Published in final edited form as:
Birth Defects Res. 2023 September 01; 115(15): 1438–1449. doi:10.1002/bdr2.2224.

Are individual-level risk factors for gastroschisis modified by neighborhood-level socioeconomic factors?

Dayna T. Neo[1], **Chantel L. Martin**[1,2], **Suzan L. Carmichael**[3,4], **Muge Gucsavas-Calikoglu**[5], **Kristin M. Conway**[6], **Shannon Pruitt Evans**[7,8], **Marcia L. Feldkamp**[9], **Suzanne M. Gilboa**[7], **Tabassum Z. Insaf**[10,11], **Fadi I. Musfee**[12,13], **Gary M. Shaw**[3], **Charles Shumate**[14], **Martha M. Werler**[15], **Andrew F. Olshan**[1], **Tania A. Desrosiers**[1],
National Birth Defects Prevention Study

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

[2]Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[3]Department of Pediatrics, Stanford University School of Medicine, Stanford, California, USA

[4]Department of Obstetrics and Gynecology, Stanford University School of Medicine, Stanford, California, USA

[5]Department of Pediatrics, Division of Genetics and Metabolism, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

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

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

[8]Eagle Global Scientific LLC, San Antonio, Texas, USA

[9]Division of Medical Genetics, Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, Utah, USA

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

[11]Department of Epidemiology and Biostatistics, School of Public Health, University at Albany, Rensselaer, New York, USA

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

Correspondence: Dayna T. Neo, Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA. dneo@email.unc.edu.

CONFLICT OF INTEREST STATEMENT
The authors declare no conflicts of interest.

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

[13]Arkansas Center for Birth Defects Research and Prevention, Fay W. Boozman College of Public Health, University of Arkansas for Medical Sciences, Little, Arkansas, USA

[14]Texas Department of State Health Services, Birth Defects Epidemiology and Surveillance Branch, Austin, Texas, USA

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

Abstract

Background: Two strong risk factors for gastroschisis are young maternal age (<20 years) and low/normal pre-pregnancy body mass index (BMI), yet the reasons remain unknown. We explored whether neighborhood-level socioeconomic position (nSEP) during pregnancy modified these associations.

Methods: We analyzed data from 1269 gastroschisis cases and 10,217 controls in the National Birth Defects Prevention Study (1997–2011). To characterize nSEP, we applied the neighborhood deprivation index and used generalized estimating equations to calculate odds ratios and relative excess risk due to interaction.

Results: Elevated odds of gastroschisis were consistently associated with young maternal age and low/normal BMI, regardless of nSEP. High-deprivation neighborhoods modified the association with young maternal age. Infants of young mothers in high-deprivation areas had lower odds of gastroschisis (adjusted odds ratio [aOR]: 3.1, 95% confidence interval [CI]: 2.6, 3.8) than young mothers in low-deprivation areas (aOR: 6.6; 95% CI: 4.6, 9.4). Mothers of low/normal BMI had approximately twice the odds of having an infant with gastroschisis compared to mothers with overweight/obese BMI, regardless of nSEP (aOR range: 1.5–2.3).

Conclusion: Our findings suggest nSEP modified the association between gastroschisis and maternal age, but not BMI. Further research could clarify whether the modification is due to unidentified biologic and/or non-biologic factors.

Keywords

age; birth defects; BMI; gastroschisis; neighborhood; socioeconomic

1 | INTRODUCTION

Gastroschisis is an abdominal birth defect characterized by the protrusion of intestines and sometimes other abdominal organs outside the body (Facts about Gastroschisis | CDC, n.d.; Jones et al., 2016; Stallings et al., 2019). The prevalence of gastroschisis in the United States increased between 1995 and 2005, possibly driven by the increasing prevalence among young mothers: the percentage increase in the prevalence of gastroschisis among mothers younger than 20 years was 6.5% compared with an increase of 0.2% among mothers 35 years or older (Kirby et al., 2013). However, a more recent study showed a decline in the prevalence of gastroschisis using administrative data between 2010 and 2018 (Bhatt et al., 2022).

Many epidemiologic studies of gastroschisis have consistently observed strong associations with young maternal age (Gill et al., 2012; Mac Bird et al., 2009; Reefhuis & Honein, 2004) and low body mass index (BMI) (Siega-Riz et al., 2009), with odds ratio estimates for maternal age <20 years ranging between 6 and 7 (Gill et al., 2012; Reefhuis & Honein, 2004) and for low BMI between 2 and 3 (Draper et al., 2008; Lam et al., 1999). These associations are contrary to many other birth defects (and other adverse pregnancy outcomes) where older maternal age and high BMI increase risk. Thus, these unique associations are likely to provide strong clues about the etiology of gastroschisis, which remains nearly completely unknown. Although a few studies have observed a familial recurrence of cases indicating a genetic contribution to gastroschisis (Feldkamp et al., 2011; Kohl et al., 2010; Torfs & Curry, 1993), it is unlikely that genetics is the sole cause of this birth defect due to the rapidly increasing prevalence. Rather, it is likely that the etiology of gastroschisis is multifactorial involving both genetic and non-genetic risk factors.

