Clubfoot (n=2423)		Cleft lip w/wo cleft palate (n=1281)		Cleft palate (n=952)		Craniosynostosis (n=931)	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Maternal age										
Aged 10-15	39	(0.21)	10	(0.41)	2	(0.16)	2	(0.21)	5	(0.54)
Aged 15-19	1085	(5.98)	167	(6.89)	91	(7.10)	59	(6.20)	58	(6.23)
Aged 20-24	3540	(19.50)	574	(23.69)	291	(22.72)	178	(18.70)	159	(17.08)
Aged 25-29	4746	(26.15)	633	(26.12)	327	(25.53)	256	(26.89)	243	(26.10)
Aged 30-34	5215	(28.73)	609	(25.13)	344	(26.85)	286	(30.04)	266	(28.57)
Aged 35-39	2863	(15.77)	330	(13.62)	171	(13.35)	143	(15.02)	161	(17.29)
Aged 40-44	619	(3.41)	95	(3.92)	54	(4.22)	25	(2.63)	36	(3.87)
Aged 45 and above	45	(0.25)	5	(0.21)	1	(0.08)	3	(0.32)	3	(0.32)
Maternal race										
White	13966	(77.48)	1959	(81.15)	1036	(81.45)	784	(82.96)	764	(82.59)
Black	1812	(10.05)	217	(8.99)	86	(6.76)	71	(7.51)	53	(5.73)
Asian	743	(4.12)	65	(2.69)	41	(3.22)	40	(4.23)	19	(2.05)
Native American	66	(0.37)	16	(0.66)	11	(0.86)	3	(0.32)	5	(0.54)
Other	1438	(7.98)	157	(6.50)	98	(7.70)	47	(4.97)	84	(9.08)
Maternal ethnicity										
Hispanic	2772	(15.53)	318	(13.32)	189	(15.17)	117	(12.59)	146	(15.89)
Non-Hispanic	15073	(84.47)	2069	(86.68)	1057	(84.83)	812	(87.41)	773	(84.11)
Maternal education										
Some high school	2842	(15.86)	414	(17.32)	262	(20.71)	154	(16.47)	137	(14.86)
High school graduate	4119	(22.99)	611	(25.56)	341	(26.96)	251	(26.84)	218	(23.64)
Some college	4832	(26.97)	697	(29.16)	332	(26.25)	250	(26.74)	248	(26.90)
College graduate	3028	(16.90)	353	(14.77)	170	(13.44)	136	(14.55)	177	(19.20)
Advanced education	3096	(17.28)	315	(13.18)	160	(12.65)	144	(15.40)	142	(15.40)
Maternal body-mass index										
Underweight	598	(3.56)	89	(3.96)	44	(3.74)	24	(2.74)	21	(2.43)
Normal weight	8178	(48.64)	963	(42.88)	537	(45.66)	398	(45.38)	363	(42.01)
Overweight	4183	(24.88)	584	(26.00)	297	(25.26)	228	(26.00)	230	(26.62)
Obese	3853	(22.92)	610	(27.16)	298	(25.34)	227	(25.88)	250	(28.94)
Maternal pre-pregnancy diabetes										
No	17949	(99.37)	2388	(99.00)	1251	(98.58)	930	(98.41)	910	(98.48)
Yes	113	(0.63)	24	(1.00)	18	(1.42)	15	(1.59)	14	(1.52)
Smoked tobacco at all during pregnancy										
No	15204	(84.65)	1869	(77.71)	987	(78.02)	747	(79.05)	751	(81.45)
Yes	2758	(15.35)	536	(22.29)	278	(21.98)	198	(20.95)	171	(18.55)
Drank alcohol at all during pregnancy										
No	17778	(99.39)	2371	(99.08)	1253	(99.52)	934	(99.26)	907	(99.02)
Yes	110	(0.61)	22	(0.92)	6	(0.48)	7	(0.74)	9	(0.98)
Tract-level median household income										
Low	4536	(24.99)	701	(28.95)	371	(28.96)	229	(24.05)	232	(24.92)
Medium-low	4546	(25.05)	671	(27.72)	365	(28.49)	277	(29.10)	260	(27.93)
Medium-high	4527	(24.94)	535	(22.10)	302	(23.58)	219	(23.00)	233	(25.03)
High	4541	(25.02)	514	(21.23)	243	(18.97)	227	(23.84)	206	(22.13)
Infant sex										
Female	8854	(48.78)	987	(40.75)	455	(35.52)	519	(54.52)	323	(34.69)
Male	9298	(51.22)	1435	(59.25)	826	(64.48)	433	(45.48)	608	(65.31)

(Continued on Next Page...)

Table 2.4: Distribution of maternal and infant characteristics by case status, New York State outside New York City, 2002 to 2015 *(continued)*

	Controls (n=18,153)		Clubfoot (n=2423)		Cleft lip w/wo cleft palate (n=1281)		Cleft palate (n=952)		Craniosynostosis (n=931)	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Plurality										
Multiple birth	696	(3.85)	142	(5.87)	53	(4.15)	32	(3.37)	60	(6.46)
Singleton birth	17397	(96.15)	2279	(94.13)	1224	(95.85)	917	(96.63)	869	(93.54)
Infant gestation length										
Very preterm	320	(1.76)	106	(4.37)	36	(2.81)	38	(3.99)	36	(3.87)
Preterm	1652	(9.10)	357	(14.73)	173	(13.51)	117	(12.29)	106	(11.39)
Full-term	16181	(89.14)	1960	(80.89)	1072	(83.68)	797	(83.72)	789	(84.75)
Infant birthweight										
Very low	248	(1.37)	74	(3.06)	26	(2.03)	25	(2.63)	33	(3.54)
Low	1029	(5.67)	300	(12.40)	142	(11.09)	113	(11.87)	75	(8.06)
Normal	16596	(91.46)	2025	(83.68)	1099	(85.79)	803	(84.35)	810	(87.00)
High	272	(1.50)	21	(0.87)	14	(1.09)	11	(1.16)	13	(1.40)
Season of conception										
Winter	4567	(25.16)	610	(25.18)	295	(23.03)	279	(29.31)	241	(25.89)
Spring	4252	(23.42)	541	(22.33)	317	(24.75)	202	(21.22)	209	(22.45)
Summer	4578	(25.22)	629	(25.96)	330	(25.76)	195	(20.48)	230	(24.70)
Autumn	4756	(26.20)	643	(26.54)	339	(26.46)	276	(28.99)	251	(26.96)
Season of birth										
Winter	4193	(23.10)	550	(22.70)	304	(23.73)	206	(21.64)	208	(22.34)
Spring	4536	(24.99)	628	(25.92)	320	(24.98)	197	(20.69)	240	(25.78)
Summer	4846	(26.70)	651	(26.87)	348	(27.17)	275	(28.89)	247	(26.53)
Autumn	4578	(25.22)	594	(24.52)	309	(24.12)	274	(28.78)	236	(25.35)
RUCA score										
Metropolitan	15414	(84.91)	1970	(81.37)	1028	(80.25)	782	(82.14)	775	(83.24)
Micropolitan	1471	(8.10)	239	(9.87)	140	(10.93)	95	(9.98)	87	(9.34)
Town	665	(3.66)	100	(4.13)	59	(4.61)	46	(4.83)	31	(3.33)
Rural	603	(3.32)	112	(4.63)	54	(4.22)	29	(3.05)	38	(4.08)

Note:
Tobacco smoking and alcohol consumption are defined as having ever smoked tobacco or consumed alcohol during pregnancy, respectively.
RUCA = Rural-Urban Commuting Area;
RUCA categories are defined as follows: Metropolitan contains scores 1-3, Micropolitan contains scores 4-6, Town contains scores 7-9, and Rural contains score 10.

Table 2.5: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs, New York State outside New York City, 2002 to 2015

	12-week model		16-week model	
Pollutant	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Clubfoot				
Ozone mean	1.03	(0.94 - 1.13)	1.00	(0.91 - 1.10)
Ozone peak	1.02	(0.95 - 1.08)	1.00	(0.93 - 1.07)
$PM_{2.5}$ mean	0.87	(0.70 - 1.08)	0.88	(0.70 - 1.10)
$PM_{2.5}$ peak	0.91	(0.82 - 1.02)	0.92	(0.82 - 1.03)
Cleft lip with or without cleft palate				
Ozone mean	0.94	(0.83 - 1.07)	0.96	(0.83 - 1.10)
Ozone peak	0.95	(0.87 - 1.04)	0.96	(0.87 - 1.06)
$PM_{2.5}$ mean	0.75	(0.56 - 1.01)	0.74	(0.54 - 1.00)
$PM_{2.5}$ peak	0.87	(0.74 - 1.01)	0.87	(0.74 - 1.02)
Cleft Palate				
Ozone mean	1.04	(0.90 - 1.20)	1.05	(0.89 - 1.23)
Ozone peak	0.99	(0.89 - 1.10)	1.00	(0.90 - 1.12)
$PM_{2.5}$ mean	0.81	(0.57 - 1.14)	0.78	(0.55 - 1.11)
$PM_{2.5}$ peak	0.89	(0.74 - 1.07)	0.86	(0.71 - 1.04)
Craniosynostosis				
Ozone mean	0.97	(0.83 - 1.13)	0.87	(0.72 - 1.05)
Ozone peak	0.97	(0.86 - 1.08)	0.92	(0.81 - 1.04)
$PM_{2.5}$ mean	1.01	(0.70 - 1.45)	1.02	(0.70 - 1.49)
$PM_{2.5}$ peak	0.99	(0.82 - 1.20)	0.98	(0.80 - 1.19)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, and conception season. RR applies to a 10-unit increase over two standard deviations above the mean.

Week 0 was week of conception. Week 12 was the end of the first trimester of pregnancy.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Table 2.6: Lag risk ratios for covariate models of air pollutant and clubfoot pairs New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	1.02	(0.97 - 1.07)	1.01	(1.00 - 1.03)	0.96	(0.88 - 1.04)	0.96	(0.90 - 1.02)
-3	1.01	(0.99 - 1.04)	1.01	(1.00 - 1.03)	0.97	(0.92 - 1.02)	0.97	(0.92 - 1.01)
-2	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.97	(0.94 - 1.01)	0.97	(0.94 - 1.00)
-1	1.00	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.95 - 1.01)	0.98	(0.95 - 1.00)
0	1.00	(0.98 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.95 - 1.02)	0.98	(0.95 - 1.01)
1	1.00	(0.97 - 1.02)	1.01	(1.00 - 1.01)	0.99	(0.94 - 1.03)	0.99	(0.96 - 1.01)
2	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	0.99	(0.95 - 1.04)	0.99	(0.96 - 1.02)
3	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	1.00	(0.96 - 1.04)	0.99	(0.96 - 1.02)
4	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.01)	1.00	(0.97 - 1.04)	1.00	(0.97 - 1.03)
5	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.03)
6	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.01	(0.97 - 1.04)	1.00	(0.98 - 1.03)
7	1.00	(0.97 - 1.03)	0.99	(0.99 - 1.00)	1.01	(0.95 - 1.07)	1.00	(0.98 - 1.03)
8	1.00	(0.96 - 1.05)	0.99	(0.98 - 1.00)	1.01	(0.92 - 1.10)	1.01	(0.98 - 1.03)
9			0.99	(0.98 - 1.00)			1.01	(0.98 - 1.04)
10			0.99	(0.98 - 1.00)			1.01	(0.97 - 1.05)
11			0.99	(0.97 - 1.00)			1.01	(0.96 - 1.07)
12			0.99	(0.97 - 1.00)			1.01	(0.94 - 1.09)
Weekly peak concentration								
-4	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.97	(0.93 - 1.02)	0.98	(0.93 - 1.03)
-3	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.95 - 1.01)	0.98	(0.96 - 1.01)
-2	1.01	(1.00 - 1.02)	1.01	(1.00 - 1.02)	0.99	(0.97 - 1.01)	0.99	(0.97 - 1.01)
-1	1.00	(1.00 - 1.01)	1.01	(1.00 - 1.01)	0.99	(0.98 - 1.01)	0.99	(0.97 - 1.01)
0	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.02)
1	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.02)
2	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.02)
3	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	1.00	(0.98 - 1.02)
4	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.00)	1.00	(0.98 - 1.02)	1.00	(0.98 - 1.02)
5	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
6	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
7	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	0.99	(0.96 - 1.02)	1.00	(0.98 - 1.02)
8	0.99	(0.98 - 1.01)	1.00	(0.99 - 1.00)	0.98	(0.94 - 1.03)	1.00	(0.98 - 1.02)
9			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
10			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
11			0.99	(0.98 - 1.00)			1.00	(0.97 - 1.03)
12			0.99	(0.98 - 1.00)			1.00	(0.94 - 1.05)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, and conception season.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 2.7: Lag risk ratios for covariate models of air pollutant and cleft lip with or without cleft palate pairs New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	**0.89**	**(0.80 - 0.98)**	0.92	(0.83 - 1.00)	0.98	(0.92 - 1.04)	0.98	(0.93 - 1.04)
-3	1.00	(0.96 - 1.05)	0.98	(0.94 - 1.02)	0.98	(0.93 - 1.03)	0.98	(0.93 - 1.03)
-2	1.05	(1.00 - 1.11)	1.02	(0.98 - 1.07)	0.98	(0.94 - 1.03)	0.98	(0.94 - 1.03)
-1	**1.05**	**(1.00 - 1.11)**	1.04	(0.99 - 1.09)	0.98	(0.94 - 1.02)	0.98	(0.95 - 1.02)
0	1.03	(0.99 - 1.08)	**1.04**	**(1.00 - 1.09)**	0.98	(0.95 - 1.01)	0.98	(0.95 - 1.02)
1	1.01	(0.96 - 1.06)	1.03	(1.00 - 1.07)	0.98	(0.95 - 1.00)	0.98	(0.96 - 1.01)
2	0.99	(0.94 - 1.04)	1.02	(0.98 - 1.06)	0.98	(0.96 - 1.00)	0.98	(0.96 - 1.01)
3	0.98	(0.93 - 1.03)	1.00	(0.97 - 1.04)	0.98	(0.96 - 1.00)	0.98	(0.96 - 1.00)
4	0.99	(0.94 - 1.03)	0.99	(0.95 - 1.03)	0.98	(0.95 - 1.01)	**0.98**	**(0.96 - 1.00)**
5	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.01)	0.98	(0.95 - 1.01)	0.98	(0.96 - 1.00)
6	1.01	(0.95 - 1.07)	0.97	(0.94 - 1.00)	0.98	(0.94 - 1.02)	0.98	(0.96 - 1.00)
7	1.00	(0.95 - 1.05)	0.97	(0.94 - 1.00)	0.98	(0.93 - 1.03)	0.98	(0.96 - 1.01)
8	0.95	(0.86 - 1.05)	0.97	(0.93 - 1.02)	0.98	(0.92 - 1.04)	0.98	(0.95 - 1.01)
9			0.98	(0.94 - 1.03)			0.98	(0.95 - 1.02)
10			1.00	(0.96 - 1.04)			0.98	(0.94 - 1.02)
11			1.02	(0.98 - 1.06)			0.98	(0.94 - 1.03)
12			1.03	(0.94 - 1.13)			0.98	(0.93 - 1.03)
Weekly peak concentration								
-4	**0.91**	**(0.85 - 0.97)**	**0.93**	**(0.88 - 0.98)**	0.96	(0.91 - 1.02)	0.99	(0.96 - 1.02)
-3	0.99	(0.96 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.98	(0.94 - 1.01)	0.99	(0.97 - 1.02)
-2	1.03	(0.99 - 1.06)	1.00	(0.99 - 1.02)	0.99	(0.97 - 1.01)	0.99	(0.97 - 1.01)
-1	**1.03**	**(1.00 - 1.07)**	**1.02**	**(1.00 - 1.04)**	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.01)
0	1.03	(1.00 - 1.06)	**1.03**	**(1.01 - 1.06)**	1.00	(0.98 - 1.03)	0.99	(0.97 - 1.01)
1	1.02	(0.98 - 1.05)	**1.03**	**(1.01 - 1.06)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
2	1.01	(0.97 - 1.04)	**1.03**	**(1.01 - 1.05)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.00)
3	1.00	(0.97 - 1.04)	1.02	(1.00 - 1.04)	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.00)
4	1.01	(0.98 - 1.04)	1.01	(0.99 - 1.02)	1.00	(0.98 - 1.03)	0.99	(0.98 - 1.00)
5	1.01	(0.98 - 1.05)	0.99	(0.98 - 1.01)	0.99	(0.97 - 1.01)	0.99	(0.98 - 1.00)
6	1.01	(0.97 - 1.05)	0.98	(0.96 - 1.00)	0.98	(0.96 - 1.01)	0.99	(0.98 - 1.00)
7	0.99	(0.96 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.97	(0.93 - 1.01)	0.99	(0.98 - 1.01)
8	0.94	(0.88 - 1.00)	**0.97**	**(0.95 - 0.99)**	0.95	(0.89 - 1.02)	0.99	(0.98 - 1.01)
9			**0.97**	**(0.95 - 0.99)**			0.99	(0.97 - 1.01)
10			**0.98**	**(0.97 - 1.00)**			0.99	(0.97 - 1.01)
11			1.00	(0.98 - 1.03)			0.99	(0.97 - 1.02)
12			1.04	(0.99 - 1.09)			0.99	(0.97 - 1.02)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, and conception season.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 2.8: Lag risk ratios for covariate models of air pollutant and cleft palate pairs New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	1.01	(0.97 - 1.04)	0.95	(0.85 - 1.07)	**0.92**	**(0.85 - 0.99)**	**0.91**	**(0.82 - 1.00)**
-3	1.00	(0.98 - 1.03)	1.01	(0.96 - 1.05)	**0.93**	**(0.87 - 0.99)**	**0.93**	**(0.86 - 1.00)**
-2	1.00	(0.98 - 1.03)	1.03	(0.98 - 1.09)	**0.94**	**(0.89 - 0.99)**	0.95	(0.89 - 1.00)
-1	1.00	(0.98 - 1.02)	1.04	(0.98 - 1.10)	**0.95**	**(0.91 - 0.99)**	0.96	(0.92 - 1.01)
0	1.00	(0.99 - 1.02)	1.03	(0.98 - 1.08)	**0.96**	**(0.93 - 1.00)**	0.98	(0.94 - 1.02)
1	1.00	(0.99 - 1.02)	1.01	(0.97 - 1.06)	0.97	(0.94 - 1.00)	0.99	(0.95 - 1.04)
2	1.00	(0.99 - 1.01)	1.00	(0.96 - 1.04)	0.98	(0.96 - 1.01)	1.00	(0.95 - 1.05)
3	1.00	(0.99 - 1.01)	0.99	(0.94 - 1.03)	1.00	(0.97 - 1.02)	1.01	(0.96 - 1.06)
4	1.00	(0.99 - 1.02)	0.98	(0.94 - 1.03)	1.01	(0.98 - 1.04)	1.02	(0.97 - 1.07)
5	1.00	(0.98 - 1.02)	0.98	(0.94 - 1.03)	1.02	(0.98 - 1.06)	1.02	(0.97 - 1.07)
6	1.00	(0.98 - 1.02)	0.99	(0.95 - 1.03)	1.03	(0.98 - 1.08)	1.02	(0.98 - 1.06)
7	1.00	(0.97 - 1.03)	1.00	(0.96 - 1.04)	1.04	(0.99 - 1.10)	1.02	(0.98 - 1.05)
8	1.00	(0.97 - 1.03)	1.01	(0.97 - 1.06)	1.05	(0.99 - 1.13)	1.01	(0.98 - 1.05)
9			1.02	(0.97 - 1.08)			1.01	(0.96 - 1.05)
10			1.03	(0.97 - 1.08)			1.00	(0.94 - 1.06)
11			1.01	(0.97 - 1.06)			0.98	(0.90 - 1.07)
12			0.97	(0.87 - 1.09)			0.97	(0.87 - 1.09)
Weekly peak concentration								
-4	0.97	(0.89 - 1.05)	0.98	(0.92 - 1.04)	**0.96**	**(0.92 - 1.00)**	**0.95**	**(0.90 - 1.00)**
-3	0.98	(0.95 - 1.02)	0.99	(0.96 - 1.02)	**0.96**	**(0.93 - 1.00)**	**0.96**	**(0.92 - 1.00)**
-2	1.00	(0.96 - 1.05)	1.00	(0.98 - 1.02)	**0.97**	**(0.94 - 1.00)**	0.97	(0.94 - 1.00)
-1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.03)	**0.97**	**(0.95 - 1.00)**	0.98	(0.96 - 1.01)
0	1.02	(0.99 - 1.06)	1.01	(0.98 - 1.04)	**0.98**	**(0.96 - 1.00)**	0.99	(0.97 - 1.02)
1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.97 - 1.00)	1.00	(0.98 - 1.02)
2	1.01	(0.97 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.00)	1.01	(0.98 - 1.03)
3	1.00	(0.96 - 1.04)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.01)	1.01	(0.98 - 1.04)
4	0.99	(0.95 - 1.02)	1.00	(0.98 - 1.02)	1.00	(0.99 - 1.02)	1.01	(0.99 - 1.04)
5	0.98	(0.94 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.03)	1.01	(0.99 - 1.04)
6	0.98	(0.93 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.04)	1.01	(0.99 - 1.03)
7	0.99	(0.95 - 1.03)	0.99	(0.96 - 1.02)	1.02	(0.99 - 1.05)	1.01	(0.99 - 1.03)
8	1.03	(0.95 - 1.11)	0.99	(0.96 - 1.02)	1.03	(0.99 - 1.07)	1.00	(0.99 - 1.02)
9			0.99	(0.97 - 1.02)			1.00	(0.97 - 1.02)
10			1.00	(0.98 - 1.02)			0.99	(0.96 - 1.02)
11			1.01	(0.98 - 1.04)			0.98	(0.94 - 1.02)
12			1.03	(0.97 - 1.09)			0.97	(0.91 - 1.03)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, and conception season.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 2.9: Lag risk ratios for covariate models of air pollutant and craniosynostosis pairs New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	0.95	(0.86 - 1.05)	0.91	(0.81 - 1.02)	1.01	(0.88 - 1.15)	0.86	(0.70 - 1.05)
-3	0.98	(0.94 - 1.03)	0.98	(0.93 - 1.03)	1.02	(0.94 - 1.11)	1.03	(0.94 - 1.13)
-2	1.00	(0.96 - 1.05)	1.01	(0.96 - 1.07)	1.03	(0.97 - 1.09)	**1.12**	**(1.02 - 1.24)**
-1	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.08)	1.03	(0.98 - 1.09)	**1.14**	**(1.03 - 1.28)**
0	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.07)	1.03	(0.97 - 1.10)	**1.11**	**(1.01 - 1.23)**
1	1.01	(0.97 - 1.06)	1.01	(0.96 - 1.05)	1.03	(0.96 - 1.11)	1.06	(0.98 - 1.15)
2	1.01	(0.96 - 1.05)	1.00	(0.95 - 1.04)	1.02	(0.95 - 1.10)	1.00	(0.93 - 1.08)
3	1.00	(0.95 - 1.04)	0.99	(0.94 - 1.04)	1.01	(0.95 - 1.09)	0.96	(0.88 - 1.04)
4	0.99	(0.94 - 1.04)	0.99	(0.94 - 1.04)	1.00	(0.95 - 1.06)	0.93	(0.85 - 1.01)
5	0.99	(0.94 - 1.04)	1.00	(0.95 - 1.04)	0.99	(0.94 - 1.03)	**0.92**	**(0.85 - 1.00)**
6	0.99	(0.95 - 1.03)	1.01	(0.97 - 1.05)	0.97	(0.92 - 1.02)	**0.93**	**(0.87 - 1.00)**
7	1.00	(0.95 - 1.05)	1.03	(0.98 - 1.07)	0.95	(0.86 - 1.04)	0.96	(0.89 - 1.03)
8	1.02	(0.92 - 1.14)	1.04	(0.99 - 1.09)	0.92	(0.79 - 1.07)	1.00	(0.91 - 1.09)
9			1.04	(0.98 - 1.10)			1.03	(0.93 - 1.15)
10			1.02	(0.96 - 1.07)			1.05	(0.94 - 1.16)
11			0.96	(0.92 - 1.01)			1.02	(0.93 - 1.13)
12			**0.87**	**(0.77 - 0.98)**			0.94	(0.76 - 1.15)
Weekly peak concentration								
-4	0.96	(0.89 - 1.04)	0.97	(0.93 - 1.01)	0.94	(0.84 - 1.05)	0.99	(0.91 - 1.07)
-3	1.00	(0.96 - 1.04)	0.98	(0.95 - 1.00)	1.02	(0.96 - 1.08)	1.00	(0.96 - 1.05)
-2	1.01	(0.97 - 1.06)	0.99	(0.97 - 1.00)	1.05	(0.99 - 1.12)	1.01	(0.98 - 1.05)
-1	1.01	(0.97 - 1.06)	0.99	(0.98 - 1.01)	1.05	(0.99 - 1.12)	1.02	(0.98 - 1.06)
0	1.01	(0.97 - 1.04)	1.00	(0.99 - 1.01)	1.03	(0.98 - 1.09)	1.02	(0.98 - 1.06)
1	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.02)	1.01	(0.95 - 1.06)	1.02	(0.97 - 1.06)
2	0.98	(0.94 - 1.03)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.04)	1.01	(0.97 - 1.05)
3	0.98	(0.94 - 1.02)	1.01	(0.99 - 1.03)	0.97	(0.92 - 1.03)	1.00	(0.97 - 1.04)
4	0.98	(0.95 - 1.02)	1.01	(0.99 - 1.03)	0.97	(0.93 - 1.02)	1.00	(0.97 - 1.02)
5	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.03)	0.98	(0.93 - 1.04)	0.99	(0.96 - 1.02)
6	1.00	(0.96 - 1.05)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.06)	0.98	(0.95 - 1.02)
7	1.02	(0.98 - 1.06)	1.01	(0.99 - 1.02)	1.00	(0.94 - 1.06)	0.98	(0.94 - 1.02)
8	1.02	(0.94 - 1.11)	1.00	(0.99 - 1.01)	0.99	(0.88 - 1.12)	0.98	(0.94 - 1.02)
9			0.99	(0.98 - 1.01)			0.98	(0.94 - 1.02)
10			0.99	(0.97 - 1.01)			0.99	(0.95 - 1.02)
11			0.98	(0.95 - 1.01)			1.00	(0.95 - 1.05)
12			0.97	(0.92 - 1.01)			1.02	(0.94 - 1.11)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, and conception season.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Figures

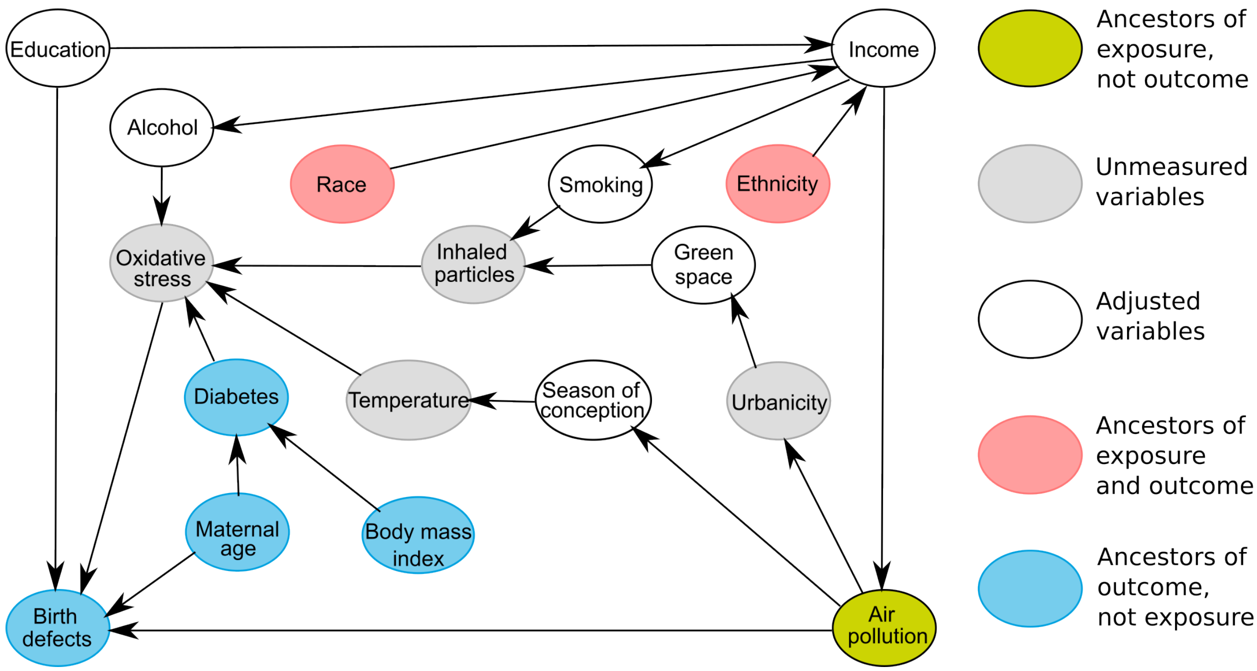
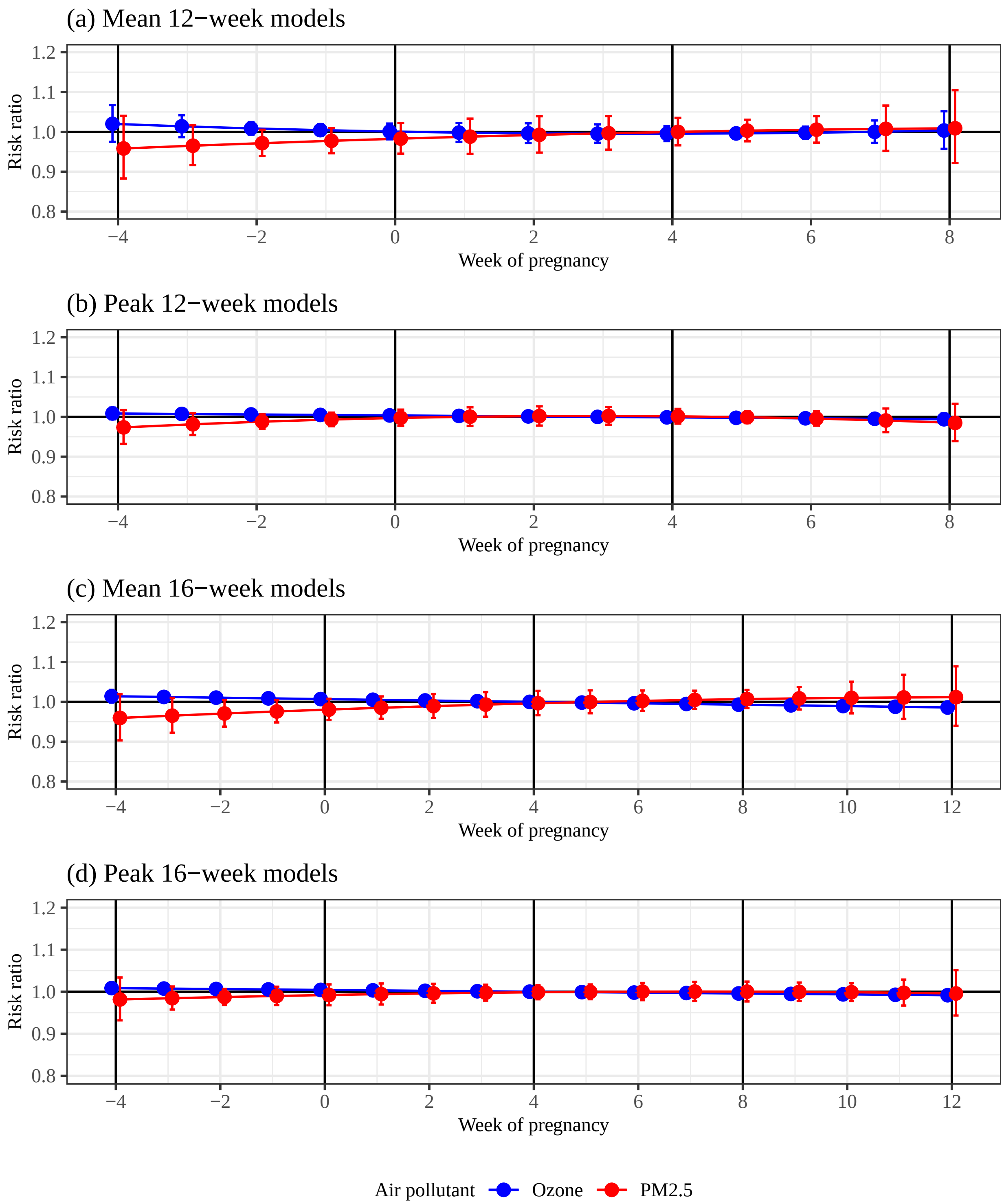
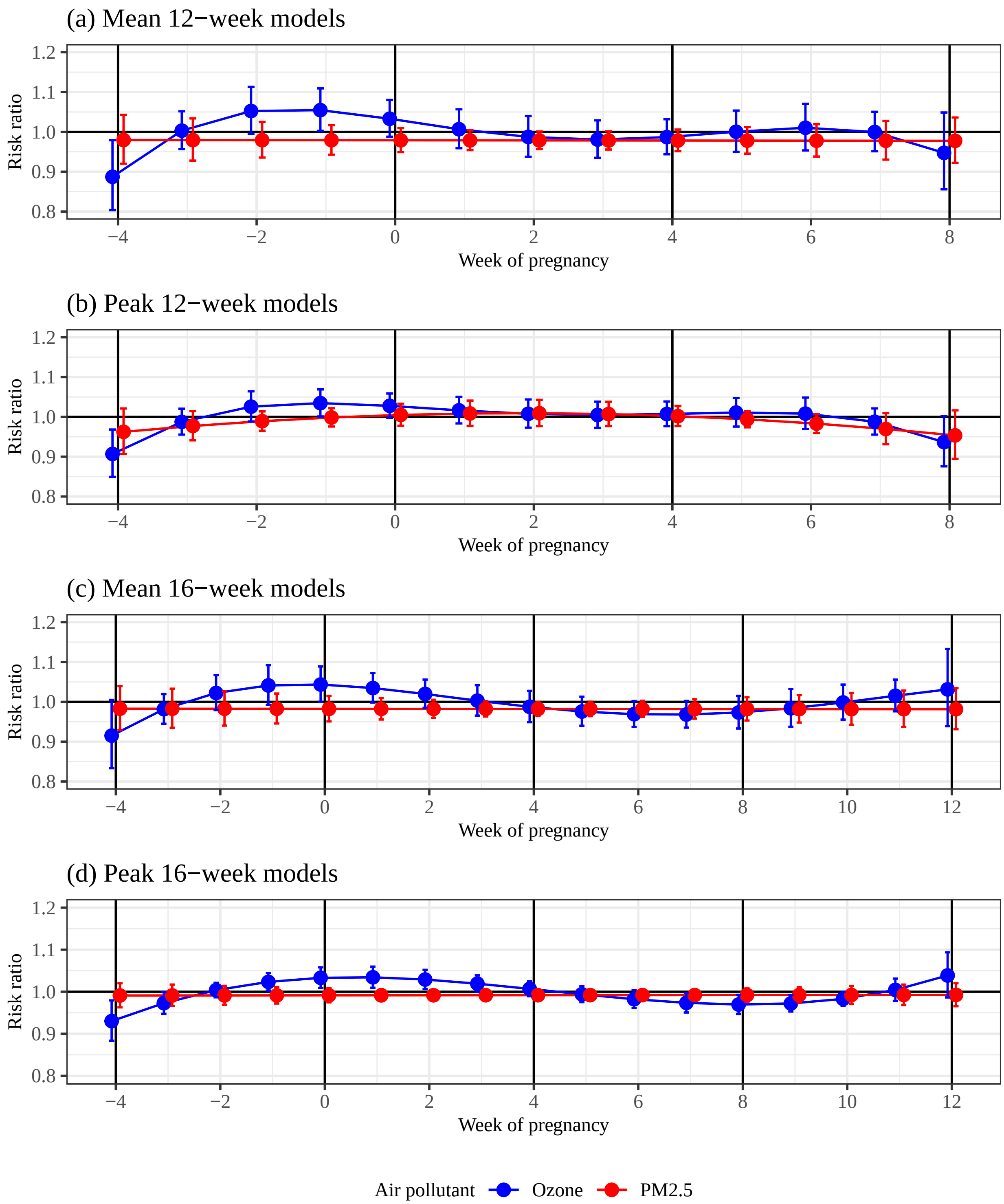


Figure 2.1: Directed acyclic graph of the relationship between air pollutants and birth defects



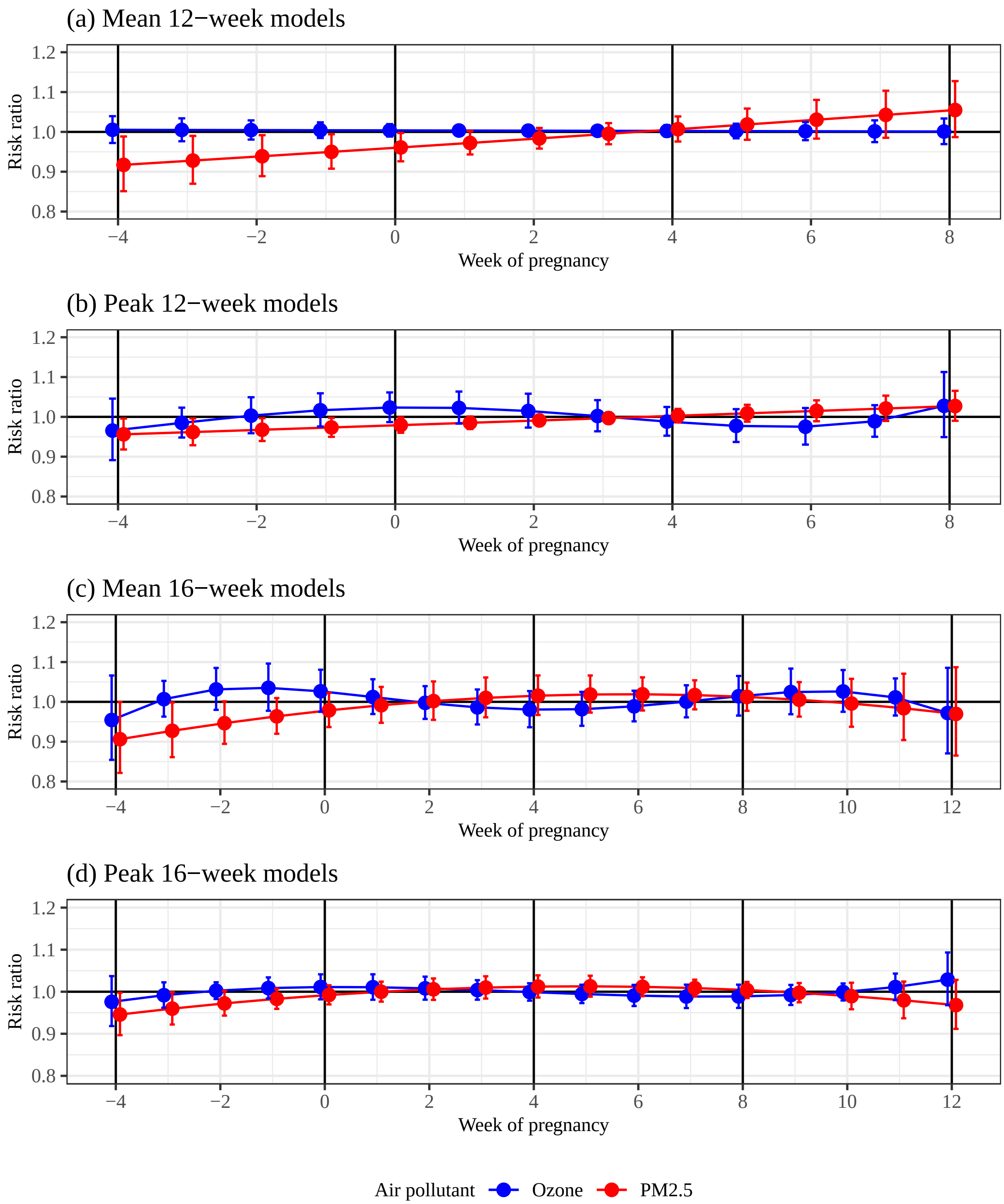
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, and conception season. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for PM2.5) over two standard deviations above the mean.

