HHS Public Access

Author manuscript

Birth Defects Res. Author manuscript; available in PMC 2024 November 01.

Published in final edited form as:

Birth Defects Res. 2023 November 01; 115(18): 1758–1769. doi:10.1002/bdr2.2250.

Is gastroschisis associated with county-level socio-environmental quality during pregnancy?

Alison K. Krajewski[1], **Achal Patel**[2], **Christine L. Gray**[3], **Lynne C. Messer**[4], **Corinna Y. Keeler**[2], **Peter H. Langlois**[5], **Jennita Reefhuis**[6], **Suzanne M. Gilboa**[6], **Martha M. Werler**[7], **Gary M. Shaw**[8], **Suzan L. Carmichael**[8], **Wendy N. Nembhard**[9], **Tabassum Z. Insaf**[10,11], **Marcia L. Feldkamp**[12], **Kristin M. Conway**[13], **Danelle T. Lobdell**[1], **Tania A. Desrosiers**[2], **The National Birth Defects Prevention Study**

[1]United States Environmental Protection Agency (U.S. EPA), Office of Research and Development, Center for Public Health & Environmental Assessment, Research Triangle Park, North Carolina, USA

[2]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[3]Duke Global Health Institute, Durham, North Carolina, USA

[4]OHSU-PSU School of Public Health, Portland, Oregon, USA

[5]Department of Epidemiology, Human Genetics, and Environmental Sciences, University of Texas School of Public Health—Austin Regional Campus, Austin, Texas, USA

[6]Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities, Division of Birth Defects and Infant Disorders, Atlanta, Georgia, USA

[7]Department of Epidemiology, Boston University, School of Public Health, Boston, Massachusetts, USA

[8]Stanford University, School of Medicine, Stanford, California, USA

[9]Department of Epidemiology, University of Arkansas for Medical Sciences, Fay W. Boozman College of Public Health, Little Rock, Arkansas, USA

[10]New York State Department of Health, Center for Environmental Health, Bureau of Environmental and Occupational Epidemiology, Albany, New York, USA

[11]Department of Epidemiology and Biostatistics, University at Albany, Albany, New York, USA

Correspondence Alison K. Krajewski, U.S. EPA, Office of Research and Development, Center of Public Health and Environmental Assessment, 109 T.W. Alexander Drive, MD B-243-01, Research Triangle Park, NC 27711, USA. krajewski.alison@epa.gov.

CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflict of interest.

DISCLAIMER

The views expressed in this manuscript are those of the authors and do not necessarily reflect the views, policies, or official positions of the U.S. Environmental Protection Agency, the Centers of Disease Control and Prevention, the California Department of Public Health, the New York State Department of Health, or the North Carolina Division of Public Health. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

[12]Department of Pediatrics, Division of Medical Genetics, University of Utah, Salt Lake City, Utah, USA

[13]Department of Epidemiology, The University of Iowa, College of Public Health, Iowa City, Iowa, USA

Abstract

Background: Gastroschisis prevalence more than doubled between 1995 and 2012. While there are individual-level risk factors (e.g., young maternal age, low body mass index), the impact of environmental exposures is not well understood.

Methods: We used the U.S. Environmental Protection Agency's Environmental Quality Index (EQI) as a county-level estimate of cumulative environmental exposures for five domains (air, water, land, sociodemographic, and built) and overall from 2006 to 2010. Adjusted odds ratios (aOR) and 95% confidence interval (CI) were estimated from logistic regression models between EQI tertiles (better environmental quality (reference); mid; poorer) and gastroschisis in the National Birth Defects Prevention Study from births delivered between 2006 and 2011. Our analysis included 594 cases with gastroschisis and 4105 infants without a birth defect (controls).

Results: Overall EQI was modestly associated with gastroschisis (aOR [95% CI]: 1.29 [0.98, 1.71]) for maternal residence in counties with poorer environmental quality, compared to the reference (better environmental quality). Within domain-specific indices, only the sociodemographic domain (aOR: 1.51 [0.99, 2.29]) was modestly associated with gastroschisis, when comparing poorer to better environmental quality.

Conclusions: Future work could elucidate pathway(s) by which components of the sociodemographic domain or possibly related psychosocial factors like chronic stress potentially contribute to risk of gastroschisis.

Keywords

gastroschisis; environmental quality index; EQI; sociodemographic; environmental quality

1 | INTRODUCTION

Gastroschisis is a major abdominal birth defect resulting in the developing intestines and sometimes other gastrointestinal organs forming outside the abdomen in the surrounding amniotic fluid, requiring immediate surgical intervention after birth (Feldkamp et al., 2007). Gastroschisis is generally not associated with genetic conditions, with fewer than 2% of cases having chromosomal abnormalities (Mastroiacovo et al., 2007). However, familial occurrence is around 3% (Salinas-Torres et al., 2018), suggesting underlying genetic susceptibility. While advances in prenatal diagnosis, surgical outcomes, and clinical management have significantly improved survival rates to over 90%, many individuals living with gastroschisis have long-term morbidity and substantial health care costs associated with their condition (Harris et al., 2016; Skarsgard, 2016).

Recent population-based studies in the United States (U.S.) estimate that gastroschisis affects approximately 4 to 5 infants per 10,000 births, meaning that nearly 2000 babies

are born every year with this condition (Mai et al., 2019; Stallings et al., 2019). Prevalence varies by race/ethnicity and is lower for non-Hispanic Black infants compared to non-Hispanic White infants (Baldacci et al., 2020; Mac Bird et al., 2009; Mai et al., 2019). Notably, the prevalence of gastroschisis has been steadily increasing over time, more than doubling between 1995 and 2012 in the U.S. (Jones et al., 2016) and around the world (Castilla et al., 2008; Egger et al., 2022; Kazaura et al., 2004). The reasons for this increase are unknown but suspected to be related to concurrent shifts in non-genetic risk factors and/or environmental exposures. Spatial clustering in the distribution of gastroschisis-affected births (Bassil et al., 2016; Elliott et al., 2009; Liu et al., 2021; Root et al., 2009; Yazdy et al., 2015) supports the hypothesis that environmental and sociodemographic factors play a role in the etiology of gastroschisis, which otherwise remains largely unexplained.

Established risk factors for gastroschisis include young maternal age (<20 years), low pre-pregnancy body mass index (BMI < 18.5 kg/m^2), smoking, medication use and to a lesser degree, alcohol use during pregnancy (Baldacci et al., 2020; Fisher et al., 2022; Mac Bird et al., 2009; Raitio et al., 2020; Rasmussen & Frías, 2008; Siega-Riz et al., 2009; Werler et al., 1992). While various individual environmental factors such as pesticides, solvents, polycyclic aromatic hydrocarbons, air pollution, and certain medications have been investigated in relation to gastroschisis (Agopian et al., 2013; Huybrechts et al., 2023; Kielb et al., 2014; Lupo et al., 2012; Padula et al., 2021; Torfs et al., 1996; Waller et al., 2010), few studies have considered multiple co-occurring environmental exposures across different domains, which could potentially have synergistic effects on embryogenesis (Rager et al., 2020). Investigation of the relationship between gastroschisis and the contextual maternal socio-environment during early pregnancy can potentially further our understanding of the increasing prevalence, spatial variability, and etiology of gastroschisis.

In this study, we used the U.S. Environmental Protection Agency (EPA)'s Environmental Quality Index (EQI) to investigate whether the environmental quality of the county of residence during early pregnancy is associated with gastroschisis in the National Birth Defects Prevention Study (NBDPS). The EQI is an aggregate environmental index incorporating a wide spectrum of environmental data that can be used to generate geographic-based estimates of cumulative environmental exposures across five domains: air, water, land, sociodemographic, and built environment (Lobdell et al., 2011; Messer et al., 2014; United States Environmental Protection Agency, 2020a, 2020b, 2020c), and has been used in prior studies of health outcomes including birth defects, infant mortality, preterm birth, asthma, mortality, and cancer (Gray et al., 2018; Jagai et al., 2017; Jian et al., 2017; Krajewski et al., 2021; Patel et al., 2018; Rappazzo et al., 2015).

2 | METHODS

2.1 | Study population

The NBDPS is a population-based, multi-center case–control study designed to investigate environmental and genetic risk factors for major structural birth defects in the U.S. (Reefhuis et al., 2015). Cases of gastroschisis and other eligible birth defects diagnosed among infants, stillbirths, and terminations with dates of delivery on or after October 1, 1997 and estimated dates of delivery on or before December 31, 2011 were identified by active,

population-based birth defects surveillance programs in Arkansas (1998–2011; statewide), California (1997–2011; selected counties), Georgia (1997–2011; selected counties), Iowa (1997–2011; statewide), Massachusetts (1997–2011; selected counties), New Jersey (1998–2002; statewide), New York (1997–2002 & 2004–2011; selected counties), North Carolina (2003–2011; selected counties), Texas (1997–2011; selected counties), and Utah (2003–2011; statewide). Clinical geneticists reviewed abstracted information to confirm diagnoses and exclude cases with known or strongly suspected single gene conditions or chromosomal abnormalities (Rasmussen et al., 2003). Infants without a major birth defect were selected as controls by sampling birth certificates or hospital discharge records in the same geographic area and time period as cases. Mothers of eligible cases and controls were invited to participate in the NBDPS and complete a 1-h telephone interview in English or Spanish between 6 weeks and 24 months after delivery. The interview covered a comprehensive range of topics including sociodemographic information, pregnancy history, maternal health and health behavioral factors, medication use, and occupational and residential histories. Overall, 65% of mothers of gastroschisis cases and 65% of mothers of controls participated in the interview. On average, interviews were conducted within 12 months after delivery (10 months for cases; 9 months for controls). For this analysis, we restricted our study sample to cases and controls conceived between 2006 and 2011 to match the period of time for which EQI data were available. We used the maternal residence corresponding to the beginning of pregnancy, based on the estimated date for conception, to better align our exposure period with the critical time window of embryologic development during which gastroschisis likely occurs (gestational weeks 4–8).

2.2 | Exposure data

The EQI is a county-level estimate of ambient environmental quality developed by the U.S. EPA. Detailed information about how the EQI was constructed has been published (United States Environmental Protection Agency, 2020a, 2020b, 2020c). In brief, national data on various sources of environmental exposures between 2006 and 2010 were compiled to represent cumulative environmental quality across five domains: *air* (43 variables), representing the six criteria air pollutants (i.e., particulate matter, photochemical oxidants including ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead) and hazardous air pollutants (e.g., perchloroethylene emitted from facilities); *water* (51 variables), representing overall water quality, general water contamination, recreational water quality, drinking water quality, atmospheric deposition, drought, and chemical contamination; *land* (18 variables), representing agriculture, pesticides, contaminants, facilities, and radon; *built* (15 variables), representing roads, highway/road safety, public transit behavior, business environment, and subsidized housing environment; and *sociodemographic* (12 variables), representing socioeconomics and crime. A summary of the data sources for each domain can be found in Table S1. To construct the EQI, variables in each of the five domains were reduced using principal components analysis (PCA), with the first component retained as that domain's index value. The domain-specific indices were valence-corrected to ensure that directionality of the variables was consistent with higher values reflecting poorer environmental quality and lower values reflecting better environmental quality. Subsequently, the five domain-specific indices were further reduced in a second PCA, in which the first component was retained as the value for the overall EQI. This

analytic process ultimately yields for each individual U.S. county an aggregate measure of environmental quality over time (2006–2010) that corresponds to the five specific domains as well as overall (i.e., six measures per county). The EQI is publicly available from U.S. EPA: https://www.epa.gov/healthresearch/environmental-quality-index-eqi.

2.3 | Exposure assignment

During the NBDPS interview, women were asked to provide their residential history, including addresses and dates, for each place they lived from 3 months before they became pregnant to the end of their pregnancy. Residential addresses reported by NBDPS participants were centrally geocoded by the Agency for Toxic Substances and Disease Registry's Geospatial Research, Analysis, and Services Program using Centrus (Pitney Bowes Software 2012, version 6.0). Data from New Jersey was not included in this analysis because geocoded data were not available. Self-reported address(es) was successfully geocoded for 97% of all NBDPS participants. The NBDPS participant's residence corresponding to the beginning of pregnancy (based on estimated date of conception) was linked to the EQI using county Federal Information Processing Standard (FIPS) codes.

2.4 | Statistical analysis

We categorized the observed distribution of the overall EQI and domain-specific indices within our study sample into tertiles based on the national distribution of the EQI across all U.S. counties (United States Environmental Protection Agency, 2020b). The EQI is structured such that higher values reflect poorer environmental quality, and lower values reflect better environmental quality. Thus, in our analysis, our tertiles corresponded to *better* environmental quality (tertile 1), *mid-range* environmental quality (tertile 2), and *poorer* environmental quality (tertile 3).

Potential confounders selected a priori and ascertained from the NBDPS interview included: maternal age at conception, race/ethnicity, completed years of education (as a proxy for individual socioeconomic status, or SES), smoking during pregnancy, alcohol use during pregnancy, pre-pregnancy BMI, and rural–urban continuum codes (RUCC). RUCC data was obtained from the US Department of Agriculture (United States Department of Agriculture, 2019). Reducing from nine classification categories to four, we used the following RUCC categories: metropolitan urbanized (RUCC1); non-metropolitan urbanized (RUCC2); less urbanized (RUCC3); and thinly populated (RUCC4) (Krajewski et al., 2021; Luben et al., 2009; Messer et al., 2010). The final minimally sufficient adjustment set was determined using a Directed Acyclic Graph (DAG) and included: maternal age (<20 years; ≥20 years), race/ethnicity (non-Hispanic White; non-Hispanic Black; Hispanic; other), education (<high school; high school; >high school), and BMI (underweight <18 kg/m^2; normal 18 to <25 kg/m^2; overweight/obese ≥25 kg/m^2). We used logistic regression to estimate unadjusted and adjusted odds ratios (aOR) and 95% confidence intervals (CI) for the association between gastroschisis and the overall EQI, as well as the associations between gastroschisis and each of the five domain-specific indices, comparing poorer environmental quality and mid-range environmental quality to a common reference category reflecting better environmental quality. When domain-specific findings were of interest, the other domains were included in the statistical models as covariates. Lastly, we used stratified analyses to explore

whether maternal age (<20 vs. ≥20 years) might modify the association between EQI and gastroschisis rather than operate as a confounder. Statistical analyses were performed by AKK using SAS version 9.4 (Cary, NC) and independently replicated (CYK).