Figure 2.2: Clubfoot models: Risk ratios by week of pregnancy



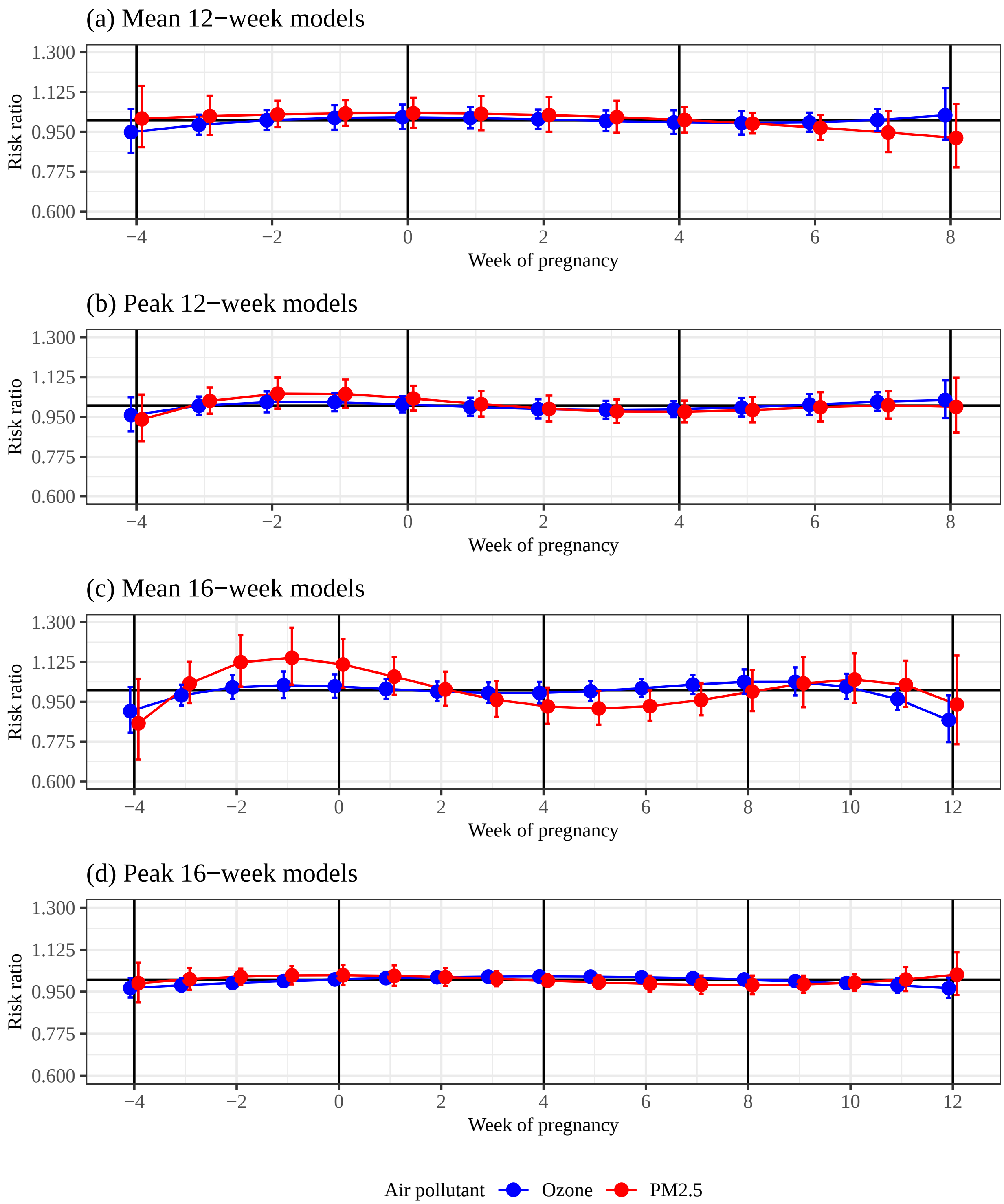
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, and conception season. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 2.3: Cleft lip with or without cleft palate models: Risk ratios by week of pregnancy



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, and conception season. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 2.4: Cleft palate models: Risk ratios by week of pregnancy



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, and conception season. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 2.5: Craniosynostosis models: Risk ratios by week of pregnancy

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3. Green Space, Individual Air Pollutants and Risk of Birth Defects

3.1 Background

In NYS, birth defects result in 20% of deaths among infants between one month and one year old[1] and babies born with birth defects are ten times more likely to die before they are a year old than babies without birth defects.[2] About 6000 children of the roughly 125,000 children born in NYS outside NYC each year are diagnosed with birth defects before age 3.[3] Approximately 30%-40% of birth defects have known causes related to genetics, environment, and maternal health.[4,5]

The connection between birth defects and maternal smoking via oxidative stress is well documented.[6–11] Some of these components are believed to cause epigenetic changes in the developing fetus and to trigger oxidative stress. Many components of cigarette smoke are also found in PM.[12]

Pregnant women exposed to higher concentrations of air pollution show more markers of DNA damage that are associated with oxidative stress than pregnant women exposed to lower concentrations of air pollution.[13] Given similarities between cigarette smoke and some forms of air pollution, notably $PM_{2.5}$, a link between air pollution and birth defects is possible.

The three birth defects investigated in this study include clubfoot, oral clefts, and craniosynostosis, which are among the more common birth defects in NYS, with over 100 cases born with each birth defect annually.[2] They were selected because they are posited to be susceptible to oxidative stress caused by similar routes of exposure. All three birth defects have an increased risk of developing if the mother smokes[6–11] and can be diagnosed prenatally.[14–16]

Air pollution may be a risk factor for development of oral clefts, clubfoot, and craniosynostosis in the fetus. Results of research have been inconclusive.[9,10] Studies have not been directly comparable, however. They vary in whether they use monitored or modeled pollution data, size of the study area, availability of pollution data throughout the study area, and frequency of pollution measurements.

Studies on the relationship between trees and air pollution have found that trees reduce various types of air pollution by either absorbing them (for example, carbon dioxide (CO_2)) or by trapping them in their leaves (for example, $PM_{2.5}$).[17,18] While trees and shrubs have been shown to remove O_3 and $PM_{2.5}$ from the air, published research on the relationship between grasses and air pollution could not be located. A 2018 literature review stated the need for more research on the connection between green space and air pollution.[18] Another review from 2019 found mixed results when assessing the relationship between green space and air pollution, notably for ozone.[19]

Green space is poorly studied in birth defects research. The only study the authors could find focused on heart defects and concluded that increasing green space was protective against being born with a heart defect.[20] Among birth outcomes research (mostly birthweight and preterm birth), results are mixed. Most studies occur in urban areas and rely on the NDVI, which does not differentiate between grasses and trees. Among studies with multiple buffers, those that see an effect tend to see the same or similar protective effects for birthweight across buffers under 1000 meters.[21–25] In urban areas, green space tends to be associated with higher birthweight and fewer preterm births, especially among women of lower education levels or socio-economic status.[26–28]

This study explored the association between maternal exposure to $PM_{2.5}$ and O_3 during the first trimester of pregnancy using statewide time-varying data for the exposures and a statewide dataset for the outcomes from 2002 to 2015 in NYS. This study used a case-cohort design with logistic regression to determine whether green space affected the relationship between select measures of air pollution and select birth defects.

3.2 Methods

3.2.1 Study population

Cases were identified through the NYS CMR, as described under Chapter 2 methods. Case categories included infants born with clubfoot, infants born with cleft lip with or without cleft palate, infants born with cleft palate, and infants born with craniosynostosis. Controls were selected from NYS Vital Records and matched on year of birth, three controls for each case, for the birth years 2002 to 2015 with mother residing in NYS outside NYC at time of birth.

3.2.2 Exposure assessment

This study used the Downscaler air pollution model[29,30] described in Chapter 2. Weekly average and peak measures of modeled $PM_{2.5}$ and O_3 were calculated for the period inclusive of four weeks prior to pregnancy until week 12 of gestation. $PM_{2.5}$ and O_3 exposure were calculated from the modeled estimates of $PM_{2.5}$ and O_3, respectively, in the census tract where the residence at birth was geocoded.

Green space was calculated using the NLCD for 2011[31]. This year was used because it is closest to 2010, which was the year used for the Census data. For this aim, three green space measures were created, for forests, grassland, and water, as well as measures combining them. Trees actively block and absorb several kinds of air pollution, grasses are associated with other health benefits, and little research is published on the relationship between water and air pollution. The forest measure was the proportion of pixel areas in the buffer that fall into the categories of deciduous, evergreen, or mixed forests or woody and emergent herbaceous wetlands. The grassland measure was the proportion of pixel areas that fall into the categories of scrub, grasslands, pasture, and cultivation. The green measure included both forest and grassland. The nature measure included forest, grassland, and water.

Several buffers were created around each maternal residence, including 50m, 100m, 200m, 300m, 400m, and 500m radius. From the three green space variables, two composite variables were created for use in the models. The first variable measured four categories of grasses and trees (grasses and trees below their respective medians, grasses and trees above their respective medians, grasses below their median and trees above their median, and grasses above their median and trees below their median). The second variable combined grasses and trees into a total green space variable, then measured four categories of green space and water (green space and water below their respective medians, green space and water above their respective medians, green space below their median and water above their median, and green space above their median and water below their median).

3.2.3 Statistical analysis

This study used data from Chapter 2 with the following addition. Buffers of 50m, 100m, 200m, 300m, 400m, and 500m were created around the mother's residence. Each buffer was overlaid on the simplified NLCD grid containing the four categories grasses, trees, water, and other. Proportions were calculated for the amounts of the buffer area that fell into each category. These proportions were then linked back to the birth data using mother's residence. The full set of data that were spatially joined is shown in 3.1.

Univariate and bivariate analyses described in Chapter 2 informed this study. The cross-basis settings described in Chapter 2 were used in the models for this study. For the multivariate analysis, a series of distributed lag logistic models were run using the R package dlnm[32] for each case group and combination of O_3 and $PM_{2.5}$. These models have been used previously to study birth outcomes.[33] Since an estimate of reasonable lag was not available, but people can experience both chronic and acute (same day) effects of inhaling $PM_{2.5}$, this study used several possible lag weeks ranging from one month before estimated conception to estimated end of first trimester, each one week apart, to cover the critical windows for the birth defects of interest.

For clarity the lag weeks were as follows, all calculated from estimated conception date. For the first run with 16 weeks, the last week of the first trimester (week 12) of pregnancy was lag 0, the week of conception was lag 12, and the week one month before conception was lag 16. For the second run with 12 weeks, lag 0 was the last week of the second month (week 8) of pregnancy, lag 8 was the week of conception, and lag 12 was the week one month before conception. The first run was intended to capture any association in the first trimester. The second run was intended to focus on the second month of pregnancy, when cranial features develop.

This approach allowed modeling of the change in values from week to week, any possible effect of exposure a few weeks prior to the critical window of weeks 3 to 12 of pregnancy, and the week during that time that shows the strongest association with each outcome.[34] Running the models using weekly peaks as well as weekly averages captured spikes in exposure that would be smoothed away (and masked) when considering an average. One set of models contained means for O_3 or $PM_{2.5}$; the other set contained peaks for O_3 or $PM_{2.5}$.

Using the model settings selected in Chapter 2, the full covariate models were run with these settings to determine the significant weeks. The full models included the season of conception, since the mother may have spent more time indoors in colder months and some components of $PM_{2.5}$ increase in colder weather while others decrease, and the $PM_{2.5}$ measures alone would not be sufficient to capture that variation. Maternal education level and smoking were included. All categorical variables were coded as described in Chapter 2. Green space was included as either grass-tree or green-water composites for each of the six buffers. Tract-level median household income was included as a proxy for SES. Four models were run for each case group: $PM_{2.5}$ or O_3, with either mean or peak values. The full lagged model was as follows:

$logit(RR_{bd}) = \beta_0 + \sum(\alpha_j Air) + \beta_1 Education + \beta_2 Season + \beta_3 Smoking + \beta_4 Income + \beta_5 Green$

- $\alpha_j Air$ = series of betas for each week of estimates for each air pollutant ($PM_{2.5}$ or O_3)
- bd = birth defect (clubfoot, cleft lip with or without cleft palate, cleft palate, or craniosynostosis)
- $Green$ = green space measure (grass-tree composite or green-water composite)

Prediction models were used to evaluate the results. For the prediction models to calculate RRs, the cross-prediction was centered on the point at approximately two standard deviations from the mean, as described in Chapter 2. Predictive risk ratios were calculated for 10 units above the centering value. Models were run for all combinations of air pollution measure, green space measure and buffer, and birth defect group, at both 12 and 16 weeks, as previously noted.

Models were run the first time with iterative elimination of insignificant lags (see Appendix A: Supplemental Tables for Chapter 3 for full results). This analysis revealed that in general, results were consistent across all buffers. When models were run a second time to include estimates for all lags, only the 300 meter buffers were run. Spatial joining of birth residences to land cover and census tracts was completed in ArcGIS.[35] Green space buffers were calculated in ArcGIS. All other analyses were completed in R.[36]

3.3 Results

3.3.1 Descriptive analysis

As described in Chapter 2 (see Table 2.4), controls included 18,153 births that were conceived between February 1, 2002 and December 31, 2015 and born to mothers living in NYS outside NYC across all four case groups. Cases included 2423 births with clubfoot, 952 births with cleft palate, 1281 births with cleft lip with or without cleft palate, and 931 births with craniosynostosis after excluding genetic syndromes. Across all controls, 78.9% of mothers reported white race and 84.5% of mothers reported non-Hispanic ethnicity. Among the case groups, 82.5%-84.4% of mothers reported white race and 84.1%-87.4% of mothers reported non-Hispanic ethnicity. Across all controls, 15.4% of mothers reported smoking while pregnant; among cases, 18.6%-22.3% of mothers reported smoking while pregnant. Across all controls, 61.2% of mothers reported education above high school; among cases, 52.3%-61.5% of mothers reported education above high school. Across all controls, 28.7% of mothers reported ages between 30 and 34; among cases, 25.1%-30.0% of mothers reported ages between 30 and 34.

As described in Chapter 2 (see Table 2.3), exposures were assigned to all cases and controls throughout the study period based on census tract of mother's residence and estimated week of conception. The mean weekly O_3 mean concentration was 37.2ppb for all controls and 36.1 to 37.6ppb for the case groups. The mean weekly O_3 peak concentration was 48.3ppb for all controls and 46.7 to 48.9ppb for the case groups. The mean weekly $PM_{2.5}$ mean was $10.0\frac{\mu g}{m^3}$ for all controls and 9.8 to $10.1\frac{\mu g}{m^3}$ for the case groups. The mean weekly $PM_{2.5}$ peak was $16.8\frac{\mu g}{m^3}$ for all controls and 16.3 to $17.0\frac{\mu g}{m^3}$ for the case groups.

Overall, there was a lot of overlap between residences at birth with grasses and residences at birth with trees. Over half of the residences at birth had no green space for either definition within the 50m and 100m buffers for all of the case groups. Over half of the residences at birth had no grasses or water for any of the case groups within the 200m and 300m buffers. Over half of the residences at birth had no water for any of the case groups within the 400m and 500m buffers. At the 500m buffer, about 80% of residences at birth had some kind of green space around the residence. Water made up the smallest proportion of natural area, with fewer than 1% of residences at birth near water at the 50m buffer and about 25% of the residences at birth near water at the 500m buffer. Models for cleft palate at the 50m buffer containing grasses, trees, and water were excluded due to fewer than 5 cases having residences at birth within 50m of water (see Table 3.1).

In evaluations, chi-square tests of whether different green space types were present or not showed strong associations between grasses and trees and between green space and water for all buffer sizes. Correlation tests of proportions showed strong associations between grasses and trees for all buffers except 50m and between green space and water for the 100m and 500m buffers, with a weak association for the 200m buffer. For this reason, composite variables were created for the models. One variable categorized grasses and trees; the other categorized grasses, trees, and water.

3.3.2 Multivariate Analysis

In the 300 meter buffers evaluations with all lags, results for both green space measures were nearly identical (for results for the other buffers, see Appendix A: Supplemental Tables for Chapter 3). For clubfoot, the cumulative effect of O_3 was higher in the 12-week evaluation than in the 16-week evaluation and the cumulative effect of $PM_{2.5}$ was lower than O_3 for all evaluations. For cleft lip with or without cleft palate, all cumulative effects were low for both O_3 and $PM_{2.5}$, with cumulative effects of $PM_{2.5}$ lower than O_3. For cleft palate, O_3 mean had the highest cumulative effect in both evaluations and PM had the lowest effect. For craniosynostosis, $PM_{2.5}$ had a higher cumulative effect than O_3 for all evaluations.

When evaluating risk during individual weeks, for most evaluations, results were similar across all buffers, so individual weeks are shown for only the 300 meter buffer. The 300 meter buffer has been used in other studies[22,24,37,38], making results easier to compare across studies, and it is central in the buffer values used in this study.

Clubfoot

In the 300 meter buffer evaluations with all lags, the effect of O_3 on the risk of clubfoot was highest before conception for all evaluations. The effect of weekly $PM_{2.5}$ mean concentrations was highest in week 8 of pregnancy for the 12-week evaluation and in week 12 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ peak concentrations was highest in weeks 2 to 3 of pregnancy for the 12-week evaluation and in weeks 7 to 8 of pregnancy for the 16-week evaluation. See Figures 3.2 and 3.6 and Tables 3.3 and 3.4 for full results.

Cleft lip with or without cleft palate

In the 300 meter buffer evaluations with all lags, the effect of O_3 on the risk of cleft lip with or without cleft palate was highest around conception for all evaluations, and all of the weeks of highest effect were significant. The effect of weekly $PM_{2.5}$ mean concentrations was consistently low for all evaluations. The effect of weekly $PM_{2.5}$ peak concentrations was highest in weeks 1 to 2 of pregnancy for the 12-week evaluation and consistently low for the 16-week evaluation. See Figures 3.3 and 3.7 and Tables 3.5 and 3.6 for full results.

Cleft palate

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean concentrations on the risk of cleft palate was consistently low for the 12-week evaluation and highest around conception for the 16-week evaluation. The effect of weekly O_3 peak concentrations was highest in week 8 of pregnancy for the 12-week evaluation and week 12 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ mean concentrations was highest in week 8 of pregnancy for the 12-week evaluation and highest in weeks 5 to 6 for the 16-week evaluation. The effect of weekly $PM_{2.5}$ peak concentrations was highest in week 8 of pregnancy for the 12-week evaluation and highest in weeks 4 to 5 for the 16-week evaluation. See Figures 3.4 and 3.8 and Tables 3.7 and 3.8 for full results.

Craniosynostosis

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean concentrations on the risk of craniosynostosis was highest in week 8 of pregnancy for the 12-week evaluation and weeks 8 to 9 for the 16-week evaluation. The effect of weekly O_3 peak concentrations was highest in week 8 of pregnancy for the 12-week evaluation and weeks 3 to 5 for the 16-week evaluation. The effect of weekly $PM_{2.5}$ concentrations was highest before conception for all evaluations, with significant results for weekly $PM_{2.5}$ mean concentrations in the 16 week evaluation. See Figures 3.5 and 3.9 and Tables 3.9 and 3.10 for full results.

3.4 Discussion

This study proposed that green space has an effect on the relationship between select measures of air pollution and select birth defects. Results varied by evaluation (12 or 16 week), case group, and air pollution measure. Overall, there was no cumulative association between air pollution and birth defects in any of the evaluations, but some weeks were associated with the birth defects of interest.

Green space is poorly studied in birth defects research. Research available suggested green space has a protective effect against heart defects as measured using the NDVI at 500 meter and 1000 meter buffers, with results consistent across both buffers.[20] Consistent with that study, critical weeks (weeks in which an association was present) tended to be consistent across buffers and green space measures, suggesting that in most cases, buffer size does not affect the associations between case groups and air pollutant measures. Because results were similar across buffers, results here focus on the 300 meter buffer.

3.4.1 Clubfoot

The higher effect of a 10-unit increase of O_3 on clubfoot around conception suggest clubfoot risk is affected more by pre-conception exposure to O_3. The higher effect of a 10-unit increase of mean $PM_{2.5}$ in the second and third months of pregnancy suggest clubfoot risk is affected more by exposure to mean $PM_{2.5}$ during the critical window of development. The higher effect of a 10-unit increase of peak $PM_{2.5}$ in the first and second months of pregnancy suggest clubfoot risk is affected more by exposure to peak $PM_{2.5}$ just before and during the critical window of development. Results were consistent for both green space measures, suggesting the inclusion of water with green space did not affect clubfoot risk.

The lack of strong associations between the air pollutant measures and clubfoot was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between these measures and clubfoot. In general, weekly risk ratios were consistent with equivalent results without green space, and any differences were tiny. Results were consistent for both green space measures. Overall, the association between clubfoot and air pollution was not affected by green space.

3.4.2 Cleft lip with or without cleft palate

The increased effect of a 10-unit increase of O_3 on cleft lip with or without cleft palate risk around conception suggest cleft lip with or without cleft palate risk is affected more by exposure to O_3 in early pregnancy. The effect of a 10-unit increase of mean $PM_{2.5}$ on cleft lip with or without cleft palate risk was consistently low. The effect of a 10-unit increase of peak $PM_{2.5}$ on cleft lip with or without cleft palate risk was consistently low in the 16-week evaluation, but highest in the first month of pregnancy in the 12-week evaluation, suggesting cleft lip with or without cleft palate risk is affected more by exposure to O_3 in early pregnancy. Results were consistent for both green space measures, suggesting the inclusion of water with green space did not affect cleft lip with or without cleft palate risk.

The lack of strong associations between the air pollutant measures and cleft lip with or without cleft palate was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between these measures and cleft lip with or without cleft palate. In general, weekly risk ratios were consistent with equivalent results without green space. The largest differences between the evaluations were for O_3, for which some of the low risk ratios were lower than in the evaluation without green space and some of the high risk ratios were higher than in the evaluation without green space. Results were consistent for both green space measures. Overall, the association between cleft lip with or without cleft palate and O_3 may have been affected by green space, but the association between cleft lip with or without cleft palate and $PM_{2.5}$ was not affected by green space.

3.4.3 Cleft palate

The increased effect of a 10-unit increase of mean O_3 on cleft palate risk around conception suggest cleft palate risk is affected more by exposure to mean O_3 in early pregnancy. The increased effect of a 10-unit increase of peak O_3 on cleft palate risk at the end of the second and third months of pregnancy suggest cleft palate risk is affected more by exposure to peak O_3 around the end of the critical window. The increased effect of a 10-unit increase of $PM_{2.5}$ on cleft palate risk during the second month of pregnancy suggest cleft palate risk is affected more by exposure to $PM_{2.5}$ during the critical window. Results were consistent for both green space measures, suggesting the inclusion of water with green space did not affect cleft palate risk.

The lack of strong associations between O_3 and cleft palate was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between O_3 and cleft palate. The strong associations between $PM_{2.5}$ and cleft palate only up to conception was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between $PM_{2.5}$ and cleft palate. In general, weekly risk ratios were consistent with equivalent results without green space. Results were consistent for both green space measures. Overall, the association between cleft palate and air pollution was not affected by green space.

3.4.4 Craniosynostosis

The increased effect of a 10-unit increase of mean O_3 on craniosynostosis risk at the end of the second month of pregnancy suggest craniosynostosis risk is affected more by exposure to mean O_3 toward the end of the critical window. The increased effect of a 10-unit increase of peak O_3 on craniosynostosis risk before conception and during the first and second months of pregnancy suggest craniosynostosis risk is affected by exposure to peak O_3 before and in the early part of pregnancy, including during the critical window. The increased effect of a 10-unit increase of $PM_{2.5}$ on craniosynostosis risk around conception suggest craniosynostosis risk is affected more by exposure to $PM_{2.5}$ in early pregnancy. Results were consistent for both green space measures, suggesting the inclusion of water with green space did not affect cleft palate risk.

The lack of strong associations between O_3 and craniosynostosis was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between O_3 and craniosynostosis. The strong associations between $PM_{2.5}$ and craniosynostosis only up to conception was consistent with equivalent results without green space, suggesting that green space does not affect the relationship between $PM_{2.5}$ and craniosynostosis. In general, weekly risk ratios were consistent with equivalent results without green space. The largest differences between the evaluations were for $PM_{2.5}$, for which several risk ratios, including the lowest and highest ones, were higher than in the evaluation without green space. Results were consistent for both green space measures. Overall, the association between craniosynostosis and $PM_{2.5}$ may have been affected by green space, but the association between craniosynostosis and O_3 was not affected by green space.

3.4.5 Strengths and limitations

Strengths of this study included that birth defect cases covered fourteen years and most of NYS. Birth defects studied are well-diagnosed, so case misclassification is unlikely, and a sensitivity analysis of the one birth defect known to have misclassification issues was not significant. Air pollutant exposure was available daily and residential information was available at point level for most births, allowing greater granularity both temporally and spatially than many currently published studies. The NLCD data covered the entire state at a small enough resolution to see variation even within 50 meter buffers and classified trees separately from grasses to allow for them to be analyzed separately.

Limitations of this study include possible exposure misclassification that is presumed to be non-differential, which would bias results toward the null. Air pollutant exposures were assigned based on the mother's geocoded residence at birth, but no information was available regarding the mother's activity patterns, including how much time she spent at that residence during her pregnancy, so we cannot assess if assigned exposures are an accurate reflection of actual exposures. However, a sensitivity test of geocoding results showed no issues when ungeocoded births were assigned to ZIP code centroids and research suggests that mothers who move during pregnancy tend to move to areas with similar levels of air pollution.[39] In NYS, smoking is known to be under-reported on birth certificates[40], but even with presumed non-differential under-reporting, mothers of cases reported smoking more frequently than mothers of controls. Income is based on median census tract income, but the mother's household may have an income much higher or lower than the median in her census tract of residence, which could bias results toward the null.

3.5 Conclusion

In conclusion, green space may affect the relationship between O_3 and cleft lip with or without cleft palate and the relationship between $PM_{2.5}$ and craniosynostosis. More research is needed on the relationship between green space and birth defects, and their association with air pollution, especially cleft lip with or without cleft palate and craniosynostosis.

Tables

Table 3.1: Description of green space around mother's residence at birth, New York State outside New York City, 2002 to 2015

Green Space		Controls (n=18,153) n	(%)	Clubfoot (n=2423) n	(%)	Cleft lip w/wo cleft palate (n=1281) n	(%)	Cleft palate (n=952) n	(%)	Craniosynostosis (n=931) n	(%)
50 meter buffer											
	Yes	3146	(17.33)	474	(19.56)	257	(20.06)	178	(18.70)	194	(20.84)
Grass	No	15006	(82.67)	1949	(80.44)	1024	(79.94)	774	(81.30)	737	(79.16)
	Yes	3973	(21.89)	590	(24.35)	322	(25.14)	229	(24.05)	242	(25.99)
Trees	No	14179	(78.11)	1833	(75.65)	959	(74.86)	723	(75.95)	689	(74.01)
	Yes	5470	(30.13)	803	(33.14)	436	(34.04)	299	(31.41)	330	(35.45)
Green	No	12682	(69.87)	1620	(66.86)	845	(65.96)	653	(68.59)	601	(64.55)
	Yes	103	(0.57)	11	(0.45)	9	(0.70)	4	(0.42)	9	(0.97)
Water	No	18049	(99.43)	2412	(99.55)	1272	(99.30)	948	(99.58)	922	(99.03)
	Yes	5495	(30.27)	809	(33.39)	439	(34.27)	299	(31.41)	332	(35.66)
Nature	No	12657	(69.73)	1614	(66.61)	842	(65.73)	653	(68.59)	599	(64.34)
100 meter buffer											
	Yes	4173	(22.99)	635	(26.21)	356	(27.79)	242	(25.42)	251	(26.96)
Grass	No	13979	(77.01)	1788	(73.79)	925	(72.21)	710	(74.58)	680	(73.04)
	Yes	5944	(32.75)	834	(34.42)	474	(37.00)	336	(35.29)	349	(37.49)
Trees	No	12208	(67.25)	1589	(65.58)	807	(63.00)	616	(64.71)	582	(62.51)
	Yes	7090	(39.06)	1006	(41.52)	563	(43.95)	387	(40.65)	416	(44.68)
Green	No	11062	(60.94)	1417	(58.48)	718	(56.05)	565	(59.35)	515	(55.32)
	Yes	349	(1.92)	54	(2.23)	25	(1.95)	11	(1.16)	19	(2.04)
Water	No	17803	(98.08)	2369	(97.77)	1256	(98.05)	941	(98.84)	912	(97.96)
	Yes	7160	(39.44)	1017	(41.97)	568	(44.34)	387	(40.65)	420	(45.11)
Nature	No	10992	(60.56)	1406	(58.03)	713	(55.66)	565	(59.35)	511	(54.89)
200 meter buffer											
	Yes	6073	(33.46)	887	(36.61)	502	(39.19)	344	(36.13)	367	(39.42)
Grass	No	12079	(66.54)	1536	(63.39)	779	(60.81)	608	(63.87)	564	(60.58)

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Table 3.1: Description of green space around mother's residence at birth, New York State outside New York City, 2002 to 2015 *(continued)*

		Controls (n=18,153)		Clubfoot (n=2423)		Cleft lip w/wo cleft palate (n=1281)		Cleft palate (n=952)		Craniosynostosis (n=931)	
Green Space		**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
	Yes	8617	(47.47)	1194	(49.28)	651	(50.82)	476	(50.00)	482	(51.77)
Trees	No	9535	(52.53)	1229	(50.72)	630	(49.18)	476	(50.00)	449	(48.23)
	Yes	9412	(51.85)	1317	(54.35)	713	(55.66)	522	(54.83)	528	(56.71)
Green	No	8740	(48.15)	1106	(45.65)	568	(44.34)	430	(45.17)	403	(43.29)
	Yes	1131	(6.23)	157	(6.48)	96	(7.49)	52	(5.46)	58	(6.23)
Water	No	17021	(93.77)	2266	(93.52)	1185	(92.51)	900	(94.54)	873	(93.77)
	Yes	9557	(52.65)	1331	(54.93)	722	(56.36)	526	(55.25)	536	(57.57)
Nature	No	8595	(47.35)	1092	(45.07)	559	(43.64)	426	(44.75)	395	(42.43)
300 meter buffer											
	Yes	7910	(43.58)	1110	(45.81)	626	(48.87)	453	(47.58)	458	(49.19)
Grass	No	10242	(56.42)	1313	(54.19)	655	(51.13)	499	(52.42)	473	(50.81)
	Yes	10377	(57.17)	1431	(59.06)	777	(60.66)	580	(60.92)	560	(60.15)
Trees	No	7775	(42.83)	992	(40.94)	504	(39.34)	372	(39.08)	371	(39.85)
	Yes	11271	(62.09)	1543	(63.68)	838	(65.42)	630	(66.18)	611	(65.63)
Green	No	6881	(37.91)	880	(36.32)	443	(34.58)	322	(33.82)	320	(34.37)
	Yes	2112	(11.64)	315	(13.00)	161	(12.57)	110	(11.55)	124	(13.32)
Water	No	16040	(88.36)	2108	(87.00)	1120	(87.43)	842	(88.45)	807	(86.68)
	Yes	11463	(63.15)	1569	(64.75)	849	(66.28)	636	(66.81)	618	(66.38)
Nature	No	6689	(36.85)	854	(35.25)	432	(33.72)	316	(33.19)	313	(33.62)
400 meter buffer											
	Yes	9567	(52.70)	1340	(55.30)	744	(58.08)	535	(56.20)	535	(57.47)
Grass	No	8585	(47.30)	1083	(44.70)	537	(41.92)	417	(43.80)	396	(42.53)
	Yes	11784	(64.92)	1626	(67.11)	860	(67.14)	646	(67.86)	625	(67.13)
Trees	No	6368	(35.08)	797	(32.89)	421	(32.86)	306	(32.14)	306	(32.87)
	Yes	12790	(70.46)	1752	(72.31)	925	(72.21)	704	(73.95)	677	(72.72)
Green	No	5362	(29.54)	671	(27.69)	356	(27.79)	248	(26.05)	254	(27.28)

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Table 3.1: Description of green space around mother's residence at birth, New York State outside New York City, 2002 to 2015 *(continued)*

		Controls (n=18,153)		Clubfoot (n=2423)		Cleft lip w/wo cleft palate (n=1281)		Cleft palate (n=952)		Craniosynostosis (n=931)	
Green Space		**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
	Yes	3266	(17.99)	490	(20.22)	244	(19.05)	169	(17.75)	171	(18.37)
Water	No	14886	(82.01)	1933	(79.78)	1037	(80.95)	783	(82.25)	760	(81.63)
	Yes	12982	(71.52)	1784	(73.63)	938	(73.22)	713	(74.89)	686	(73.68)
Nature	No	5170	(28.48)	639	(26.37)	343	(26.78)	239	(25.11)	245	(26.32)
500 meter buffer											
	Yes	11089	(61.09)	1539	(63.52)	840	(65.57)	596	(62.61)	611	(65.63)
Grass	No	7063	(38.91)	884	(36.48)	441	(34.43)	356	(37.39)	320	(34.37)
	Yes	12910	(71.12)	1750	(72.22)	936	(73.07)	705	(74.05)	683	(73.36)
Trees	No	5242	(28.88)	673	(27.78)	345	(26.93)	247	(25.95)	248	(26.64)
	Yes	14073	(77.53)	1911	(78.87)	1016	(79.31)	761	(79.94)	738	(79.27)
Green	No	4079	(22.47)	512	(21.13)	265	(20.69)	191	(20.06)	193	(20.73)
	Yes	4492	(24.75)	625	(25.79)	332	(25.92)	244	(25.63)	238	(25.56)
Water	No	13660	(75.25)	1798	(74.21)	949	(74.08)	708	(74.37)	693	(74.44)
	Yes	14240	(78.45)	1939	(80.02)	1025	(80.02)	775	(81.41)	749	(80.45)
Nature	No	3912	(21.55)	484	(19.98)	256	(19.98)	177	(18.59)	182	(19.55)

Note:

Grass is defined as scrub, grasslands, pasture, or cultivation.

Trees is defined as deciduous, evergreen, or mixed forests or woody or emergent herbaceous wetlands.

Green combines any grasses or any trees. Nature combines any grasses, trees, or water.

Table 3.2: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs with green space, 300m buffer, New York State outside New York City, 2002 to 2015

		12-week model		16-week model	
Pollutant	**Green space**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Clubfoot					
Ozone mean	grass-trees	1.03	(0.94 - 1.13)	0.99	(0.90 - 1.10)
	green-water	1.03	(0.94 - 1.13)	0.99	(0.90 - 1.10)
Ozone peak	grass-trees	1.02	(0.95 - 1.09)	1.00	(0.93 - 1.07)
	green-water	1.02	(0.95 - 1.09)	1.00	(0.93 - 1.07)
$PM_{2.5}$ mean	grass-trees	0.89	(0.71 - 1.11)	0.90	(0.72 - 1.14)
	green-water	0.89	(0.71 - 1.11)	0.90	(0.72 - 1.14)
$PM_{2.5}$ peak	grass-trees	0.93	(0.83 - 1.04)	0.93	(0.83 - 1.05)
	green-water	0.93	(0.83 - 1.04)	0.93	(0.83 - 1.05)
Cleft lip with or without cleft palate					
Ozone mean	grass-trees	0.93	(0.82 - 1.06)	0.94	(0.82 - 1.09)
	green-water	0.93	(0.82 - 1.06)	0.94	(0.82 - 1.09)
Ozone peak	grass-trees	0.96	(0.87 - 1.05)	0.97	(0.88 - 1.06)
	green-water	0.96	(0.87 - 1.05)	0.97	(0.88 - 1.06)
$PM_{2.5}$ mean	grass-trees	0.79	(0.59 - 1.06)	0.77	(0.57 - 1.05)
	green-water	0.79	(0.59 - 1.06)	0.77	(0.57 - 1.05)
$PM_{2.5}$ peak	grass-trees	0.89	(0.76 - 1.04)	0.89	(0.76 - 1.05)
	green-water	0.89	(0.76 - 1.04)	0.89	(0.76 - 1.05)
Cleft Palate					
Ozone mean	grass-trees	1.04	(0.90 - 1.20)	1.04	(0.89 - 1.23)
	green-water	1.04	(0.90 - 1.20)	1.04	(0.89 - 1.23)
Ozone peak	grass-trees	0.99	(0.89 - 1.10)	1.00	(0.90 - 1.12)
	green-water	0.99	(0.89 - 1.10)	1.00	(0.90 - 1.12)
$PM_{2.5}$ mean	grass-trees	0.81	(0.57 - 1.14)	0.78	(0.55 - 1.12)
	green-water	0.81	(0.57 - 1.14)	0.78	(0.55 - 1.12)
$PM_{2.5}$ peak	grass-trees	0.89	(0.74 - 1.07)	0.86	(0.71 - 1.04)
	green-water	0.89	(0.74 - 1.07)	0.86	(0.71 - 1.04)
Craniosynostosis					
Ozone mean	grass-trees	0.96	(0.82 - 1.12)	0.86	(0.71 - 1.03)
	green-water	0.96	(0.82 - 1.12)	0.86	(0.71 - 1.03)
Ozone peak	grass-trees	0.97	(0.87 - 1.09)	0.92	(0.81 - 1.05)
	green-water	0.97	(0.87 - 1.09)	0.92	(0.81 - 1.05)
$PM_{2.5}$ mean	grass-trees	1.09	(0.76 - 1.59)	1.11	(0.76 - 1.64)
	green-water	1.09	(0.76 - 1.59)	1.11	(0.76 - 1.64)
$PM_{2.5}$ peak	grass-trees	1.03	(0.85 - 1.25)	1.02	(0.84 - 1.25)
	green-water	1.03	(0.85 - 1.25)	1.02	(0.84 - 1.25)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, green space, and conception season. RR applies to a 10-unit increase over two standard deviations above the mean. For green space, grass-trees is a composite variable of grasses and trees and green-water is a composite of grasses, trees, and water.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Table 3.3: Lag risk ratios for covariate models of air pollutant and clubfoot pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	1.02	(0.97 - 1.07)	1.01	(1.00 - 1.03)	0.96	(0.89 - 1.04)	0.96	(0.91 - 1.02)
-3	1.01	(0.99 - 1.04)	1.01	(1.00 - 1.03)	0.97	(0.92 - 1.02)	0.97	(0.93 - 1.01)
-2	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.97	(0.94 - 1.01)	0.97	(0.94 - 1.01)
-1	1.00	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.95 - 1.01)	0.98	(0.95 - 1.01)
0	1.00	(0.98 - 1.02)	1.01	(1.00 - 1.02)	↑0.99	(0.95 - 1.02)	0.98	(0.96 - 1.01)
1	1.00	(0.97 - 1.02)	↓1.00	(1.00 - 1.01)	0.99	(0.95 - 1.04)	0.99	(0.96 - 1.01)
2	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	0.99	(0.95 - 1.04)	0.99	(0.96 - 1.02)
3	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	1.00	(0.96 - 1.04)	0.99	(0.96 - 1.03)
4	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.01)	1.00	(0.97 - 1.04)	1.00	(0.97 - 1.03)
5	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.03)
6	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.01	(0.97 - 1.04)	1.00	(0.98 - 1.03)
7	1.00	(0.97 - 1.03)	0.99	(0.99 - 1.00)	1.01	(0.95 - 1.07)	↑1.01	(0.98 - 1.03)
8	1.00	(0.96 - 1.05)	0.99	(0.98 - 1.00)	1.01	(0.92 - 1.11)	1.01	(0.99 - 1.03)
9			0.99	(0.98 - 1.00)			1.01	(0.98 - 1.04)
10			0.99	(0.98 - 1.00)			1.01	(0.97 - 1.05)
11			0.99	(0.97 - 1.00)			1.01	(0.96 - 1.07)
12			0.99	(0.97 - 1.00)			↑1.02	(0.94 - 1.09)
Weekly peak concentration								
-4	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	↑0.98	(0.93 - 1.02)	0.98	(0.93 - 1.04)
-3	1.01	(1.00 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.96 - 1.01)	↑0.99	(0.96 - 1.01)
-2	1.01	(1.00 - 1.02)	1.01	(1.00 - 1.02)	0.99	(0.97 - 1.01)	0.99	(0.97 - 1.01)
-1	1.00	(1.00 - 1.01)	1.01	(1.00 - 1.01)	0.99	(0.98 - 1.01)	0.99	(0.97 - 1.01)
0	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.02)
1	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	↑1.00	(0.97 - 1.02)
2	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.02)
3	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.02)
4	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.00)	1.00	(0.98 - 1.02)	1.00	(0.98 - 1.02)
5	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
6	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
7	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	0.99	(0.96 - 1.02)	1.00	(0.98 - 1.02)
8	0.99	(0.98 - 1.01)	1.00	(0.99 - 1.00)	↑0.99	(0.94 - 1.03)	1.00	(0.98 - 1.02)
9			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
10			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
11			0.99	(0.98 - 1.00)			1.00	(0.97 - 1.03)
12			0.99	(0.98 - 1.00)			1.00	(0.95 - 1.05)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.4: Lag risk ratios for covariate models of air pollutant and clubfoot pairs with grasses, trees, and water, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	1.02	(0.97 - 1.07)	1.01	(1.00 - 1.03)	0.96	(0.89 - 1.04)	0.96	(0.91 - 1.02)
-3	1.01	(0.99 - 1.04)	1.01	(1.00 - 1.03)	0.97	(0.92 - 1.02)	0.97	(0.93 - 1.01)
-2	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.97	(0.94 - 1.01)	0.97	(0.94 - 1.01)
-1	1.00	(0.99 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.95 - 1.01)	0.98	(0.95 - 1.01)
0	1.00	(0.98 - 1.02)	1.01	(1.00 - 1.02)	↑0.99	(0.95 - 1.02)	0.98	(0.96 - 1.01)
1	1.00	(0.97 - 1.02)	↓1.00	(1.00 - 1.01)	0.99	(0.95 - 1.04)	0.99	(0.96 - 1.01)
2	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	0.99	(0.95 - 1.04)	0.99	(0.96 - 1.02)
3	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	1.00	(0.96 - 1.04)	0.99	(0.96 - 1.03)
4	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.01)	1.00	(0.97 - 1.04)	1.00	(0.97 - 1.03)
5	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.03)
6	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.01	(0.97 - 1.04)	1.00	(0.98 - 1.03)
7	1.00	(0.97 - 1.03)	0.99	(0.99 - 1.00)	1.01	(0.95 - 1.07)	↑1.01	(0.98 - 1.03)
8	1.00	(0.96 - 1.05)	0.99	(0.98 - 1.00)	1.01	(0.92 - 1.11)	1.01	(0.99 - 1.03)
9			0.99	(0.98 - 1.00)			1.01	(0.98 - 1.04)
10			0.99	(0.98 - 1.00)			1.01	(0.97 - 1.05)
11			0.99	(0.97 - 1.00)			1.01	(0.96 - 1.07)
12			0.99	(0.97 - 1.00)			↑1.02	(0.94 - 1.09)
Weekly peak concentration								
-4	1.01	(0.99 - 1.02)	1.01	(1.00 - 1.02)	↑0.98	(0.93 - 1.02)	0.98	(0.93 - 1.04)
-3	1.01	(1.00 - 1.02)	1.01	(1.00 - 1.02)	0.98	(0.96 - 1.01)	↑0.99	(0.96 - 1.01)
-2	1.01	(1.00 - 1.02)	1.01	(1.00 - 1.02)	0.99	(0.97 - 1.01)	0.99	(0.97 - 1.01)
-1	1.00	(1.00 - 1.01)	1.01	(1.00 - 1.01)	0.99	(0.98 - 1.01)	0.99	(0.97 - 1.01)
0	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.02)
1	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.02)	↑1.00	(0.97 - 1.02)
2	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.02)
3	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.02)
4	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.00)	1.00	(0.98 - 1.02)	1.00	(0.98 - 1.02)
5	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
6	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.01)	1.00	(0.98 - 1.02)
7	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	0.99	(0.96 - 1.02)	1.00	(0.98 - 1.02)
8	0.99	(0.98 - 1.01)	1.00	(0.99 - 1.00)	↑0.99	(0.94 - 1.03)	1.00	(0.98 - 1.02)
9			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
10			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.02)
11			0.99	(0.98 - 1.00)			1.00	(0.97 - 1.03)
12			0.99	(0.98 - 1.00)			1.00	(0.95 - 1.05)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.5: Lag risk ratios for covariate models of air pollutant and cleft lip with or without cleft palate pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	↓**0.88**	**(0.80 - 0.97)**	↓**0.91**	**(0.83 - 1.00)**	0.98	(0.92 - 1.05)	↑0.99	(0.93 - 1.04)
-3	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.02)	0.98	(0.93 - 1.04)	↑0.99	(0.94 - 1.04)
-2	1.05	(0.99 - 1.11)	1.02	(0.98 - 1.07)	0.98	(0.94 - 1.03)	↑0.99	(0.94 - 1.03)
-1	↑**1.06**	**(1.00 - 1.11)**	1.04	(0.99 - 1.09)	0.98	(0.95 - 1.02)	↑0.99	(0.95 - 1.02)
0	↑1.04	(0.99 - 1.08)	↑**1.05**	**(1.00 - 1.09)**	0.98	(0.95 - 1.01)	↑0.99	(0.95 - 1.02)
1	1.01	(0.96 - 1.06)	↑**1.04**	**(1.00 - 1.07)**	0.98	(0.96 - 1.01)	↑0.99	(0.96 - 1.01)
2	0.99	(0.94 - 1.04)	1.02	(0.99 - 1.06)	0.98	(0.96 - 1.00)	↑0.99	(0.96 - 1.01)
3	0.98	(0.94 - 1.03)	1.00	(0.97 - 1.04)	0.98	(0.96 - 1.01)	↑0.99	(0.97 - 1.00)
4	0.99	(0.94 - 1.03)	0.99	(0.95 - 1.03)	0.98	(0.95 - 1.01)	0.98	(0.97 - 1.00)
5	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.01)	0.98	(0.95 - 1.02)	0.98	(0.97 - 1.00)
6	1.01	(0.95 - 1.07)	0.97	(0.94 - 1.00)	0.98	(0.94 - 1.02)	0.98	(0.96 - 1.01)
7	1.00	(0.95 - 1.05)	0.97	(0.93 - 1.00)	0.98	(0.93 - 1.03)	0.98	(0.96 - 1.01)
8	0.95	(0.85 - 1.05)	0.97	(0.93 - 1.01)	0.98	(0.93 - 1.04)	0.98	(0.96 - 1.01)
9			0.98	(0.94 - 1.03)			0.98	(0.95 - 1.02)
10			1.00	(0.95 - 1.04)			0.98	(0.94 - 1.02)
11			↓1.01	(0.98 - 1.06)			0.98	(0.94 - 1.03)
12			1.03	(0.94 - 1.13)			0.98	(0.93 - 1.04)
Weekly peak concentration								
-4	**0.91**	**(0.85 - 0.97)**	**0.93**	**(0.88 - 0.98)**	0.96	(0.91 - 1.02)	0.99	(0.96 - 1.02)
-3	0.99	(0.95 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.98	(0.94 - 1.02)	0.99	(0.97 - 1.02)
-2	1.03	(0.99 - 1.06)	1.00	(0.99 - 1.02)	0.99	(0.97 - 1.02)	0.99	(0.97 - 1.02)
-1	**1.03**	**(1.00 - 1.07)**	**1.02**	**(1.00 - 1.05)**	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.01)
0	1.03	(1.00 - 1.06)	**1.03**	**(1.01 - 1.06)**	↑1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
1	1.02	(0.98 - 1.05)	↑**1.04**	**(1.01 - 1.06)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
2	1.01	(0.97 - 1.05)	**1.03**	**(1.01 - 1.05)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
3	↑1.01	(0.97 - 1.04)	**1.02**	**(1.00 - 1.04)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.00)
4	1.01	(0.98 - 1.04)	1.01	(0.99 - 1.03)	1.00	(0.98 - 1.03)	0.99	(0.98 - 1.00)
5	1.01	(0.98 - 1.05)	0.99	(0.98 - 1.01)	↑1.00	(0.98 - 1.02)	0.99	(0.98 - 1.00)
6	1.01	(0.97 - 1.05)	0.98	(0.96 - 1.00)	↑0.99	(0.96 - 1.01)	0.99	(0.98 - 1.00)
7	0.99	(0.95 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.97	(0.93 - 1.01)	0.99	(0.98 - 1.01)
8	0.94	(0.88 - 1.00)	**0.97**	**(0.95 - 0.99)**	↑0.96	(0.90 - 1.02)	0.99	(0.98 - 1.01)
9			**0.97**	**(0.95 - 0.99)**			0.99	(0.98 - 1.01)
10			**0.98**	**(0.97 - 1.00)**			0.99	(0.97 - 1.02)
11			1.00	(0.98 - 1.03)			0.99	(0.97 - 1.02)
12			1.04	(0.99 - 1.10)			0.99	(0.97 - 1.02)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.6: Lag risk ratios for covariate models of air pollutant and cleft lip with or without cleft palate pairs with grasses, trees, and water, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	**↓0.88**	**(0.80 - 0.97)**	**↓0.91**	**(0.83 - 1.00)**	0.98	(0.92 - 1.05)	↑0.99	(0.93 - 1.04)
-3	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.02)	0.98	(0.93 - 1.04)	↑0.99	(0.94 - 1.04)
-2	1.05	(0.99 - 1.11)	1.02	(0.98 - 1.07)	0.98	(0.94 - 1.03)	↑0.99	(0.94 - 1.03)
-1	**↑1.06**	**(1.00 - 1.11)**	1.04	(0.99 - 1.09)	0.98	(0.95 - 1.02)	↑0.99	(0.95 - 1.02)
0	↑1.04	(0.99 - 1.08)	**↑1.05**	**(1.00 - 1.09)**	0.98	(0.95 - 1.01)	↑0.99	(0.95 - 1.02)
1	1.01	(0.96 - 1.06)	**↑1.04**	**(1.00 - 1.07)**	0.98	(0.96 - 1.01)	↑0.99	(0.96 - 1.01)
2	0.99	(0.94 - 1.04)	1.02	(0.99 - 1.06)	0.98	(0.96 - 1.00)	↑0.99	(0.96 - 1.01)
3	0.98	(0.94 - 1.03)	1.00	(0.97 - 1.04)	0.98	(0.96 - 1.01)	↑0.99	(0.97 - 1.00)
4	0.99	(0.94 - 1.03)	0.99	(0.95 - 1.03)	0.98	(0.95 - 1.01)	0.98	(0.97 - 1.00)
5	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.01)	0.98	(0.95 - 1.02)	0.98	(0.97 - 1.00)
6	1.01	(0.95 - 1.07)	0.97	(0.94 - 1.00)	0.98	(0.94 - 1.02)	0.98	(0.96 - 1.01)
7	1.00	(0.95 - 1.05)	0.97	(0.93 - 1.00)	0.98	(0.93 - 1.03)	0.98	(0.96 - 1.01)
8	0.95	(0.85 - 1.05)	0.97	(0.93 - 1.01)	0.98	(0.93 - 1.04)	0.98	(0.96 - 1.01)
9			0.98	(0.94 - 1.03)			0.98	(0.95 - 1.02)
10			1.00	(0.95 - 1.04)			0.98	(0.94 - 1.02)
11			↓1.01	(0.98 - 1.06)			0.98	(0.94 - 1.03)
12			1.03	(0.94 - 1.13)			0.98	(0.93 - 1.04)
Weekly peak concentration								
-4	**0.91**	**(0.85 - 0.97)**	**0.93**	**(0.88 - 0.98)**	0.96	(0.91 - 1.02)	0.99	(0.96 - 1.02)
-3	0.99	(0.95 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.98	(0.94 - 1.02)	0.99	(0.97 - 1.02)
-2	1.03	(0.99 - 1.06)	1.00	(0.99 - 1.02)	0.99	(0.97 - 1.02)	0.99	(0.97 - 1.02)
-1	**1.03**	**(1.00 - 1.07)**	**1.02**	**(1.00 - 1.05)**	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.01)
0	1.03	(1.00 - 1.06)	**1.03**	**(1.01 - 1.06)**	↑1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
1	1.02	(0.98 - 1.05)	**↑1.04**	**(1.01 - 1.06)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
2	1.01	(0.97 - 1.05)	**1.03**	**(1.01 - 1.05)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)
3	↑1.01	(0.97 - 1.04)	**1.02**	**(1.00 - 1.04)**	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.00)
4	1.01	(0.98 - 1.04)	1.01	(0.99 - 1.03)	1.00	(0.98 - 1.03)	0.99	(0.98 - 1.00)
5	1.01	(0.98 - 1.05)	0.99	(0.98 - 1.01)	↑1.00	(0.98 - 1.02)	0.99	(0.98 - 1.00)
6	1.01	(0.97 - 1.05)	0.98	(0.96 - 1.00)	↑0.99	(0.96 - 1.01)	0.99	(0.98 - 1.00)
7	0.99	(0.95 - 1.02)	**0.97**	**(0.95 - 1.00)**	0.97	(0.93 - 1.01)	0.99	(0.98 - 1.01)
8	0.94	(0.88 - 1.00)	**0.97**	**(0.95 - 0.99)**	↑0.96	(0.90 - 1.02)	0.99	(0.98 - 1.01)
9			**0.97**	**(0.95 - 0.99)**			0.99	(0.98 - 1.01)
10			**0.98**	**(0.97 - 1.00)**			0.99	(0.97 - 1.02)
11			1.00	(0.98 - 1.03)			0.99	(0.97 - 1.02)
12			1.04	(0.99 - 1.10)			0.99	(0.97 - 1.02)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.7: Lag risk ratios for covariate models of air pollutant and cleft palate pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	↓1.00	(0.97 - 1.04)	0.95	(0.85 - 1.07)	**0.92**	**(0.85 - 0.99)**	0.91	(0.82 - 1.00)
-3	1.00	(0.98 - 1.03)	1.01	(0.96 - 1.05)	**0.93**	**(0.87 - 0.99)**	**0.93**	**(0.86 - 1.00)**
-2	1.00	(0.98 - 1.03)	1.03	(0.98 - 1.09)	**0.94**	**(0.89 - 0.99)**	0.95	(0.89 - 1.00)
-1	1.00	(0.98 - 1.02)	1.04	(0.98 - 1.10)	**0.95**	**(0.91 - 0.99)**	0.96	(0.92 - 1.01)
0	1.00	(0.99 - 1.02)	1.03	(0.98 - 1.08)	**0.96**	**(0.93 - 1.00)**	0.98	(0.94 - 1.02)
1	1.00	(0.99 - 1.02)	1.01	(0.97 - 1.06)	0.97	(0.94 - 1.00)	0.99	(0.95 - 1.04)
2	1.00	(0.99 - 1.01)	1.00	(0.96 - 1.04)	0.98	(0.96 - 1.01)	1.00	(0.95 - 1.05)
3	1.00	(0.99 - 1.01)	0.99	(0.94 - 1.03)	1.00	(0.97 - 1.02)	1.01	(0.96 - 1.06)
4	1.00	(0.99 - 1.02)	0.98	(0.94 - 1.03)	1.01	(0.98 - 1.04)	1.02	(0.97 - 1.07)
5	1.00	(0.98 - 1.02)	0.98	(0.94 - 1.02)	1.02	(0.98 - 1.06)	1.02	(0.97 - 1.07)
6	1.00	(0.98 - 1.02)	0.99	(0.95 - 1.03)	1.03	(0.98 - 1.08)	1.02	(0.98 - 1.06)
7	1.00	(0.97 - 1.03)	1.00	(0.96 - 1.04)	1.04	(0.98 - 1.10)	1.02	(0.98 - 1.05)
8	1.00	(0.97 - 1.03)	1.01	(0.97 - 1.07)	1.05	(0.99 - 1.13)	1.01	(0.98 - 1.05)
9			↑1.03	(0.97 - 1.08)			1.01	(0.96 - 1.05)
10			1.03	(0.98 - 1.08)			1.00	(0.94 - 1.06)
11			1.01	(0.97 - 1.06)			0.98	(0.90 - 1.07)
12			0.97	(0.87 - 1.09)			0.97	(0.87 - 1.09)
Weekly peak concentration								
-4	0.97	(0.89 - 1.05)	0.98	(0.92 - 1.04)	**0.96**	**(0.92 - 1.00)**	**0.95**	**(0.90 - 1.00)**
-3	0.98	(0.95 - 1.02)	0.99	(0.96 - 1.02)	**0.96**	**(0.93 - 1.00)**	**0.96**	**(0.92 - 1.00)**
-2	1.00	(0.96 - 1.05)	1.00	(0.98 - 1.02)	**0.97**	**(0.94 - 1.00)**	0.97	(0.94 - 1.00)
-1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.03)	**0.97**	**(0.95 - 1.00)**	0.98	(0.96 - 1.01)
0	1.02	(0.99 - 1.06)	1.01	(0.98 - 1.04)	**0.98**	**(0.96 - 1.00)**	0.99	(0.97 - 1.02)
1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.97 - 1.00)	1.00	(0.98 - 1.02)
2	1.01	(0.97 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)	1.01	(0.98 - 1.03)
3	1.00	(0.96 - 1.04)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.01)	1.01	(0.98 - 1.04)
4	0.99	(0.95 - 1.02)	1.00	(0.98 - 1.02)	1.00	(0.99 - 1.02)	1.01	(0.99 - 1.04)
5	0.98	(0.94 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.03)	1.01	(0.99 - 1.04)
6	0.98	(0.93 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.04)	1.01	(0.99 - 1.03)
7	0.99	(0.95 - 1.03)	0.99	(0.96 - 1.02)	1.02	(0.99 - 1.05)	1.01	(0.99 - 1.03)
8	1.03	(0.95 - 1.11)	0.99	(0.96 - 1.02)	1.03	(0.99 - 1.07)	1.00	(0.99 - 1.02)
9			0.99	(0.97 - 1.02)			1.00	(0.97 - 1.02)
10			1.00	(0.98 - 1.02)			0.99	(0.96 - 1.02)
11			1.01	(0.98 - 1.04)			0.98	(0.94 - 1.02)
12			1.03	(0.97 - 1.09)			0.97	(0.91 - 1.03)

Note:
RR = risk ratio; CI = confidence interval; PM = particulate matter
↑= RR is higher than in the original model; ↓= RR is lower than in the original model
Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.
RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for $PM_{2.5}$) over two standard deviations above the mean.
Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.8: Lag risk ratios for covariate models of air pollutant and cleft palate pairs with grasses, trees, and water, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	↓1.00	(0.97 - 1.04)	0.95	(0.85 - 1.07)	**0.92**	**(0.85 - 0.99)**	0.91	(0.82 - 1.00)
-3	1.00	(0.98 - 1.03)	1.01	(0.96 - 1.05)	**0.93**	**(0.87 - 0.99)**	**0.93**	**(0.86 - 1.00)**
-2	1.00	(0.98 - 1.03)	1.03	(0.98 - 1.09)	**0.94**	**(0.89 - 0.99)**	0.95	(0.89 - 1.00)
-1	1.00	(0.98 - 1.02)	1.04	(0.98 - 1.10)	**0.95**	**(0.91 - 0.99)**	0.96	(0.92 - 1.01)
0	1.00	(0.99 - 1.02)	1.03	(0.98 - 1.08)	**0.96**	**(0.93 - 1.00)**	0.98	(0.94 - 1.02)
1	1.00	(0.99 - 1.02)	1.01	(0.97 - 1.06)	0.97	(0.94 - 1.00)	0.99	(0.95 - 1.04)
2	1.00	(0.99 - 1.01)	1.00	(0.96 - 1.04)	0.98	(0.96 - 1.01)	1.00	(0.95 - 1.05)
3	1.00	(0.99 - 1.01)	0.99	(0.94 - 1.03)	1.00	(0.97 - 1.02)	1.01	(0.96 - 1.06)
4	1.00	(0.99 - 1.02)	0.98	(0.94 - 1.03)	1.01	(0.98 - 1.04)	1.02	(0.97 - 1.07)
5	1.00	(0.98 - 1.02)	0.98	(0.94 - 1.02)	1.02	(0.98 - 1.06)	1.02	(0.97 - 1.07)
6	1.00	(0.98 - 1.02)	0.99	(0.95 - 1.03)	1.03	(0.98 - 1.08)	1.02	(0.98 - 1.06)
7	1.00	(0.97 - 1.03)	1.00	(0.96 - 1.04)	1.04	(0.98 - 1.10)	1.02	(0.98 - 1.05)
8	1.00	(0.97 - 1.03)	1.01	(0.97 - 1.07)	1.05	(0.99 - 1.13)	1.01	(0.98 - 1.05)
9			↑1.03	(0.97 - 1.08)			1.01	(0.96 - 1.05)
10			1.03	(0.98 - 1.08)			1.00	(0.94 - 1.06)
11			1.01	(0.97 - 1.06)			0.98	(0.90 - 1.07)
12			0.97	(0.87 - 1.09)			0.97	(0.87 - 1.09)
Weekly peak concentration								
-4	0.97	(0.89 - 1.05)	0.98	(0.92 - 1.04)	**0.96**	**(0.92 - 1.00)**	**0.95**	**(0.90 - 1.00)**
-3	0.98	(0.95 - 1.02)	0.99	(0.96 - 1.02)	**0.96**	**(0.93 - 1.00)**	**0.96**	**(0.92 - 1.00)**
-2	1.00	(0.96 - 1.05)	1.00	(0.98 - 1.02)	**0.97**	**(0.94 - 1.00)**	0.97	(0.94 - 1.00)
-1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.03)	**0.97**	**(0.95 - 1.00)**	0.98	(0.96 - 1.01)
0	1.02	(0.99 - 1.06)	1.01	(0.98 - 1.04)	**0.98**	**(0.96 - 1.00)**	0.99	(0.97 - 1.02)
1	1.02	(0.98 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.97 - 1.00)	1.00	(0.98 - 1.02)
2	1.01	(0.97 - 1.06)	1.01	(0.98 - 1.04)	0.99	(0.98 - 1.01)	1.01	(0.98 - 1.03)
3	1.00	(0.96 - 1.04)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.01)	1.01	(0.98 - 1.04)
4	0.99	(0.95 - 1.02)	1.00	(0.98 - 1.02)	1.00	(0.99 - 1.02)	1.01	(0.99 - 1.04)
5	0.98	(0.94 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.03)	1.01	(0.99 - 1.04)
6	0.98	(0.93 - 1.02)	0.99	(0.97 - 1.02)	1.01	(0.99 - 1.04)	1.01	(0.99 - 1.03)
7	0.99	(0.95 - 1.03)	0.99	(0.96 - 1.02)	1.02	(0.99 - 1.05)	1.01	(0.99 - 1.03)
8	1.03	(0.95 - 1.11)	0.99	(0.96 - 1.02)	1.03	(0.99 - 1.07)	1.00	(0.99 - 1.02)
9			0.99	(0.97 - 1.02)			1.00	(0.97 - 1.02)
10			1.00	(0.98 - 1.02)			0.99	(0.96 - 1.02)
11			1.01	(0.98 - 1.04)			0.98	(0.94 - 1.02)
12			1.03	(0.97 - 1.09)			0.97	(0.91 - 1.03)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.9: Lag risk ratios for covariate models of air pollutant and craniosynostosis pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	0.95	(0.85 - 1.05)	0.91	(0.81 - 1.01)	↑1.02	(0.89 - 1.17)	↑0.87	(0.71 - 1.07)
-3	0.98	(0.94 - 1.02)	0.98	(0.93 - 1.02)	↑1.03	(0.94 - 1.12)	↑1.04	(0.95 - 1.13)
-2	1.00	(0.96 - 1.04)	1.01	(0.96 - 1.07)	1.03	(0.98 - 1.10)	↑**1.13**	**(1.02 - 1.25)**
-1	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.08)	↑1.04	(0.98 - 1.10)	↑**1.15**	**(1.03 - 1.28)**
0	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.07)	↑1.04	(0.97 - 1.11)	↑**1.12**	**(1.01 - 1.23)**
1	1.01	(0.97 - 1.06)	1.01	(0.96 - 1.05)	1.03	(0.96 - 1.11)	1.06	(0.98 - 1.15)
2	1.01	(0.96 - 1.05)	1.00	(0.95 - 1.04)	↑1.03	(0.95 - 1.11)	↑1.01	(0.94 - 1.09)
3	1.00	(0.95 - 1.05)	0.99	(0.94 - 1.04)	↑1.02	(0.95 - 1.09)	0.96	(0.89 - 1.05)
4	0.99	(0.94 - 1.05)	0.99	(0.94 - 1.04)	↑1.01	(0.95 - 1.07)	↑0.94	(0.86 - 1.02)
5	0.99	(0.94 - 1.04)	1.00	(0.95 - 1.04)	0.99	(0.95 - 1.04)	↑0.93	(0.85 - 1.00)
6	0.99	(0.95 - 1.03)	1.01	(0.97 - 1.05)	0.97	(0.92 - 1.03)	↑0.94	(0.87 - 1.00)
7	1.00	(0.95 - 1.05)	↓1.02	(0.98 - 1.07)	0.95	(0.87 - 1.05)	0.96	(0.89 - 1.04)
8	1.02	(0.91 - 1.14)	1.04	(0.98 - 1.09)	↑0.93	(0.80 - 1.08)	1.00	(0.91 - 1.09)
9			1.04	(0.98 - 1.10)			1.03	(0.93 - 1.15)
10			↓1.01	(0.96 - 1.07)			1.05	(0.95 - 1.17)
11			0.96	(0.91 - 1.01)			↑1.03	(0.93 - 1.14)
12			**0.87**	**(0.77 - 0.98)**			↑0.95	(0.77 - 1.16)
Weekly peak concentration								
-4	0.96	(0.89 - 1.04)	0.97	(0.93 - 1.01)	↑0.95	(0.85 - 1.06)	0.99	(0.91 - 1.08)
-3	1.00	(0.96 - 1.04)	0.98	(0.95 - 1.01)	1.02	(0.97 - 1.08)	↑1.01	(0.96 - 1.05)
-2	↑1.02	(0.97 - 1.06)	0.99	(0.97 - 1.01)	1.05	(0.99 - 1.12)	↑1.02	(0.98 - 1.05)
-1	1.01	(0.97 - 1.06)	0.99	(0.98 - 1.01)	1.05	(0.99 - 1.12)	1.02	(0.98 - 1.06)
0	1.01	(0.97 - 1.04)	1.00	(0.99 - 1.01)	1.03	(0.98 - 1.09)	1.02	(0.98 - 1.06)
1	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.02)	1.01	(0.95 - 1.07)	1.02	(0.98 - 1.06)
2	0.98	(0.94 - 1.03)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.05)	1.01	(0.98 - 1.05)
3	0.98	(0.94 - 1.02)	1.01	(0.99 - 1.03)	↑0.98	(0.93 - 1.03)	↑1.01	(0.97 - 1.04)
4	0.98	(0.95 - 1.02)	1.01	(0.99 - 1.03)	↑0.98	(0.93 - 1.02)	1.00	(0.97 - 1.03)
5	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.03)	0.98	(0.93 - 1.04)	0.99	(0.96 - 1.02)
6	1.00	(0.96 - 1.05)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.06)	0.98	(0.95 - 1.02)
7	1.02	(0.98 - 1.06)	1.01	(0.99 - 1.02)	1.00	(0.94 - 1.07)	0.98	(0.94 - 1.02)
8	1.02	(0.94 - 1.11)	1.00	(0.99 - 1.01)	↑1.00	(0.89 - 1.13)	0.98	(0.94 - 1.02)
9			0.99	(0.98 - 1.01)			0.98	(0.95 - 1.02)
10			0.99	(0.97 - 1.01)			0.99	(0.96 - 1.03)
11			0.98	(0.95 - 1.01)			1.00	(0.96 - 1.05)
12			0.97	(0.92 - 1.01)			1.02	(0.94 - 1.12)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 3.10: Lag risk ratios for covariate models of air pollutant and craniosynostosis pairs with grasses, trees, and water, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	0.95	(0.85 - 1.05)	0.91	(0.81 - 1.01)	↑1.02	(0.89 - 1.17)	↑0.87	(0.71 - 1.07)
-3	0.98	(0.94 - 1.02)	0.98	(0.93 - 1.02)	↑1.03	(0.94 - 1.12)	↑1.04	(0.95 - 1.13)
-2	1.00	(0.96 - 1.04)	1.01	(0.96 - 1.07)	1.03	(0.98 - 1.10)	**↑1.13**	**(1.02 - 1.25)**
-1	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.08)	↑1.04	(0.98 - 1.10)	**↑1.15**	**(1.03 - 1.28)**
0	1.01	(0.96 - 1.07)	1.02	(0.97 - 1.07)	↑1.04	(0.97 - 1.11)	**↑1.12**	**(1.01 - 1.23)**
1	1.01	(0.97 - 1.06)	1.01	(0.96 - 1.05)	1.03	(0.96 - 1.11)	1.06	(0.98 - 1.15)
2	1.01	(0.96 - 1.05)	1.00	(0.95 - 1.04)	↑1.03	(0.95 - 1.11)	↑1.01	(0.94 - 1.09)
3	1.00	(0.95 - 1.05)	0.99	(0.94 - 1.04)	↑1.02	(0.95 - 1.09)	0.96	(0.89 - 1.05)
4	0.99	(0.94 - 1.05)	0.99	(0.94 - 1.04)	↑1.01	(0.95 - 1.07)	↑0.94	(0.86 - 1.02)
5	0.99	(0.94 - 1.04)	1.00	(0.95 - 1.04)	0.99	(0.95 - 1.04)	↑0.93	(0.85 - 1.00)
6	0.99	(0.95 - 1.03)	1.01	(0.97 - 1.05)	0.97	(0.92 - 1.03)	↑0.94	(0.87 - 1.00)
7	1.00	(0.95 - 1.05)	↓1.02	(0.98 - 1.07)	0.95	(0.87 - 1.05)	0.96	(0.89 - 1.04)
8	1.02	(0.91 - 1.14)	1.04	(0.98 - 1.09)	↑0.93	(0.80 - 1.08)	1.00	(0.91 - 1.09)
9			1.04	(0.98 - 1.10)			1.03	(0.93 - 1.15)
10			↓1.01	(0.96 - 1.07)			1.05	(0.95 - 1.17)
11			0.96	(0.91 - 1.01)			↑1.03	(0.93 - 1.14)
12			**0.87**	**(0.77 - 0.98)**			↑0.95	(0.77 - 1.16)
Weekly peak concentration								
-4	0.96	(0.89 - 1.04)	0.97	(0.93 - 1.01)	↑0.95	(0.85 - 1.06)	0.99	(0.91 - 1.08)
-3	1.00	(0.96 - 1.04)	0.98	(0.95 - 1.01)	1.02	(0.97 - 1.08)	↑1.01	(0.96 - 1.05)
-2	↑1.02	(0.97 - 1.06)	0.99	(0.97 - 1.01)	1.05	(0.99 - 1.12)	↑1.02	(0.98 - 1.05)
-1	1.01	(0.97 - 1.06)	0.99	(0.98 - 1.01)	1.05	(0.99 - 1.12)	1.02	(0.98 - 1.06)
0	1.01	(0.97 - 1.04)	1.00	(0.99 - 1.01)	1.03	(0.98 - 1.09)	1.02	(0.98 - 1.06)
1	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.02)	1.01	(0.95 - 1.07)	1.02	(0.98 - 1.06)
2	0.98	(0.94 - 1.03)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.05)	1.01	(0.98 - 1.05)
3	0.98	(0.94 - 1.02)	1.01	(0.99 - 1.03)	↑0.98	(0.93 - 1.03)	↑1.01	(0.97 - 1.04)
4	0.98	(0.95 - 1.02)	1.01	(0.99 - 1.03)	↑0.98	(0.93 - 1.02)	1.00	(0.97 - 1.03)
5	0.99	(0.95 - 1.03)	1.01	(0.99 - 1.03)	0.98	(0.93 - 1.04)	0.99	(0.96 - 1.02)
6	1.00	(0.96 - 1.05)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.06)	0.98	(0.95 - 1.02)
7	1.02	(0.98 - 1.06)	1.01	(0.99 - 1.02)	1.00	(0.94 - 1.07)	0.98	(0.94 - 1.02)
8	1.02	(0.94 - 1.11)	1.00	(0.99 - 1.01)	↑1.00	(0.89 - 1.13)	0.98	(0.94 - 1.02)
9			0.99	(0.98 - 1.01)			0.98	(0.95 - 1.02)
10			0.99	(0.97 - 1.01)			0.99	(0.96 - 1.03)
11			0.98	(0.95 - 1.01)			1.00	(0.96 - 1.05)
12			0.97	(0.92 - 1.01)			1.02	(0.94 - 1.12)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

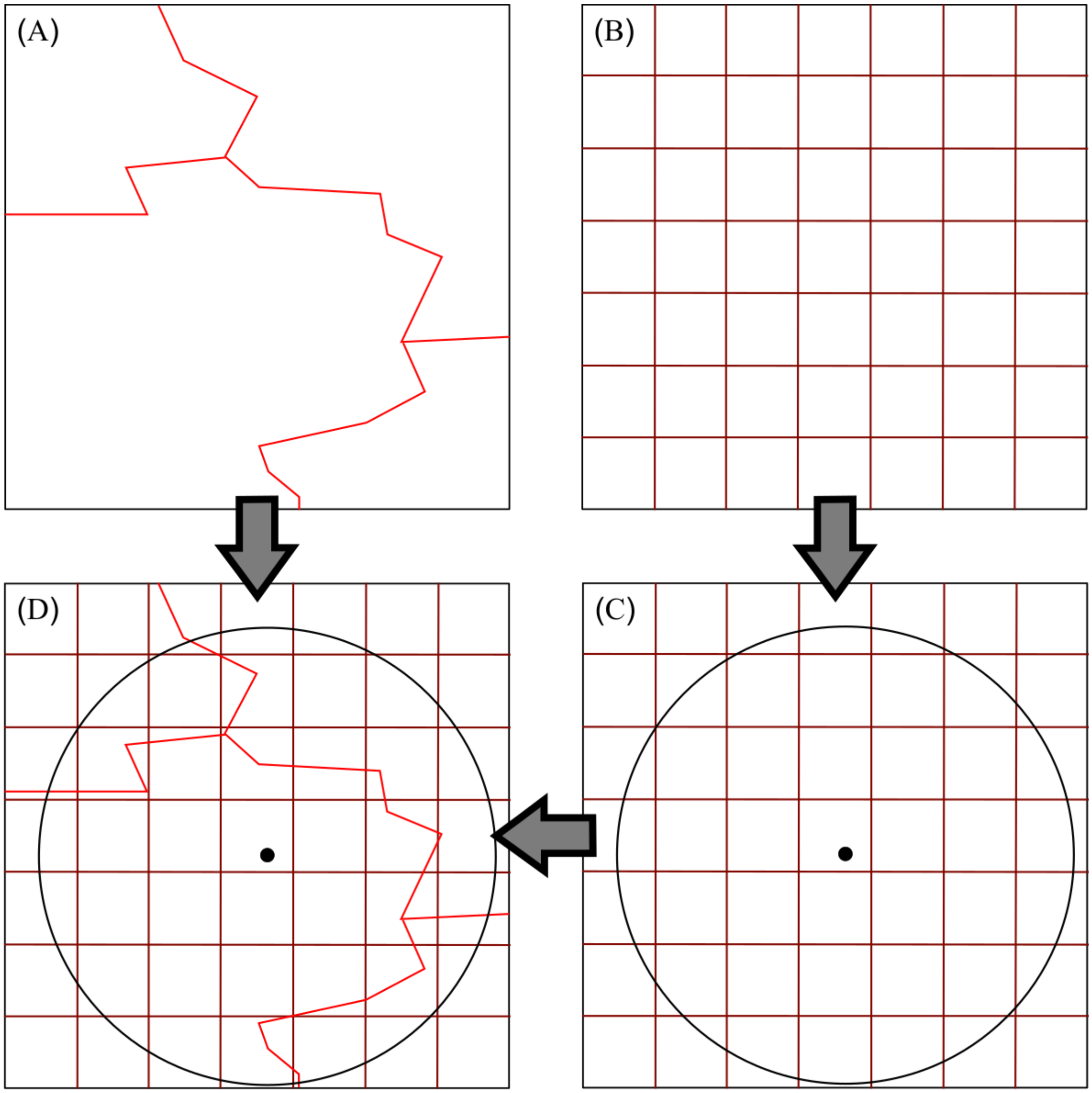
↑= RR is higher than in the original model; ↓= RR is lower than in the original model

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and green space.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

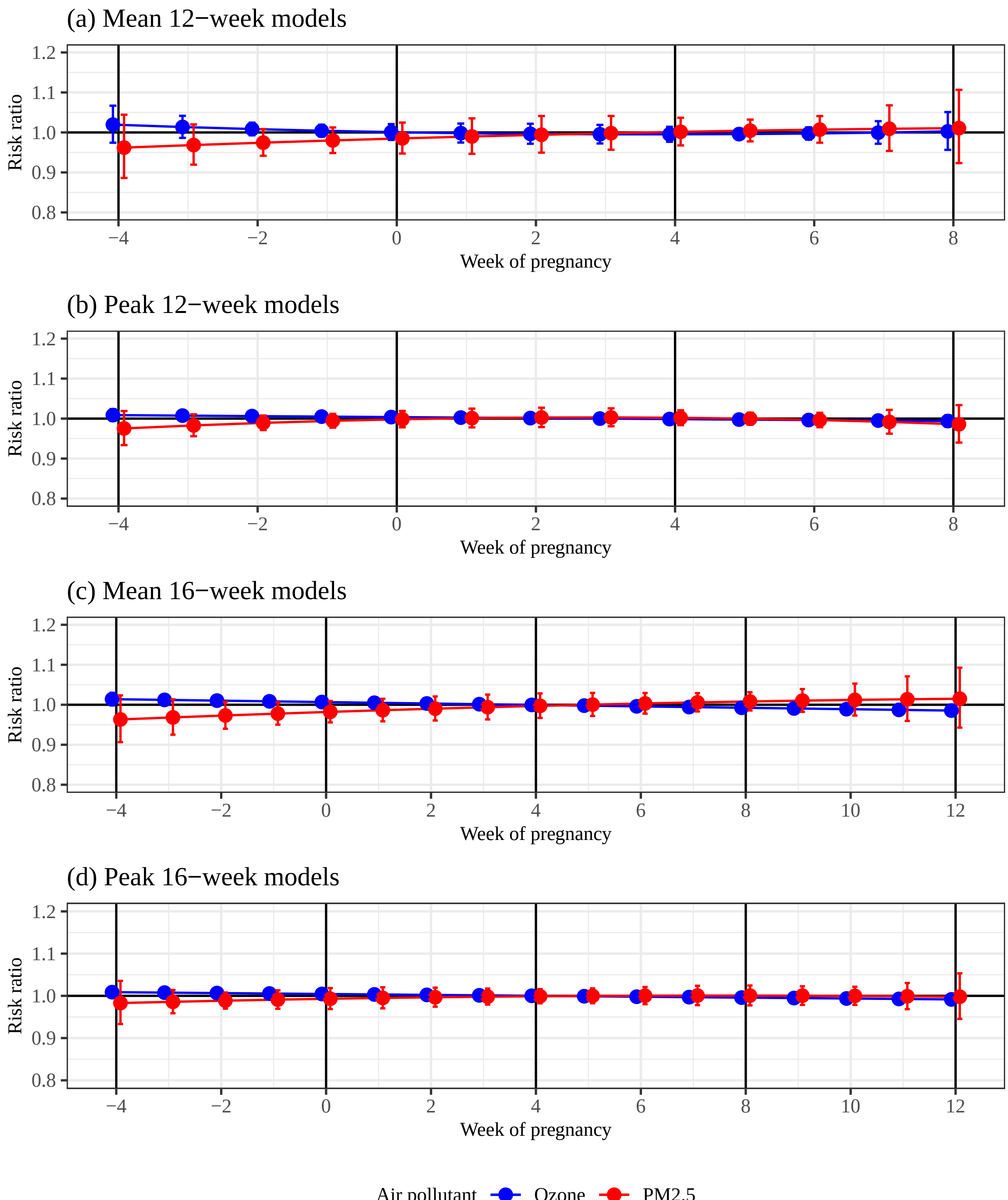
Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Figures