3 | RESULTS

The total number of eligible gastroschisis cases and controls with dates of conception between January 1, 2006 and December 31, 2011 was 629 and 4368, respectively. Of those cases and controls, we successfully linked 94% to the EQI (298 participants were missing a FIPS code), yielding exposure data for 4699 study participants across 369 unique residential counties.

Our final sample for analysis consisted of 594 gastroschisis cases and 4105 controls (Table 1). Over 90% of cases were diagnosed with an isolated occurrence of gastroschisis, whereas the remaining case infants had at least one additional co-occurring birth defect. Mothers of case infants were more likely than mothers of control infants to be younger than 20 years at conception (37.7% vs. 10.9%, respectively) and have a pre-pregnancy BMI 18 to <25 kg/m^2 (60.4% vs. 47.7%, respectively). The largest proportion of mothers of both cases (47.5%) and controls (56.6%) identifying as non-Hispanic White. Among cases, mothers were more likely to have completed high school (36.7%) or more than high school (36.9%); however, among controls, the largest proportion of mothers were likely to have completed more than a high school education (60.2%). The majority of cases (84.3%) and controls (86.3%) were born in metropolitan urbanized areas (RUCC 1).

The overall EQI was associated with an increased risk of gastroschisis (Figure 1; Table 2). Compared to mothers who lived in counties with better environmental quality, mothers who lived in counties with either poorer or mid-range environmental quality were approximately 30% more likely to have a pregnancy affected by gastroschisis (aOR: 1.31 [95% CI: 0.99, 1.73] for poorer quality; aOR: 1.29 [0.98, 1.71] for mid-range quality). The patterns of association varied in the domain specific indices. Mothers who lived in counties with poorer quality within the sociodemographic domain were nearly twice as likely to have an infant with gastroschisis (OR: 1.86 [1.28, 2.73]), with some attenuation after multivariable adjustment (aOR:1.51 [0.99, 2.29]). In the land domain, we observed elevated odds with gastroschisis among mothers who lived in counties with poorer land quality (aOR: 1.17 [0.92, 1.49]). We also observed lower odds with gastroschisis in the mid-range quality of the water domain (aOR: 0.72 [0.49, 1.03]) and built domain (aOR:0.74 [0.55, 0.99]). The associations were similar when including RUCC as a covariate (Table S2).

Analyses stratified by maternal age (Table 3) revealed no meaningful differences by age in the association between the overall EQI and gastroschisis, with aOR of 1.13 for mothers <20 years and aOR of 1.33 for mothers ≥20. Within domain specific indices, the moderate association observed in the primary analyses between gastroschisis and poorer quality in the sociodemographic domain appeared to be driven by the strata of mothers ≥20 years at conception (aOR: 1.88 [1.13, 3.14]) compared to mothers <20 years (aOR: 0.95 [0.47, 1.92]). Furthermore, there was increased odds of gastroschisis among mothers <20 years living in counties with poorer quality in the water domain (aOR: 1.37 [0.66, 2.82]) and in the

land domain (aOR:1.43 [0.91, 2.25]). The associations were similar when including RUCC as a covariate (Table S3).

4 | DISCUSSION

In this study using the EQI as a measure of the environmental quality of a mother's county of residence during pregnancy, we found that overall EQI was not strongly associated with an increased risk of having an infant with gastroschisis in the NBDPS study population. Within the specific domains that comprise the EQI—air, water, land, sociodemographic, and built environment—we observed varied patterns of association. There was an elevated effect estimate for the sociodemographic domain, whereby mothers living in counties with poorer quality sociodemographic environment having 50% increased odds of gastroschisis in adjusted models (90% when restricted only to mothers ≥20 years at conception) compared to mothers living in counties with better quality sociodemographic environment. Additionally, the was an observed pattern of increased odds of gastroschisis among mothers who lived in counties with poorer quality in the land domain, while there was decreased odds among mothers who lived in counties with mid-range quality in the water and built domains.

Our study is among the first to explore associations between gastroschisis and cumulative residential environmental quality across multiple domains. A previous study conducted in Texas by Krajewski et al. (2021) investigated potential associations between the EQI and various types of birth defects including gastroschisis. In that study, maternal residence at delivery in counties with the poorest overall environmental quality was associated with a higher prevalence of gastroschisis (prevalence ratio [PR] = 1.55 [95% CI = 1.30, 1.86]), adjusting for maternal age, race/ethnicity, education, smoking, and RUCC. Within the domain specific indices, the adjusted PRs (95% CI) comparing the poorest quality to the best quality were: air 1.06 (0.76, 1.46); water 1.00 (0.69, 1.43); land 0.95 (0.74, 1.23); sociodemographic 1.53 (1.02, 2.31); and built 0.67 (0.48, 0.92). While our study did not observe as strong of an association with the EQI both overall and domain specific, our results were generally consistent with their findings, particularly the sociodemographic domain finding. Because Texas participated in the NBDPS and contributed cases of gastroschisis from selected counties delivered between 2007 and 2010, there is a relatively small overlap in the case series between our study and the Texas EQI study. However, there are differences between the studies that make them unique and inform comparison of results. The Texas EQI study was a cohort analysis that included over 1.6 million births from across the state (not just from the geographically smaller NBDPS study area) and used maternal address at delivery as documented on the birth certificate to link to the EQI. Whereas we categorized exposure in our study based on the national distribution (in tertiles) of the EQI across all U.S. counties, the Texas study categorized exposure based on their within-sample distribution (in quartiles) among the baseline population of livebirths in their study, precluding direct comparison of the EQI categories between studies. Results from our study may be more generalizable and directly comparable to other studies that, like ours, standardize their population to the national EQI distribution.

In our study the association with the sociodemographic domain persisted after adjustment for individual-level sociodemographic risk factors for gastroschisis (maternal age, education,

and race/ethnicity), suggesting that while individual-level factors might partially mediate or confound the total observed effect of the sociodemographic domain estimated by the crude ORs, the county-level sociodemographic environment during early pregnancy may also have an independent role in the causal pathway(s) for gastroschisis (Robert, 1999). These findings are consistent with a recent study that investigated the association between >1200 cases of gastroschisis in the NBDPS and neighborhood-level socioeconomic position using two separate indices—the Neighborhood Deprivation Index (NDI), and the Neighborhood Socioeconomic Position Index (nSEPI) (Neo et al., 2023). In that study, women who lived in low socioeconomic-position neighborhoods during early pregnancy were more likely to deliver an infant with gastroschisis compared to women residing in high socioeconomic-position neighborhoods (OR for NDI: 2.31 [95% CI: 1.98, 2.71]; OR for nSEPI: 2.42 [95% CI: 2.06, 2.83]). Adjustment for individual-level factors including maternal race/ethnicity, household income, and education attenuated the observed associations, yet remained modestly elevated (aOR for NDI: 1.28 [95% CI: 1.04, 1.49]; aOR for nSEPI: 1.32 [95% CI: 1.09, 1.61]).