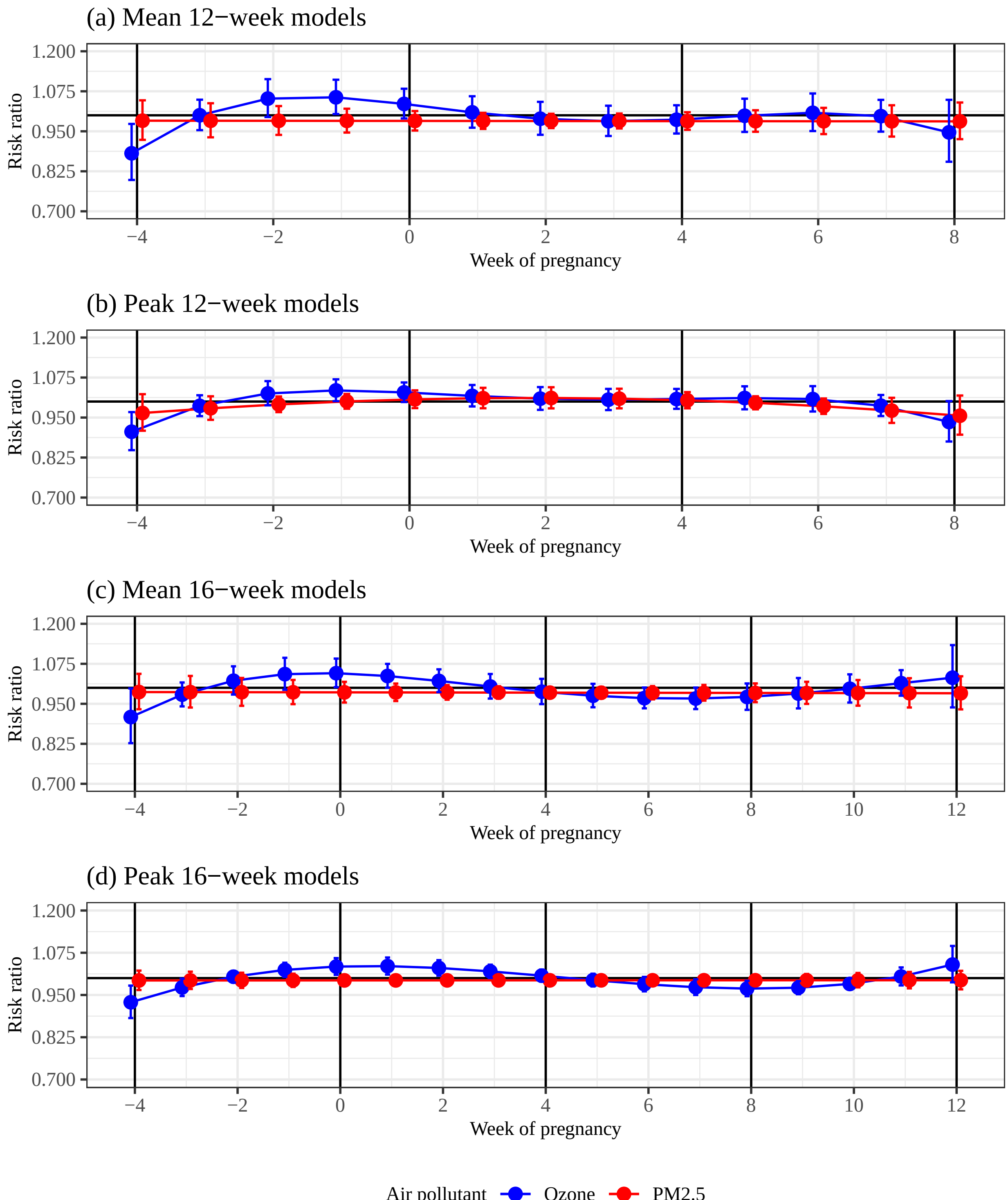
(A) Census tracts layer; (B) National Land Cover Database (NLCD) grid layer; (C) Buffer with maternal residence at centroid overlaid on NLCD grid layer; (D) All layers overlaid together with maternal residence

Figure 3.1: Method by which point, tract-level, and grid data were spatially joined



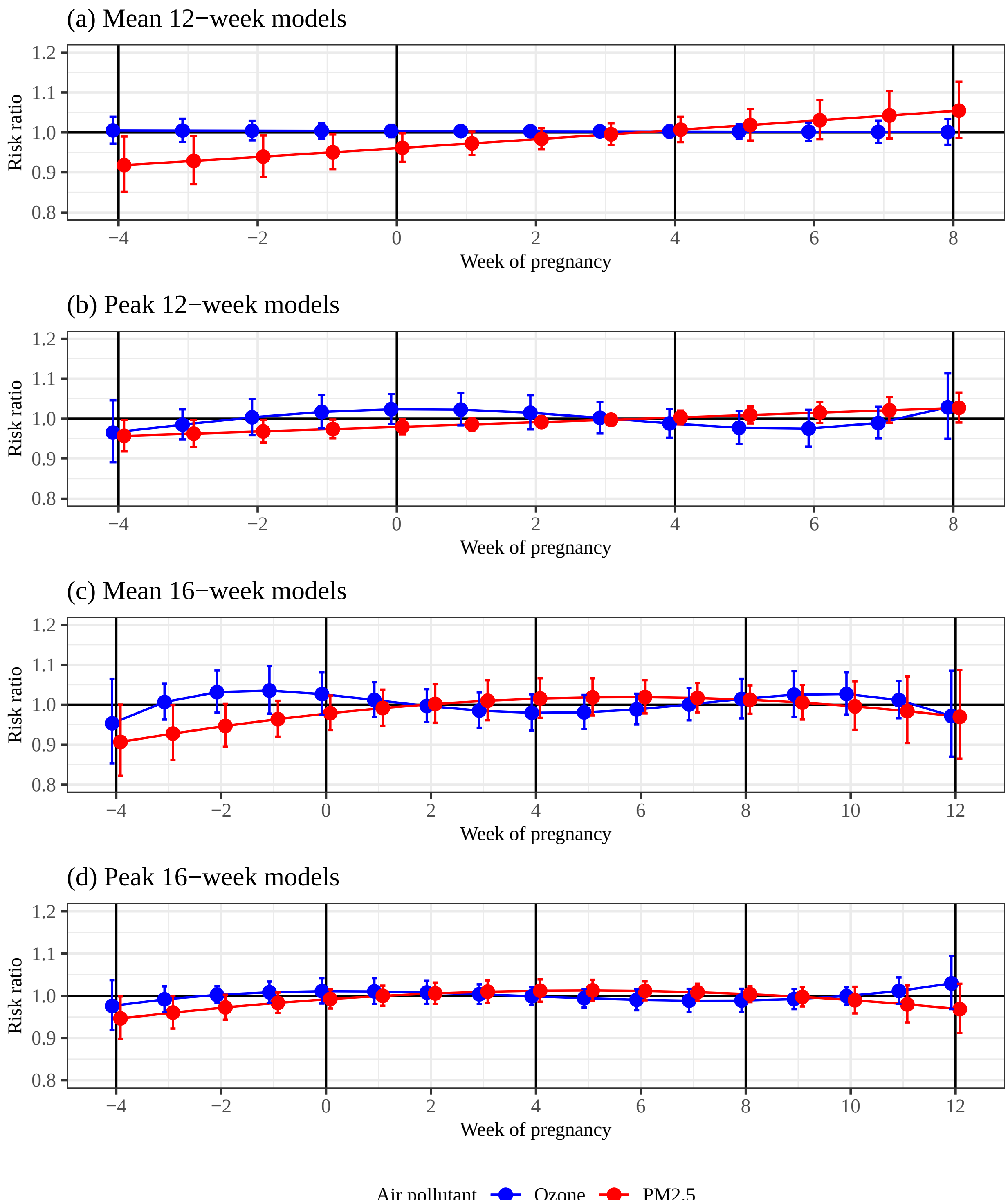
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.2: Clubfoot models: Risk ratios by week of pregnancy with grasses and trees



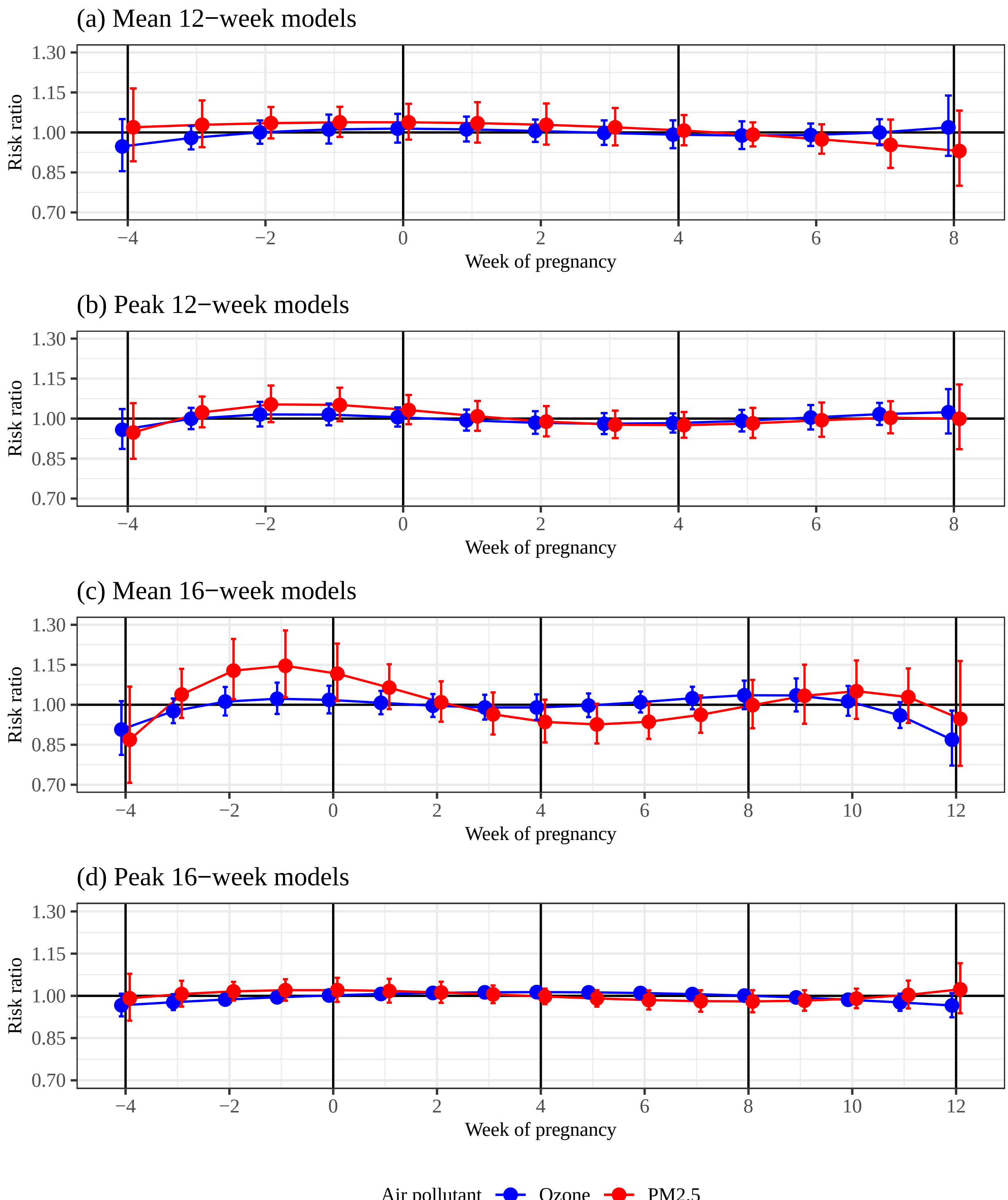
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.3: Cleft lip with or without cleft palate models: Risk ratios by week of pregnancy with grasses and trees



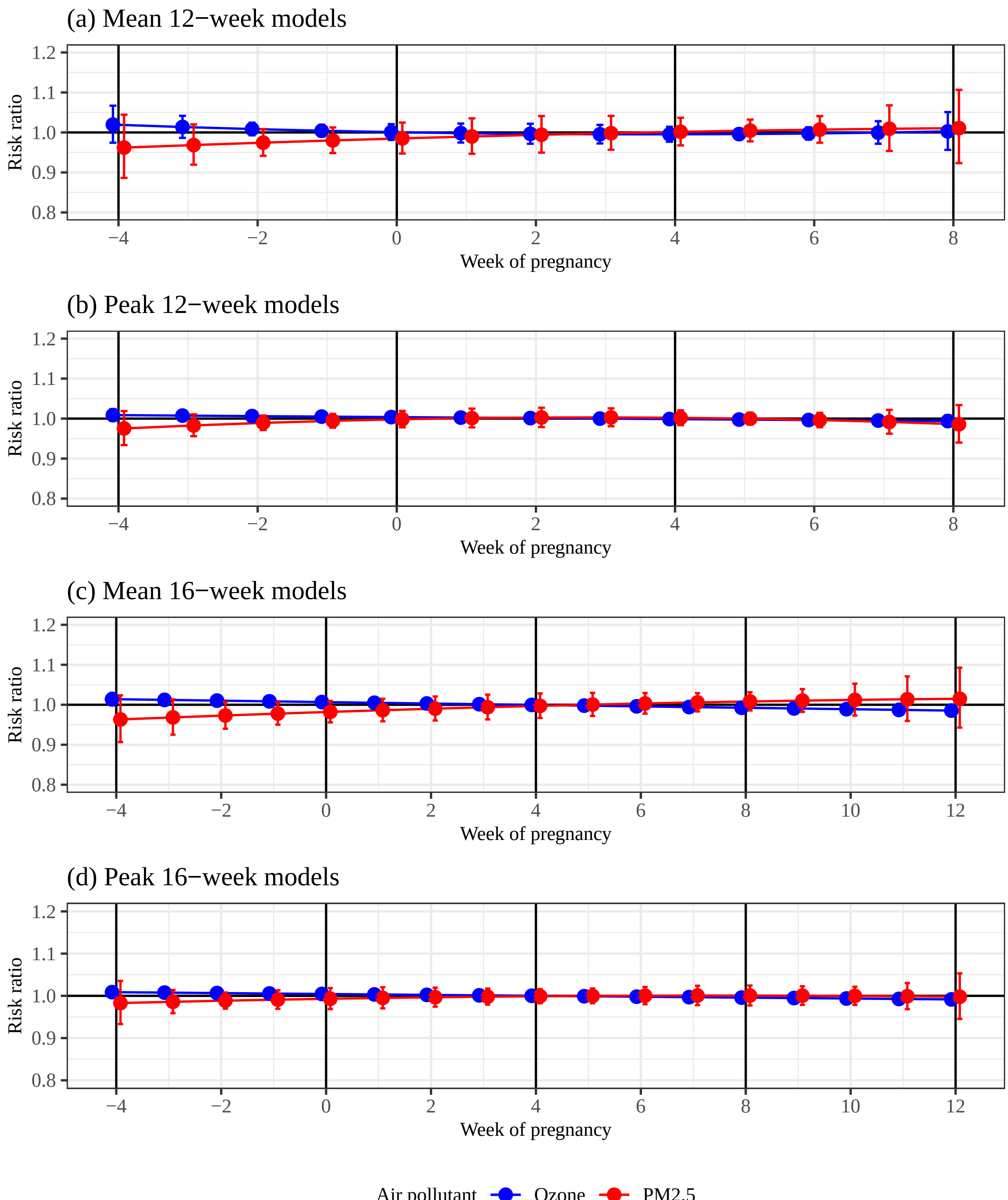
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.4: Cleft palate models: Risk ratios by week of pregnancy with grasses and trees



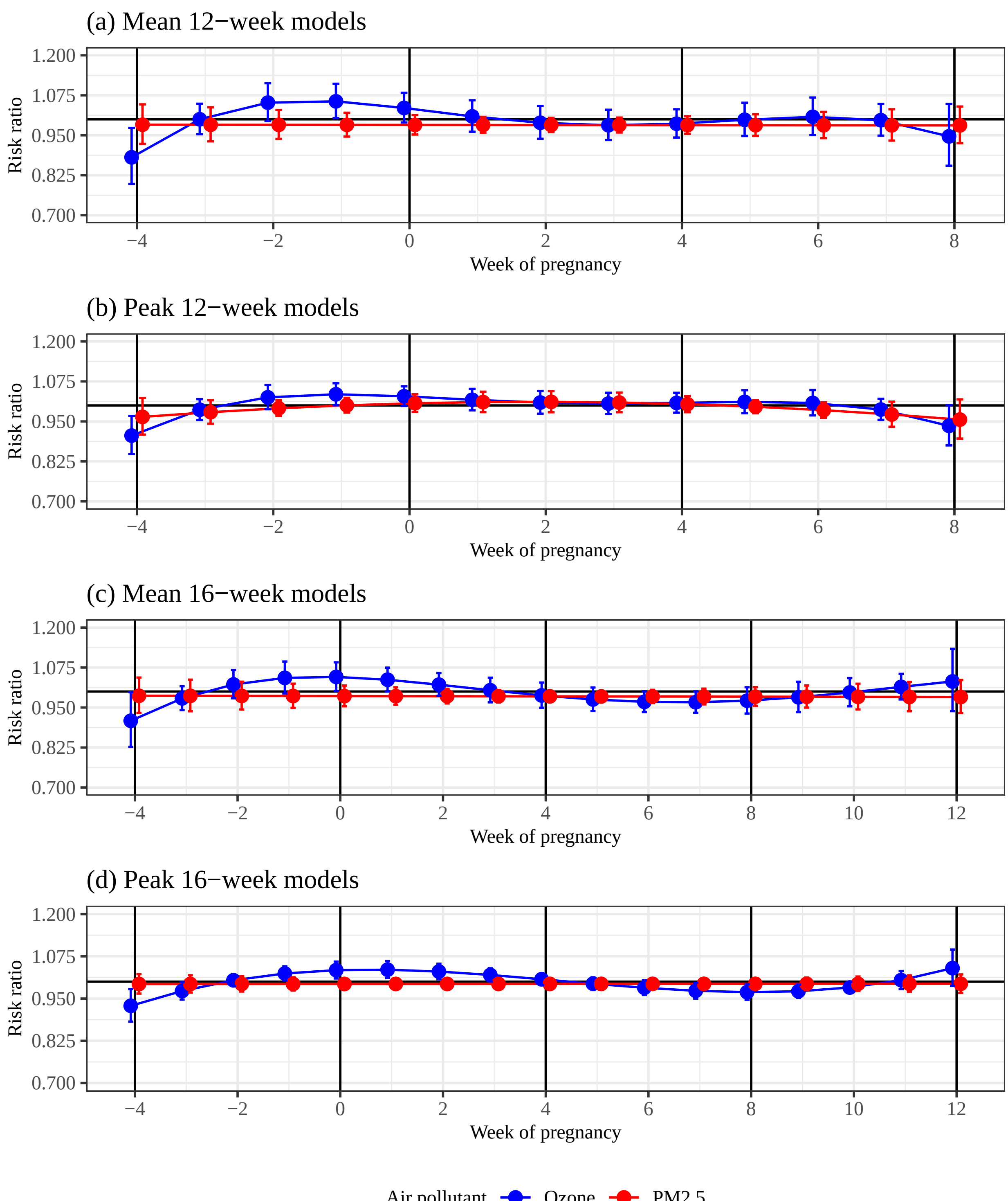
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.5: Craniosynostosis models: Risk ratios by week of pregnancy with grasses and trees



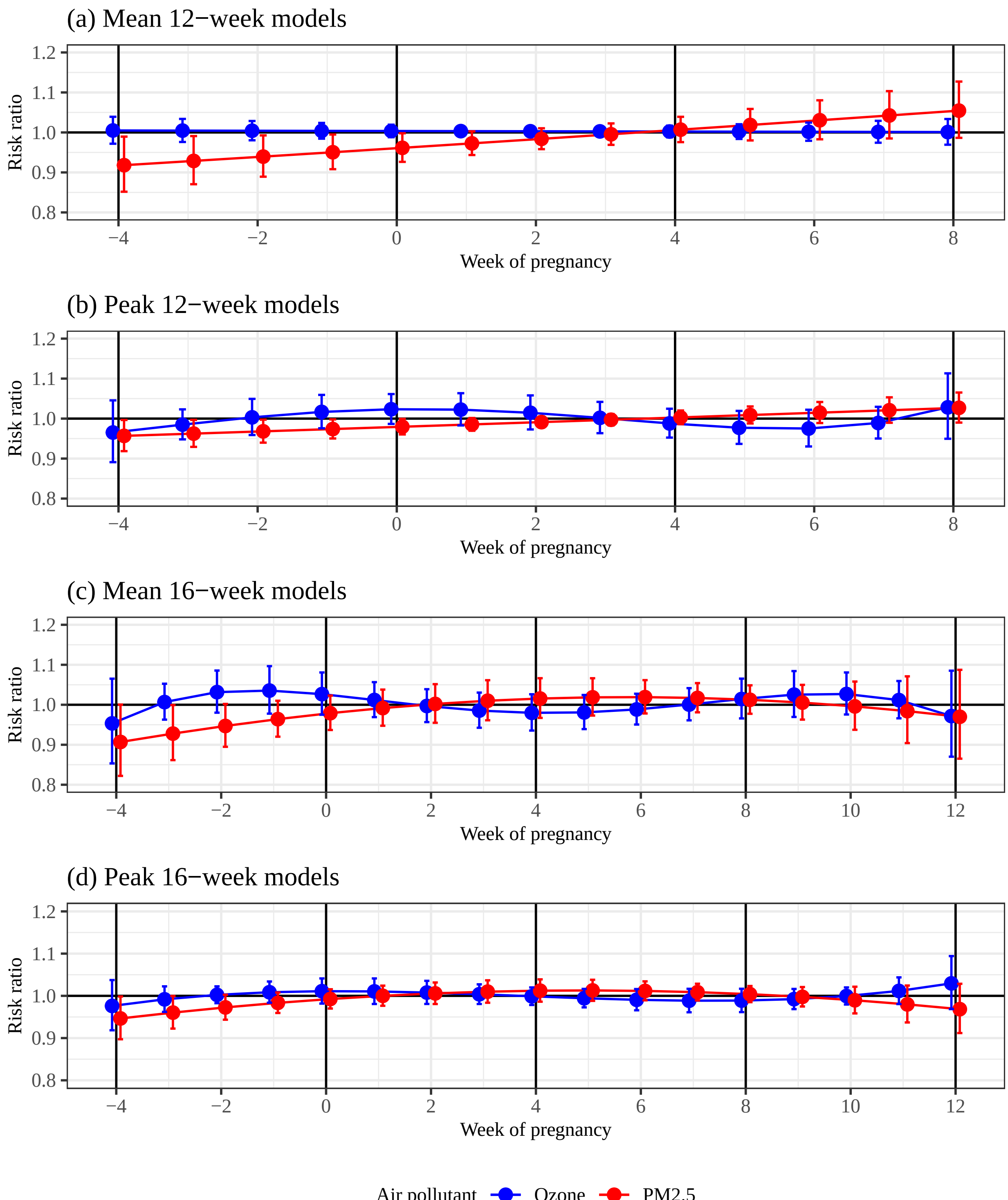
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.6: Clubfoot models: Risk ratios by week of pregnancy with grasses, trees, and water



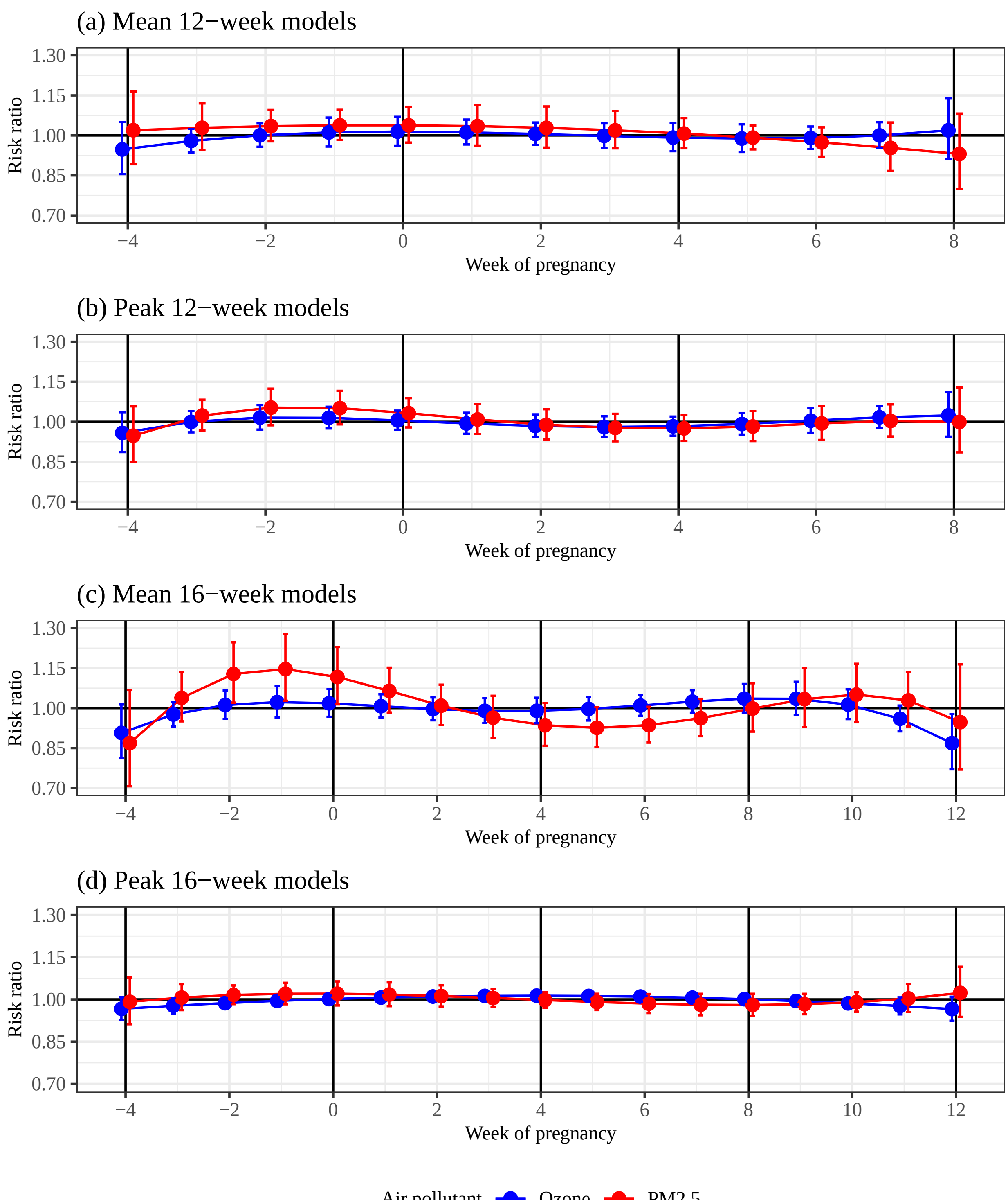
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.7: Cleft lip with or without cleft palate models: Risk ratios by week of pregnancy with grasses, trees, and water



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.8: Cleft palate models: Risk ratios by week of pregnancy with grasses, trees, and water



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 3.9: Craniosynostosis models: Risk ratios by week of pregnancy with grasses, trees, and water

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4. Green Space, Mixed Air Pollutants and Risk of Birth Defects

4.1 Background

In NYS, birth defects result in 20% of deaths among infants between one month and one year old[1] and babies born with birth defects are ten times more likely to die before they are a year old than babies without birth defects.[2] About 6000 children of the roughly 125,000 children born in NYS outside NYC each year are diagnosed with birth defects before age 3.[3] Approximately 30%-40% of birth defects have known causes related to genetics, environment, and maternal health.[4,5]

The connection between birth defects and maternal smoking via oxidative stress is well documented.[6–11] Some of these components are believed to cause epigenetic changes in the developing fetus and to trigger oxidative stress. Many components of cigarette smoke are also found in PM.[12]

Pregnant women exposed to higher concentrations of air pollution show more markers of DNA damage that are associated with oxidative stress than pregnant women exposed to lower concentrations of air pollution.[13] Given similarities between cigarette smoke and some forms of air pollution, notably $PM_{2.5}$, a link between air pollution and birth defects is possible.

The three birth defects investigated in this study include clubfoot, oral clefts, and craniosynostosis, which are among the more common birth defects in NYS, with over 100 cases born with each birth defect annually.[2] They were selected because they are posited to be susceptible to oxidative stress caused by similar routes of exposure. All three birth defects have an increased risk of developing if the mother smokes[6–11] and can be diagnosed prenatally.[14–16]

Air pollution may be a risk factor for development of oral clefts, clubfoot, and craniosynostosis in the fetus. Results of research have been inconclusive.[9,10] Studies have not been directly comparable, however. They vary in whether they use monitored or modeled pollution data, size of the study area, availability of pollution data throughout the study area, and frequency of pollution measurements.

PM and O_3 were studied together in relation to birth defects because they are prevalent in NYS, with exposures averaging $11.2\frac{\mu g}{m^3}$ for $PM_{2.5}$ and 38ppb for ozone.[17] Both exposures have been linked to asthma[18,19] and other health outcomes and have been studied as possible causal factors in the development of birth outcomes and birth defects. Air pollution is a composite of chemicals suspended in the air that, when inhaled, can cause damage to human health. O_3 is produced by chemical reactions in the air between PM and NO_x. Because O_3 is a by-product of PM, there may be an inverse relationship between them.

There is very little research on how multi-pollutant models affect the relationships between air pollutants and birth defects. What little research was available on the birth defects of interest showed mixed results. Two studies showed a difference in effect of O_3 when adding other pollutants including $PM_{2.5}$ to the model.[20,21] Two other studies showed a difference in effect of $PM_{2.5}$ when adding O_3 to the model.[22,23] The other studies showed no difference in effect between single-pollutant and multi-pollutant models.[24,25]

This study explored the association between maternal exposure to $PM_{2.5}$ and O_3 during the first trimester of pregnancy using statewide time-varying data for the exposures and a statewide dataset for the outcomes from 2002 to 2015 in NYS. This study used a case-cohort design with logistic regression to determine the relationship between select measures of mixed air pollution and select birth defects.

4.2 Methods

4.2.1 Study population

Cases were identified through the NYS CMR, as described in Chapter 2 methods. Case categories included infants born with clubfoot, infants born with cleft lip with or without cleft palate, infants born with cleft palate, and infants born with craniosynostosis. Controls were selected from NYS Vital Records and matched on year of birth, three controls for each case, for the birth years 2002 to 2015 with mother residing in NYS outside NYC at time of birth.

4.2.2 Exposure assessment

This study used the Downscaler air pollution model[26,27] described in Chapter 2. Consistent with the previous studies, weekly average and peak measures of modeled $PM_{2.5}$ and O_3 were calculated for the period inclusive of four weeks prior to pregnancy until week 12 of gestation. $PM_{2.5}$ and O_3 exposure were calculated from the modeled estimates of $PM_{2.5}$ and O_3, respectively, in the census tract where the residence at birth was geocoded.

Green space was calculated using the NLCD for 2011[28], as described in Chapter 3 methods. Green space was a composite measure of trees, including deciduous, evergreen, or mixed forests or woody and emergent herbaceous wetlands, and grasses, including scrub, grasslands, pasture, and cultivation. This composite variable measured four categories of grasses and trees (grasses and trees below their respective medians, grasses and trees above their respective medians, grasses below their median and trees above their median, and grasses above their median and trees below their median). Buffers of 50m, 100m, 200m, 300m, 400m, and 500m radius around each maternal residence were created.

4.2.3 Statistical analysis

Univariate and bivariate analyses described in Chapter 2 informed this study. The cross-basis settings described in Chapter 2 were used in the models for this study. Models were adjusted for the following covariates from birth certificate data: mother's education level, mother's smoking, and season of conception, for median tract-level income from the US Census[29], and for green space around the mother's residence. All categorical variables were coded as described in Chapter 2.

For the multivariate analysis, a series of distributed lag logistic models were run using the R package dlnm[30] for each case group and combination of O_3 and $PM_{2.5}$. These models have been used previously to study birth outcomes.[31] Since an estimate of reasonable lag was not available, but people can experience both chronic and acute (same day) effects of inhaling $PM_{2.5}$, this study used several possible lag weeks ranging from one month before estimated conception to estimated end of first trimester, each one week apart, to cover the critical windows for the birth defects of interest.

For clarity the lag weeks were as follows, all calculated from estimated conception date. For the first run, and the only run for clubfoot, the last week of the first trimester (week 12) of pregnancy was lag 0, the week of conception was lag 12, and the week one month before conception was lag 16. For the second run for the other three case groups, lag 0 was the last week of the second month (week 8) of pregnancy, lag 8 was the week of conception, and lag 12 was the week one month before conception. The first run was intended to capture any association in the first trimester. The second run was intended to focus on the second month of pregnancy, when cranial features develop, which is not relevant for clubfoot.

This approach allowed modeling of the change in values from week to week, any possible effect of exposure a few weeks prior to the critical window of weeks 3 to 12 of pregnancy, and the week during that time that shows the strongest association with each outcome.[32] Running the models using weekly peaks as well as weekly averages captured spikes in exposure that would be smoothed away (and masked) when considering an average. One set of models contained means for O_3 or $PM_{2.5}$; the other set contained peaks for O_3 or $PM_{2.5}$.

Using the model settings determined in Chapter 2, the full covariate models were run with these settings to determine the significant lags. The full models included the season of conception, since the mother may have spent more time indoors in colder months and some components of $PM_{2.5}$ increase in colder weather while others decrease, and the $PM_{2.5}$ measures alone would not be sufficient to capture that variation. Maternal education level and smoking were included. Green space was included as a grass-tree composite for each of the six buffers. Tract-level median household income was included as a proxy for SES. Two models were run for each case group: means or peaks in multi-pollutant models containing both $PM_{2.5}$ and O_3. The full lagged model was as follows:

$logit(RR_{bd}) = \beta_0 + \sum(\alpha_a O_3) + \sum(\alpha_b PM_{2.5}) + \beta_1 Education + \beta_2 Season + \beta_3 Smoking + \beta_4 Income + \beta_5 Green$

- $alpha_a O_3$ and $alpha_b PM_{2.5}$ = two series of several betas, with one beta for each week of pollutant estimates

- bd = birth defect (clubfoot, cleft lip with or without cleft palate, cleft palate, or craniosynostosis)

Prediction models were used to evaluate the results. For the prediction models to calculate RRs, the cross-prediction was centered on the point at approximately two standard deviations from the mean, as described in Chapter 2. Predictive risk ratios were calculated for 10 units above the centering value. Models were run for all combinations of air pollution measure, green space measure and buffer, and birth defect group, at both 12 and 16 weeks, as previously noted.

Models were run the first time with iterative elimination of insignificant lags (see Appendix B: Supplemental Tables for Chapter 4 for full results). This analysis revealed that in general, results were consistent across all buffers. When models were run a second time to include estimates for all lags, only the 300 meter buffers were run. Spatial joining of birth residences to land cover and census tracts was completed in ArcGIS.[33] Green space buffers were calculated in ArcGIS. All other analyses were completed in R.[34]

4.3 Results

4.3.1 Descriptive analysis

As described in Chapter 2 (see Table 2.4), controls included 18,153 births that were conceived between February 1, 2002 and December 31, 2015 and born to mothers living in NYS outside NYC across all four case groups. Cases included 2423 births with clubfoot, 952 births with cleft palate, 1281 births with cleft lip with or without cleft palate, and 931 births with craniosynostosis after excluding genetic syndromes. Across all controls, 78.9% of mothers reported white race and 84.5% of mothers reported non-Hispanic ethnicity. Among the case groups, 82.5%-84.4% of mothers reported white race and 84.1%-87.4% of mothers reported non-Hispanic ethnicity. Across all controls, 15.4% of mothers reported smoking while pregnant; among cases, 18.6%-22.3% of mothers reported smoking while pregnant. Across all controls, 61.2% of mothers reported education above high school; among cases, 52.3%-61.5% of mothers reported education above high school. Across all controls, 28.7% of mothers reported ages between 30 and 34; among cases, 25.1%-30.0% of mothers reported ages between 30 and 34.

As described in Chapter 2 (see Table 2.3), exposures were assigned to all cases and controls throughout the study period based on census tract of mother's residence and estimated week of conception. The mean weekly O_3 mean concentration was 37.2ppb for all controls and 36.1 to 37.6ppb for the case groups. The mean weekly O_3 peak concentration was 48.3ppb for all controls and 46.7 to 48.9ppb for the case groups. The mean weekly $PM_{2.5}$ mean was $10.0\frac{\mu g}{m^3}$ for all controls and 9.8 to $10.1\frac{\mu g}{m^3}$ for the case groups. The mean weekly $PM_{2.5}$ peak was $16.8\frac{\mu g}{m^3}$ for all controls and 16.3 to $17.0\frac{\mu g}{m^3}$ for the case groups.

As described in Chapter 3 (see Table 3.1), overall, there was a lot of overlap between residences at birth with grasses and residences at birth with trees. Over half of the residences at birth had no green space within the 50m and 100m buffers for any of the case groups. Over half of the residences at birth had no grasses for any of the case groups within the 200m and 300m buffers. At the 500m buffer, about 80% of residences at birth had some kind of green space around the residence. In evaluations, chi-square tests of whether different green space types were present or not showed strong associations between grasses and trees for all buffer sizes. Correlation tests of proportions showed strong associations between grasses and trees for all buffers except 50m, so a composite variable was used for the models.

4.3.2 Multivariate Analysis

As shown in Table 4.1, in the 300 meter buffer evaluations with all lags, the cumulative effect of air pollution was not associated with any of the birth defects studied during the time period of one month prior to conception through the end of the third month of pregnancy. In general, the effect of O_3 on the risk of developing the birth defect was at or above RR 1.0 for clubfoot and cleft palate and below RR 1.0 for cleft lip with or without cleft palate and craniosynostosis. The effect of $PM_{2.5}$ on the risk of developing the birth defect was lower than for O_3 for all birth defects except craniosynostosis, for which the RR was above 1.0. These patterns held true in both the 12-week and 16-week evaluations. For results for the other buffers, see Appendix B: Supplemental Tables for Chapter 4.

When evaluating risk during individual weeks, for most evaluations, results were similar across all buffers, so individual weeks are shown for only the 300m buffer. The 300m buffer has been used in other studies[35–38], making results easier to compare across studies, and it is central in the buffer values used in this study.

Clubfoot

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean and peak concentrations on the risk of clubfoot was highest before conception for all evaluations, with significant associations in the 16-week evaluations. The effect of weekly $PM_{2.5}$ mean concentrations was highest in week 8 of pregnancy for the 12-week evaluation and in week 12 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ peak concentrations was highest in weeks 3 to 4 of pregnancy for the 12-week evaluation and in week 12 of pregnancy for the 16-week evaluation. See Figure 4.1 and Table 4.2 for full results.

Cleft lip with or without cleft palate

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean and peak concentrations on the risk of cleft lip with or without cleft palate was highest before conception for the 12-week evaluations and around conception for the 16-week evaluations, with significant associations in all evaluations. The effect of weekly $PM_{2.5}$ mean concentrations was consistently low for all evaluations. The effect of weekly $PM_{2.5}$ peak concentrations was highest in week 12 of pregnancy for the 16-week evaluation and consistently low for the 12-week evaluation. See Figure 4.2 and Table 4.3 for full results.

Cleft palate

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean concentrations on the risk of cleft palate was highest before conception for both evaluations. The effect of weekly

O_3 peak concentrations on the risk of cleft palate was highest around conception for the 12-week evaluation and in week 12 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ mean concentrations was highest in week 8 of pregnancy for the 12-week evaluation and in weeks 5 to 6 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ peak concentrations was highest in week 8 of pregnancy for the 12-week evaluation and in weeks 4 to 5 of pregnancy for the 16-week evaluation. See Figure 4.3 and Table 4.4 for full results.

Craniosynostosis

In the 300 meter buffer evaluations with all lags, the effect of weekly O_3 mean concentrations on the risk of cleft palate was highest in week 8 of pregnancy for the 12-week evaluation and in weeks 7 to 8 of pregnancy for the 16-week evaluation. The effect of weekly O_3 peak concentrations on the risk of cleft palate was highest in week 8 of pregnancy for the 12-week evaluation and in weeks 4 to 5 of pregnancy for the 16-week evaluation. The effect of weekly $PM_{2.5}$ mean concentrations was highest before conception for the 12-week evaluation and around conception for the 16-week evaluation. The effect of weekly $PM_{2.5}$ peak concentrations was highest before conception for the 12-week evaluation and in week 12 for the 16-week evaluation. See Figure 4.4 and Table 4.5 for full results.

4.4 Discussion

This study proposed that there is a mixed effect on the relationships between select measures of air pollution and select birth defects. Results varied by evaluation (12- or 16-week), case group, and air pollution measure. Overall, the only cumulative association was between clubfoot and O_3 in the 16-week evaluation of the mean air pollutant measure. No prior research was identified on clubfoot and mixed air pollutants, so the reason O_3 would have a significantly lower effect on clubfoot after adjusting for $PM_{2.5}$ is unknown.

Little research has been done on mixtures of air pollutants and the birth defects of interest. In all, six studies were identified, all of which evaluated cleft lip with or without cleft palate and cleft palate alone and one of which evaluated craniosynostosis. No studies were identified that evaluated clubfoot. In general, these studies found that there was little change in significance or effect of O_3 or PM on the birth defect when the other pollutant was added to the evaluation.