The salient utility of the EQI is that it reflects cumulative, simultaneous exposures from multiple components of the total environment in which people live, allowing for estimation of ambient county-level environmental quality that are known to impact health and can be actionable targets for intervention. The sociodemographic domain was constructed using county-level data about household income and poverty, housing quality, education, unemployment, and crime (United States Environmental Protection Agency, 2020b). Previous studies have observed associations between adverse pregnancy outcomes and these same neighborhood-level socioeconomic Census indicators (Carmichael et al., 2003; Lupo et al., 2015; Neo et al., 2023; O'Campo et al., 2008; Vinikoor-Imler et al., 2011; Wasserman et al., 1998). While our study design cannot elucidate the exact mechanisms by which such features of the social environment might contribute to the occurrence of gastroschisis, one reasonable hypothesis to be explored in future studies is whether community-level measures of socio-economic position might serve as markers for individual health behaviors (Vinikoor-Imler et al., 2011) and/or psychosocial stress, which has been previously associated with gastroschisis (Carmichael, Ma, Tinker, Shaw, & National Birth Defects Prevention Study, 2017; Ortega-García et al., 2013; Werler et al., 2018).

The cornerstone of our study was the availability of self-reported residential histories for NBDPS participants, which enabled direct linkage with the EQI to obtain a database-driven, historically comprehensive estimate of exposure profiles across various environmental and social domains within residential counties. A strength of the EQI is that specific domains are constructed separately and take into account various components from multiple documented sources, as well as across multiple routes of exposure. Analytically, this structure allowed us to investigate the potential association between gastroschisis and each individual domain while controlling for concurrent exposure profiles represented by the other domains. Despite these advantages, the EQI has limitations in the context of our study. As an ecologic index of cumulative exposures measured over 5 years (2006–2010), the EQI does not capture annual exposure variability, which may have introduced some degree of exposure misclassification. Furthermore, the EQI is assessed at the county level, which is likely to have more heterogenous composition than smaller geographic units such as Census tracts or blocks.

Heterogeneity within the county scale may also have introduced non-differential exposure misclassification, which could have diluted any underlying associations in our data between individual environmental domains and gastroschisis. Previous research has demonstrated that the association between area-level socioeconomic factors and gastroschisis varies depending on the neighborhood scale used for analysis (Root et al., 2011). Another potential source of exposure misclassification is that our analysis focused exclusively on maternal residence at conception whereas it's possible that an earlier time period could have more relevance, such as maternal residence in the year(s) before conception (which was not collected in the NBDPS). However, because the critical window of development for gastroschisis is during early pregnancy, maternal residence at conception is a highly plausible exposure window and the availability of residential data for early pregnancy (vs. knowing only maternal residence at delivery, for example) is a strength of our study. The NBDPS design has several other strengths that impart advantages to our study, including a geographically and demographically diverse study population ascertained over multiple years, as well as expert diagnosis and systematic classification of gastroschisis cases.

As the prevalence of gastroschisis more than doubled between 1995 and 2012 in the U.S., so does the importance of identifying potential environmental factors that can be mitigated to reduce the occurrence of this severe birth defect. The results of our study suggest that overall, the socio-environmental quality of a mother's residential county at conception as measured by the EQI is not strongly associated with having an infant with gastroschisis, but there is a modest increase in odds for mothers living in counties with the lowest quality of the EQI's sociodemographic domain, particularly for mothers 20 years and older at conception. Research is needed to elucidate possible mechanisms underlying the association between gastroschisis and residential sociodemographic factors, and to understand the relative contributions to the etiology of gastroschisis of individual-level versus neighborhood-level SES and other socio-environmental factors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors wish to acknowledge the participants of the National Birth Defects Prevention Study, and the support provided by the EPA's Environmental Quality Index team: Stephanie A. DeFlorio-Barker, Jyotsna S. Jagai, Monica P. Jimenez, and Kristen M. Rappazzo.

FUNDING INFORMATION

This project was supported through funding from the Centers for Disease Control and Prevention (CDC) to the North Carolina Center for Birth Defects Research and Prevention at the University of North Carolina at Chapel Hill (grant number U01DD001231), and through CDC cooperative agreements under PA #96043, PA #02081, FOA #DD09–001, FOA #DD13–003, and NOFO #DD18–001 to the Centers for Birth Defects Research and Prevention participating in the National Birth Defects Prevention Study (NBDPS) and/or the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS).

DATA AVAILABILITY STATEMENT

Data from the National Birth Defects Prevention Study (NBDPS) and the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS) are not released to the public. Qualified researchers can be granted access to NBDPS and/or BD-STEPS data for analysis through collaboration with one of the Centers for Birth Defects Research and Prevention (CBDRP). Information for access is available at https://www.cdc.gov/ncbddd/birthdefects/nbdps-public-access-procedures.html. The Environmental Quality Index (EQI) data are available from the US Environmental Protection Agency at https://www.epa.gov/healthresearch/environmental-quality-index-eqi.

REFERENCES

Agopian AJ, Langlois PH, Cai Y, Canfield MA, & Lupo PJ (2013). Maternal residential atrazine exposure and gastroschisis by maternal age. Maternal and Child Health Journal, 17(10), 1768–1775. 10.1007/s10995-012-1196-3 [PubMed: 23184502]

Baldacci S, Santoro M, Coi A, Mezzasalma L, Bianchi F, & Pierini A (2020). Lifestyle and sociodemographic risk factors for gastroschisis: A systematic review and meta-analysis. Archives of Disease in Childhood, 105(8), 756–764. 10.1136/archdischild-2019-318412 [PubMed: 32051127]

Bassil KL, Yang J, Arbour L, Moineddin R, Brindle ME, Hazell E, & Skarsgard ED (2016). Spatial variability of gastroschisis in Canada, 2006–2011: An exploratory analysis. Canadian Journal of Public Health, 107(1), e62–e67. 10.17269/cjph.107.5084 [PubMed: 27348112]

Carmichael SL, Ma C, Tinker S, Shaw GM, & National Birth Defects Prevention Study. (2017). Maternal stressors and social support and risks of delivering babies with gastroschisis or hypospadias. American Journal of Epidemiology, 185(12), 1240–1246. 10.1093/aje/kww121 [PubMed: 28505275]

Carmichael SL, Nelson V, Shaw GM, Wasserman CR, & Croen LA (2003). Socio-economic status and risk of conotruncal heart defects and orofacial clefts. Paediatric and Perinatal Epidemiology, 17(3), 264–271. 10.1046/j.1365-3016.2003.00498.x [PubMed: 12839538]

Castilla EE, Mastroiacovo P, & Orioli IM (2008). Gastroschisis: International epidemiology and public health perspectives. American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 148C(3), 162–179. 10.1002/ajmg.c.30181 [PubMed: 18655097]

Egger PA, de Souza MP, Riedo CO, et al. (2022). Gastroschisis annual incidence, mortality, and trends in extreme southern Brazil. Jornal de Pediatria, 98(1), 69–75. 10.1016/j.jped.2021.04.007 [PubMed: 34115974]

Elliott L, Loomis D, Lottritz L, Slotnick RN, Oki E, & Todd R (2009). Case-control study of a gastroschisis cluster in Nevada. Archives of Pediatrics & Adolescent Medicine, 163(11), 1000–1006. 10.1001/archpediatrics.2009.186 [PubMed: 19884590]

Feldkamp ML, Carey JC, & Sadler TW (2007). Development of gastroschisis: Review of hypotheses, a novel hypothesis, and implications for research. American Journal of Medical Genetics. Part A, 143A(7), 639–652. 10.1002/ajmg.a.31578 [PubMed: 17230493]

Fisher SC, Howley MM, Romitti PA, Desrosiers TA, Jabs EW, Browne ML, & the National Birth Defects Prevention Study. (2022). Maternal periconceptional alcohol consumption and gastroschisis in the National Birth Defects Prevention Study, 1997–2011. Paediatric and Perinatal Epidemiology, 36(6), 782–791. 10.1111/ppe.12882 [PubMed: 35437856]

Gray CL, Lobdell DT, Rappazzo KM, Jian Y, Jagai JS, Messer LC, Patel AP, DeFlorio-Barker SA, Lyttle C, Solway J, & Rzhetsky A (2018). Associations between environmental quality and adult asthma prevalence in medical claims data. Environmental Research, 166, 529–536. 10.1016/j.envres.2018.06.020 [PubMed: 29957506]

Harris EL, Hart SJ, Minutillo C, Ravikumara M, Warner TM, Williams Y, Nathan EA, & Dickinson JE (2016). The long-term neurodevelopmental and psychological outcomes of gastroschisis: A cohort study. Journal of Pediatric Surgery, 51(4), 549–553. 10.1016/j.jpedsurg.2015.08.062 [PubMed: 26490011]

Huybrechts KF, Straub L, Karlsson P, Pazzagli L, Furu K, Gissler M, Hernandez-Diaz S, Nørgaard M, Zoega H, Bateman BT, Cesta CE, Cohen JM, Leinonen MK, Reutfors J, Selmer RM, Suarez EA, Ulrichsen SP, & Kieler H (2023). Association of in utero antipsychotic medication exposure with risk of congenital malformations in Nordic countries and the US. JAMA Psychiatry, 80(2), 156–166. 10.1001/jamapsychiatry.2022.4109 [PubMed: 36477338]

Jagai JS, Messer LC, Rappazzo KM, Gray CL, Grabich SC, & Lobdell DT (2017). County-level cumulative environmental quality associated with cancer incidence [published correction appears in Cancer. 2019 May 15;125(10): 1756]. Cancer, 123(15), 2901–2908. 10.1002/cncr.30709 [PubMed: 28480506]

Jian Y, Messer LC, Jagai JS, Rappazzo KM, Gray CL, Grabich SC, & Lobdell DT (2017). Associations between environmental quality and mortality in the contiguous United States, 2000–2005. Environmental Health Perspectives, 125(3), 355–362. 10.1289/EHP119 [PubMed: 27713110]

Jones AM, Isenburg J, Salemi JL, Arnold KE, Mai CT, Aggarwal D, Arias W, Carrino GE, Ferrell E, Folorunso O, Ibe B, Kirby RS, Krapfl HR, Marengo LK, Mosley BS, Nance AE, Romitti PA, Spadafino J, Stock J, & Honein MA (2016). Increasing prevalence of Gastroschisis—14 states, 1995–2012. Morbidity and Mortality Weekly Report, 65(2), 23–26. 10.15585/mmwr.mm6502a2 [PubMed: 26796490]

Kazaura MR, Lie RT, Irgens LM, Didriksen A, Kapstad M, Egenaes J, & Bjerkedal T (2004). Increasing risk of gastroschisis in Norway: An age-period-cohort analysis. American Journal of Epidemiology, 159(4), 358–363. 10.1093/aje/kwh051 [PubMed: 14769639]

Kielb C, Lin S, Herdt-Losavio M, Bell E, Chapman B, Rocheleau CM, Lawson C, Waters M, Stewart P, Olney RS, Romitti PA, Cao Y, Druschel C, & National Birth Defects Prevention Study. (2014). Maternal periconceptional occupational exposure to pesticides and selected musculoskeletal birth defects. International Journal of Hygiene and Environmental Health, 217(2–3), 248–254. 10.1016/j.ijheh.2013.06.003 [PubMed: 23871272]

Krajewski AK, Rappazzo KM, Langlois PH, Messer LC, & Lobdell DT (2021). Associations between cumulative environmental quality and ten selected birth defects in Texas. Birth Defects Research, 113(2), 161–172. 10.1002/bdr2.1788 [PubMed: 32864854]

Liu S, Evans J, Boutin A, Luo W, Gheorghe M, Auger N, Arbour L, Moore A, Joseph KS, & Little J (2021). Time trends, geographic variation and risk factors for gastroschisis in Canada: A population-based cohort study 2006–2017. Paediatric and Perinatal Epidemiology, 35(6), 664–673. 10.1111/ppe.12800 [PubMed: 34472132]

Lobdell DT, Jagai JS, Rappazzo K, & Messer LC (2011). Data sources for an environmental quality index: Availability, quality, and utility. American Journal of Public Health, 101(1), S277–S285. 10.2105/AJPH.2011.300184 [PubMed: 21836111]

Luben TJ, Messer LC, Mendola P, Carozza SE, Horel SA, & Langlois PH (2009). Urban-rural residence and the occurrence of neural tube defects in Texas, 1999–2003. Health & Place, 15(3), 848–854. 10.1016/j.healthplace.2009.02.006 [PubMed: 19299192]

Lupo PJ, Danysh HE, Symanski E, Langlois PH, Cai Y, & Swartz MD (2015). Neighborhood-based socioeconomic position and risk of oral clefts among offspring. American Journal of Public Health, 105(12), 2518–2525. 10.2105/AJPH.2015.302804 [PubMed: 26469673]

Lupo PJ, Langlois PH, Reefhuis J, Lawson CC, Symanski E, Desrosiers TA, Khodr ZG, Agopian AJ, Waters MA, Duwe KN, Finnell RH, Mitchell LE, Moore CA, Romitti PA, Shaw GM, & for the National Birth Defects Prevention Study. (2012). Maternal occupational exposure to polycyclic aromatic hydrocarbons: Effects on gastroschisis among offspring in the National Birth Defects Prevention Study. Environmental Health Perspectives, 120(6), 910–915. 10.1289/ehp.1104305 [PubMed: 22330681]

Mac Bird T, Robbins JM, Druschel C, Cleves MA, Yang S, Hobbs CA, & National Birth Defects Prevention Study. (2009). Demographic and environmental risk factors for gastroschisis and omphalocele in the National Birth Defects Prevention Study. Journal of Pediatric Surgery, 44(8), 1546–1551. 10.1016/j.jpedsurg.2008.10.109 [PubMed: 19635303]

Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ, Lupo PJ, Riehle-Colarusso T, Cho SJ, Aggarwal D, Kirby RS, & National Birth Defects Prevention Network. (2019). National

population-based estimates for major birth defects, 2010–2014. Birth Defects Research, 111(18), 1420–1435. 10.1002/bdr2.1589 [PubMed: 31580536]

Mastroiacovo P, Lisi A, Castilla EE, Martínez-Frías ML, Bermejo E, Marengo L, Kucik J, Siffel C, Halliday J, Gatt M, Annerèn G, Bianchi F, Canessa MA, Danderfer R, De Walle H, Harris J, Li Z, Lowry RB, McDonell R, … Yevtushok L (2007). Gastroschisis and associated defects: An international study. American Journal of Medical Genetics. Part A, 143A(7), 660–671. 10.1002/ajmg.a.31607 [PubMed: 17357116]

Messer LC, Jagai JS, Rappazzo KM, & Lobdell DT (2014). Construction of an environmental quality index for public health research. Environmental Health, 13(1), 39. 10.1186/1476-069X-13-39 [PubMed: 24886426]

Messer LC, Luben TJ, Mendola P, Carozza SE, Horel SA, & Langlois PH (2010). Urban-rural residence and the occurrence of cleft lip and cleft palate in Texas, 1999–2003. Annals of Epidemiology, 20(1), 32–39. 10.1016/j.annepidem.2009.09.006 [PubMed: 20006274]

Neo DT, Desrosiers TA, Martin CL, Carmichael SL, Gucsavas-Calikoglu M, Conway KM, Evans SP, Feldkamp ML, Gilboa SM, Insaf TZ, Musfee FI, Shaw GM, Shumate CJ, Werler MM, Olshan AF, & the National Birth Defects Prevention Study. (2023). Neighborhood-level socioeconomic position during early pregnancy and risk of Gastroschisis. Epidemiology, 34(4), 576–588. 10.1097/EDE.0000000000001621 [PubMed: 36976718]

O'Campo P, Burke JG, Culhane J, Elo IT, Eyster J, Holzman C, Messer LC, Kaufman JS, & Laraia BA (2008). Neighborhood deprivation and preterm birth among non-Hispanic black and white women in eight geographic areas in the United States. American Journal of Epidemiology, 167(2), 155–163. 10.1093/aje/kwm277 [PubMed: 17989062]

Ortega-García JA, Soldin OP, Sánchez-Sauco MF, Cánovas-Conesa A, Gomaríz-Peñalver V, Jaimes-Vega D, Perales J, Cárceles-Alvarez A, Martínez-Ros M, & Ruiz D (2013). Violence against women and gastroschisis: A case-control study. International Journal of Environmental Research and Public Health, 10(10), 5178–5190. 10.3390/ijerph10105178 [PubMed: 24142184]

Padula AM, Yang W, Schultz K, Lee C, Lurmann F, Hammond SK, & Shaw GM (2021). Gene-environment interactions between air pollution and biotransformation enzymes and risk of birth defects. Birth Defects Research, 113(9), 676–686. 10.1002/bdr2.1880 [PubMed: 33569925]

Patel AP, Jagai JS, Messer LC, Gray CL, Rappazzo KM, Deflorio-Barker SA, & Lobdell DT (2018). Associations between environmental quality and infant mortality in the United States, 2000–2005. Archives of Public Health, 76, 60. 10.1186/s13690-018-0306-0 [PubMed: 30356923]

Rager JE, Bangma J, Carberry C, Chao A, Grossman J, Lu K, Manuck TA, Sobus JR, Szilagyi J, & Fry RC (2020). Review of the environmental prenatal exposome and its relationship to maternal and fetal health. Reproductive Toxicology, 98, 1–12. 10.1016/j.reprotox.2020.02.004 [PubMed: 32061676]

Raitio A, Tauriainen A, Leinonen MK, Syvänen J, Kemppainen T, Löyttyniemi E, Sankilampi U, Gissler M, Hyvärinen A, & Helenius I (2020). Maternal risk factors for gastroschisis: A population-based case-control study. Birth Defects Research, 112(13), 989–995. 10.1002/bdr2.1703 [PubMed: 32406607]

Rappazzo KM, Messer LC, Jagai JS, Gray CL, Grabich SC, & Lobdell DT (2015). The associations between environmental quality and preterm birth in the United States, 2000–2005: A cross-sectional analysis. Environmental Health, 14, 50. Published 2015 Jun 9. 10.1186/s12940-015-0038-3 [PubMed: 26051702]

Rasmussen SA, & Frías JL (2008). Non-genetic risk factors for gastroschisis. American Journal of Medical Genetics. Part C, Seminars in Medical Genetics, 148C(3), 199–212. 10.1002/ajmg.c.30175 [PubMed: 18655102]

Rasmussen SA, Olney RS, Holmes LB, Lin AE, Keppler-Noreuil KM, Moore CA, & the National Birth Defects Prevention Study. (2003). Guidelines for case classification for the National Birth Defects Prevention Study. Birth Defects Research. Part A, Clinical and Molecular Teratology, 67(3), 193–201. 10.1002/bdra.10012 [PubMed: 12797461]

Reefhuis J, Gilboa SM, Anderka M, Browne ML, Feldkamp ML, Hobbs CA, Jenkins MM, Langlois PH, Newsome KB, Olshan AF, Romitti PA, Shapira SK, Shaw GM, Tinker SC, Honein MA, & the National Birth Defects Prevention Study. (2015). The National Birth Defects Prevention Study: A

review of the methods. Birth Defects Research. Part A, Clinical and Molecular Teratology, 103(8), 656–669. 10.1002/bdra.23384 [PubMed: 26033852]

Robert SA (1999). Socioeconomic position and health: The independent contribution of community socioeconomic context. Annual Review of Sociology, 25, 489–516.

Root ED, Meyer RE, & Emch M (2011). Socioeconomic context and gastroschisis: Exploring associations at various geographic scales. Social Science & Medicine, 72(4), 625–633. 10.1016/j.socscimed.2010.11.025 [PubMed: 21216059]

Root ED, Meyer RE, & Emch ME (2009). Evidence of localized clustering of gastroschisis births in North Carolina, 1999–2004. Social Science & Medicine, 68(8), 1361–1367. 10.1016/j.socscimed.2009.01.034 [PubMed: 19231056]

Salinas-Torres VM, Salinas-Torres RA, Cerda-Flores RM, & Martínez-de-Villarreal LE (2018). Familial occurrence of gastroschisis: A population-based overview on recurrence risk, sex-dependent influence, and geographical distribution. Pediatric Surgery International, 34(3), 277–282. 10.1007/s00383-018-4224-6 [PubMed: 29335896]

Siega-Riz AM, Herring AH, Olshan AF, Smith J, & Moore C (2009). National Birth Defects Prevention Study. The joint effects of maternal prepregnancy body mass index and age on the risk of gastroschisis. Paediatric and Perinatal Epidemiology, 23(1), 51–57. 10.1111/j.1365-3016.2008.00990.x