4.4.1 Clubfoot

In the mixed pollutant evaluations, the increased effect of 10-unit increases of O_3 on clubfoot before conception suggest clubfoot risk is affected more by pre-conception exposure to O_3. The higher effect of a 10-unit increase of mean $PM_{2.5}$ in the second and third months of pregnancy suggest clubfoot risk is affected more by exposure to mean $PM_{2.5}$ during the critical window of development. The higher effect of a 10-unit increase of peak $PM_{2.5}$ in the first and third months of pregnancy suggest clubfoot risk is affected more by exposure to peak $PM_{2.5}$ just before and at the end of the critical window of development.

The effects of O_3 and mean $PM_{2.5}$ on clubfoot risk were consistent with single-pollutant models. The effects of peak $PM_{2.5}$ on clubfoot risk differed from single-pollutant models, suggesting peak O_3 may affect the association between peak $PM_{2.5}$ and clubfoot risk. In general, weekly risk ratios were higher than equivalent results above 1.0 and lower than equivalent results below 1.0 in the single-pollutant models for all weeks for which risk ratios differed, though differences were small. Overall, the association between O_3 and clubfoot was not affected by $PM_{2.5}$, but the association between $PM_{2.5}$ and clubfoot was affected by O_3.

4.4.2 Cleft lip with or without cleft palate

In the mixed pollutant evaluations, the increased effect of 10-unit increases of O_3 on cleft lip with or without cleft palate before and around conception suggest cleft lip with or without cleft palate risk is affected more by pre-conception exposure to O_3. The effect of a 10-unit increase of mean $PM_{2.5}$ on cleft lip with or without cleft palate risk was consistently low. The effect of a 10-unit increase of peak $PM_{2.5}$ on cleft lip with or without cleft palate risk was consistently low in the 12-week evaluation, but highest in the third month of pregnancy in the 16-week evaluation, suggesting cleft lip with or without cleft palate risk is affected more by exposure to O_3 during the critical window. Week 12 is three weeks after the mandible should have finished forming, so the the reason for the higher effect that week is unclear.

The effects of O_3 and mean $PM_{2.5}$ on cleft lip with or without cleft palate risk were consistent with single-pollutant models. The effects of peak $PM_{2.5}$ on cleft lip with or without cleft palate risk differed from single-pollutant models, suggesting peak O_3 may affect the association between peak $PM_{2.5}$ and cleft lip with or without cleft palate risk. In general, weekly risk ratios were higher than equivalent results above 1.0 for all weeks for which risk ratios differed and either lower or higher than equivalent results below 1.0 depending on the week in the single-pollutant models, though differences were small. Overall, the association between O_3 and cleft lip with or without cleft palate was weakly affected by $PM_{2.5}$, but the association between $PM_{2.5}$ and cleft lip with or without cleft palate was affected by O_3.

Of the six studies that evaluated the effect of air pollution on risk of cleft lip with or without cleft palate in both single-pollutant and mixed pollutant models, two used Downscaler[22,23]. Neither of these studies reported significant effects of either air pollutant on the risk of cleft lip with or without cleft palate. Both noted that results for O_3 were similar in the single-pollutant and multi-pollutant evaluations, and that results for $PM_{2.5}$ were slightly higher in the multi-pollutant evaluation than in the single-pollutant evaluation, which was consistent with our results for peak $PM_{2.5}$, but not mean $PM_{2.5}$. Only one of the studies, which used monitoring station data to evaluate O_3 and PM_{10}, reported any significant associations, but even that study noted that results were similar between single-pollutant and multi-pollutant evaluations.[25] Another study using monitoring station data reported that while not significant, results for O_3 were higher in the multi-pollutant evaluation than in the single-pollutant evaluation[21], which was consistent with our results for peak O_3, but not mean O_3.

4.4.3 Cleft palate

In the mixed pollutant evaluations, the increased effect of 10-unit increases of mean O_3 on cleft palate before conception suggest cleft palate risk is affected more by pre-conception exposure to mean O_3. The increased effect of 10-unit increases of peak O_3 on cleft palate around conception and in the third month of pregnancy suggest cleft palate risk is affected more by pre-conception exposure to peak O_3 and exposure at the end of the critical window. The effect of a 10-unit increase of $PM_{2.5}$ on cleft palate risk was highest in the second month of pregnancy, suggesting cleft palate risk is affected more by exposure to O_3 during the critical window.

The effects of $PM_{2.5}$ and mean O_3 on cleft palate risk were consistent with single-pollutant models. The effects of peak O_3 on cleft palate risk differed from single-pollutant models, suggesting peak $PM_{2.5}$ may affect the association between peak O_3 and cleft palate risk. In general, weekly risk ratios differed from equivalent results for several weeks in the single-pollutant models for all evaluations, though differences were small. Overall, the association between $PM_{2.5}$ and cleft palate was weakly affected by O_3, but the association between O_3 and cleft palate was affected by $PM_{2.5}$.

Of the six studies that evaluated the effect of air pollution on risk of cleft palate in both single-pollutant and mixed pollutant models, two used Downscaler[22,23]. Neither of these studies reported significant effects of either air pollutant on the risk of cleft palate. Both noted that results for O_3 were similar in the single-pollutant and multi-pollutant evaluations, and that results for $PM_{2.5}$ were slightly higher in the multi-pollutant evaluation than in the single-pollutant evaluation. Only one of the studies, which used monitoring station data to evaluate O_3, $PM_{2.5}$, and PM_{10}, reported any significant associations.[20] That study noted that significant results varied between single-pollutant and multi-pollutant evaluations, though they included additional pollutants in the model and were not consistent about using continuous or categorized exposures. Another study using monitoring station data reported that while not significant, results for O_3 were higher in the multi-pollutant evaluation than in the single-pollutant evaluation.[21]

4.4.4 Craniosynostosis

In the mixed pollutant evaluations, the increased effect of 10-unit increases of O_3 on cleft palate in the second month of pregnancy suggest cleft palate risk is affected more by exposure to O_3 during the critical window. The increased effect of 10-unit increases of mean $PM_{2.5}$ on cleft palate before and around conception suggest cleft palate risk is affected more by pre-conception exposure to mean $PM_{2.5}$. The increased effect of 10-unit increases of peak $PM_{2.5}$ on cleft palate around conception and in the third month of pregnancy suggest cleft palate risk is affected more by pre-conception exposure to peak $PM_{2.5}$ and exposure at the end of the critical window.

The effects of O_3 and mean $PM_{2.5}$ on cleft palate risk were mostly consistent with single-pollutant models. The effects of peak $PM_{2.5}$ on cleft palate risk differed from single-pollutant models, suggesting peak O_3 may affect the association between peak $PM_{2.5}$ and cleft palate risk. In general, weekly risk ratios differed from equivalent results for several weeks in the single-pollutant models for all evaluations, though differences were small. Overall, the association between O_3 and cleft palate was weakly affected by $PM_{2.5}$, but the association between $PM_{2.5}$ and cleft palate was affected by O_3. Only one study we found evaluated the effect of air pollution on risk of craniosynostosis in both single-pollutant and mixed pollutant models.[23] This study, which used Downscaler, reported similar results for O_3 in the evaluations, but differing results between the evaluations for $PM_{2.5}$, which is consistent with our study.

4.4.5 Strengths and limitations

Strengths of this study included that birth defect cases covered fourteen years and most of NYS. Birth defects studied are well-diagnosed, so case misclassification is unlikely, and a sensitivity analysis of the one birth defect known to have misclassification issues was not significant. Air pollutant exposure was available daily and residential information was available at point level for most births, allowing greater granularity both temporally and spatially than many currently published studies. The NLCD data covered the entire state at a small enough resolution to see variation even within 50 meter buffers and classified trees separately from grasses to allow for them to be analyzed separately.

Limitations of this study include possible exposure misclassification that is presumed to be non-differential, which would bias results toward the null. Air pollutant exposures were assigned based on the mother's geocoded residence at birth, but no information was available regarding the mother's activity patterns, including how much time she spent at that residence during her pregnancy, so we cannot assess if assigned exposures are an accurate reflection of actual exposures. However, a sensitivity test of geocoding results showed no issues when ungeocoded births were assigned to ZIP code centroids and research suggests that mothers who move during pregnancy tend to move to areas with similar levels of air pollution.[39] In NYS, smoking is known to be under-reported on birth certificates[40], but even with presumed non-differential under-reporting, mothers of cases reported smoking more frequently than mothers of controls. Income is based on median census tract income, but the mother's household may have an income much higher or lower than the median in her census tract of residence, which could bias results toward the null.

4.5 Conclusion

In conclusion, including both O_3 and $PM_{2.5}$ in the evaluations did not affect the associations between the mean air pollutant measures and risk of any of the birth defects. Including both O_3 and $PM_{2.5}$ in the evaluations affected the associations between peak $PM_{2.5}$ and clubfoot, cleft lip with or without cleft palate, and craniosynostosis and between peak O_3 and cleft palate. More research is needed on multi-pollutant effects and birth defects.

Tables

Table 4.1: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	12-week model		16-week model	
Pollutant	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Clubfoot				
Ozone mean	1.04	(0.95 - 1.15)	1.00	(0.91 - 1.11)
Ozone peak	1.04	(0.97 - 1.11)	1.02	(0.94 - 1.10)
$PM_{2.5}$ mean	0.88	(0.70 - 1.10)	0.91	(0.72 - 1.15)
$PM_{2.5}$ peak	0.91	(0.80 - 1.03)	0.92	(0.81 - 1.05)
Cleft lip with or without cleft palate				
Ozone mean	0.95	(0.83 - 1.09)	0.97	(0.84 - 1.12)
Ozone peak	0.98	(0.89 - 1.08)	0.99	(0.89 - 1.10)
$PM_{2.5}$ mean	0.80	(0.59 - 1.09)	0.79	(0.57 - 1.08)
$PM_{2.5}$ peak	0.90	(0.76 - 1.07)	0.90	(0.75 - 1.07)
Cleft Palate				
Ozone mean	1.07	(0.92 - 1.24)	1.07	(0.91 - 1.26)
Ozone peak	1.00	(0.90 - 1.12)	1.04	(0.92 - 1.17)
$PM_{2.5}$ mean	0.80	(0.56 - 1.13)	0.77	(0.53 - 1.11)
$PM_{2.5}$ peak	0.89	(0.74 - 1.09)	0.84	(0.69 - 1.03)
Craniosynostosis				
Ozone mean	0.94	(0.80 - 1.11)	0.85	(0.70 - 1.02)
Ozone peak	0.96	(0.85 - 1.09)	0.91	(0.80 - 1.04)
$PM_{2.5}$ mean	1.13	(0.77 - 1.65)	1.19	(0.80 - 1.76)
$PM_{2.5}$ peak	1.05	(0.85 - 1.29)	1.08	(0.87 - 1.34)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

Models were adjusted for maternal education level, maternal smoking, tract-level median income, green space, and conception season.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

Table 4.2: Lag risk ratios for covariate models of air pollutant and clubfoot pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	1.02	(0.97 - 1.08)	↑**1.02**	**(1.00 - 1.04)**	↓0.94	(0.86 - 1.03)	↓**0.93**	**(0.87 - 0.99)**
-3	↑1.02	(0.99 - 1.05)	↑**1.02**	**(1.00 - 1.03)**	↓0.95	(0.90 - 1.01)	↓**0.94**	**(0.90 - 0.99)**
-2	1.01	(1.00 - 1.03)	↑**1.02**	**(1.00 - 1.03)**	0.97	(0.93 - 1.00)	↓**0.96**	**(0.92 - 0.99)**
-1	↑1.01	(0.99 - 1.03)	**1.01**	**(1.00 - 1.03)**	0.98	(0.94 - 1.01)	↓**0.97**	**(0.94 - 1.00)**
0	↑1.01	(0.98 - 1.03)	**1.01**	**(1.00 - 1.02)**	0.99	(0.95 - 1.03)	0.98	(0.95 - 1.00)
1	1.00	(0.98 - 1.03)	↑1.01	(1.00 - 1.02)	↑1.00	(0.95 - 1.05)	↓0.98	(0.96 - 1.01)
2	1.00	(0.97 - 1.03)	↑1.01	(1.00 - 1.01)	↑1.00	(0.95 - 1.05)	0.99	(0.96 - 1.02)
3	1.00	(0.97 - 1.02)	1.00	(1.00 - 1.01)	↑1.01	(0.96 - 1.05)	↑1.00	(0.97 - 1.03)
4	1.00	(0.97 - 1.02)	1.00	(0.99 - 1.01)	↑1.01	(0.97 - 1.05)	↑1.01	(0.97 - 1.04)
5	↓0.99	(0.98 - 1.01)	1.00	(0.99 - 1.00)	↑1.01	(0.98 - 1.04)	↑1.01	(0.98 - 1.04)
6	↓0.99	(0.98 - 1.01)	↓0.99	(0.99 - 1.00)	1.01	(0.98 - 1.05)	↑1.02	(0.99 - 1.04)
7	↓0.99	(0.96 - 1.03)	0.99	(0.98 - 1.00)	1.01	(0.95 - 1.07)	↑1.02	(0.99 - 1.04)
8	↓0.99	(0.94 - 1.05)	**0.99**	**(0.98 - 1.00)**	1.01	(0.91 - 1.11)	↑1.02	(1.00 - 1.05)
9			**0.99**	**(0.98 - 1.00)**			↑1.02	(0.99 - 1.05)
10			↓**0.98**	**(0.97 - 1.00)**			↑1.02	(0.98 - 1.06)
11			↓**0.98**	**(0.97 - 1.00)**			↑1.02	(0.97 - 1.08)
12			↓**0.98**	**(0.96 - 0.99)**			1.02	(0.95 - 1.10)
Weekly peak concentration								
-4	1.01	(1.00 - 1.03)	**1.01**	**(1.00 - 1.03)**	↓0.96	(0.92 - 1.01)	↓0.96	(0.91 - 1.02)
-3	1.01	(1.00 - 1.03)	**1.01**	**(1.00 - 1.02)**	↓0.97	(0.94 - 1.00)	↓0.97	(0.94 - 1.00)
-2	1.01	(1.00 - 1.02)	**1.01**	**(1.00 - 1.02)**	↓0.98	(0.96 - 1.00)	↓0.98	(0.96 - 1.00)
-1	↑1.01	(1.00 - 1.02)	**1.01**	**(1.00 - 1.02)**	0.99	(0.97 - 1.01)	0.99	(0.96 - 1.01)
0	↑1.01	(1.00 - 1.01)	↑**1.01**	**(1.00 - 1.01)**	1.00	(0.98 - 1.02)	0.99	(0.97 - 1.02)
1	1.00	(1.00 - 1.01)	↑1.01	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.97 - 1.02)
2	1.00	(1.00 - 1.01)	1.00	(1.00 - 1.01)	1.00	(0.98 - 1.03)	1.00	(0.98 - 1.02)
3	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.01)	↑1.01	(0.98 - 1.03)	1.00	(0.98 - 1.02)
4	1.00	(0.99 - 1.01)	1.00	(1.00 - 1.01)	↑1.01	(0.99 - 1.03)	1.00	(0.98 - 1.02)
5	1.00	(0.99 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.99 - 1.02)	1.00	(0.98 - 1.02)
6	1.00	(0.98 - 1.01)	1.00	(0.99 - 1.00)	1.00	(0.98 - 1.02)	1.00	(0.98 - 1.02)
7	↓0.99	(0.98 - 1.01)	1.00	(0.99 - 1.00)	0.99	(0.96 - 1.02)	1.00	(0.98 - 1.03)
8	0.99	(0.98 - 1.01)	↓0.99	(0.99 - 1.00)	0.99	(0.94 - 1.03)	1.00	(0.98 - 1.03)
9			0.99	(0.99 - 1.00)			1.00	(0.98 - 1.03)
10			0.99	(0.98 - 1.00)			1.00	(0.98 - 1.03)
11			0.99	(0.98 - 1.00)			1.00	(0.97 - 1.04)
12			0.99	(0.98 - 1.00)			↑1.01	(0.95 - 1.06)

Note:
RR = risk ratio; CI = confidence interval; PM = particulate matter
↑= RR is higher than in the single-pollutant models; ↓= RR is lower than in the single-pollutant models
Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, green space, ozone, and $PM_{2.5}$.
RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.
Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 4.3: Lag risk ratios for covariate models of air pollutant and cleft lip with or without cleft palate pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	**0.88**	**(0.80 - 0.97)**	**0.91**	**(0.83 - 1.00)**	↓0.97	(0.91 - 1.04)	0.99	(0.93 - 1.05)
-3	1.00	(0.95 - 1.05)	0.98	(0.94 - 1.02)	↓0.97	(0.92 - 1.03)	0.99	(0.93 - 1.04)
-2	1.05	(1.00 - 1.12)	1.02	(0.98 - 1.07)	0.98	(0.93 - 1.03)	0.99	(0.94 - 1.04)
-1	**1.06**	**(1.01 - 1.11)**	1.04	(0.99 - 1.10)	0.98	(0.94 - 1.02)	0.99	(0.95 - 1.03)
0	1.04	(0.99 - 1.09)	**1.05**	**(1.00 - 1.09)**	0.98	(0.95 - 1.01)	0.99	(0.95 - 1.02)
1	1.01	(0.96 - 1.06)	1.04	(1.00 - 1.08)	0.98	(0.96 - 1.01)	0.99	(0.96 - 1.02)
2	0.99	(0.94 - 1.05)	1.02	(0.98 - 1.06)	0.98	(0.96 - 1.01)	0.99	(0.96 - 1.01)
3	0.98	(0.94 - 1.03)	1.00	(0.96 - 1.05)	↑0.99	(0.96 - 1.01)	0.99	(0.97 - 1.01)
4	0.99	(0.95 - 1.03)	0.99	(0.95 - 1.03)	↑0.99	(0.96 - 1.02)	↑0.99	(0.97 - 1.00)
5	1.00	(0.95 - 1.06)	0.98	(0.94 - 1.01)	↑0.99	(0.95 - 1.03)	↑0.99	(0.97 - 1.01)
6	1.01	(0.95 - 1.07)	0.97	(0.94 - 1.00)	↑0.99	(0.95 - 1.04)	↑0.99	(0.96 - 1.01)
7	1.00	(0.95 - 1.05)	0.97	(0.94 - 1.00)	↑0.99	(0.94 - 1.05)	↑0.99	(0.96 - 1.01)
8	0.95	(0.85 - 1.05)	0.97	(0.93 - 1.02)	↑0.99	(0.93 - 1.06)	↑0.99	(0.95 - 1.02)
9			↑0.99	(0.94 - 1.04)			↑0.99	(0.95 - 1.03)
10			1.00	(0.95 - 1.05)			↑0.99	(0.94 - 1.03)
11			↑1.02	(0.98 - 1.06)			↑0.99	(0.93 - 1.04)
12			1.03	(0.94 - 1.14)			↑0.99	(0.93 - 1.05)
Weekly peak concentration								
-4	**0.91**	**(0.85 - 0.97)**	**0.93**	**(0.88 - 0.98)**	↑0.99	(0.92 - 1.05)	0.99	(0.96 - 1.02)
-3	0.99	(0.95 - 1.02)	0.97	(0.95 - 1.00)	↑0.99	(0.95 - 1.03)	0.99	(0.96 - 1.02)
-2	1.03	(0.99 - 1.07)	↑1.01	(0.99 - 1.02)	0.99	(0.96 - 1.02)	0.99	(0.97 - 1.02)
-1	↑**1.04**	**(1.00 - 1.07)**	↑**1.03**	**(1.00 - 1.05)**	↓0.99	(0.97 - 1.02)	0.99	(0.97 - 1.01)
0	1.03	(1.00 - 1.06)	↑**1.04**	**(1.01 - 1.06)**	↓0.99	(0.96 - 1.02)	0.99	(0.97 - 1.01)
1	1.02	(0.98 - 1.05)	**1.04**	**(1.01 - 1.06)**	↓0.99	(0.96 - 1.03)	0.99	(0.98 - 1.01)
2	1.01	(0.97 - 1.05)	**1.03**	**(1.01 - 1.06)**	↓0.99	(0.96 - 1.03)	0.99	(0.98 - 1.01)
3	1.01	(0.97 - 1.04)	**1.02**	**(1.00 - 1.04)**	↓0.99	(0.96 - 1.03)	0.99	(0.98 - 1.00)
4	1.01	(0.98 - 1.04)	1.01	(0.99 - 1.03)	↓0.99	(0.97 - 1.02)	0.99	(0.98 - 1.00)
5	1.01	(0.98 - 1.05)	↑1.00	(0.98 - 1.01)	↓0.99	(0.97 - 1.02)	0.99	(0.98 - 1.01)
6	1.01	(0.97 - 1.05)	0.98	(0.96 - 1.01)	0.99	(0.97 - 1.02)	0.99	(0.98 - 1.01)
7	0.99	(0.95 - 1.02)	**0.97**	**(0.95 - 1.00)**	↑0.99	(0.95 - 1.04)	↑1.00	(0.98 - 1.01)
8	0.94	(0.87 - 1.01)	**0.97**	**(0.95 - 0.99)**	↑0.99	(0.93 - 1.07)	↑1.00	(0.98 - 1.01)
9			**0.97**	**(0.95 - 0.99)**			↑1.00	(0.98 - 1.02)
10			0.98	(0.97 - 1.00)			↑1.00	(0.97 - 1.02)
11			↑1.01	(0.98 - 1.03)			↑1.00	(0.97 - 1.03)
12			1.04	(0.99 - 1.10)			↑1.00	(0.97 - 1.03)

Note:
RR = risk ratio; CI = confidence interval; PM = particulate matter
↑= RR is higher than in the single-pollutant models; ↓= RR is lower than in the single-pollutant models
Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, green space, ozone, and $PM_{2.5}$.
RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.
Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 4.4: Lag risk ratios for covariate models of air pollutant and cleft palate pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	↑1.02	(0.98 - 1.06)	↑0.96	(0.86 - 1.08)	↓**0.91**	**(0.84 - 0.98)**	↓**0.89**	**(0.80 - 1.00)**
-3	↑1.02	(0.99 - 1.05)	↑1.02	(0.97 - 1.06)	↓**0.92**	**(0.86 - 0.98)**	↓**0.92**	**(0.85 - 1.00)**
-2	↑1.01	(0.99 - 1.04)	↑1.04	(0.99 - 1.10)	↓**0.93**	**(0.88 - 0.99)**	↓**0.94**	**(0.89 - 1.00)**
-1	↑1.01	(0.99 - 1.03)	1.04	(0.98 - 1.11)	↓**0.94**	**(0.90 - 0.99)**	0.96	(0.91 - 1.01)
0	↑1.01	(0.99 - 1.03)	1.03	(0.98 - 1.09)	**0.96**	**(0.92 - 0.99)**	0.98	(0.93 - 1.03)
1	↑1.01	(0.99 - 1.02)	↑1.02	(0.97 - 1.06)	0.97	(0.94 - 1.00)	0.99	(0.95 - 1.04)
2	1.00	(0.99 - 1.02)	1.00	(0.96 - 1.05)	0.98	(0.96 - 1.01)	↑1.01	(0.95 - 1.06)
3	1.00	(0.99 - 1.02)	0.99	(0.94 - 1.03)	1.00	(0.97 - 1.02)	1.01	(0.96 - 1.07)
4	1.00	(0.99 - 1.02)	0.98	(0.93 - 1.03)	1.01	(0.98 - 1.04)	1.02	(0.97 - 1.08)
5	1.00	(0.98 - 1.02)	0.98	(0.93 - 1.02)	1.02	(0.98 - 1.07)	1.02	(0.97 - 1.08)
6	1.00	(0.97 - 1.02)	↓0.98	(0.94 - 1.02)	↑1.04	(0.99 - 1.09)	1.02	(0.98 - 1.07)
7	↓0.99	(0.97 - 1.02)	↓0.99	(0.95 - 1.03)	↑1.05	(0.99 - 1.12)	1.02	(0.98 - 1.06)
8	↓0.99	(0.96 - 1.03)	↓1.00	(0.95 - 1.06)	↑1.07	(0.99 - 1.14)	1.01	(0.98 - 1.06)
9			↓1.02	(0.96 - 1.08)			1.01	(0.96 - 1.06)
10			↓1.02	(0.97 - 1.08)			↓0.99	(0.93 - 1.06)
11			1.01	(0.96 - 1.07)			0.98	(0.89 - 1.08)
12			↑0.99	(0.88 - 1.11)			↓0.96	(0.85 - 1.09)
Weekly peak concentration								
-4	0.97	(0.90 - 1.05)	↑0.99	(0.93 - 1.06)	↓**0.95**	**(0.91 - 0.99)**	↓**0.94**	**(0.88 - 0.99)**
-3	↑0.99	(0.95 - 1.03)	↑1.01	(0.97 - 1.04)	**0.96**	**(0.92 - 0.99)**	↓**0.95**	**(0.91 - 1.00)**
-2	↑1.01	(0.96 - 1.06)	↑1.01	(0.99 - 1.04)	↓**0.96**	**(0.93 - 1.00)**	0.97	(0.94 - 1.00)
-1	1.02	(0.98 - 1.07)	↑1.02	(0.99 - 1.04)	**0.97**	**(0.95 - 1.00)**	0.98	(0.96 - 1.01)
0	↑1.03	(0.99 - 1.07)	↑1.02	(0.99 - 1.05)	**0.98**	**(0.96 - 1.00)**	↑1.00	(0.97 - 1.02)
1	↑1.03	(0.99 - 1.07)	1.01	(0.98 - 1.04)	↓0.98	(0.97 - 1.00)	↑1.01	(0.98 - 1.03)
2	↑1.02	(0.98 - 1.06)	↓1.00	(0.98 - 1.03)	0.99	(0.98 - 1.01)	1.01	(0.98 - 1.04)
3	↑1.01	(0.97 - 1.05)	1.00	(0.97 - 1.02)	1.00	(0.98 - 1.01)	↑1.02	(0.99 - 1.05)
4	0.99	(0.95 - 1.03)	↓0.99	(0.97 - 1.01)	↑1.01	(0.99 - 1.02)	↑1.02	(0.99 - 1.05)
5	0.98	(0.94 - 1.02)	↓0.98	(0.96 - 1.01)	1.01	(0.99 - 1.04)	↑1.02	(0.99 - 1.05)
6	↓0.97	(0.93 - 1.02)	↓0.98	(0.95 - 1.01)	↑1.02	(0.99 - 1.05)	↑1.02	(0.99 - 1.04)
7	↓0.98	(0.94 - 1.02)	↓0.98	(0.95 - 1.01)	↑1.03	(0.99 - 1.06)	1.01	(0.99 - 1.03)
8	↓1.01	(0.93 - 1.10)	↓0.98	(0.95 - 1.01)	1.03	(0.99 - 1.08)	1.00	(0.98 - 1.03)
9			0.99	(0.96 - 1.01)			↓0.99	(0.97 - 1.02)
10			1.00	(0.98 - 1.02)			↓0.98	(0.95 - 1.02)
11			↑1.02	(0.99 - 1.06)			↓0.97	(0.92 - 1.02)
12			↑1.05	(0.98 - 1.12)			↓0.95	(0.89 - 1.02)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

↑= RR is higher than in the single-pollutant models; ↓= RR is lower than in the single-pollutant models

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, green space, ozone, and $PM_{2.5}$.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and μg/m³ for $PM_{2.5}$) over two standard deviations above the mean.

Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Table 4.5: Lag risk ratios for covariate models of air pollutant and craniosynostosis pairs with grasses and trees, 300m buffer, New York State outside New York City, 2002 to 2015

	Ozone				$PM_{2.5}$			
	12-week model		16-week model		12-week model		16-week model	
Week	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**	**RR**	**(95% CI)**
Weekly mean concentration								
-4	0.95	(0.85 - 1.06)	↑0.94	(0.83 - 1.07)	↑1.05	(0.91 - 1.22)	↑0.91	(0.72 - 1.15)
-3	0.98	(0.93 - 1.03)	↓0.97	(0.92 - 1.02)	↑1.05	(0.96 - 1.16)	↑1.05	(0.95 - 1.15)
-2	↓0.99	(0.95 - 1.04)	↓0.99	(0.93 - 1.05)	↑1.05	(0.99 - 1.12)	↓1.12	(1.00 - 1.24)
-1	↓1.00	(0.95 - 1.06)	↓0.99	(0.93 - 1.06)	↑1.05	(0.99 - 1.11)	↓1.13	(1.00 - 1.27)
0	↓1.00	(0.95 - 1.06)	↓0.99	(0.94 - 1.05)	1.04	(0.97 - 1.12)	↓1.10	(0.99 - 1.22)
1	↓1.00	(0.95 - 1.05)	↓0.99	(0.94 - 1.04)	1.03	(0.95 - 1.12)	↓1.05	(0.96 - 1.15)
2	↓0.99	(0.95 - 1.04)	↓0.99	(0.94 - 1.04)	↓1.02	(0.94 - 1.11)	1.01	(0.92 - 1.09)
3	↓0.99	(0.94 - 1.04)	0.99	(0.94 - 1.05)	↓1.01	(0.94 - 1.09)	0.96	(0.88 - 1.06)
4	0.99	(0.93 - 1.04)	↑1.00	(0.95 - 1.06)	↓1.00	(0.94 - 1.06)	0.94	(0.85 - 1.03)
5	0.99	(0.94 - 1.04)	↑1.01	(0.96 - 1.06)	↓0.98	(0.93 - 1.03)	↓0.92	(0.85 - 1.01)
6	↑1.00	(0.95 - 1.04)	↑1.03	(0.98 - 1.07)	↓0.96	(0.91 - 1.03)	↓0.93	(0.86 - 1.01)
7	↑1.01	(0.96 - 1.07)	↑1.04	(0.99 - 1.09)	0.95	(0.85 - 1.05)	↓0.95	(0.88 - 1.03)
8	↑1.05	(0.93 - 1.18)	1.04	(0.98 - 1.10)	0.93	(0.78 - 1.09)	↓0.98	(0.89 - 1.09)
9			↓1.03	(0.97 - 1.10)			↓1.02	(0.91 - 1.15)
10			1.01	(0.95 - 1.07)			1.05	(0.94 - 1.18)
11			↓0.95	(0.90 - 1.01)			↑1.06	(0.95 - 1.19)
12			**0.87**	**(0.77 - 0.99)**			↑1.03	(0.83 - 1.30)
Weekly peak concentration								
-4	↑0.97	(0.89 - 1.06)	↓0.96	(0.91 - 1.00)	↑0.97	(0.86 - 1.11)	↑1.01	(0.93 - 1.11)
-3	↓0.99	(0.95 - 1.04)	↓0.97	(0.94 - 1.00)	↑1.03	(0.97 - 1.10)	↑1.02	(0.97 - 1.07)
-2	↓1.00	(0.95 - 1.05)	↓0.98	(0.96 - 1.00)	1.05	(0.98 - 1.14)	1.02	(0.99 - 1.06)
-1	↓1.00	(0.95 - 1.05)	0.99	(0.98 - 1.01)	1.05	(0.98 - 1.12)	1.02	(0.98 - 1.06)
0	↓1.00	(0.96 - 1.04)	1.00	(0.99 - 1.01)	1.03	(0.97 - 1.10)	↓1.01	(0.97 - 1.06)
1	0.99	(0.95 - 1.04)	1.01	(0.99 - 1.02)	1.01	(0.95 - 1.08)	↓1.01	(0.97 - 1.05)
2	↑0.99	(0.94 - 1.04)	1.01	(0.99 - 1.03)	0.99	(0.93 - 1.06)	↓1.00	(0.96 - 1.04)
3	↑0.99	(0.94 - 1.03)	1.01	(0.99 - 1.04)	0.98	(0.92 - 1.04)	↓1.00	(0.96 - 1.03)
4	↑0.99	(0.95 - 1.03)	↑1.02	(0.99 - 1.04)	0.98	(0.92 - 1.04)	↓0.99	(0.96 - 1.02)
5	↑1.00	(0.95 - 1.04)	↑1.02	(0.99 - 1.04)	0.98	(0.92 - 1.05)	0.99	(0.95 - 1.02)
6	↑1.01	(0.95 - 1.06)	1.01	(0.99 - 1.03)	0.99	(0.92 - 1.06)	0.98	(0.95 - 1.02)
7	1.02	(0.97 - 1.07)	1.01	(0.99 - 1.02)	↓0.99	(0.93 - 1.06)	0.98	(0.94 - 1.02)
8	↑1.03	(0.94 - 1.13)	1.00	(0.99 - 1.02)	↓0.98	(0.86 - 1.13)	0.98	(0.95 - 1.03)
9			0.99	(0.98 - 1.01)			↑0.99	(0.95 - 1.03)
10			0.99	(0.96 - 1.01)			↑1.00	(0.96 - 1.04)
11			↓0.97	(0.94 - 1.01)			↑1.02	(0.97 - 1.08)
12			↓0.96	(0.92 - 1.01)			↑1.04	(0.95 - 1.14)

Note:

RR = risk ratio; CI = confidence interval; PM = particulate matter

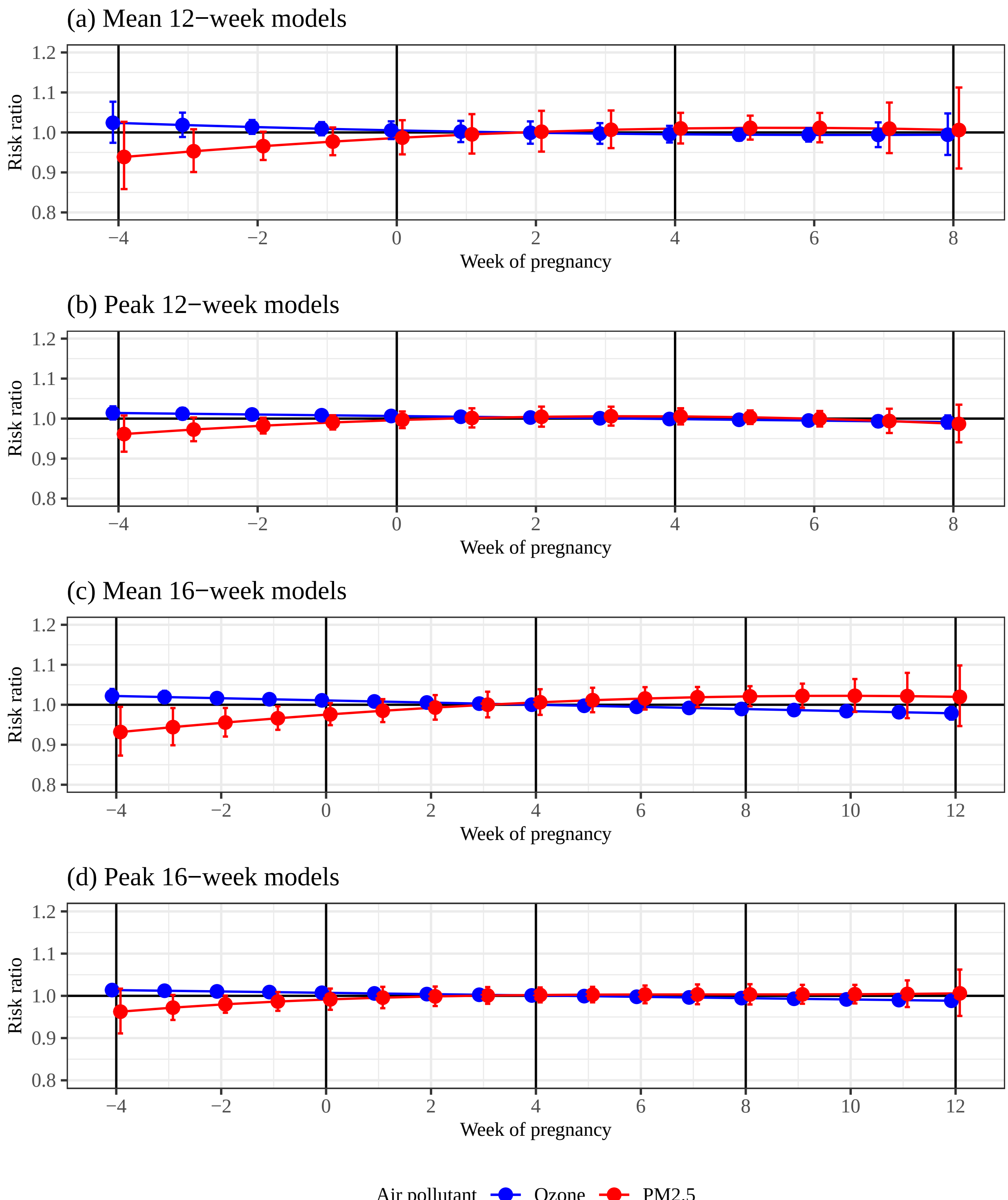
↑= RR is higher than in the single-pollutant models; ↓= RR is lower than in the single-pollutant models

Models were adjusted for maternal education level, maternal smoking, tract-level median income, conception season, green space, ozone, and $PM_{2.5}$.

RR applies to a 10-unit increase from the previous week in the air pollutant (ppb for ozone and $\mu g/m^3$ for $PM_{2.5}$) over two standard deviations above the mean.

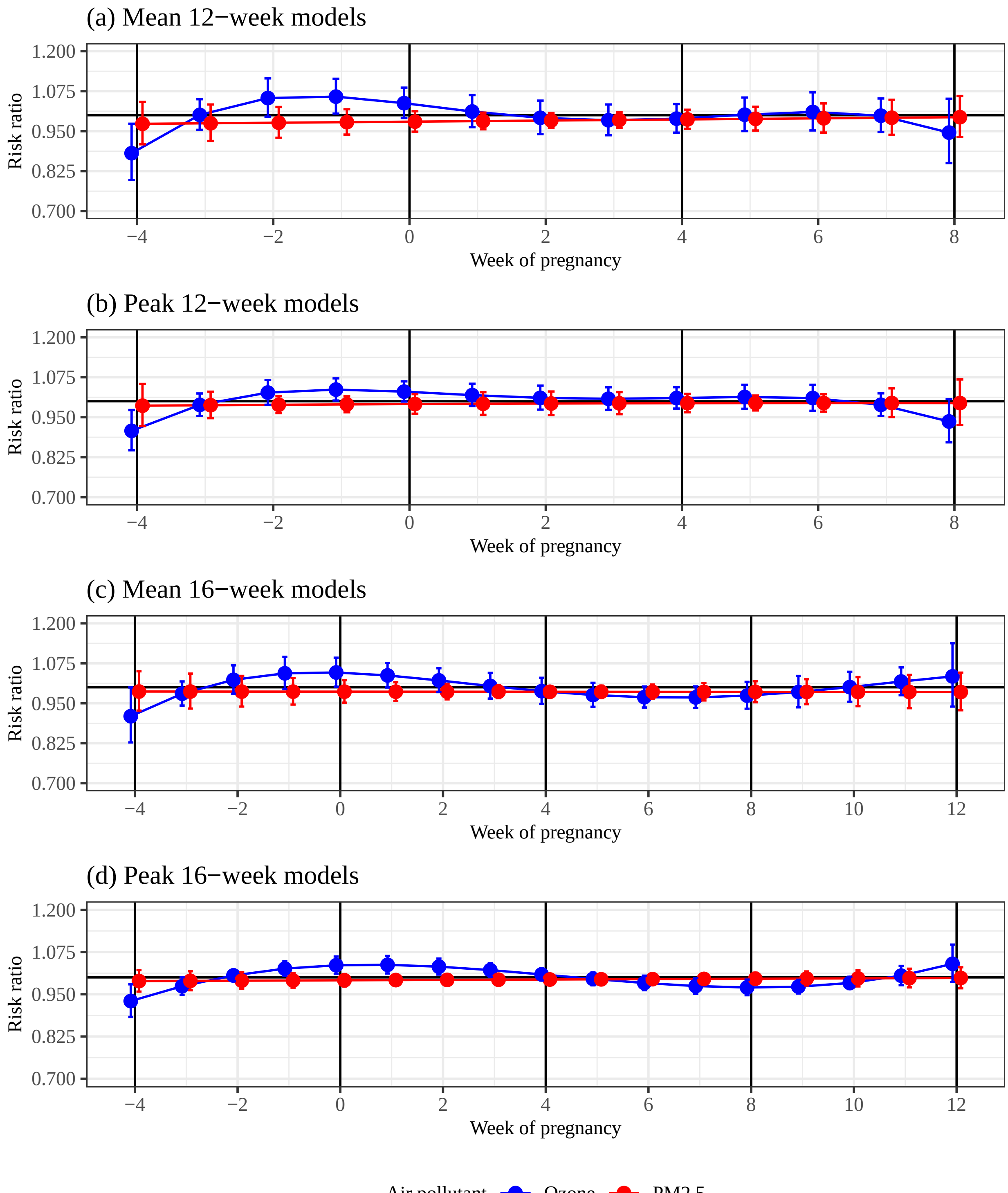
Week 0 refers to the week of conception. Week 12 refers to the end of the first trimester of pregnancy.