Skarsgard ED (2016 Jun). Management of gastroschisis. Current Opinion in Pediatrics, 28(3), 363–369. [PubMed: 26974976]

Stallings EB, Isenburg JL, Short TD, Heinke D, Kirby RS, Romitti PA, Canfield MA, O'Leary LA, Liberman RF, Forestieri NE, Nembhard WN, Sandidge T, Nestoridi E, Salemi JL, Nance AE, Duckett K, Ramirez GM, Shan X, Shi J, & Lupo PJ (2019). Population-based birth defects data in the United States, 2012–2016: A focus on abdominal wall defects. Birth Defects Research, 111(18), 1436–1447. 10.1002/bdr2.1607 [PubMed: 31642616]

Torfs CP, Katz EA, Bateson TF, Lam PK, & Curry CJ (1996). Maternal medications and environmental exposures as risk factors for gastroschisis. Teratology, 54(2), 84–92. 10.1002/(SICI)1096-9926(199606)54:2<84::AID-TERA4>3.0.CO;2-4 [PubMed: 8948544]

United States Department of Agricultures (USDA). (2019). Rural-Urban Continuum Codes. https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/

United States Environmental Protection Agency (US EPA). (2020a). Environmental dataset gateway download locations. EQI. https://edg.epa.gov/data/Public/ORD/NHEERL/EQI

United States Environmental Protection Agency (US EPA). (2020b). Environmental quality index 2006–2010, Technical Report.

United States Environmental Protection Agency (US EPA). (2020c). Environmental dataset gateway download locations. EQI. [Dataset]. https://edg.epa.gov/data/Public/ORD/NHEERL/EQI

Vinikoor-Imler LC, Messer LC, Evenson KR, & Laraia BA (2011). Neighborhood conditions are associated with maternal health behaviors and pregnancy outcomes. Social Science & Medicine, 73(9), 1302–1311. 10.1016/j.socscimed.2011.08.012 [PubMed: 21920650]

Waller SA, Paul K, Peterson SE, & Hitti JE (2010). Agricultural-related chemical exposures, season of conception, and risk of gastroschisis in Washington state [published correction appears in Am J Obstet Gynecol. 2010 Aug;203(2):183]. American Journal of Obstetrics and Gynecology, 202(3), 241.e1–241. e2416. 10.1016/j.ajog.2010.01.023

Wasserman CR, Shaw GM, Selvin S, Gould JB, & Syme SL (1998). Socioeconomic status, neighborhood social conditions, and neural tube defects. American Journal of Public Health, 88(11), 1674–1680. 10.2105/ajph.88.11.1674 [PubMed: 9807535]

Werler MM, Guéry E, Waller DK, & Parker SE (2018). Gastroschisis and cumulative stressor exposures. Epidemiology, 29(5), 721–728. [PubMed: 29863532]

Werler MM, Mitchell AA, & Shapiro S (1992). First trimester maternal medication use in relation to gastroschisis. Teratology, 45(4), 361–367. [PubMed: 1533958]

Yazdy MM, Werler MM, Feldkamp ML, Shaw GM, Mosley BS, Vieira VM, & The National Birth Defects Prevention Study. (2015). Spatial analysis of gastroschisis in the National Birth Defects Prevention Study. Birth Defects Research. Part A, Clinical and Molecular Teratology, 103(6), 544–553. 10.1002/bdra.23375 [PubMed: 25850424]

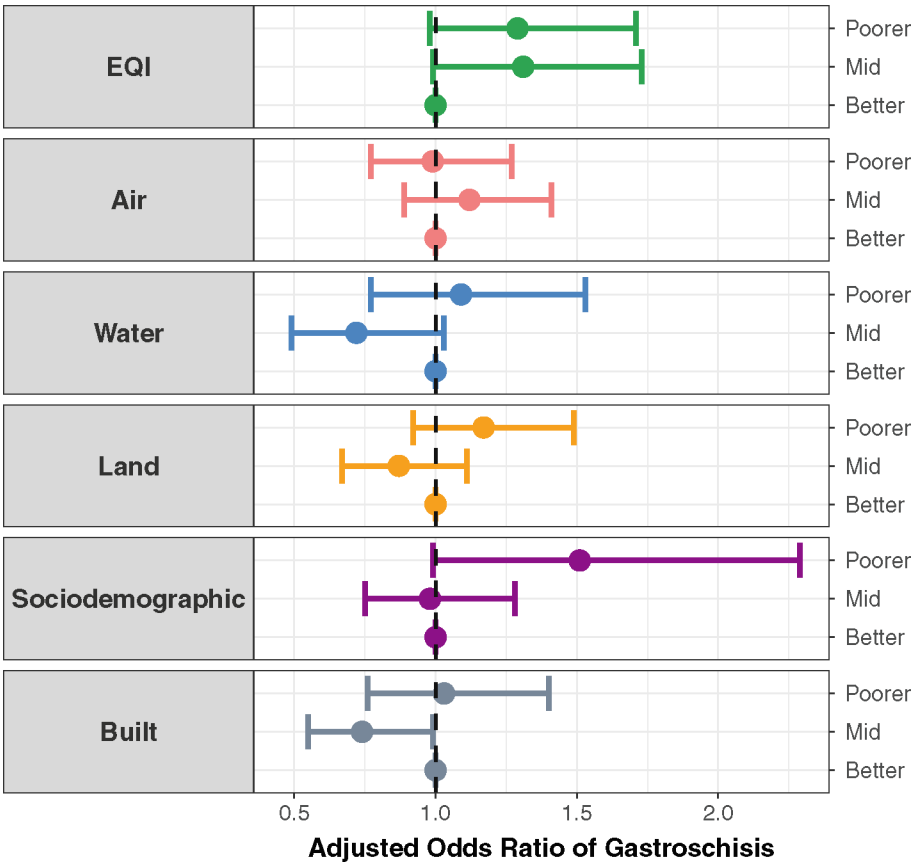

FIGURE 1.

Adjusted odds ratios with 95% confidence intervals for the association between the Environmental Quality Index (EQI) overall and gastroschisis (top panel), and between the five domain-specific indices and gastroschisis (lower panels). Odds ratios are estimating the relative risk of having a pregnancy with gastroschisis among women whose residential county at conception was estimated to have poorer environmental quality or mid-range environmental quality compared to better environmental quality (referent), as measured by the EQI. All models were adjusted for maternal age, race/ethnicity, education, and pre-pregnancy body mass index. Each domain-specific model was further adjusted for the other EQI domains.

TABLE 1

Maternal characteristics for cases with gastroschisis and control infants without a birth defect, National Birth Defects Prevention Study, 2006–2011.