Figures



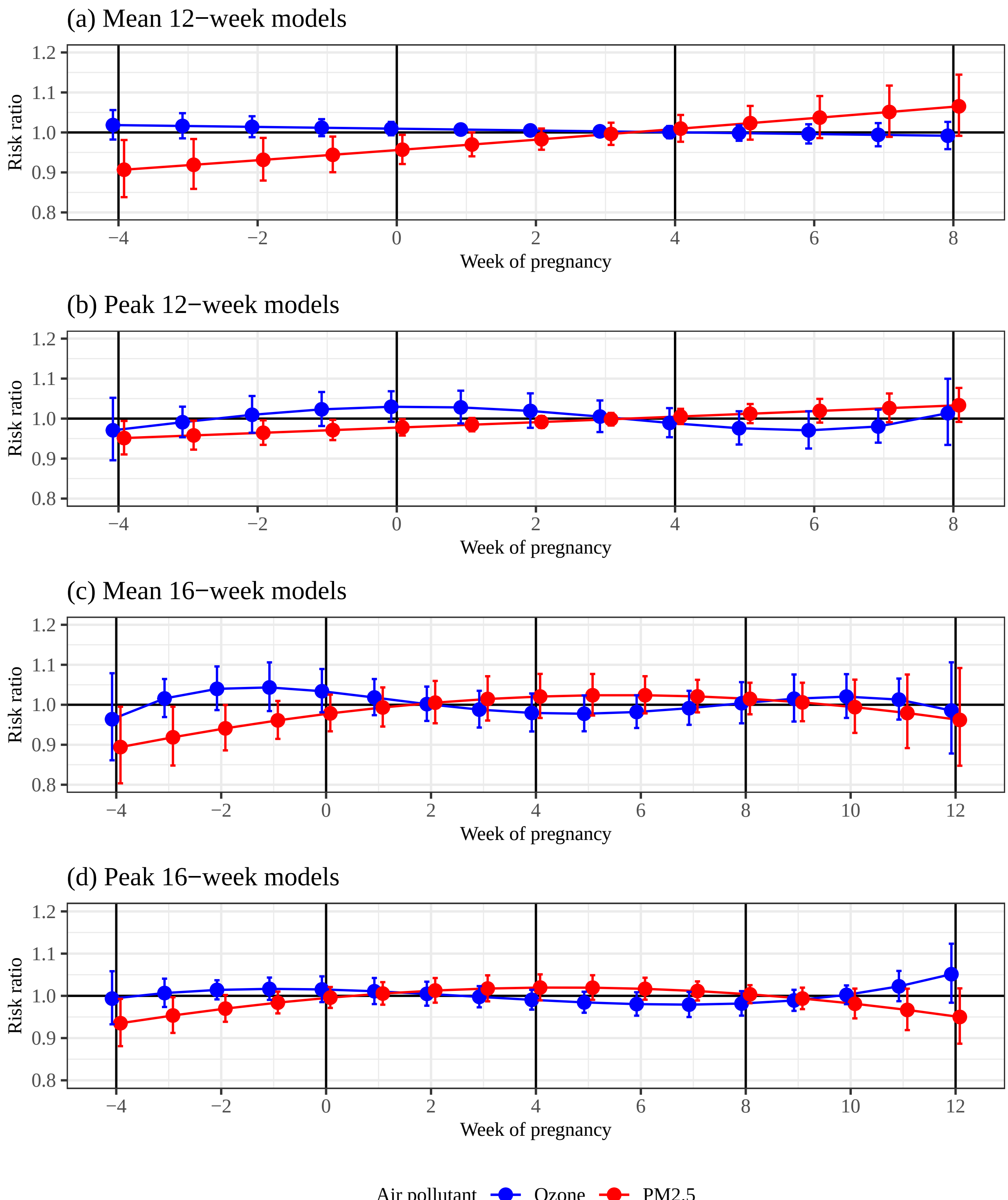
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 4.1: Clubfoot models: Risk ratios by week of pregnancy with grasses and trees



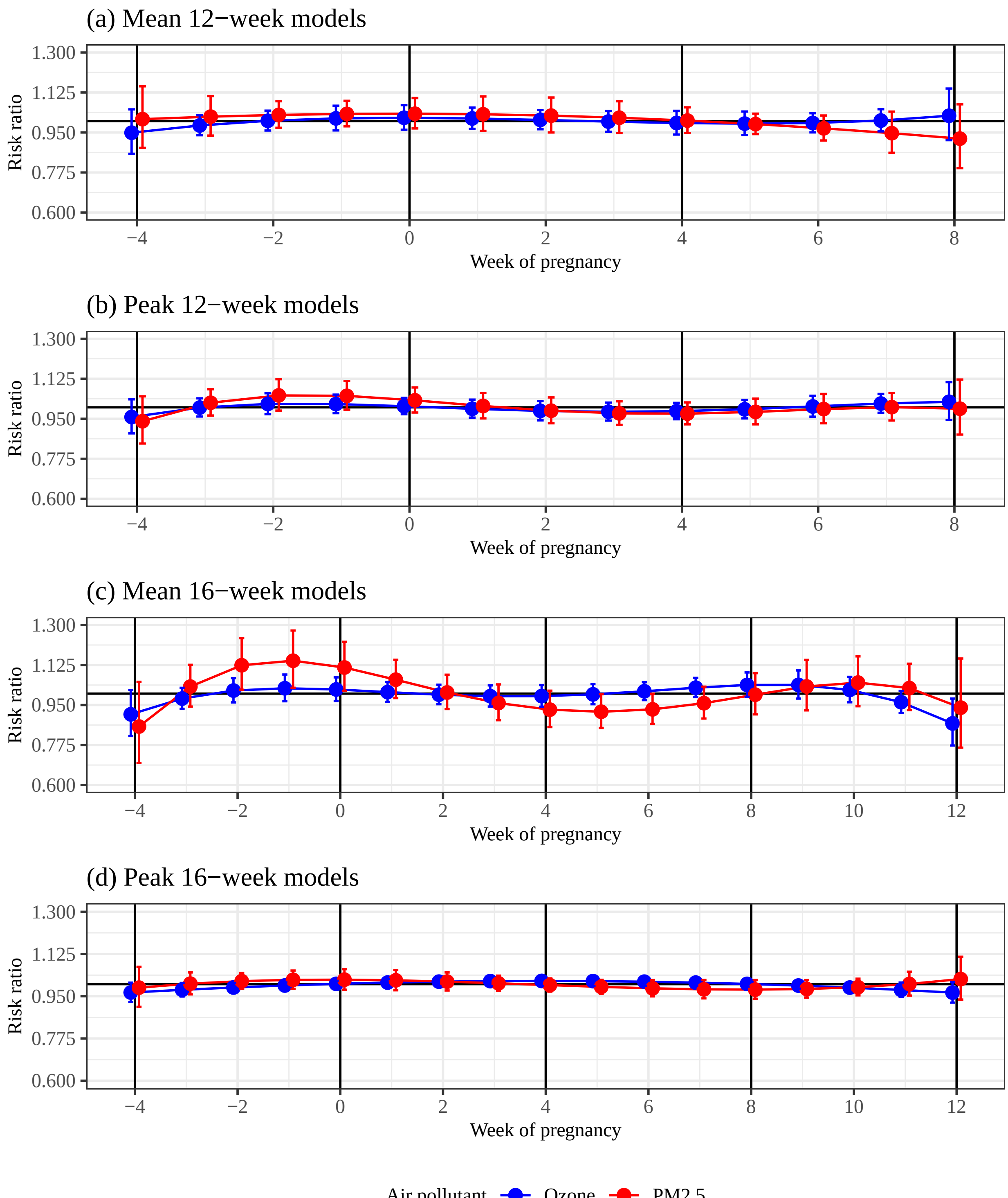
Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 4.2: Cleft lip with or without cleft palate models: Risk ratios by week of pregnancy with grasses and trees



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 4.3: Cleft palate models: Risk ratios by week of pregnancy with grasses and trees



Note: Models were adjusted for maternal education level, maternal smoking, tract−level median income, conception season, and the indicated green space variable. Week 0 was the week of conception. Week 8 was the end of the second month of pregnancy. Week 12 was the end of the first trimester of pregnancy. Risk ratio applies to a 10−unit increase from the previous week in the air pollutant (ppb for ozone and µg/m³ for PM2.5) over two standard deviations above the mean.

Figure 4.4: Craniosynostosis models: Risk ratios by week of pregnancy with grasses and trees

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5. Summary

This series of studies explored the relationship between air pollution, as defined by Downscaler estimates of O_3 and $PM_{2.5}$ and the birth defects clubfoot, oral clefts, and craniosynostosis for the years 2002 to 2015 using a case-cohort design. This topic was chosen because there has been little to no research on the association between air pollution and either clubfoot or craniosynostosis and research on air pollution and oral clefts has shown mixed results. However, all of these birth defects are associated with maternal smoking, so we hypothesized that inhaling $PM_{2.5}$, which contains many of the same components as cigarette smoke, could be associated with increased risk of these birth defects.

Distributed lag models were used to assess the the risk of each birth defect group over time. The first study evaluated the relationship between each birth defect and each air pollutant separately. The second study evaluated the role of green space, as developed using the NLCD, in altering this relationship by evaluating a series of buffer sizes ranging from 50m to 500m around the mother's residence at birth. The third study evaluated the relationship between air pollution and birth defects when both pollutants were combined in the same model. Additional covariates included maternal education, maternal smoking, tract-level median income, and season of conception.

5.1 Clubfoot

All three studies showed that 10ppb increases in weekly O_3 mean and peak concentrations had the highest effect on risk of developing clubfoot when exposure occurred before conception. Including green space and $PM_{2.5}$ in the evaluations did not change these results. All three studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ mean concentrations had the highest effect when exposure occurred in week 8 of pregnancy in the 12-week evaluation and in or near week 12 of pregnancy in the 16-week evaluation. All three studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ peak concentrations had the highest effect when exposure occurred in the first month of pregnancy in the 12-week evaluation. The first two studies showed that $10\frac{\mu g}{m^3}$ increases in weekly

$PM_{2.5}$ peak concentrations had the highest effect when exposure occurred in the second month of pregnancy in the 12-week evaluation, but in the third evaluation with peak O_3, the highest effect occurred in week 12 of pregnancy.

Including green space in the evaluations did not alter the weeks of highest effect very much. Including mean O_3 and mean $PM_{2.5}$ in the same evaluation did not alter the results for mean O_3 or mean $PM_{2.5}$ very much. Including peak O_3 and peak $PM_{2.5}$ in the same evaluation shifted the week in which peak $PM_{2.5}$ had the highest effect to week 12 of pregnancy.

To our knowledge, only one published study has analyzed the association between clubfoot and PM.[1] That study did not find an association between PM_{10} and clubfoot. No studies have looked at $PM_{2.5}$ or O_3 and clubfoot. In summary, green space does not affect the relationship between air pollution and risk of clubfoot. Pre-conception exposure to O_3 and exposure to $PM_{2.5}$ in the first and second months of pregnancy have the highest effects on risk of clubfoot. Peak O_3 affects the relationship between peak $PM_{2.5}$ and the risk of clubfoot.

5.2 Cleft lip with or without cleft palate

All three studies showed that 10ppb increases in weekly O_3 mean and peak concentrations had the highest effect on risk of developing cleft lip with or without cleft palatewhen exposure occurred around conception in the 16-week evaluation. Including green space and $PM_{2.5}$ in the evaluations did not change these results. The first two studies showed that 10ppb increases in weekly O_3 mean and peak concentrations had the highest effect on risk of developing cleft lip with or without cleft palatewhen exposure occurred around conception in the 12-week evaluation, but in the third study with $PM_{2.5}$, the highest effect occurred before conception.

All three studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ mean concentrations had weekly RRs that were consistently below 1.0 with no high points. The first two studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ peak concentrations had the highest effect on risk of developing cleft lip with or without cleft palatewhen exposure occurred in the first month of pregnancy in the 12-week evaluation, but in the 16-week evaluation, all weeks had RRs that were consistently below 1.0.

The third study showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ peak concentrations had weekly RRs that were consistently below 1.0 with no high points in the 12-week evaluation, but in the 16-week evaluation, the highest effect occurred in week 12 of pregnancy.

Including green space in the evaluations did not alter the weeks of highest effect very much. Including mean O_3 and mean $PM_{2.5}$ in the same evaluation shifted the weeks in which mean O_3 had the highest effect to before pregnancy, while results for mean $PM_{2.5}$ were unchanged. Including peak O_3 and peak $PM_{2.5}$ in the same evaluation shifted the weeks in which peak O_3 had the highest effect to before conception and the week in which peak $PM_{2.5}$ had the highest effect to week 12 of pregnancy.

Of the 17 published studies we identified that looked at PM and cleft lip with or without cleft palate, three found significant associations. Of these, one found an association with PM_{10} exposure in the second month of pregnancy[1] and another found a general spatial association with PM_{10} exposure[2]. None of the nine that looked at $PM_{2.5}$ found associations. This is not consistent with our results, which suggested an association with $PM_{2.5}$ in the first month of pregnancy. Of these published studies, nine also looked at O_3 and cleft lip with or without cleft palate, but only one found associations in the first two months of pregnancy[3]. This result is not consistent with ours, so studies that used multi-week means may have diluted their results.

In summary, exposure to O_3 before of during conception and exposure to $PM_{2.5}$ in the first month of pregnancy or at the end of the first trimester have the highest effects on risk of cleft lip with or without cleft palate. Green space does not affect the relationship between air pollution and risk of cleft lip with or without cleft palate. O_3 and $PM_{2.5}$ affect the relationships between each other and the risk of cleft lip with or without cleft palate.

5.3 Cleft palate

The first two studies showed that 10ppb increases in weekly O_3 mean concentrations had weekly RRs that were consistently around 1.0 with no high points in the 12-week evaluation, but in the 16-week evaluations, the highest effect occurred around conception. The third study showed that

10ppb increases in weekly O_3 mean concentrations had the highest effect on risk of developing cleft palate before conception. The first study showed that 10ppb increases in weekly O_3 peak concentrations had the highest effect on risk of developing cleft palate around conception. The second study showed that 10ppb increases in weekly O_3 peak concentrations had the highest effect on risk of developing cleft palate in week 8 of pregnancy in the 12-week evaluation and in week 12 of pregnancy in the 16-week evaluation. The third study showed that 10ppb increases in weekly O_3 peak concentrations had the highest effect on risk of developing cleft palate in around conception in the 12-week evaluation and in week 12 of pregnancy in the 16-week evaluation.

All three studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ mean and peak concentrations had the highest effect on risk of developing cleft palate in week 8 of pregnancy in the 12-week evaluation and in the second month of pregnancy in the 16-week evaluation. Including green space in the evaluations only changed the results for peak O_3, shifting its week of highest effect to week 8 of pregnancy. Including O_3 and $PM_{2.5}$ in the same evaluation shifted the weeks in which O_3 had the highest effect to before pregnancy, while results for $PM_{2.5}$ were unchanged.

Of the 16 published studies we identified that looked at PM and cleft palate alone, four found significant associations. Of these, two found associations with $PM_{2.5}$ around the second month of pregnancy[4,5] and one found an association with PM_{10} at that time[6], while two found associations with earlier PM_{10} exposure[1,5] The three that found associations during the second month are consistent with our results. Of these published studies, 12 also looked at O_3 and cleft palate, but none found associations. This is not consistent with our results. However, our results showed highest effects before and around conception, but all studies except one only considered times during pregnancy.

In summary, exposure to O_3 before and around conception and exposure to $PM_{2.5}$ in the second month of pregnancy have the highest effects on risk of cleft palate. Green space affects the relationship between peak O_3 and risk of cleft palate. $PM_{2.5}$ affects the relationship between O_3 and the risk of cleft palate.

5.4 Craniosynostosis

All three studies showed that 10ppb increases in weekly O_3 mean concentrations had the highest effect on risk of developing craniosynostosis when exposure occurred around week 8 of pregnancy. All three studies showed that 10ppb increases in weekly O_3 peak concentrations had the highest effect on risk of developing craniosynostosis when exposure occurred around week 8 of pregnancy in the 12-week evaluations and in the first month of pregnancy in the 16-week evaluations. Including green space and $PM_{2.5}$ in the evaluations did not change these results.

The first two studies showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ mean and peak concentrations had the highest effect on risk of developing craniosynostosis when exposure occurred around conception. The third study showed that $10\frac{\mu g}{m^3}$ increases in weekly $PM_{2.5}$ mean and peak concentrations had the highest effect on risk of developing craniosynostosis when exposure occurred before conception in the 12-week evaluations. In the 16-week mean $PM_{2.5}$ evaluation, the highest effect occurred around conception, but in the 16-week peak $PM_{2.5}$ evaluation, the highest effect occurred in week 12 of pregnancy. Including green space in the evaluations did not change these results.

Including green space in the evaluations did not alter the weeks of highest effect very much. Including O_3 and $PM_{2.5}$ in the same evaluation shifted the weeks in which mean $PM_{2.5}$ had the highest effect to before conception or week 12 of pregnancy, while results for O_3 were unchanged.

To our knowledge, only two published studies has analyzed the association between craniosynostosis alone and $PM_{2.5}$ and O_3. One found no association using a two-month average of exposure[7] and the other found strong associations with both $PM_{2.5}$ and O_3 using exposure averaged over the first trimester[8], which makes comparison to our study difficult. In our evaluations, the week of highest effect for O_3 was week 8 of pregnancy, so it makes sense that a study looking at the entire first trimester could find an association, but a study looking at only the first two months would not. In most of our evaluations, the weeks of highest effect for $PM_{2.5}$ were before and during conception, while these studies considered only time periods during pregnancy.

In summary, exposure to $PM_{2.5}$ before and around conception and exposure to O_3 around week

8 of pregnancy have the highest effects on risk of craniosynostosis. Green space does not affect the relationship between air pollution and risk of craniosynostosis. O_3 affects the relationship between $PM_{2.5}$ and the risk of craniosynostosis.

5.5 Limitations and suggestions for further research

These studies had several limitations that provide opportunities for further research. They relied on birth mother's residence at birth to assign exposure for both air pollution and green space, which measures potential exposure assuming the mother spent a lot of time outside at that residence. Including both maternal mobility (moving during pregnancy) and the amount of time the mother spends outside at home, as well as other places she frequents (such as workplace) could improve estimates of exposure during pregnancy. These studies did not account for indoor air pollution at all, which could result in exposure misclassification especially during winter months. We tried to account for this by including season of conception in the evaluations. We suggest that studies account for both indoor and outdoor exposure to address this. To estimate green space, we used only one year of the NLCD, but it is possible that green space around a mother's home shifted as buildings were built or land was reclaimed, which could result in misclassification of green space. A more complex model that uses the NLCD's datasets that calculate changes in categorization between vintages could address this.

Race was not included in the models in our studies because in 2019 when the studies were being prepared, there was contention in the literature regarding whether race should be included in models if it was not of direct interest in the study. At that time, race was considered a proxy for lived experience related to social status and access to care, but we had no reason to believe biologically that race itself was associated with birth defects. Since then, a lot of research has been done on environmental justice that suggests race should be included in models as a proxy for lived experience that it is difficult to capture in other ways, especially with surveillance data. A next step for this research could be to compare results for births of white and black mothers, and possibly Asian mothers, since among our samples, white mothers had higher proportions of births with birth defects than black or Asian mothers.

We found that including green space as a confounder in the models affected the relationship between O_3 and cleft palate. We would like to explore this further by stratifying green space and rerunning the models to test effect modification.

5.6 Conclusion

Past studies have struggled with small sample sizes or poor spatial and temporal granularity. Utilizing address-level data from large state and national birth defect registries would help advance this research. We are unsure if the modest results we found are clinically meaningful, so we suggest future research on these birth defects should focus on exposure to air pollution around conception and month 2 of pregnancy. Studies of cleft palate should include green space. Studies of birth defects should include mixed air pollution effects.

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A. Supplemental Tables for Chapter 3

Table A.1: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Pollutant	Green space	Weeks	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Clubfoot								
Ozone mean	grass-trees	16	0.98 (0.90 - 1.08)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.10)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.09)
	green-water	16	0.98 (0.89 - 1.08)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.10)
Ozone peak	grass-trees	16	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.05)
	green-water	16	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.06)	0.99 (0.93 - 1.06)
$PM_{2.5}$ mean	grass-trees	16	1.01 (0.84 - 1.20)	1.00 (0.84 - 1.20)	1.01 (0.84 - 1.20)	1.00 (0.84 - 1.19)	1.00 (0.84 - 1.20)	1.00 (0.84 - 1.20)
	green-water	16	1.00 (0.84 - 1.20)	1.00 (0.84 - 1.19)	1.00 (0.84 - 1.20)	1.01 (0.84 - 1.20)	1.01 (0.85 - 1.21)	1.00 (0.84 - 1.20)
$PM_{2.5}$ peak	grass-trees	16	0.98 (0.88 - 1.08)	0.97 (0.88 - 1.08)	0.98 (0.88 - 1.08)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.08)
	green-water	16	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.08)	0.98 (0.88 - 1.08)	0.97 (0.88 - 1.08)
Cleft lip with or without cleft palate								
Ozone mean	grass-trees	12	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.05)
		16	0.97 (0.88 - 1.08)	0.97 (0.87 - 1.07)	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.08)	0.97 (0.87 - 1.07)
	green-water	12	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.05)
		16	0.97 (0.88 - 1.08)	0.97 (0.87 - 1.07)	0.97 (0.88 - 1.08)	0.97 (0.88 - 1.08)	0.97 (0.87 - 1.07)	0.97 (0.87 - 1.07)
Ozone peak	grass-trees	12	0.96 (0.87 - 1.05)	0.96 (0.87 - 1.05)	0.96 (0.87 - 1.05)	0.96 (0.87 - 1.05)	0.96 (0.87 - 1.05)	0.95 (0.87 - 1.04)
		16	0.97 (0.88 - 1.06)	0.97 (0.88 - 1.06)	0.97 (0.88 - 1.06)	0.97 (0.88 - 1.06)	0.97 (0.88 - 1.06)	0.96 (0.88 - 1.06)
	green-water	12	0.95 (0.87 - 1.04)	0.96 (0.87 - 1.05)	0.95 (0.87 - 1.04)	0.96 (0.87 - 1.04)	0.95 (0.87 - 1.04)	0.95 (0.87 - 1.04)
		16	0.96 (0.88 - 1.06)	0.96 (0.88 - 1.06)	0.96 (0.88 - 1.06)	0.96 (0.88 - 1.06)	0.96 (0.87 - 1.06)	0.96 (0.87 - 1.06)
$PM_{2.5}$ mean	grass-trees	12	0.88 (0.72 - 1.07)	0.89 (0.73 - 1.08)	0.88 (0.73 - 1.08)	0.88 (0.72 - 1.08)	0.88 (0.72 - 1.08)	0.88 (0.72 - 1.08)
		16	0.86 (0.70 - 1.06)	0.87 (0.71 - 1.07)	0.87 (0.70 - 1.07)	0.87 (0.70 - 1.07)	0.86 (0.70 - 1.06)	0.87 (0.70 - 1.07)
	green-water	12	0.88 (0.72 - 1.07)	0.89 (0.73 - 1.08)	0.88 (0.72 - 1.08)	0.88 (0.72 - 1.07)	0.88 (0.72 - 1.08)	0.89 (0.73 - 1.08)
		16	0.86 (0.70 - 1.06)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.86 (0.70 - 1.07)	0.87 (0.70 - 1.07)	0.87 (0.71 - 1.07)
$PM_{2.5}$ peak	grass-trees	12	0.92 (0.82 - 1.04)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.04)	0.93 (0.82 - 1.04)	0.93 (0.82 - 1.04)
		16	0.95 (0.86 - 1.06)	0.96 (0.86 - 1.07)	0.96 (0.86 - 1.06)	0.96 (0.86 - 1.06)	0.95 (0.86 - 1.06)	0.96 (0.86 - 1.06)
	green-water	12	0.92 (0.82 - 1.04)	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.04)	0.92 (0.82 - 1.04)	0.93 (0.82 - 1.04)	0.93 (0.82 - 1.05)
		16	0.95 (0.86 - 1.06)	0.96 (0.86 - 1.07)	0.96 (0.86 - 1.07)	0.95 (0.86 - 1.06)	0.96 (0.86 - 1.06)	0.96 (0.86 - 1.07)

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Table A.1: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Pollutant	Green space	Weeks	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Cleft palate								
Ozone mean	grass-trees	12	1.01 (0.91 - 1.13)	1.01 (0.91 - 1.13)	1.01 (0.91 - 1.12)	1.01 (0.91 - 1.12)	1.01 (0.91 - 1.12)	1.01 (0.91 - 1.12)
		16	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.16)
	green-water	12	NA	1.01 (0.91 - 1.12)	1.01 (0.91 - 1.13)	1.01 (0.91 - 1.13)	1.01 (0.91 - 1.13)	1.01 (0.91 - 1.12)
		16	NA	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)	1.03 (0.91 - 1.17)
Ozone peak	grass-trees	12	1.01 (0.91 - 1.11)	1.01 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)
		16	1.01 (0.94 - 1.10)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)
	green-water	12	NA	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)	1.00 (0.91 - 1.11)
		16	NA	1.02 (0.92 - 1.13)	1.01 (0.93 - 1.10)	1.01 (0.94 - 1.10)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)
$PM_{2.5}$ mean	grass-trees	12	0.80 (0.57 - 1.13)	0.80 (0.57 - 1.14)	0.81 (0.57 - 1.14)	0.81 (0.57 - 1.14)	0.81 (0.57 - 1.14)	0.82 (0.58 - 1.15)
		16	0.77 (0.54 - 1.09)	0.77 (0.54 - 1.09)	0.78 (0.55 - 1.10)	0.77 (0.55 - 1.10)	0.78 (0.55 - 1.10)	0.78 (0.55 - 1.11)
	green-water	12	NA	0.79 (0.56 - 1.12)	0.80 (0.57 - 1.13)	0.81 (0.57 - 1.14)	0.81 (0.57 - 1.14)	0.81 (0.58 - 1.15)
		16	NA	0.75 (0.53 - 1.07)	0.77 (0.54 - 1.09)	0.78 (0.55 - 1.10)	0.78 (0.55 - 1.10)	0.78 (0.55 - 1.11)
$PM_{2.5}$ peak	grass-trees	12	0.90 (0.76 - 1.08)	0.89 (0.74 - 1.07)	0.91 (0.76 - 1.08)	0.91 (0.76 - 1.08)	0.91 (0.76 - 1.08)	0.91 (0.77 - 1.09)
		16	0.91 (0.78 - 1.08)	0.91 (0.78 - 1.08)	0.92 (0.78 - 1.08)	0.91 (0.77 - 1.08)	0.87 (0.72 - 1.05)	0.92 (0.78 - 1.09)
	green-water	12	NA	0.90 (0.75 - 1.07)	0.90 (0.76 - 1.08)	0.91 (0.76 - 1.08)	0.91 (0.76 - 1.08)	0.91 (0.76 - 1.08)
		16	NA	0.86 (0.71 - 1.03)	0.91 (0.78 - 1.08)	0.92 (0.78 - 1.08)	0.87 (0.72 - 1.05)	0.91 (0.77 - 1.08)
Craniosynostosis								
Ozone mean	grass-trees	12	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)
		16	0.94 (0.82 - 1.08)	0.94 (0.82 - 1.08)	0.94 (0.82 - 1.08)	0.94 (0.81 - 1.07)	0.94 (0.81 - 1.07)	0.94 (0.82 - 1.08)
	green-water	12	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.12)	0.98 (0.86 - 1.13)
		16	0.94 (0.82 - 1.08)	0.94 (0.82 - 1.08)	0.94 (0.82 - 1.08)	0.94 (0.82 - 1.08)	0.94 (0.81 - 1.08)	0.94 (0.82 - 1.08)
Ozone peak	grass-trees	12	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.08)	0.98 (0.88 - 1.09)
		16	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)
	green-water	12	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.08)	0.98 (0.88 - 1.09)
		16	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)	0.94 (0.84 - 1.04)
$PM_{2.5}$ mean	grass-trees	12	0.91 (0.69 - 1.20)	0.92 (0.70 - 1.21)	0.92 (0.70 - 1.21)	0.92 (0.70 - 1.21)	0.91 (0.69 - 1.20)	0.91 (0.69 - 1.20)
		16	1.10 (0.75 - 1.62)	1.12 (0.76 - 1.65)	1.10 (0.75 - 1.62)	1.12 (0.76 - 1.64)	1.09 (0.74 - 1.61)	1.09 (0.74 - 1.60)
	green-water	12	0.91 (0.69 - 1.20)	0.91 (0.69 - 1.21)	0.92 (0.69 - 1.21)	0.91 (0.69 - 1.19)	0.90 (0.69 - 1.19)	0.90 (0.68 - 1.19)
		16	1.11 (0.76 - 1.63)	1.11 (0.76 - 1.63)	1.10 (0.75 - 1.62)	1.09 (0.74 - 1.60)	1.08 (0.73 - 1.58)	1.07 (0.73 - 1.57)

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Table A.1: Cumulative risk ratios for covariate models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Pollutant	Green space	Weeks	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
$PM_{2.5}$ peak	grass-trees	12	1.03 (0.85 - 1.24)	1.03 (0.85 - 1.25)	1.02 (0.85 - 1.24)	1.03 (0.85 - 1.25)	1.02 (0.84 - 1.24)	1.02 (0.84 - 1.24)
		16	0.97 (0.83 - 1.14)	0.97 (0.83 - 1.14)	0.97 (0.83 - 1.14)	0.97 (0.83 - 1.14)	0.97 (0.82 - 1.14)	0.97 (0.82 - 1.14)
	green-water	12	1.03 (0.85 - 1.24)	1.03 (0.85 - 1.24)	1.02 (0.85 - 1.24)	1.02 (0.84 - 1.23)	1.01 (0.84 - 1.23)	1.01 (0.84 - 1.23)
		16	0.97 (0.83 - 1.14)	0.97 (0.83 - 1.14)	0.97 (0.83 - 1.14)	0.96 (0.82 - 1.13)	0.96 (0.82 - 1.13)	0.96 (0.82 - 1.13)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable.

For green space, grass-trees is a composite variable of grasses and trees and green-water is a composite of grasses, trees, and water.

For the initial analysis, clubfoot was not run for the 12-week model.

Table A.2: Risk ratios for covariate clubfoot 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
-4	NA	NA	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)
-3	NA	NA	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)
-2	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
-1	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
0	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
1	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
2	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
3	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
4	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)
5	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
6	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
7	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)
8	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
9	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
10	**0.99 (0.97 - 1.00)**	**0.99 (0.97 - 1.00)**	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
11	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)
12	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
-4	NA	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)
-3	NA	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.03)
-2	1.02 (1.00 - 1.04)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
-1	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
0	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
1	1.01 (1.00 - 1.02)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.01 (1.00 - 1.01)
2	1.01 (1.00 - 1.02)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
3	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
4	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)
5	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
6	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)

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Table A.2: Risk ratios for covariate clubfoot 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
7	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)	0.99 (0.99 - 1.00)
8	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
9	**0.99 (0.98 - 1.00)**	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
10	**0.99 (0.97 - 1.00)**	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
11	**0.98 (0.97 - 1.00)**	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)
12	**0.98 (0.96 - 1.00)**	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)	0.99 (0.97 - 1.00)
Weekly Ozone peak concentration, composite of grass and trees within buffer						
2	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.04)
3	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)
4	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
5	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
6	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
7	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
8	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
9	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)	0.99 (0.98 - 1.00)
10	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**
11	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**
12	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
2	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**
3	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)	1.02 (1.00 - 1.03)
4	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.03)	1.01 (1.00 - 1.02)
5	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)	1.01 (1.00 - 1.02)
6	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)	1.00 (1.00 - 1.01)
7	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
8	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)	1.00 (0.99 - 1.00)
9	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**
10	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**	**0.99 (0.98 - 1.00)**
11	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**
12	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**	**0.98 (0.96 - 1.00)**

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Table A.2: Risk ratios for covariate clubfoot 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
9	**0.96 (0.83 - 1.10)**	**0.96 (0.83 - 1.11)**	**0.96 (0.84 - 1.11)**	**0.96 (0.83 - 1.10)**	**0.96 (0.83 - 1.10)**	**0.96 (0.83 - 1.10)**
10	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.12)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)
11	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)
12	0.99 (0.86 - 1.15)	1.00 (0.86 - 1.15)	1.00 (0.86 - 1.15)	0.99 (0.86 - 1.15)	0.99 (0.86 - 1.15)	0.99 (0.86 - 1.15)
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
9	0.96 (0.83 - 1.10)	0.96 (0.83 - 1.11)	0.96 (0.83 - 1.10)	0.96 (0.83 - 1.10)	0.96 (0.84 - 1.11)	0.96 (0.84 - 1.11)
10	1.02 (0.93 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)
11	1.04 (0.94 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)
12	**0.99 (0.86 - 1.14)**	**0.99 (0.86 - 1.15)**	**0.99 (0.86 - 1.15)**	**1.00 (0.86 - 1.15)**	**0.99 (0.86 - 1.15)**	**0.99 (0.86 - 1.14)**
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
5	1.05 (0.98 - 1.12)	1.05 (0.98 - 1.12)	1.05 (0.98 - 1.12)	1.04 (0.98 - 1.12)	1.04 (0.98 - 1.12)	1.05 (0.98 - 1.12)
6	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)
7	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)
8	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)
9	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)
10	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**
11	1.02 (0.98 - 1.07)	1.02 (0.98 - 1.07)	1.02 (0.99 - 1.07)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.07)	1.02 (0.99 - 1.07)
12	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.04)	0.96 (0.90 - 1.04)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
5	1.05 (0.98 - 1.12)	1.05 (0.98 - 1.12)	1.04 (0.98 - 1.12)	1.05 (0.98 - 1.12)	1.05 (0.98 - 1.12)	1.05 (0.98 - 1.12)
6	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)
7	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)
8	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)
9	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)
10	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**	**1.03 (0.99 - 1.08)**
11	1.02 (0.98 - 1.07)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.07)	1.02 (0.99 - 1.07)	1.02 (0.98 - 1.06)
12	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.04)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)

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Table A.2: Risk ratios for covariate clubfoot 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	**50m buffer**	**100m buffer**	**200m buffer**	**300m buffer**	**400m buffer**	**500m buffer**

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.3: Risk ratios for covariate cleft lip with or without cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
0	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.97)	0.88 (0.80 - 0.97)	0.88 (0.80 - 0.97)	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.98)
1	1.00 (0.96 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)
2	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)
3	1.06 (1.00 - 1.11)	1.06 (1.00 - 1.11)	1.05 (1.00 - 1.11)	1.06 (1.00 - 1.11)	1.05 (1.00 - 1.11)	1.05 (1.00 - 1.11)
4	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)
5	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)
6	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)
7	0.98 (0.93 - 1.03)	0.98 (0.93 - 1.03)	0.98 (0.94 - 1.03)	0.98 (0.94 - 1.03)	0.98 (0.93 - 1.03)	0.98 (0.94 - 1.03)
8	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)
9	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**
10	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)
11	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)
12	**0.95 (0.86 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
0	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.97)	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.98)	0.88 (0.80 - 0.98)
1	1.00 (0.96 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)
2	1.05 (1.00 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.11)
3	1.06 (1.00 - 1.11)	1.06 (1.00 - 1.11)	1.05 (1.00 - 1.11)	1.05 (1.00 - 1.11)	1.05 (1.00 - 1.11)	1.05 (1.00 - 1.11)
4	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)	1.03 (0.99 - 1.08)
5	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)	1.01 (0.96 - 1.06)
6	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)	0.99 (0.94 - 1.04)
7	0.98 (0.93 - 1.03)	0.98 (0.93 - 1.03)	0.98 (0.94 - 1.03)	0.98 (0.93 - 1.03)	0.98 (0.94 - 1.03)	0.98 (0.93 - 1.03)
8	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)	0.99 (0.94 - 1.03)
9	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**	**1.00 (0.95 - 1.05)**
10	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)	1.01 (0.95 - 1.07)
11	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)	1.00 (0.95 - 1.05)
12	**0.95 (0.86 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**	**0.95 (0.85 - 1.05)**

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Table A.3: Risk ratios for covariate cleft lip with or without cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone peak concentration, composite of grass and trees within buffer						
0	0.91 (0.85 - 0.97)	0.91 (0.85 - 0.97)	0.91 (0.85 - 0.97)	0.91 (0.85 - 0.97)	0.91 (0.85 - 0.97)	0.91 (0.85 - 0.97)
1	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)
2	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)
3	1.03 (1.00 - 1.07)	1.03 (1.00 - 1.07)	1.03 (1.00 - 1.07)	1.03 (1.00 - 1.07)	1.03 (1.00 - 1.07)	1.03 (1.00 - 1.07)
4	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)
5	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)
6	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)
7	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)
8	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)
9	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)
10	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)
11	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)
12	0.94 (0.88 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.88 - 1.00)	0.94 (0.88 - 1.00)	0.94 (0.88 - 1.00)
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
0	**0.91 (0.85 - 0.97)**	**0.91 (0.85 - 0.97)**	**0.91 (0.85 - 0.97)**	**0.91 (0.85 - 0.97)**	**0.91 (0.85 - 0.97)**	**0.91 (0.85 - 0.97)**
1	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)
2	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.02 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.06)
3	**1.04 (1.00 - 1.07)**	**1.03 (1.00 - 1.07)**	**1.03 (1.00 - 1.07)**	**1.03 (1.00 - 1.07)**	**1.03 (1.00 - 1.07)**	**1.03 (1.00 - 1.07)**
4	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)
5	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)	1.02 (0.98 - 1.05)
6	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)
7	1.00 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.00 (0.97 - 1.04)
8	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)
9	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)
10	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)	1.01 (0.97 - 1.05)
11	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.95 - 1.02)	0.99 (0.95 - 1.02)
12	0.94 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.88 - 1.00)	0.94 (0.88 - 1.00)	0.94 (0.87 - 1.00)

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Table A.3: Risk ratios for covariate cleft lip with or without cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
11	**0.85 (0.70 - 1.02)**	**0.86 (0.71 - 1.03)**	**0.85 (0.71 - 1.02)**	**0.85 (0.71 - 1.02)**	**0.85 (0.71 - 1.02)**	**0.85 (0.71 - 1.02)**
12	1.04 (0.87 - 1.24)	1.04 (0.87 - 1.24)	1.04 (0.87 - 1.24)	1.04 (0.87 - 1.24)	1.04 (0.87 - 1.24)	1.04 (0.87 - 1.24)
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
11	0.85 (0.70 - 1.02)	0.85 (0.71 - 1.03)	0.85 (0.70 - 1.02)	0.84 (0.70 - 1.02)	0.85 (0.70 - 1.02)	0.85 (0.71 - 1.02)
12	**1.04 (0.87 - 1.24)**	**1.04 (0.87 - 1.25)**	**1.04 (0.87 - 1.25)**	**1.04 (0.87 - 1.25)**	**1.04 (0.87 - 1.25)**	**1.05 (0.87 - 1.25)**
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
9	1.03 (0.94 - 1.14)	1.04 (0.94 - 1.14)	1.03 (0.94 - 1.14)	1.03 (0.94 - 1.14)	1.03 (0.94 - 1.14)	1.03 (0.94 - 1.14)
10	0.96 (0.90 - 1.02)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)
11	0.94 (0.88 - 1.01)	0.95 (0.88 - 1.01)	0.95 (0.88 - 1.01)	0.95 (0.88 - 1.01)	0.95 (0.88 - 1.01)	0.95 (0.88 - 1.01)
12	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.08)
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
9	1.03 (0.94 - 1.14)	1.04 (0.94 - 1.14)	1.04 (0.94 - 1.14)	1.03 (0.94 - 1.14)	1.04 (0.94 - 1.14)	1.04 (0.94 - 1.14)
10	0.96 (0.90 - 1.02)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.02)	0.96 (0.90 - 1.02)	0.96 (0.90 - 1.03)	0.96 (0.90 - 1.03)
11	0.94 (0.88 - 1.01)	0.95 (0.88 - 1.01)	0.94 (0.88 - 1.01)	0.94 (0.88 - 1.01)	0.94 (0.88 - 1.01)	0.95 (0.88 - 1.01)
12	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.09)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.08)	0.99 (0.90 - 1.09)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.4: Risk ratios for covariate cleft lip with or without cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
7	1.06 (0.95 - 1.19)	1.07 (0.95 - 1.19)	1.06 (0.95 - 1.19)	1.07 (0.95 - 1.19)	1.06 (0.95 - 1.19)	1.06 (0.95 - 1.19)
8	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.90 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.90 (0.81 - 1.01)
9	0.98 (0.90 - 1.07)	0.98 (0.90 - 1.06)	0.98 (0.90 - 1.06)	0.98 (0.90 - 1.06)	0.98 (0.90 - 1.07)	0.98 (0.90 - 1.07)
10	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)
11	0.95 (0.85 - 1.06)	0.95 (0.85 - 1.06)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.06)
12	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
7	1.06 (0.95 - 1.19)	1.07 (0.95 - 1.19)	1.06 (0.95 - 1.18)	1.06 (0.95 - 1.19)	1.06 (0.95 - 1.18)	1.06 (0.95 - 1.18)
8	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)	0.91 (0.81 - 1.01)
9	0.98 (0.90 - 1.07)	0.97 (0.89 - 1.06)	0.98 (0.90 - 1.07)	0.98 (0.90 - 1.07)	0.98 (0.90 - 1.07)	0.98 (0.90 - 1.06)
10	1.00 (0.92 - 1.09)	1.00 (0.91 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)
11	0.95 (0.85 - 1.06)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)	0.95 (0.85 - 1.07)
12	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.97 - 1.21)	1.08 (0.96 - 1.21)	1.08 (0.96 - 1.21)	1.08 (0.97 - 1.21)
Weekly Ozone peak concentration, composite of grass and trees within buffer						
-4	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.98)
-3	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)
-2	1.00 (0.99 - 1.02)	1.00 (0.99 - 1.02)	1.00 (0.99 - 1.02)	1.00 (0.99 - 1.02)	1.00 (0.99 - 1.02)	1.00 (0.99 - 1.02)
-1	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.04)	1.02 (1.00 - 1.05)
0	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)
1	1.04 (1.01 - 1.06)	1.04 (1.01 - 1.06)	1.04 (1.01 - 1.06)	1.04 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)
2	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**
3	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**
4	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.02)**	**1.01 (0.99 - 1.02)**
5	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**
6	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)
7	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)
8	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)
9	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)
10	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**