	Cases (*n* = 594) *n* (%)	**Controls (*n* = 4105) *n* (%)**
Age at conception		
<20 years	224 (37.7)	446 (10.9)
≥20 years	370 (62.3)	3659 (89.1)
Race/ethnicity		
Non-Hispanic White	282 (47.5)	2322 (56.6)
Non-Hispanic Black	63 (10.6)	403 (9.8)
Hispanic	198 (33.3)	1079 (26.3)
Other	51 (8.6)	301 (7.3)
Completed years of education		
< High school	114 (19.2)	607 (14.8)
High school	218 (36.7)	870 (21.2)
> High school	219 (36.9)	2473 (60.2)
Missing	43 (7.2)	155 (3.8)
Pre-pregnancy BMI		
Underweight (<18 kg/m^2)	54 (9.1)	193 (4.7)
Normal weight (18- < 25 kg/m^2)	359 (60.4)	1956 (47.7)
Overweight or Obese (≥25 kg/m^2)	160 (26.9)	1777 (43.3)
Missing	21 (3.5)	179 (4.4)
Residential RUCC		
Metropolitan urbanized (RUCC1)	501 (84.3)	3542 (86.3)
Non-metropolitan urbanized (RUCC2)	27 (4.6)	195 (4.8)
Less urbanized (RUCC3)	60 (10.1)	314 (7.7)
Thinly populated (RUCC4)	6 (1.0)	54 (1.3)

Abbreviations: BMI, body mass index; RUCC, rural-urban continuum code.

TABLE 2

Associations between gastroschisis and environmental quality (overall and domain-specific) of maternal county of residence during early pregnancy as measured by the Environmental Quality Index, National Birth Defects Prevention Study, 2006–2011.

	Cases (*n* = 594)	Controls (*n* = 4105)	OR (95% CI)	aOR[a] (95% CI)
Overall EQI				
Better environmental quality (<−0.32)	94 (15.8)	763 (18.6)	Reference	Reference
Mid-range (−0.32–0.49)	235 (39.6)	1596 (38.9)	1.20 (0.39, 1.54)	1.31 (0.99, 1.73)
Poorer environmental quality (>0.49)	265 (44.6)	1746 (42.5)	1.23 (0.96, 1.58)	1.29 (0.98, 1.71)
Air domain				
Better environmental quality (<−0.32)	226 (38.1)	1586 (38.6)	Reference	Reference
Mid-range (−0.32–0.42)	213 (35.9)	1312 (32.0)	1.09 (0.88, 1.34)	1.12 (0.89, 1.41)
Poorer environmental quality (>0.42)	155 (26.1)	1207 (29.4)	0.94 (0.75, 1.18)	0.99 (0.77, 1.27)
Water domain				
Better environmental quality (<−0.40)	62 (10.4)	462 (11.3)	Reference	Reference
Mid-range (−0.40–0.70)	178 (30.0)	1356 (33.0)	0.80 (0.58, 1.12)	0.72 (0.49, 1.03)
Poorer environmental quality (>0.70)	354 (59.6)	2287 (55.7)	1.08 (0.80, 1.48)	1.09 (0.77, 1.53)
Land domain				
Better environmental quality (<−0.25)	205 (34.5)	1574 (38.3)	Reference	Reference
Mid-range (−0.25–0.53)	146 (24.6)	1189 (29.0)	0.90 (0.72, 1.14)	0.87 (0.67, 1.11)
Poorer environmental quality (>0.53)	243 (41.0)	1342 (32.7)	1.27 (1.02, 1.58)	1.17 (0.92, 1.49)
Sociodemographic domain				
Better environmental quality (<−0.22)	405 (68.2)	3072 (74.8)	Reference	Reference
Mid-range (−0.22–0.52)	152 (25.6)	872 (21.2)	1.10 (0.86, 1.39)	0.98 (0.75, 1.28)
Poorer environmental quality (>0.52)	37 (6.2)	161 (3.9)	1.87 (1.28, 2.73)	1.51 (0.99, 2.29)
Built environment domain				
Better environmental quality (<−0.35)	100 (16.8)	707 (17.2)	Reference	Reference
Mid-range (−0.35–0.40)	198 (33.3)	1802 (43.9)	0.79 (0.60, 1.04)	0.74 (0.55, 0.99)
Poorer environmental quality (>0.40)	296 (49.8)	1596 (38.9)	1.21 (0.93, 1.58)	1.03 (0.76, 1.40)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; EQI, Environmental Quality Index; OR, odds ratio.

[a]All models adjusted for maternal age, race/ethnicity, education, and pre-pregnancy body mass index. Each domain-specific model was further adjusted for the other domains.

TABLE 3

Maternal age-stratified associations between gastroschisis and environmental quality (overall and domain-specific) of maternal county of residence during early pregnancy as measured by the Environmental Quality Index, National Birth Defects Prevention Study, 2006–2011.

	Unadjusted OR (95% CI)		**Adjusted[a] aOR (95% CI)**	
	<20 years (*n* = 670)	**≥20 years (*n* = 4029)**	**<20 years (*n* = 670)**	**≥20 years (*n* = 4029)**
EQI overall				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	1.30 (0.81, 2.08)	1.23 (0.89, 1.69)	1.13 (0.68, 1.87)	1.32 (0.94, 1.86)
Poorer environmental quality	1.08 (0.69, 1.70)	1.27 (0.93, 1.74)	1.13 (0.70, 1.85)	1.33 (0.95, 1.88)
Air domain				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	0.92 (0.63, 1.35)	1.21 (0.93, 1.58)	1.03 (0.68, 1.58)	1.18 (0.88, 1.56)
Poorer environmental quality	0.78 (0.50, 1.21)	1.01 (0.76, 1.34)	0.95 (0.59, 1.52)	1.03 (0.76, 1.39)
Water domain				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	0.63 (0.32, 1.25)	0.73 (0.49, 1.08)	0.74 (0.35, 1.57)	0.74 (0.48, 1.13)
Poorer environmental quality	1.12 (0.57, 2.18)	1.01 (0.70, 1.45)	1.37 (0.66, 2.82)	1.03 (0.70, 1.52)
Land domain				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	0.79 (0.50, 1.25)	0.89 (0.68, 1.18)	0.84 (0.52, 1.38)	0.89 (0.66, 1.20)
Poorer environmental quality	1.59 (1.04, 2.42)	0.99 (0.75, 1.30)	1.43 (0.91, 2.25)	1.04 (0.78, 1.41)
Sociodemographic domain				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	0.67 (0.44, 1.02)	1.20 (0.89, 1.63)	0.73 (0.47, 1.15)	1.20 (0.86, 1.66)
Poorer environmental quality	0.90 (0.46, 1.74)	2.04 (1.26, 3.31)	0.95 (0.47, 1.92)	1.88 (1.13, 3.14)
Built environment domain				
Better environmental quality	Reference	Reference	Reference	Reference
Mid-range	0.78 (0.46, 1.34)	0.78 (0.56, 1.09)	0.69 (0.39, 1.23)	0.73 (0.51, 1.05)
Poorer environmental quality	0.86 (0.50, 1.46)	1.20 (0.87, 1.66)	0.69 (0.38, 1.24)	1.17 (0.82, 1.66)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; EQI, Environmental Quality Index; OR, odds ratio.

[a]All models adjusted for maternal race/ethnicity, education, pre-pregnancy body mass index. Each domain-specific model was further adjusted for the other domains.