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Table A.4: Risk ratios for covariate cleft lip with or without cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
11	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**
12	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.10)**	**1.04 (0.99 - 1.10)**	**1.04 (0.99 - 1.09)**
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
-4	**0.93 (0.88 - 0.98)**	**0.93 (0.88 - 0.98)**	**0.93 (0.88 - 0.98)**	**0.93 (0.88 - 0.98)**	**0.93 (0.88 - 0.98)**	**0.93 (0.88 - 0.98)**
-3	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)
-2	**1.00 (0.99 - 1.02)**	**1.00 (0.99 - 1.02)**	**1.00 (0.99 - 1.02)**	**1.00 (0.99 - 1.02)**	**1.00 (0.99 - 1.02)**	**1.00 (0.99 - 1.02)**
-1	**1.02 (1.00 - 1.05)**	**1.02 (1.00 - 1.05)**	**1.02 (1.00 - 1.05)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**
0	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)
1	1.03 (1.01 - 1.06)	1.04 (1.01 - 1.06)	1.04 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)	1.03 (1.01 - 1.06)
2	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**	**1.03 (1.01 - 1.05)**
3	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**	**1.02 (1.00 - 1.04)**
4	**1.01 (0.99 - 1.02)**	**1.01 (0.99 - 1.02)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.02)**
5	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**	**0.99 (0.98 - 1.01)**
6	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)
7	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)	0.97 (0.95 - 1.00)
8	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)
9	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)	0.97 (0.95 - 0.99)
10	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**	**0.98 (0.97 - 1.00)**
11	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**	**1.00 (0.98 - 1.03)**
12	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.10)**	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.09)**	**1.04 (0.99 - 1.09)**
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
11	**0.90 (0.74 - 1.09)**	**0.91 (0.75 - 1.10)**	**0.91 (0.75 - 1.09)**	**0.90 (0.75 - 1.09)**	**0.90 (0.74 - 1.09)**	**0.90 (0.75 - 1.09)**
12	0.96 (0.79 - 1.16)	0.96 (0.79 - 1.17)	0.96 (0.79 - 1.16)	0.96 (0.79 - 1.16)	0.96 (0.79 - 1.16)	0.96 (0.79 - 1.16)
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
11	**0.90 (0.74 - 1.09)**	**0.91 (0.75 - 1.09)**	**0.90 (0.75 - 1.09)**	**0.90 (0.75 - 1.09)**	**0.91 (0.75 - 1.10)**	**0.91 (0.75 - 1.10)**
12	**0.96 (0.79 - 1.16)**	**0.96 (0.79 - 1.16)**	**0.96 (0.79 - 1.16)**	**0.96 (0.79 - 1.16)**	**0.96 (0.79 - 1.16)**	**0.96 (0.79 - 1.16)**
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
11	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)
12	0.98 (0.89 - 1.09)	0.99 (0.89 - 1.09)	0.98 (0.89 - 1.09)	0.99 (0.89 - 1.09)	0.99 (0.89 - 1.09)	0.99 (0.89 - 1.09)

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Table A.4: Risk ratios for covariate cleft lip with or without cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
11	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)	0.97 (0.88 - 1.07)
12	0.98 (0.89 - 1.09)	0.99 (0.89 - 1.09)	0.99 (0.89 - 1.09)	0.98 (0.89 - 1.09)	0.98 (0.89 - 1.09)	0.99 (0.89 - 1.09)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.5: Risk ratios for covariate cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
11	1.04 (0.92 - 1.17)	1.04 (0.92 - 1.18)	1.04 (0.92 - 1.17)	1.04 (0.92 - 1.17)	1.04 (0.92 - 1.17)	1.04 (0.92 - 1.17)
12	0.97 (0.87 - 1.10)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
11	NA	1.04 (0.92 - 1.17)	1.05 (0.93 - 1.18)	1.04 (0.92 - 1.18)	1.04 (0.92 - 1.17)	1.04 (0.92 - 1.17)
12	NA	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)	0.97 (0.86 - 1.09)
Weekly Ozone peak concentration, composite of grass and trees within buffer						
3	NA	0.98 (0.90 - 1.06)	0.97 (0.90 - 1.06)	0.97 (0.90 - 1.06)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)
4	1.01 (0.93 - 1.10)	**1.06 (1.00 - 1.12)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**
5	**1.06 (1.00 - 1.13)**	1.05 (0.99 - 1.11)	1.05 (0.99 - 1.10)	1.05 (0.99 - 1.10)	1.05 (0.99 - 1.10)	1.05 (0.99 - 1.10)
6	1.02 (0.97 - 1.08)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)
7	0.96 (0.92 - 1.01)	0.96 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)
8	**0.94 (0.89 - 0.99)**	**0.95 (0.90 - 1.00)**	0.95 (0.91 - 1.00)	0.95 (0.91 - 1.00)	0.95 (0.91 - 1.00)	0.95 (0.90 - 1.00)
9	0.96 (0.91 - 1.00)	0.97 (0.92 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)
10	1.01 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)
11	**1.05 (0.98 - 1.11)**	**1.03 (0.98 - 1.09)**	**1.03 (0.98 - 1.09)**	**1.03 (0.98 - 1.09)**	**1.03 (0.98 - 1.09)**	**1.03 (0.98 - 1.09)**
12	**1.01 (0.92 - 1.09)**	**1.01 (0.93 - 1.10)**	**1.01 (0.93 - 1.10)**	**1.01 (0.93 - 1.10)**	**1.01 (0.93 - 1.10)**	**1.01 (0.93 - 1.10)**
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
3	**NA**	**0.97 (0.89 - 1.06)**	**0.97 (0.89 - 1.06)**	**0.97 (0.89 - 1.06)**	**0.97 (0.89 - 1.06)**	**0.97 (0.89 - 1.06)**
4	**NA**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**	**1.06 (1.00 - 1.11)**
5	**NA**	**1.05 (0.99 - 1.11)**	**1.05 (0.99 - 1.10)**	**1.05 (0.99 - 1.10)**	**1.05 (0.99 - 1.10)**	**1.05 (0.99 - 1.10)**
6	NA	1.01 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)	1.00 (0.96 - 1.05)
7	NA	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.96 (0.92 - 1.01)
8	NA	0.95 (0.91 - 1.00)	0.95 (0.91 - 1.00)	0.95 (0.91 - 1.00)	0.95 (0.91 - 1.00)	**0.95 (0.90 - 1.00)**
9	NA	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)	0.97 (0.93 - 1.01)
10	NA	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)	1.00 (0.95 - 1.06)
11	NA	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)
12	NA	1.01 (0.93 - 1.09)	1.01 (0.93 - 1.09)	1.01 (0.93 - 1.10)	1.01 (0.93 - 1.10)	1.01 (0.93 - 1.10)

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Table A.5: Risk ratios for covariate cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
0	0.92 (0.85 - 0.99)	0.92 (0.85 - 0.99)	0.92 (0.85 - 0.99)	0.92 (0.85 - 0.99)	0.92 (0.85 - 0.99)	0.92 (0.85 - 0.99)
1	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)
2	0.94 (0.89 - 0.99)	0.94 (0.89 - 0.99)	0.94 (0.89 - 0.99)	0.94 (0.89 - 0.99)	0.94 (0.89 - 0.99)	0.94 (0.89 - 0.99)
3	0.95 (0.91 - 0.99)	0.95 (0.91 - 0.99)	0.95 (0.91 - 0.99)	0.95 (0.91 - 0.99)	0.95 (0.91 - 0.99)	0.95 (0.91 - 1.00)
4	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)
5	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
6	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)
7	0.99 (0.97 - 1.02)	0.99 (0.97 - 1.02)	1.00 (0.97 - 1.02)	1.00 (0.97 - 1.02)	1.00 (0.97 - 1.02)	1.00 (0.97 - 1.02)
8	1.01 (0.97 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)
9	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)
10	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)
11	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
12	1.05 (0.99 - 1.13)	1.05 (0.99 - 1.13)	1.05 (0.99 - 1.13)	1.05 (0.99 - 1.13)	1.06 (0.99 - 1.13)	1.06 (0.99 - 1.13)
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
0	NA	**0.92 (0.85 - 0.99)**	**0.92 (0.85 - 0.99)**	**0.92 (0.85 - 0.99)**	**0.92 (0.85 - 0.99)**	**0.92 (0.85 - 0.99)**
1	NA	**0.93 (0.87 - 0.99)**	**0.93 (0.87 - 0.99)**	**0.93 (0.87 - 0.99)**	**0.93 (0.87 - 0.99)**	**0.93 (0.87 - 0.99)**
2	NA	**0.94 (0.89 - 0.99)**	**0.94 (0.89 - 0.99)**	**0.94 (0.89 - 0.99)**	**0.94 (0.89 - 0.99)**	**0.94 (0.89 - 0.99)**
3	NA	**0.95 (0.91 - 0.99)**	**0.95 (0.91 - 0.99)**	**0.95 (0.91 - 0.99)**	**0.95 (0.91 - 0.99)**	**0.95 (0.91 - 0.99)**
4	NA	**0.96 (0.92 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**
5	NA	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
6	NA	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)	0.98 (0.96 - 1.01)
7	NA	0.99 (0.97 - 1.02)	0.99 (0.97 - 1.02)	1.00 (0.97 - 1.02)	1.00 (0.97 - 1.02)	1.00 (0.97 - 1.02)
8	NA	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)
9	NA	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)
10	NA	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.08)
11	NA	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
12	NA	1.05 (0.98 - 1.12)	1.05 (0.99 - 1.13)	1.05 (0.99 - 1.13)	1.06 (0.99 - 1.13)	1.06 (0.99 - 1.13)

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Table A.5: Risk ratios for covariate cleft palate 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
0	NA	**0.96 (0.92 - 1.00)**	NA	NA	NA	NA
1	NA	**0.96 (0.93 - 1.00)**	NA	NA	NA	NA
2	0.95 (0.90 - 1.00)	0.97 (0.94 - 1.00)	0.95 (0.90 - 1.00)	0.95 (0.90 - 1.00)	0.95 (0.90 - 1.00)	0.95 (0.90 - 1.00)
3	0.96 (0.92 - 1.00)	0.97 (0.95 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)
4	0.96 (0.93 - 1.00)	0.98 (0.96 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)	0.96 (0.93 - 1.00)
5	**0.97 (0.95 - 1.00)**	0.99 (0.97 - 1.00)	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**
6	0.98 (0.96 - 1.00)	0.99 (0.98 - 1.01)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)
7	0.99 (0.98 - 1.01)	1.00 (0.98 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)
8	**1.00 (0.98 - 1.02)**	**1.00 (0.99 - 1.02)**	**1.00 (0.98 - 1.02)**	**1.00 (0.98 - 1.02)**	**1.00 (0.98 - 1.02)**	**1.00 (0.98 - 1.02)**
9	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**	**1.01 (0.99 - 1.03)**
10	**1.02 (0.99 - 1.05)**	**1.01 (0.99 - 1.04)**	**1.02 (0.99 - 1.05)**	**1.02 (0.99 - 1.05)**	**1.02 (0.99 - 1.05)**	**1.02 (0.99 - 1.05)**
11	1.03 (0.99 - 1.07)	1.02 (0.99 - 1.05)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)
12	1.04 (0.99 - 1.08)	1.03 (0.99 - 1.06)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
2	NA	**0.95 (0.90 - 0.99)**	**0.95 (0.90 - 1.00)**	**0.95 (0.90 - 1.00)**	**0.95 (0.90 - 1.00)**	**0.95 (0.90 - 0.99)**
3	NA	**0.95 (0.92 - 1.00)**	**0.96 (0.92 - 1.00)**	**0.96 (0.92 - 1.00)**	**0.96 (0.92 - 1.00)**	**0.96 (0.92 - 1.00)**
4	NA	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**
5	NA	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**	**0.97 (0.95 - 1.00)**
6	NA	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)	0.98 (0.96 - 1.00)
7	NA	0.99 (0.97 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)	0.99 (0.98 - 1.01)
8	NA	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)
9	NA	1.01 (0.99 - 1.03)	1.01 (0.99 - 1.03)	1.01 (0.99 - 1.03)	1.01 (0.99 - 1.03)	1.01 (0.99 - 1.03)
10	NA	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)
11	NA	1.03 (0.99 - 1.06)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)
12	NA	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.09)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.6: Risk ratios for covariate cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
5	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)
6	1.08 (0.97 - 1.19)	1.07 (0.97 - 1.19)	1.08 (0.97 - 1.19)	1.08 (0.97 - 1.20)	1.08 (0.97 - 1.19)	1.08 (0.97 - 1.19)
7	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)
8	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)
9	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)
10	1.05 (0.97 - 1.13)	1.04 (0.96 - 1.13)	1.05 (0.97 - 1.13)	1.05 (0.97 - 1.13)	1.05 (0.97 - 1.13)	1.05 (0.97 - 1.13)
11	1.09 (0.99 - 1.21)	1.09 (0.98 - 1.21)	1.10 (0.99 - 1.22)	1.10 (0.99 - 1.22)	1.10 (0.99 - 1.22)	1.10 (0.99 - 1.22)
12	0.93 (0.82 - 1.05)	0.93 (0.82 - 1.05)	0.93 (0.81 - 1.05)	0.93 (0.81 - 1.05)	0.93 (0.81 - 1.05)	0.92 (0.81 - 1.05)
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
5	NA	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)	0.95 (0.83 - 1.09)
6	NA	1.08 (0.97 - 1.20)	1.08 (0.97 - 1.20)	1.08 (0.97 - 1.20)	1.08 (0.97 - 1.19)	1.08 (0.97 - 1.20)
7	NA	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.11)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)	1.02 (0.94 - 1.10)
8	NA	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)
9	NA	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.05)
10	NA	1.05 (0.97 - 1.13)	1.04 (0.96 - 1.13)	1.05 (0.97 - 1.13)	1.05 (0.97 - 1.13)	1.05 (0.97 - 1.13)
11	NA	1.10 (0.99 - 1.22)	1.09 (0.99 - 1.21)	1.10 (0.99 - 1.22)	1.10 (0.99 - 1.22)	1.10 (0.99 - 1.22)
12	NA	0.93 (0.81 - 1.05)	0.93 (0.82 - 1.05)	0.93 (0.81 - 1.05)	0.92 (0.81 - 1.05)	0.93 (0.81 - 1.05)
Weekly Ozone peak concentration, composite of grass and trees within buffer						
1	NA	1.07 (1.00 - 1.16)	1.07 (1.00 - 1.15)	1.07 (1.00 - 1.15)	1.07 (1.00 - 1.15)	1.07 (1.00 - 1.15)
2	NA	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.05)
3	NA	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)
4	NA	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)	0.96 (0.92 - 1.00)
5	NA	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**
6	NA	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
7	NA	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)
8	0.97 (0.89 - 1.06)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)
9	1.01 (0.94 - 1.09)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)
10	1.01 (0.96 - 1.07)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (0.99 - 1.06)
11	1.01 (0.93 - 1.09)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)

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Table A.6: Risk ratios for covariate cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
12	1.01 (0.93 - 1.10)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
1	NA	1.07 (1.00 - 1.15)	NA	NA	1.07 (1.00 - 1.15)	1.07 (1.00 - 1.15)
2	NA	1.01 (0.98 - 1.05)	NA	NA	1.01 (0.98 - 1.05)	1.01 (0.98 - 1.04)
3	NA	0.98 (0.94 - 1.01)	NA	NA	0.98 (0.94 - 1.01)	0.98 (0.94 - 1.01)
4	NA	0.96 (0.92 - 1.00)	NA	NA	0.96 (0.93 - 1.00)	0.96 (0.92 - 1.00)
5	NA	**0.96 (0.93 - 1.00)**	NA	NA	**0.96 (0.93 - 1.00)**	**0.96 (0.93 - 1.00)**
6	NA	0.97 (0.94 - 1.00)	NA	NA	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
7	NA	0.99 (0.96 - 1.02)	NA	NA	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)
8	NA	1.01 (0.97 - 1.04)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)	1.01 (0.97 - 1.04)	1.01 (0.97 - 1.04)
9	NA	1.02 (0.98 - 1.06)	1.01 (0.94 - 1.10)	1.01 (0.94 - 1.10)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)
10	NA	1.03 (0.99 - 1.06)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.03 (0.99 - 1.06)	1.03 (1.00 - 1.06)
11	NA	1.02 (0.99 - 1.05)	1.00 (0.93 - 1.08)	1.00 (0.93 - 1.08)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)
12	NA	1.00 (0.93 - 1.07)	1.01 (0.93 - 1.10)	1.01 (0.93 - 1.10)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
-2	**0.86 (0.77 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.76 - 0.97)**	**0.86 (0.77 - 0.97)**
-1	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**
0	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**
1	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)
2	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)
3	1.01 (0.96 - 1.07)	1.02 (0.97 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.02 (0.97 - 1.07)	1.02 (0.97 - 1.07)
4	1.03 (0.98 - 1.08)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)
5	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
6	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
7	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)
8	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)
9	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.02 (0.97 - 1.06)
10	0.99 (0.94 - 1.06)	0.99 (0.93 - 1.05)	0.99 (0.94 - 1.06)	0.99 (0.94 - 1.06)	0.99 (0.94 - 1.06)	1.00 (0.94 - 1.06)
11	0.97 (0.89 - 1.06)	0.96 (0.88 - 1.05)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)
12	0.94 (0.83 - 1.06)	0.93 (0.83 - 1.06)	0.94 (0.83 - 1.06)	0.94 (0.83 - 1.06)	0.94 (0.83 - 1.06)	0.94 (0.83 - 1.06)

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Table A.6: Risk ratios for covariate cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
-2	NA	**0.86 (0.76 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.77 - 0.97)**	**0.86 (0.76 - 0.97)**
-1	NA	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**	**0.90 (0.83 - 0.98)**
0	NA	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**	**0.94 (0.88 - 1.00)**
1	NA	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)	0.97 (0.92 - 1.02)
2	NA	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)	0.99 (0.95 - 1.04)
3	NA	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.02 (0.97 - 1.07)	1.01 (0.96 - 1.07)
4	NA	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)
5	NA	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.98 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
6	NA	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)	1.04 (0.99 - 1.10)
7	NA	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)	1.04 (0.99 - 1.09)
8	NA	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)
9	NA	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.02 (0.97 - 1.06)
10	NA	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.05)	0.99 (0.94 - 1.06)	0.99 (0.94 - 1.06)	1.00 (0.94 - 1.06)
11	NA	0.96 (0.88 - 1.05)	0.97 (0.89 - 1.05)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)	0.97 (0.89 - 1.06)
12	NA	0.93 (0.82 - 1.05)	0.93 (0.83 - 1.06)	0.94 (0.83 - 1.06)	0.94 (0.83 - 1.06)	0.94 (0.83 - 1.06)
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
-2	NA	NA	NA	NA	**0.94 (0.88 - 1.00)**	NA
-1	NA	NA	NA	NA	0.96 (0.91 - 1.00)	NA
0	NA	NA	NA	NA	0.97 (0.94 - 1.01)	NA
1	NA	NA	NA	NA	0.99 (0.96 - 1.02)	NA
2	NA	NA	NA	0.94 (0.87 - 1.02)	1.00 (0.98 - 1.03)	NA
3	0.94 (0.86 - 1.02)	0.94 (0.86 - 1.02)	0.94 (0.86 - 1.02)	0.97 (0.93 - 1.02)	1.01 (0.98 - 1.04)	0.94 (0.86 - 1.02)
4	0.98 (0.93 - 1.03)	0.98 (0.93 - 1.03)	0.98 (0.93 - 1.03)	1.00 (0.97 - 1.03)	1.02 (0.99 - 1.05)	0.98 (0.93 - 1.03)
5	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.01 (0.98 - 1.04)
6	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.02 (0.99 - 1.05)	1.03 (0.99 - 1.07)
7	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (1.00 - 1.09)	1.03 (0.99 - 1.08)	1.02 (0.99 - 1.04)	1.04 (1.00 - 1.09)
8	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.03 (0.99 - 1.07)	1.01 (0.99 - 1.03)	1.04 (0.99 - 1.08)
9	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.01 (0.98 - 1.05)	1.00 (0.98 - 1.03)	1.02 (0.98 - 1.06)
10	1.00 (0.96 - 1.03)	0.99 (0.96 - 1.03)	1.00 (0.96 - 1.03)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)	1.00 (0.96 - 1.03)
11	0.96 (0.91 - 1.01)	0.96 (0.91 - 1.01)	0.96 (0.91 - 1.01)	0.96 (0.92 - 1.01)	0.97 (0.93 - 1.02)	0.96 (0.91 - 1.01)

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Table A.6: Risk ratios for covariate cleft palate 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
12	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	0.92 (0.85 - 1.00)	0.96 (0.90 - 1.02)	**0.91 (0.84 - 1.00)**
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
-2	NA	**0.93 (0.88 - 1.00)**	NA	NA	**0.94 (0.88 - 1.00)**	NA
-1	NA	**0.95 (0.91 - 1.00)**	NA	NA	0.96 (0.91 - 1.00)	NA
0	NA	0.97 (0.94 - 1.01)	NA	NA	0.97 (0.94 - 1.01)	NA
1	NA	0.99 (0.96 - 1.01)	NA	NA	0.99 (0.96 - 1.02)	NA
2	NA	1.00 (0.98 - 1.03)	NA	NA	1.00 (0.98 - 1.03)	0.94 (0.86 - 1.02)
3	NA	1.01 (0.98 - 1.04)	0.94 (0.86 - 1.02)	0.94 (0.86 - 1.02)	1.01 (0.98 - 1.04)	0.97 (0.93 - 1.02)
4	NA	1.02 (0.99 - 1.05)	0.98 (0.93 - 1.03)	0.98 (0.93 - 1.03)	1.02 (0.99 - 1.05)	1.00 (0.97 - 1.03)
5	NA	1.02 (0.99 - 1.05)	1.01 (0.98 - 1.04)	1.01 (0.98 - 1.04)	1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)
6	NA	1.02 (0.99 - 1.05)	1.03 (0.99 - 1.07)	1.03 (0.99 - 1.07)	1.02 (0.99 - 1.05)	1.03 (0.99 - 1.07)
7	NA	1.02 (0.99 - 1.04)	1.04 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.02 (0.99 - 1.04)	1.03 (0.99 - 1.08)
8	NA	1.01 (0.99 - 1.03)	1.03 (0.99 - 1.08)	1.04 (0.99 - 1.08)	1.01 (0.99 - 1.03)	1.03 (0.99 - 1.07)
9	NA	1.00 (0.98 - 1.02)	1.02 (0.98 - 1.06)	1.02 (0.98 - 1.06)	1.00 (0.98 - 1.03)	1.01 (0.98 - 1.05)
10	NA	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.03)	0.99 (0.96 - 1.03)	0.99 (0.96 - 1.02)	0.99 (0.96 - 1.02)
11	NA	0.97 (0.93 - 1.02)	0.96 (0.91 - 1.01)	0.96 (0.91 - 1.01)	0.97 (0.93 - 1.02)	0.96 (0.92 - 1.01)
12	NA	0.95 (0.89 - 1.02)	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	0.96 (0.90 - 1.02)	0.93 (0.85 - 1.00)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.7: Risk ratios for covariate craniosynostosis 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
6	1.07 (0.94 - 1.22)	1.07 (0.94 - 1.21)	1.07 (0.94 - 1.21)	1.06 (0.94 - 1.21)	1.06 (0.93 - 1.21)	1.06 (0.93 - 1.21)
7	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**
8	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.92 (0.84 - 1.00)**	**0.92 (0.84 - 1.00)**	**0.92 (0.84 - 1.00)**
9	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)
10	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)
11	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.19)**	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.18)**
12	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.07)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
6	1.07 (0.94 - 1.22)	1.07 (0.94 - 1.22)	1.07 (0.94 - 1.21)	1.07 (0.94 - 1.21)	1.07 (0.94 - 1.21)	1.07 (0.94 - 1.22)
7	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**
8	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.92 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**
9	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)	1.00 (0.93 - 1.07)
10	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.01 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)	1.09 (1.00 - 1.18)
11	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.18)**	**1.10 (1.01 - 1.19)**	**1.09 (1.01 - 1.18)**	**1.09 (1.01 - 1.18)**	**1.10 (1.01 - 1.19)**
12	0.94 (0.82 - 1.07)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)	0.93 (0.82 - 1.06)
Weekly Ozone peak concentration, composite of grass and trees within buffer						
4	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.05)	0.96 (0.88 - 1.05)	0.96 (0.88 - 1.05)
5	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)
6	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)
7	0.96 (0.91 - 1.00)	0.96 (0.91 - 1.00)	0.96 (0.91 - 1.00)	0.95 (0.91 - 1.00)	0.96 (0.91 - 1.00)	0.96 (0.91 - 1.00)
8	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)
9	0.96 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)
10	1.03 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)
11	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)
12	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)

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Table A.7: Risk ratios for covariate craniosynostosis 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
4	**0.96 (0.88 - 1.05)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**
5	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)	1.05 (0.99 - 1.12)
6	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)
7	**0.96 (0.91 - 1.00)**	**0.96 (0.91 - 1.00)**	**0.96 (0.91 - 1.00)**	**0.96 (0.91 - 1.00)**	**0.95 (0.91 - 1.00)**	**0.95 (0.91 - 1.00)**
8	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.98)
9	0.96 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.97 (0.92 - 1.01)	0.96 (0.92 - 1.01)	0.96 (0.92 - 1.01)
10	1.03 (0.98 - 1.09)	1.03 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)	1.04 (0.98 - 1.09)
11	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)	1.08 (1.02 - 1.15)
12	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)	0.99 (0.91 - 1.08)
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
9	**0.79 (0.63 - 1.01)**	**0.81 (0.64 - 1.02)**	**0.80 (0.63 - 1.02)**	**0.81 (0.64 - 1.02)**	**0.80 (0.63 - 1.01)**	**0.80 (0.63 - 1.02)**
10	1.13 (0.96 - 1.32)	1.12 (0.96 - 1.31)	1.13 (0.96 - 1.32)	1.13 (0.96 - 1.32)	1.13 (0.96 - 1.32)	1.12 (0.96 - 1.31)
11	1.16 (0.99 - 1.36)	1.15 (0.98 - 1.36)	1.16 (0.99 - 1.36)	1.16 (0.99 - 1.36)	1.16 (0.99 - 1.36)	1.15 (0.98 - 1.35)
12	**0.87 (0.69 - 1.11)**	**0.88 (0.69 - 1.12)**	**0.87 (0.69 - 1.11)**	**0.88 (0.69 - 1.12)**	**0.87 (0.69 - 1.11)**	**0.87 (0.69 - 1.11)**
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
9	0.80 (0.63 - 1.01)	0.81 (0.64 - 1.02)	0.80 (0.63 - 1.01)	0.80 (0.63 - 1.02)	0.80 (0.63 - 1.01)	0.79 (0.63 - 1.01)
10	1.13 (0.96 - 1.32)	1.12 (0.96 - 1.31)	1.12 (0.96 - 1.31)	1.12 (0.96 - 1.31)	1.12 (0.96 - 1.32)	1.13 (0.96 - 1.32)
11	1.16 (0.99 - 1.36)	1.15 (0.98 - 1.35)	1.16 (0.99 - 1.36)	1.15 (0.98 - 1.36)	1.16 (0.99 - 1.36)	1.16 (0.99 - 1.36)
12	0.88 (0.69 - 1.12)	0.88 (0.69 - 1.12)	0.88 (0.69 - 1.12)	0.87 (0.68 - 1.11)	0.87 (0.68 - 1.11)	0.87 (0.68 - 1.10)
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
1	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.02)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.02)	0.91 (0.82 - 1.02)
2	**1.06 (1.00 - 1.13)**	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)
3	1.10 (1.03 - 1.18)	1.10 (1.03 - 1.18)	1.10 (1.02 - 1.18)	1.10 (1.03 - 1.18)	1.10 (1.03 - 1.18)	1.10 (1.03 - 1.18)
4	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.13)	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.14)
5	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)
6	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)
7	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)
8	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)
9	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**

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Table A.7: Risk ratios for covariate craniosynostosis 12-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
10	**1.01 (0.95 - 1.08)**	**1.02 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**
11	1.03 (0.96 - 1.09)	1.03 (0.96 - 1.10)	1.03 (0.97 - 1.10)	1.03 (0.96 - 1.10)	1.03 (0.96 - 1.09)	1.03 (0.96 - 1.10)
12	0.98 (0.87 - 1.11)	0.98 (0.87 - 1.11)	0.98 (0.87 - 1.11)	0.98 (0.87 - 1.11)	0.98 (0.86 - 1.10)	0.98 (0.86 - 1.10)
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
1	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)	0.92 (0.82 - 1.03)
2	**1.07 (1.00 - 1.13)**	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)	1.06 (1.00 - 1.13)
3	1.10 (1.03 - 1.18)	1.10 (1.03 - 1.18)	1.10 (1.02 - 1.18)	1.10 (1.02 - 1.18)	1.10 (1.02 - 1.18)	1.10 (1.02 - 1.18)
4	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.13)	1.07 (1.01 - 1.13)	1.07 (1.01 - 1.14)	1.07 (1.01 - 1.13)	1.07 (1.01 - 1.13)
5	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.02 (0.96 - 1.07)	1.01 (0.96 - 1.07)	1.01 (0.96 - 1.07)
6	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.92 - 1.03)	0.97 (0.91 - 1.03)	0.97 (0.91 - 1.03)
7	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)	0.95 (0.89 - 1.01)
8	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)	0.95 (0.90 - 1.01)
9	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**	**0.98 (0.93 - 1.04)**
10	**1.01 (0.95 - 1.08)**	**1.02 (0.95 - 1.09)**	**1.01 (0.95 - 1.09)**	**1.01 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**	**1.02 (0.95 - 1.09)**
11	1.03 (0.96 - 1.09)	1.03 (0.96 - 1.10)	1.03 (0.96 - 1.10)	1.03 (0.96 - 1.09)	1.03 (0.96 - 1.09)	1.03 (0.96 - 1.09)
12	0.98 (0.87 - 1.11)	0.98 (0.87 - 1.11)	0.98 (0.87 - 1.11)	0.98 (0.86 - 1.10)	0.98 (0.86 - 1.10)	0.98 (0.86 - 1.10)

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table A.8: Risk ratios for covariate craniosynostosis 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone mean concentration, composite of grass and trees within buffer						
5	0.86 (0.75 - 0.99)	0.86 (0.75 - 0.99)	0.86 (0.75 - 0.99)	0.86 (0.75 - 0.99)	0.86 (0.75 - 0.99)	0.87 (0.75 - 0.99)
6	1.20 (1.08 - 1.33)	1.20 (1.09 - 1.34)	1.21 (1.09 - 1.34)	1.21 (1.09 - 1.34)	1.20 (1.09 - 1.34)	1.20 (1.08 - 1.33)
7	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.11 (1.03 - 1.21)	1.11 (1.03 - 1.21)
8	0.96 (0.88 - 1.05)	0.96 (0.88 - 1.05)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.04)	0.96 (0.88 - 1.05)
9	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 1.00)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 0.99)**	**0.91 (0.84 - 1.00)**	0.92 (0.84 - 1.00)
10	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.08)**	**0.99 (0.91 - 1.08)**
11	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**
12	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.86 (0.75 - 0.99)**
Weekly Ozone mean concentration, composite of grass, trees, and water within buffer						
5	0.86 (0.75 - 0.99)	0.86 (0.75 - 0.99)	0.87 (0.75 - 1.00)	0.87 (0.75 - 1.00)	0.87 (0.75 - 0.99)	0.87 (0.75 - 1.00)
6	1.20 (1.09 - 1.34)	1.20 (1.08 - 1.33)	1.21 (1.09 - 1.34)	1.20 (1.09 - 1.34)	1.20 (1.09 - 1.34)	1.20 (1.09 - 1.34)
7	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.11 (1.03 - 1.21)	1.12 (1.03 - 1.21)	1.12 (1.03 - 1.21)
8	**0.96 (0.88 - 1.05)**	**0.96 (0.88 - 1.05)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.04)**	**0.96 (0.88 - 1.05)**
9	0.91 (0.84 - 1.00)	0.91 (0.84 - 1.00)	0.91 (0.83 - 0.99)	0.91 (0.84 - 1.00)	0.91 (0.84 - 1.00)	0.91 (0.84 - 1.00)
10	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**	**0.99 (0.91 - 1.07)**
11	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.18)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**	**1.07 (0.96 - 1.19)**
12	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**	**0.87 (0.76 - 1.00)**
Weekly Ozone peak concentration, composite of grass and trees within buffer						
3	**0.93 (0.87 - 1.00)**	0.94 (0.88 - 1.00)	**0.93 (0.87 - 1.00)**	**0.94 (0.87 - 1.00)**	**0.93 (0.87 - 1.00)**	**0.93 (0.87 - 1.00)**
4	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)
5	1.01 (0.98 - 1.03)	1.01 (0.98 - 1.03)	1.01 (0.98 - 1.03)	1.01 (0.98 - 1.03)	1.01 (0.98 - 1.03)	1.01 (0.98 - 1.03)
6	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)	1.03 (1.00 - 1.06)
7	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)
8	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)
9	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.03 (1.00 - 1.06)
10	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.03)
11	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
12	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)

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Table A.8: Risk ratios for covariate craniosynostosis 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly Ozone peak concentration, composite of grass, trees, and water within buffer						
3	0.93 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.93 (0.87 - 1.00)	0.93 (0.87 - 1.00)	0.93 (0.87 - 1.00)
4	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)	0.97 (0.94 - 1.01)
5	**1.01 (0.98 - 1.03)**	**1.01 (0.98 - 1.03)**	**1.01 (0.98 - 1.03)**	**1.01 (0.98 - 1.03)**	**1.01 (0.98 - 1.03)**	**1.01 (0.98 - 1.03)**
6	**1.03 (1.00 - 1.06)**	**1.03 (1.00 - 1.06)**	**1.03 (1.00 - 1.06)**	**1.03 (1.00 - 1.06)**	**1.03 (1.00 - 1.06)**	**1.03 (1.00 - 1.06)**
7	**1.04 (1.00 - 1.07)**	**1.04 (1.00 - 1.07)**	**1.04 (1.00 - 1.07)**	**1.04 (1.00 - 1.07)**	**1.04 (1.00 - 1.07)**	**1.04 (1.00 - 1.07)**
8	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)	1.04 (1.00 - 1.07)
9	1.03 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)	1.02 (1.00 - 1.05)
10	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.03)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)	1.00 (0.98 - 1.02)
11	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)	0.97 (0.94 - 1.00)
12	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)	0.93 (0.87 - 0.99)
Weekly $PM_{2.5}$ mean concentration, composite of grass and trees within buffer						
-4	0.86 (0.70 - 1.06)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.86 (0.70 - 1.06)
-3	1.04 (0.95 - 1.14)	1.04 (0.95 - 1.14)	1.04 (0.95 - 1.13)	1.04 (0.95 - 1.14)	1.04 (0.95 - 1.13)	1.04 (0.95 - 1.13)
-2	1.13 (1.03 - 1.25)	1.13 (1.02 - 1.25)	1.13 (1.02 - 1.24)	1.13 (1.02 - 1.25)	1.13 (1.02 - 1.25)	1.13 (1.02 - 1.25)
-1	1.15 (1.03 - 1.29)	1.15 (1.03 - 1.28)	1.14 (1.03 - 1.28)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)
0	1.12 (1.02 - 1.23)	1.12 (1.01 - 1.23)	1.11 (1.01 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.01 - 1.23)
1	1.07 (0.99 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)
2	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.93 - 1.09)
3	0.96 (0.89 - 1.04)	0.96 (0.89 - 1.05)	0.96 (0.89 - 1.05)	0.96 (0.89 - 1.05)	0.96 (0.89 - 1.04)	0.96 (0.88 - 1.04)
4	0.93 (0.86 - 1.01)	0.94 (0.86 - 1.02)	0.94 (0.86 - 1.02)	0.94 (0.86 - 1.02)	0.93 (0.86 - 1.02)	0.93 (0.85 - 1.02)
5	**0.92 (0.85 - 1.00)**	**0.93 (0.85 - 1.00)**	**0.93 (0.86 - 1.00)**	**0.93 (0.85 - 1.00)**	**0.93 (0.85 - 1.00)**	**0.92 (0.85 - 1.00)**
6	**0.93 (0.87 - 1.00)**	**0.94 (0.87 - 1.00)**	**0.94 (0.87 - 1.01)**	**0.94 (0.87 - 1.01)**	**0.94 (0.87 - 1.00)**	**0.93 (0.87 - 1.00)**
7	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.04)**	**0.96 (0.89 - 1.04)**	**0.96 (0.89 - 1.04)**	**0.96 (0.89 - 1.03)**
8	1.00 (0.91 - 1.09)	1.00 (0.91 - 1.09)	1.00 (0.91 - 1.09)	1.00 (0.91 - 1.09)	1.00 (0.91 - 1.09)	1.00 (0.91 - 1.10)
9	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.04 (0.93 - 1.15)
10	**1.05 (0.95 - 1.17)**	**1.05 (0.95 - 1.17)**	**1.05 (0.95 - 1.16)**	**1.05 (0.95 - 1.17)**	**1.05 (0.95 - 1.17)**	**1.05 (0.95 - 1.17)**
11	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.13)	1.03 (0.93 - 1.14)
12	0.95 (0.77 - 1.16)	0.95 (0.77 - 1.17)	0.95 (0.77 - 1.16)	0.95 (0.77 - 1.16)	0.94 (0.77 - 1.16)	0.94 (0.76 - 1.16)

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Table A.8: Risk ratios for covariate craniosynostosis 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	50m buffer	100m buffer	200m buffer	300m buffer	400m buffer	500m buffer
Weekly $PM_{2.5}$ mean concentration, composite of grass, trees, and water within buffer						
-4	0.87 (0.70 - 1.06)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.87 (0.71 - 1.07)	0.87 (0.70 - 1.06)	0.86 (0.70 - 1.06)
-3	**1.04 (0.95 - 1.14)**	**1.04 (0.95 - 1.14)**	**1.04 (0.95 - 1.13)**	**1.04 (0.95 - 1.13)**	**1.04 (0.95 - 1.13)**	**1.04 (0.95 - 1.13)**
-2	**1.13 (1.03 - 1.25)**	**1.13 (1.02 - 1.25)**	**1.13 (1.02 - 1.25)**	**1.13 (1.02 - 1.25)**	**1.13 (1.02 - 1.25)**	**1.13 (1.02 - 1.25)**
-1	1.15 (1.03 - 1.29)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)	1.15 (1.03 - 1.28)
0	1.12 (1.02 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.01 - 1.23)	1.12 (1.02 - 1.23)
1	1.07 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)	1.06 (0.98 - 1.15)
2	1.01 (0.93 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.94 - 1.09)	1.01 (0.93 - 1.09)	1.01 (0.94 - 1.09)
3	**0.96 (0.89 - 1.04)**	**0.96 (0.89 - 1.05)**	**0.96 (0.89 - 1.05)**	**0.96 (0.89 - 1.05)**	**0.96 (0.89 - 1.04)**	**0.96 (0.89 - 1.04)**
4	0.93 (0.85 - 1.01)	0.93 (0.86 - 1.02)	0.93 (0.86 - 1.02)	0.93 (0.86 - 1.02)	0.93 (0.86 - 1.02)	0.93 (0.86 - 1.02)
5	**0.92 (0.85 - 1.00)**	0.93 (0.85 - 1.00)	0.93 (0.85 - 1.00)	0.92 (0.85 - 1.00)	0.92 (0.85 - 1.00)	0.92 (0.85 - 1.00)
6	0.93 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.94 (0.87 - 1.00)	0.93 (0.87 - 1.00)	0.93 (0.87 - 1.00)	0.93 (0.87 - 1.00)
7	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**	**0.96 (0.89 - 1.03)**
8	**1.00 (0.91 - 1.09)**	**1.00 (0.91 - 1.09)**	**1.00 (0.91 - 1.09)**	**1.00 (0.91 - 1.09)**	**1.00 (0.91 - 1.09)**	**1.00 (0.91 - 1.09)**
9	1.04 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)	1.03 (0.93 - 1.15)
10	1.05 (0.95 - 1.17)	1.05 (0.95 - 1.17)	1.05 (0.95 - 1.17)	1.05 (0.95 - 1.16)	1.05 (0.95 - 1.16)	1.05 (0.95 - 1.16)
11	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.14)	1.03 (0.93 - 1.13)	1.03 (0.93 - 1.13)	1.03 (0.93 - 1.13)
12	**0.94 (0.77 - 1.16)**	**0.95 (0.77 - 1.17)**	**0.95 (0.77 - 1.16)**	**0.94 (0.77 - 1.16)**	**0.94 (0.77 - 1.16)**	**0.94 (0.76 - 1.15)**
Weekly $PM_{2.5}$ peak concentration, composite of grass and trees within buffer						
8	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)
9	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.09)	0.97 (0.87 - 1.09)	0.98 (0.88 - 1.09)	0.98 (0.88 - 1.09)
10	1.00 (0.93 - 1.09)	1.00 (0.93 - 1.09)	1.00 (0.93 - 1.09)	1.00 (0.93 - 1.09)	1.00 (0.93 - 1.09)	1.00 (0.93 - 1.09)
11	1.03 (0.92 - 1.14)	1.03 (0.92 - 1.14)	1.02 (0.92 - 1.14)	1.03 (0.92 - 1.14)	1.02 (0.92 - 1.14)	1.02 (0.92 - 1.13)
12	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)
Weekly $PM_{2.5}$ peak concentration, composite of grass, trees, and water within buffer						
8	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)	0.96 (0.84 - 1.09)
9	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.09)	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.08)	0.97 (0.87 - 1.08)
10	1.01 (0.93 - 1.09)	1.00 (0.93 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)	1.00 (0.92 - 1.09)
11	1.03 (0.92 - 1.14)	1.02 (0.92 - 1.14)	1.02 (0.92 - 1.14)	1.02 (0.92 - 1.14)	1.02 (0.92 - 1.13)	1.02 (0.92 - 1.13)
12	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.13)	1.01 (0.90 - 1.14)	1.01 (0.90 - 1.13)

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Table A.8: Risk ratios for covariate craniosynostosis 16-week models of air pollutant and birth defects pairs with green space, New York State outside New York City, 2002 to 2015 *(continued)*

Week	**50m buffer**	**100m buffer**	**200m buffer**	**300m buffer**	**400m buffer**	**500m buffer**

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for maternal education level, maternal smoking, tract-level median income, conception season, and the indicated green space variable. Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

B. Supplemental Tables for Chapter 4

Table B.1: Cumulative risk ratios for covariate models of mixed air pollutants and birth defects, New York State outside New York City, 2002 to 2015

	16 week model		12 week model	
Buffer	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Clubfoot case group, weekly mean concentration				
50m	**0.92 (0.85-0.99)**	1.07 (0.89-1.28)		
100m	**0.92 (0.85-0.99)**	1.06 (0.88-1.28)		
200m	**0.92 (0.85-0.99)**	1.07 (0.89-1.28)		
300m	**0.92 (0.85-1.00)**	1.06 (0.88-1.27)		
400m	**0.92 (0.85-0.99)**	1.06 (0.88-1.28)		
500m	**0.92 (0.85-0.99)**	1.06 (0.88-1.28)		
Clubfoot case group, weekly peak concentration				
50m	0.98 (0.93-1.05)	1.00 (0.90-1.11)		
100m	0.98 (0.93-1.05)	1.00 (0.89-1.11)		
200m	0.98 (0.93-1.05)	1.00 (0.90-1.11)		
300m	0.99 (0.93-1.05)	0.99 (0.89-1.11)		
400m	0.98 (0.93-1.05)	1.00 (0.89-1.11)		
500m	0.98 (0.93-1.05)	1.00 (0.89-1.11)		
Cleft lip with or without cleft palate case group, weekly mean concentration				
50m	0.99 (0.89-1.11)	0.83 (0.64-1.08)	0.97 (0.87-1.09)	0.85 (0.66-1.10)
100m	0.99 (0.89-1.10)	0.85 (0.66-1.11)	0.97 (0.86-1.08)	0.87 (0.68-1.12)
200m	0.99 (0.89-1.10)	0.84 (0.65-1.09)	0.97 (0.87-1.09)	0.86 (0.67-1.11)
300m	0.99 (0.89-1.10)	0.84 (0.65-1.09)	0.97 (0.87-1.09)	0.86 (0.67-1.11)
400m	0.99 (0.89-1.11)	0.83 (0.64-1.08)	0.97 (0.87-1.09)	0.86 (0.67-1.10)
500m	0.99 (0.89-1.10)	0.84 (0.65-1.09)	0.97 (0.86-1.08)	0.86 (0.67-1.11)
Cleft lip with or without cleft palate case group, weekly peak concentration				
50m	0.99 (0.91-1.06)	0.93 (0.81-1.07)	1.01 (0.92-1.10)	0.91 (0.79-1.05)
100m	0.98 (0.91-1.06)	0.94 (0.82-1.08)	1.00 (0.92-1.10)	0.93 (0.81-1.07)
200m	0.98 (0.91-1.06)	0.94 (0.82-1.08)	1.01 (0.92-1.10)	0.92 (0.80-1.06)
300m	0.98 (0.91-1.06)	0.94 (0.82-1.08)	1.01 (0.92-1.10)	0.92 (0.80-1.06)
400m	0.99 (0.91-1.06)	0.94 (0.82-1.07)	1.01 (0.92-1.10)	0.92 (0.80-1.06)
500m	0.98 (0.91-1.06)	0.94 (0.82-1.08)	1.00 (0.92-1.10)	0.92 (0.80-1.06)
Cleft palate case group, weekly mean concentration				
50m	1.03 (0.91-1.16)	0.90 (0.67-1.21)	1.00 (0.90-1.12)	1.08 (0.86-1.36)
100m	1.03 (0.91-1.16)	0.90 (0.67-1.20)	1.00 (0.90-1.12)	1.08 (0.86-1.36)
200m	1.03 (0.91-1.16)	0.90 (0.67-1.21)	1.00 (0.90-1.12)	1.08 (0.86-1.36)
300m	1.03 (0.91-1.16)	0.90 (0.67-1.21)	1.00 (0.90-1.12)	1.08 (0.86-1.36)
400m	1.03 (0.91-1.16)	0.90 (0.67-1.22)	1.00 (0.90-1.12)	1.08 (0.86-1.36)
500m	1.02 (0.90-1.16)	0.91 (0.68-1.23)	1.00 (0.89-1.11)	1.09 (0.87-1.37)
Cleft palate case group, weekly peak concentration				
50m	1.03 (0.94-1.13)	0.90 (0.76-1.05)	1.02 (0.92-1.13)	0.95 (0.80-1.14)

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Table B.1: Cumulative risk ratios for covariate models of mixed air pollutants and birth defects, New York State outside New York City, 2002 to 2015 *(continued)*

	16 week model		12 week model	
Buffer	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
100m	1.03 (0.94-1.13)	0.89 (0.76-1.05)	1.02 (0.91-1.13)	0.94 (0.79-1.13)
200m	1.03 (0.94-1.12)	0.90 (0.77-1.06)	1.01 (0.91-1.13)	0.94 (0.79-1.13)
300m	1.03 (0.94-1.13)	0.90 (0.77-1.06)	1.01 (0.91-1.13)	0.94 (0.78-1.13)
400m	1.03 (0.94-1.13)	0.90 (0.77-1.06)	1.01 (0.91-1.13)	0.94 (0.79-1.13)
500m	1.03 (0.94-1.12)	0.90 (0.77-1.06)	1.01 (0.91-1.13)	0.95 (0.79-1.13)
Craniosynostosis case group, weekly mean concentration				
50m	0.94 (0.82-1.08)	1.03 (0.75-1.42)	0.98 (0.86-1.12)	0.91 (0.67-1.22)
100m	0.94 (0.82-1.07)	1.04 (0.76-1.44)	0.98 (0.86-1.12)	0.92 (0.68-1.23)
200m	0.94 (0.82-1.08)	1.04 (0.75-1.43)	0.98 (0.86-1.12)	0.92 (0.68-1.23)
300m	0.93 (0.81-1.07)	1.04 (0.76-1.44)	0.98 (0.86-1.12)	0.92 (0.68-1.24)
400m	0.94 (0.81-1.07)	1.03 (0.75-1.42)	0.98 (0.86-1.12)	0.91 (0.68-1.22)
500m	0.94 (0.82-1.08)	1.03 (0.75-1.42)	0.99 (0.86-1.13)	0.90 (0.67-1.21)
Craniosynostosis case group, weekly peak concentration				
50m	0.96 (0.87-1.06)	1.00 (0.84-1.19)	0.98 (0.89-1.09)	0.95 (0.80-1.13)
100m	0.96 (0.87-1.06)	1.01 (0.85-1.19)	0.98 (0.89-1.09)	0.96 (0.81-1.13)
200m	0.96 (0.87-1.06)	1.00 (0.84-1.19)	0.98 (0.89-1.09)	0.96 (0.80-1.13)
300m	0.96 (0.87-1.06)	1.01 (0.85-1.19)	0.98 (0.89-1.09)	0.96 (0.81-1.14)
400m	0.96 (0.87-1.06)	1.00 (0.84-1.18)	0.98 (0.88-1.09)	0.95 (0.80-1.13)
500m	0.96 (0.87-1.06)	1.00 (0.84-1.19)	0.98 (0.89-1.09)	0.95 (0.80-1.13)

Note:
NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter
Model was adjusted for O_3, $PM_{2.5}$, maternal education level, maternal smoking, tract-level median income, conception season, and presence of grasses or trees.
Values in bold were significant at $\alpha = 0.05$.

Table B.2: Risk ratios for covariate clubfoot mixed air pollutant models, New York State outside New York City, 2002 to 2015

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Weekly mean concentration					
50m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.23)		
	11	**0.96 (0.93-0.99)**	1.06 (0.96-1.18)		
	10	1.00 (0.97-1.03)	1.02 (0.92-1.13)		
	9	1.05 (0.98-1.13)	0.93 (0.80-1.08)		
100m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.23)		
	11	**0.96 (0.93-0.99)**	1.06 (0.95-1.17)		
	10	1.00 (0.97-1.03)	1.01 (0.92-1.12)		
	9	1.05 (0.98-1.12)	0.93 (0.81-1.08)		
200m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.24)		
	11	**0.96 (0.93-0.99)**	1.06 (0.96-1.17)		
	10	1.00 (0.97-1.03)	1.02 (0.92-1.13)		
	9	1.05 (0.98-1.13)	0.93 (0.81-1.08)		
300m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.23)		
	11	**0.96 (0.93-0.99)**	1.06 (0.95-1.17)		
	10	1.00 (0.97-1.03)	1.01 (0.91-1.12)		
	9	1.05 (0.98-1.13)	0.93 (0.80-1.08)		
400m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.23)		
	11	**0.96 (0.93-0.99)**	1.06 (0.96-1.17)		
	10	1.00 (0.97-1.03)	1.02 (0.92-1.13)		
	9	1.05 (0.98-1.13)	0.93 (0.80-1.08)		
500m buffer	12	**0.91 (0.85-0.98)**	1.06 (0.91-1.23)		
	11	**0.96 (0.93-0.99)**	1.06 (0.96-1.17)		
	10	1.00 (0.97-1.03)	1.02 (0.92-1.13)		
	9	1.05 (0.98-1.12)	0.93 (0.80-1.08)		
Weekly peak concentration					
50m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.05 (1.00-1.09)		
	9	0.99 (0.98-1.00)	1.01 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.05)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.11)		

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Table B.2: Risk ratios for covariate clubfoot mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
100m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.04 (1.00-1.09)		
	9	0.99 (0.99-1.00)	1.01 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.04)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.11)		
200m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.05 (1.00-1.09)		
	9	0.99 (0.98-1.00)	1.02 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.05)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.10)		
300m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.04 (1.00-1.09)		
	9	0.99 (0.99-1.00)	1.01 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.05)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.10)		
400m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.05 (1.00-1.09)		
	9	0.99 (0.99-1.00)	1.01 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.05)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.10)		
500m buffer	12	**0.97 (0.94-0.99)**	0.98 (0.91-1.06)		
	11	**0.97 (0.95-1.00)**	1.04 (1.00-1.09)		
	10	**0.98 (0.97-1.00)**	1.05 (1.00-1.09)		
	9	0.99 (0.98-1.00)	1.02 (0.98-1.05)		
	8	1.00 (0.99-1.01)	0.98 (0.94-1.01)		
	7	1.01 (1.00-1.03)	**0.95 (0.91-0.99)**		
	6	1.02 (1.00-1.04)	0.96 (0.92-1.00)		
	5	**1.03 (1.00-1.06)**	1.03 (0.96-1.10)		

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Table B.2: Risk ratios for covariate clubfoot mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**

Note:
NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter
Model was adjusted for O_3, $PM_{2.5}$, maternal education level, maternal smoking, tract-level median income, conception season, and presence of grasses or trees. Values in bold were significant at $\alpha = 0.05$.
Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table B.3: Risk ratios for covariate cleft lip with or without cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Weekly mean concentration					
50m buffer	12	1.09 (0.97-1.23)	0.96 (0.83-1.10)		
	11	0.96 (0.85-1.07)	0.96 (0.88-1.06)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.97 (0.93-1.02)		
	8	0.91 (0.81-1.01)	0.98 (0.90-1.06)	0.96 (0.86-1.08)	0.96 (0.84-1.11)
	7	1.05 (0.94-1.18)	0.98 (0.86-1.12)	1.04 (0.93-1.16)	0.97 (0.88-1.06)
	6			0.98 (0.90-1.07)	0.97 (0.92-1.02)
	5			0.98 (0.90-1.08)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.90-1.08)
	3			0.97 (0.86-1.09)	0.99 (0.86-1.14)
100m buffer	12	1.09 (0.97-1.23)	0.96 (0.84-1.10)		
	11	0.96 (0.85-1.07)	0.97 (0.88-1.06)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.98 (0.93-1.02)		
	8	0.90 (0.81-1.01)	0.98 (0.90-1.07)	0.96 (0.85-1.07)	0.97 (0.84-1.11)
	7	1.06 (0.94-1.19)	0.99 (0.87-1.12)	1.04 (0.93-1.16)	0.97 (0.89-1.06)
	6			0.98 (0.90-1.07)	0.98 (0.93-1.02)
	5			0.98 (0.90-1.07)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.90-1.08)
	3			0.97 (0.86-1.09)	0.99 (0.86-1.14)
200m buffer	12	1.09 (0.97-1.23)	0.96 (0.83-1.10)		
	11	0.96 (0.86-1.08)	0.96 (0.88-1.06)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.97 (0.93-1.02)		
	8	0.91 (0.81-1.01)	0.98 (0.90-1.07)	0.96 (0.85-1.08)	0.97 (0.84-1.11)
	7	1.05 (0.94-1.18)	0.98 (0.86-1.12)	1.04 (0.93-1.16)	0.97 (0.89-1.06)
	6			0.98 (0.90-1.07)	0.97 (0.93-1.02)
	5			0.98 (0.90-1.07)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.89-1.07)
	3			0.97 (0.86-1.09)	0.98 (0.85-1.13)
300m buffer	12	1.09 (0.97-1.23)	0.96 (0.83-1.10)		
	11	0.96 (0.86-1.08)	0.96 (0.88-1.06)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.97 (0.93-1.02)		
	8	0.90 (0.81-1.01)	0.98 (0.90-1.06)	0.96 (0.85-1.07)	0.97 (0.84-1.11)
	7	1.06 (0.94-1.19)	0.98 (0.86-1.12)	1.04 (0.93-1.16)	0.97 (0.89-1.06)
	6			0.98 (0.90-1.07)	0.97 (0.93-1.02)
	5			0.98 (0.90-1.07)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.89-1.07)
	3			0.97 (0.86-1.09)	0.98 (0.85-1.13)

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Table B.3: Risk ratios for covariate cleft lip with or without cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
400m buffer	12	1.10 (0.97-1.23)	0.96 (0.83-1.10)		
	11	0.96 (0.85-1.08)	0.96 (0.88-1.05)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.97 (0.93-1.02)		
	8	0.90 (0.81-1.01)	0.98 (0.90-1.07)	0.96 (0.85-1.08)	0.97 (0.84-1.11)
	7	1.05 (0.94-1.18)	0.98 (0.86-1.12)	1.04 (0.93-1.16)	0.97 (0.89-1.06)
	6			0.98 (0.90-1.07)	0.97 (0.93-1.02)
	5			0.98 (0.90-1.07)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.89-1.07)
	3			0.97 (0.86-1.09)	0.98 (0.85-1.13)
500m buffer	12	1.09 (0.97-1.23)	0.96 (0.84-1.10)		
	11	0.96 (0.85-1.07)	0.97 (0.88-1.06)		
	10	1.01 (0.92-1.10)	0.97 (0.92-1.02)		
	9	0.98 (0.90-1.07)	0.97 (0.93-1.02)		
	8	0.90 (0.81-1.01)	0.98 (0.90-1.06)	0.96 (0.85-1.07)	0.97 (0.84-1.11)
	7	1.05 (0.94-1.18)	0.98 (0.86-1.12)	1.04 (0.93-1.16)	0.97 (0.89-1.06)
	6			0.98 (0.90-1.07)	0.97 (0.93-1.02)
	5			0.98 (0.90-1.07)	0.98 (0.93-1.03)
	4			1.04 (0.93-1.17)	0.98 (0.89-1.07)
	3			0.97 (0.86-1.09)	0.98 (0.85-1.13)
Weekly peak concentration					
50m buffer	12	**1.09 (1.00-1.18)**	0.96 (0.89-1.04)		
	11	0.97 (0.91-1.04)	0.97 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.01)		
	9	1.01 (0.95-1.08)	1.00 (0.95-1.04)		
	8	0.94 (0.86-1.01)	1.01 (0.93-1.09)	0.95 (0.87-1.03)	1.01 (0.91-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.95-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	1.00 (0.90-1.10)
100m buffer	12	**1.09 (1.00-1.18)**	0.97 (0.89-1.05)		
	11	0.97 (0.91-1.04)	0.98 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.02)		
	9	1.01 (0.94-1.08)	1.00 (0.96-1.05)		
	8	0.93 (0.86-1.01)	1.01 (0.94-1.09)	0.94 (0.87-1.02)	1.01 (0.92-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.96-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	1.00 (0.90-1.10)

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Table B.3: Risk ratios for covariate cleft lip with or without cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
200m buffer	12	**1.09 (1.00-1.18)**	0.96 (0.89-1.04)		
	11	0.97 (0.91-1.04)	0.98 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.01)		
	9	1.01 (0.94-1.08)	1.00 (0.96-1.04)		
	8	0.93 (0.86-1.01)	1.01 (0.94-1.09)	0.94 (0.87-1.02)	1.01 (0.92-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.96-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	1.00 (0.90-1.10)
300m buffer	12	**1.09 (1.00-1.18)**	0.96 (0.89-1.04)		
	11	0.97 (0.91-1.04)	0.98 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.01)		
	9	1.01 (0.95-1.08)	1.00 (0.96-1.04)		
	8	0.93 (0.86-1.01)	1.01 (0.94-1.09)	0.94 (0.87-1.02)	1.01 (0.92-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.96-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	1.00 (0.90-1.10)
400m buffer	12	**1.09 (1.00-1.18)**	0.96 (0.89-1.04)		
	11	0.97 (0.91-1.04)	0.97 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.01)		
	9	1.01 (0.95-1.08)	1.00 (0.96-1.04)		
	8	0.93 (0.86-1.01)	1.01 (0.94-1.09)	0.94 (0.87-1.02)	1.01 (0.92-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.96-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	0.99 (0.90-1.10)
500m buffer	12	**1.09 (1.00-1.18)**	0.96 (0.89-1.04)		
	11	0.97 (0.91-1.04)	0.98 (0.93-1.02)		
	10	0.99 (0.94-1.04)	0.99 (0.96-1.02)		
	9	1.01 (0.94-1.08)	1.00 (0.96-1.04)		
	8	0.93 (0.86-1.01)	1.01 (0.94-1.09)	0.94 (0.87-1.02)	1.01 (0.92-1.12)
	7			1.00 (0.93-1.08)	0.99 (0.94-1.04)
	6			1.01 (0.95-1.07)	0.97 (0.92-1.03)
	5			1.01 (0.95-1.08)	0.97 (0.91-1.03)
	4			1.03 (0.96-1.11)	0.98 (0.93-1.03)
	3			1.01 (0.93-1.10)	0.99 (0.90-1.10)

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Table B.3: Risk ratios for covariate cleft lip with or without cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**

Note:

NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter

Model was adjusted for O_3, $PM_{2.5}$, maternal education level, maternal smoking, tract-level median income, conception season, and presence of grasses or trees. Values in bold were significant at $\alpha = 0.05$.

Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table B.4: Risk ratios for covariate cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Weekly mean concentration					
50m buffer	12	0.95 (0.82-1.09)	0.91 (0.73-1.14)		
	11	1.10 (0.96-1.25)	0.90 (0.81-1.00)		
	10	1.08 (0.97-1.20)	0.92 (0.81-1.04)		
	9	1.00 (0.90-1.11)	0.97 (0.85-1.10)		
	8	0.94 (0.82-1.07)	1.05 (0.95-1.16)	0.97 (0.85-1.10)	1.04 (0.82-1.30)
	7	0.98 (0.85-1.12)	1.17 (0.96-1.44)	1.04 (0.91-1.18)	1.04 (0.83-1.30)
100m buffer	12	0.95 (0.83-1.09)	0.91 (0.73-1.14)		
	11	1.10 (0.96-1.25)	0.90 (0.81-1.00)		
	10	1.08 (0.98-1.20)	0.91 (0.80-1.04)		
	9	1.00 (0.90-1.11)	0.96 (0.85-1.09)		
	8	0.94 (0.82-1.07)	1.05 (0.95-1.16)	0.97 (0.85-1.10)	1.03 (0.82-1.29)
	7	0.98 (0.85-1.12)	1.18 (0.96-1.45)	1.04 (0.91-1.18)	1.05 (0.84-1.31)
200m buffer	12	0.95 (0.83-1.09)	0.91 (0.73-1.13)		
	11	1.09 (0.96-1.25)	0.90 (0.81-1.01)		
	10	1.09 (0.98-1.20)	0.92 (0.81-1.05)		
	9	1.00 (0.90-1.11)	0.97 (0.85-1.10)		
	8	0.93 (0.82-1.06)	1.05 (0.95-1.16)	0.96 (0.85-1.10)	1.04 (0.83-1.31)
	7	0.98 (0.85-1.12)	1.17 (0.96-1.44)	1.04 (0.91-1.18)	1.04 (0.83-1.30)
300m buffer	12	0.95 (0.83-1.09)	0.91 (0.73-1.13)		
	11	1.10 (0.96-1.25)	0.90 (0.81-1.01)		
	10	1.09 (0.98-1.21)	0.92 (0.81-1.05)		
	9	1.00 (0.90-1.11)	0.97 (0.85-1.10)		
	8	0.93 (0.82-1.06)	1.05 (0.95-1.16)	0.97 (0.85-1.10)	1.04 (0.83-1.31)
	7	0.98 (0.85-1.12)	1.17 (0.96-1.44)	1.04 (0.91-1.18)	1.04 (0.83-1.30)
400m buffer	12	0.95 (0.83-1.09)	0.91 (0.73-1.13)		
	11	1.10 (0.96-1.25)	0.90 (0.81-1.00)		
	10	1.09 (0.98-1.21)	0.92 (0.81-1.05)		
	9	1.00 (0.90-1.11)	0.97 (0.85-1.10)		
	8	0.93 (0.82-1.06)	1.05 (0.95-1.16)	0.97 (0.85-1.10)	1.04 (0.83-1.31)
	7	0.98 (0.85-1.12)	1.18 (0.96-1.44)	1.04 (0.91-1.18)	1.04 (0.83-1.30)
500m buffer	12	0.95 (0.82-1.09)	0.91 (0.73-1.14)		
	11	1.09 (0.96-1.25)	0.90 (0.81-1.01)		
	10	1.09 (0.98-1.20)	0.92 (0.81-1.05)		
	9	1.00 (0.90-1.11)	0.97 (0.85-1.10)		
	8	0.93 (0.82-1.06)	1.05 (0.95-1.16)	0.96 (0.85-1.10)	1.04 (0.83-1.31)
	7	0.98 (0.85-1.12)	1.18 (0.96-1.44)	1.04 (0.91-1.18)	1.04 (0.84-1.31)

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Table B.4: Risk ratios for covariate cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Weekly peak concentration					
50m buffer	12	1.03 (0.93-1.13)	0.95 (0.84-1.07)		
	11	1.03 (0.95-1.12)	**0.93 (0.87-0.99)**		
	10	1.03 (0.97-1.10)	0.95 (0.87-1.03)		
	9	1.01 (0.93-1.09)	0.99 (0.93-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	0.99 (0.91-1.08)	1.05 (0.99-1.11)
	7			1.04 (0.98-1.11)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.06)
	5			0.96 (0.91-1.00)	1.01 (0.98-1.03)
	4			**0.94 (0.89-1.00)**	0.99 (0.98-1.01)
	3			0.97 (0.92-1.02)	0.98 (0.96-1.01)
	2			1.03 (0.97-1.09)	0.97 (0.93-1.01)
	1			**1.07 (1.01-1.14)**	0.96 (0.91-1.01)
	0			1.02 (0.94-1.12)	0.94 (0.89-1.01)
100m buffer	12	1.03 (0.93-1.13)	0.95 (0.84-1.07)		
	11	1.03 (0.95-1.11)	**0.93 (0.87-0.99)**		
	10	1.03 (0.97-1.10)	0.94 (0.87-1.03)		
	9	1.01 (0.93-1.09)	0.99 (0.93-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	1.00 (0.92-1.09)	1.04 (0.99-1.10)
	7			1.03 (0.97-1.08)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.05)
	5			0.97 (0.92-1.01)	1.01 (0.99-1.03)
	4			0.95 (0.91-1.00)	1.00 (0.98-1.02)
	3			0.97 (0.92-1.02)	0.99 (0.97-1.01)
	2			1.01 (0.97-1.05)	0.98 (0.95-1.01)
	1			1.06 (1.00-1.11)	0.97 (0.93-1.00)
	0			**1.07 (1.01-1.12)**	0.96 (0.91-1.01)
	-1			0.98 (0.90-1.07)	0.95 (0.89-1.01)
200m buffer	12	1.03 (0.93-1.13)	0.94 (0.83-1.07)		
	11	1.03 (0.95-1.11)	**0.93 (0.87-0.99)**		
	10	1.03 (0.97-1.10)	0.95 (0.87-1.03)		
	9	1.01 (0.93-1.09)	1.00 (0.93-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	1.00 (0.91-1.08)	1.04 (0.99-1.10)
	7			1.02 (0.97-1.08)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.06)
	5			0.97 (0.93-1.01)	1.01 (0.99-1.03)
	4			0.95 (0.91-1.00)	1.00 (0.98-1.02)
	3			0.97 (0.92-1.02)	0.99 (0.97-1.01)
	2			1.01 (0.97-1.05)	0.98 (0.95-1.00)
	1			1.05 (1.00-1.11)	0.97 (0.93-1.00)
	0			**1.06 (1.01-1.12)**	0.96 (0.91-1.00)
	-1			0.98 (0.90-1.07)	0.95 (0.89-1.00)

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Table B.4: Risk ratios for covariate cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
300m buffer	12	1.03 (0.93-1.13)	0.94 (0.83-1.07)		
	11	1.03 (0.95-1.11)	**0.93 (0.87-0.99)**		
	10	1.03 (0.97-1.10)	0.95 (0.87-1.03)		
	9	1.01 (0.93-1.10)	1.00 (0.93-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	1.00 (0.91-1.08)	1.04 (0.99-1.10)
	7			1.02 (0.97-1.08)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.05)
	5			0.97 (0.93-1.01)	1.01 (0.99-1.03)
	4			0.95 (0.91-1.00)	1.00 (0.98-1.02)
	3			0.97 (0.92-1.02)	0.99 (0.97-1.01)
	2			1.01 (0.97-1.05)	0.98 (0.95-1.00)
	1			1.05 (1.00-1.11)	0.97 (0.93-1.00)
	0			**1.06 (1.01-1.12)**	0.96 (0.91-1.00)
	-1			0.98 (0.90-1.07)	0.95 (0.89-1.00)
400m buffer	12	1.03 (0.93-1.13)	0.94 (0.83-1.07)		
	11	1.03 (0.95-1.11)	**0.93 (0.87-0.99)**		
	10	1.03 (0.97-1.10)	0.95 (0.87-1.03)		
	9	1.01 (0.93-1.09)	1.00 (0.94-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	1.00 (0.91-1.08)	1.04 (0.99-1.10)
	7			1.02 (0.97-1.08)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.06)
	5			0.97 (0.93-1.01)	1.01 (0.99-1.03)
	4			0.95 (0.91-1.00)	1.00 (0.98-1.02)
	3			0.97 (0.92-1.02)	0.99 (0.97-1.01)
	2			1.01 (0.97-1.05)	0.98 (0.95-1.00)
	1			1.05 (1.00-1.11)	0.97 (0.93-1.00)
	0			**1.06 (1.01-1.12)**	0.96 (0.91-1.00)
	-1			0.98 (0.90-1.07)	0.95 (0.89-1.00)
500m buffer	12	1.03 (0.93-1.13)	0.95 (0.84-1.07)		
	11	1.03 (0.95-1.11)	**0.93 (0.87-1.00)**		
	10	1.03 (0.97-1.10)	0.95 (0.87-1.03)		
	9	1.01 (0.93-1.09)	1.00 (0.93-1.06)		
	8	0.94 (0.85-1.03)	1.08 (0.96-1.22)	1.00 (0.91-1.08)	1.04 (0.99-1.10)
	7			1.02 (0.97-1.08)	1.03 (0.99-1.08)
	6			1.00 (0.95-1.06)	1.02 (0.99-1.06)
	5			0.97 (0.93-1.01)	1.01 (0.99-1.04)
	4			0.95 (0.91-1.00)	1.00 (0.98-1.02)
	3			0.97 (0.92-1.02)	0.99 (0.97-1.01)
	2			1.01 (0.97-1.05)	0.98 (0.95-1.01)
	1			1.05 (1.00-1.11)	0.97 (0.93-1.00)
	0			**1.06 (1.01-1.12)**	0.96 (0.91-1.00)
	-1			0.98 (0.90-1.07)	0.95 (0.89-1.00)

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Table B.4: Risk ratios for covariate cleft palate mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**

Note:
NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter
Model was adjusted for O_3, $PM_{2.5}$, maternal education level, maternal smoking, tract-level median income, conception season, and presence of grasses or trees. Values in bold were significant at $\alpha = 0.05$.
Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.

Table B.5: Risk ratios for covariate craniosynostosis mixed air pollutant models, New York State outside New York City, 2002 to 2015

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
Weekly mean concentration					
50m buffer	12	0.86 (0.74-1.01)	1.06 (0.82-1.36)		
	11	1.05 (0.91-1.22)	1.04 (0.80-1.35)		
	10	0.98 (0.87-1.10)	1.05 (0.85-1.29)		
	9	0.94 (0.84-1.06)	0.96 (0.78-1.17)		
	8	1.02 (0.88-1.18)	0.87 (0.67-1.13)	0.91 (0.79-1.05)	0.98 (0.76-1.25)
	7	1.09 (0.94-1.26)	1.07 (0.82-1.38)	**1.17 (1.03-1.32)**	0.96 (0.85-1.10)
	6			**1.11 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.94 (0.83-1.07)	0.98 (0.87-1.12)
	4			0.89 (0.77-1.03)	1.01 (0.79-1.29)
100m buffer	12	0.87 (0.75-1.01)	1.06 (0.82-1.36)		
	11	1.05 (0.91-1.22)	1.04 (0.80-1.35)		
	10	0.98 (0.87-1.10)	1.06 (0.86-1.30)		
	9	0.94 (0.84-1.06)	0.97 (0.79-1.18)		
	8	1.02 (0.88-1.18)	0.87 (0.67-1.14)	0.91 (0.79-1.05)	0.98 (0.76-1.26)
	7	1.09 (0.94-1.26)	1.06 (0.82-1.38)	**1.16 (1.03-1.32)**	0.96 (0.84-1.10)
	6			**1.11 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.95 (0.84-1.07)	0.99 (0.87-1.12)
	4			0.89 (0.76-1.03)	1.02 (0.80-1.31)
200m buffer	12	0.87 (0.74-1.01)	1.06 (0.82-1.36)		
	11	1.06 (0.91-1.22)	1.04 (0.80-1.34)		
	10	0.98 (0.87-1.10)	1.05 (0.86-1.30)		
	9	0.94 (0.84-1.05)	0.97 (0.79-1.18)		
	8	1.02 (0.88-1.18)	0.87 (0.67-1.13)	0.91 (0.79-1.05)	0.98 (0.76-1.26)
	7	1.09 (0.94-1.26)	1.07 (0.83-1.39)	**1.17 (1.03-1.32)**	0.97 (0.85-1.10)
	6			**1.11 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.94 (0.83-1.07)	0.99 (0.87-1.12)
	4			0.89 (0.77-1.03)	1.01 (0.79-1.30)
300m buffer	12	0.87 (0.74-1.01)	1.06 (0.82-1.36)		
	11	1.05 (0.91-1.22)	1.04 (0.80-1.35)		
	10	0.98 (0.87-1.10)	1.05 (0.86-1.30)		
	9	0.94 (0.84-1.06)	0.97 (0.79-1.18)		
	8	1.02 (0.88-1.18)	0.88 (0.67-1.14)	0.91 (0.78-1.05)	0.98 (0.76-1.26)
	7	1.09 (0.94-1.26)	1.07 (0.82-1.38)	**1.16 (1.03-1.32)**	0.97 (0.85-1.10)
	6			**1.11 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.95 (0.84-1.07)	0.99 (0.87-1.12)
	4			0.89 (0.77-1.03)	1.02 (0.80-1.30)

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Table B.5: Risk ratios for covariate craniosynostosis mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
400m buffer	12	0.86 (0.74-1.00)	1.05 (0.82-1.36)		
	11	1.06 (0.91-1.23)	1.03 (0.80-1.34)		
	10	0.98 (0.87-1.10)	1.05 (0.86-1.30)		
	9	0.94 (0.84-1.06)	0.97 (0.79-1.18)		
	8	1.02 (0.88-1.18)	0.87 (0.67-1.13)	0.91 (0.78-1.05)	0.97 (0.76-1.25)
	7	1.09 (0.94-1.26)	1.07 (0.83-1.39)	**1.16 (1.03-1.32)**	0.97 (0.85-1.10)
	6			**1.10 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.95 (0.83-1.07)	0.98 (0.87-1.12)
	4			0.89 (0.77-1.03)	1.01 (0.79-1.29)
500m buffer	12	**0.86 (0.74-1.00)**	1.06 (0.82-1.36)		
	11	1.06 (0.92-1.23)	1.03 (0.79-1.33)		
	10	0.98 (0.87-1.10)	1.06 (0.86-1.30)		
	9	0.94 (0.84-1.06)	0.97 (0.79-1.19)		
	8	1.02 (0.88-1.18)	0.87 (0.67-1.13)	0.91 (0.79-1.06)	0.97 (0.76-1.25)
	7	1.09 (0.94-1.26)	1.06 (0.82-1.38)	**1.16 (1.03-1.32)**	0.97 (0.85-1.10)
	6			**1.10 (1.01-1.21)**	0.97 (0.82-1.14)
	5			0.94 (0.83-1.07)	0.98 (0.87-1.12)
	4			0.89 (0.77-1.03)	1.01 (0.79-1.29)
Weekly peak concentration					
50m buffer	12	0.92 (0.84-1.02)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.00 (0.94-1.07)	1.01 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.81-1.08)	1.01 (0.92-1.12)	0.93 (0.80-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.05 (0.98-1.14)	0.99 (0.89-1.10)
	5			0.97 (0.90-1.05)	0.96 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.02 (0.89-1.16)
	3			1.00 (0.90-1.11)	0.99 (0.86-1.14)
100m buffer	12	0.92 (0.84-1.02)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.00 (0.94-1.07)	1.01 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.81-1.08)	1.01 (0.92-1.12)	0.93 (0.81-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.05 (0.98-1.14)	0.99 (0.90-1.10)
	5			0.97 (0.90-1.05)	0.97 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.02 (0.89-1.16)
	3			1.00 (0.90-1.11)	0.99 (0.86-1.14)

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Table B.5: Risk ratios for covariate craniosynostosis mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**
200m buffer	12	0.92 (0.84-1.02)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.00 (0.94-1.07)	1.00 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.81-1.09)	1.01 (0.92-1.12)	0.93 (0.81-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.05 (0.98-1.14)	0.99 (0.90-1.10)
	5			0.97 (0.90-1.05)	0.96 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.01 (0.89-1.16)
	3			1.00 (0.90-1.10)	0.99 (0.86-1.14)
300m buffer	12	0.92 (0.84-1.01)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.00 (0.94-1.07)	1.01 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.82-1.09)	1.01 (0.92-1.12)	0.93 (0.81-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.06 (0.98-1.14)	0.99 (0.90-1.10)
	5			0.97 (0.90-1.05)	0.97 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.02 (0.89-1.16)
	3			1.00 (0.90-1.10)	0.99 (0.86-1.14)
400m buffer	12	0.92 (0.84-1.01)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.00 (0.94-1.07)	1.00 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.81-1.08)	1.01 (0.92-1.12)	0.93 (0.80-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.05 (0.98-1.14)	0.99 (0.90-1.10)
	5			0.97 (0.90-1.05)	0.96 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.02 (0.89-1.16)
	3			1.00 (0.90-1.10)	0.99 (0.86-1.14)
500m buffer	12	0.92 (0.84-1.01)	1.06 (0.93-1.20)		
	11	0.97 (0.92-1.02)	1.05 (0.94-1.17)		
	10	1.01 (0.94-1.07)	1.00 (0.92-1.10)		
	9	1.03 (0.98-1.08)	0.96 (0.86-1.07)		
	8	1.04 (0.95-1.14)	0.94 (0.81-1.08)	1.01 (0.92-1.12)	0.93 (0.80-1.08)
	7			1.06 (0.96-1.16)	1.06 (0.93-1.21)
	6			1.05 (0.98-1.14)	0.99 (0.90-1.10)
	5			0.98 (0.90-1.06)	0.96 (0.87-1.07)
	4			**0.90 (0.81-0.99)**	1.01 (0.89-1.16)
	3			0.99 (0.90-1.10)	0.99 (0.86-1.14)

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Table B.5: Risk ratios for covariate craniosynostosis mixed air pollutant models, New York State outside New York City, 2002 to 2015 *(continued)*

		16 week model		12 week model	
Buffer	**Week**	**O_3**	**$PM_{2.5}$**	**O_3**	**$PM_{2.5}$**

Note:
NA = data not applicable; O_3 = Ozone; $PM_{2.5}$ = Fine particulate matter
Model was adjusted for O_3, $PM_{2.5}$, maternal education level, maternal smoking, tract-level median income, conception season, and presence of grasses or trees. Values in bold were significant at $\alpha = 0.05$.
Week 0 is week of conception. Week 12 is the end of the first trimester of pregnancy.