Neighborhood contextual factors have been shown to influence the risk of adverse pregnancy outcomes (Culhane & Elo, 2005). Previous studies have observed modest associations between measures of neighborhood socioeconomic characteristics that are independent of individual-level socioeconomic position (iSEP) and adverse maternal health (Penman-Aguilar et al., 2013; Vinikoor-Imler et al., 2011) and birth outcomes, such as low birth weight (O'Campo et al., 1997), preterm birth (O'Campo et al., 2008), orofacial clefts (Lupo et al., 2015), neural tube defects (Wasserman et al., 1998) and congenital heart defects (Carmichael et al., 2003; Carmichael et al., 2009). Two studies have previously examined whether neighborhood-level socioeconomic factors might influence risk of gastroschisis: the first study observed an increased risk among mothers residing in areas characterized by high poverty and unemployment in North Carolina (1998–2004) (Root et al., 2011). The second study is an analysis from our research group using data from the National Birth Defects Prevention Study (NBDPS; 1997–2011), in which we observed an increased risk of gastroschisis associated with maternal residence during early pregnancy in areas classified as low neighborhood socioeconomic position (nSEP)/high deprivation (Neo et al., 2023).

Neighborhood adverse conditions that are correlated with the neighborhood's socioeconomic position may influence the risk of gastroschisis by shaping individual-level risk factors, such as maternal age at conception or pre-pregnancy BMI. In this study, we hypothesized that neighborhood-level social and environmental factors may also have the potential to modify the well-established associations between maternal age, BMI, and gastroschisis. In other words, we hypothesized that the risk of gastroschisis for younger mothers, for example, may vary in magnitude depending on neighborhood-level socioeconomic factors. Gaining a fuller understanding of how nSEP influences the risk of gastroschisis may provide further clues toward elucidating the etiology of this important birth defect. For instance, if the associations between maternal age, BMI, and gastroschisis vary across different strata of nSEP, this may potentially suggest that these individual-level risk factors have a social or environmental component related to nSEP that may explain some of their association with gastroschisis, as opposed to acting exclusively on biological pathways independent of the social context. Thus, in this analysis, we examine whether the associations between young maternal age at conception and low or normal pre-pregnancy BMI and the risk of gastroschisis, differ by nSEP.

2 | METHODS

2.1 | Study population

This study used data from the NBDPS. Detailed study methods have been published elsewhere (Reefhuis et al., 2015). In brief, the NBDPS is a population-based, multi-site, case–control study sponsored by the Centers for Disease Control and Prevention (CDC) that investigates risk factors associated with more than 30 major birth defects, including gastroschisis. The NBDPS included pregnancies between October 1997 and December 2011 in 10 participating states: Arkansas, California, Georgia, Iowa, Massachusetts, North Carolina, New York, New Jersey, Texas, and Utah. The NBDPS was approved by the Institutional Review Board at the CDC and at each participating center.

For this analysis, we included cases that were singleton livebirths, stillbirths (fetal deaths ≥20 weeks' gestation), or terminations with a diagnosis of gastroschisis (British Pediatric Association modification of the International Classification of Diseases, 9th revision). There were seven (<1%) terminations with a diagnosis of gastroschisis. Cases of gastroschisis in the entire state (AR, IA, UT) or selected counties (CA, GA, MA, NC, NY, TX) were ascertained by local birth defects registries. Participants from NJ were not included in this analysis as geocoded addresses were unavailable. Cases with known genetic etiologies were excluded. Using standardized case classification guidelines, diagnoses were confirmed and cases were classified as "isolated" if there was no concurrent major anomaly in the same body system, "multiple" if defects were identified in multiple body systems, or "sequence" if there were additional major defects that were developmentally related to one another (Rasmussen et al., 2003; Reefhuis et al., 2015). Liveborn singleton infants without a birth defect were randomly selected as controls from hospital records and/or birth certificates from the same geographic area and time period as the cases.

Eligible mothers of case and control infants participated in a computer-assisted telephone interview (CATI) approximately 6 weeks to 24 months after their estimated date of delivery. The interview included questions regarding sociodemographic information, residential history, lifestyle and behavioral factors, medical history, and other exposures that occurred between 3 months prior to conception through the end of the pregnancy. Overall, participation rates were approximately 65% for case and 65% for control mothers.

2.2 | Defining maternal neighborhood

During the interview, mothers self-reported all residential addresses at which they lived for at least 30 days between 3 months prior to pregnancy to the end of pregnancy. For this study, we geographically defined "maternal neighborhood" as the census tract corresponding to the address mothers lived at during the periconceptional period, defined as 1 month prior to conception to the third month of pregnancy. If a participant reported multiple addresses for this period (13%), we selected the address with the longest duration. Mothers were excluded if they reported more than one address with the same length of stay during the periconceptional period on the basis that it was unclear which address would have a larger influence on the risk of gastroschisis (<1%) or if they only reported one address with a length of stay fewer than 30 days (<1%) (Figure 1).

2.3 | Geocoding addresses and linkage to US census-tract socioeconomic indicators

Maternal addresses from all NBDPS centers except NJ were centrally geocoded by the Agency for Toxic Substances and Disease Registry's Geospatial Research, Analysis, and Services Program using the Centrus software version 6.00.00 N. All successfully geocoded addresses (97% of eligible NBDPS participants) were linked by CDC to the 2000 and 2010 US Census Tracts using Arc-GIS. Census information from the 2000 US Census and 5-year American Community Survey (ACS) was linked with the NBDPS analytic data set based on Federal Information Processing Standards (FIPS) codes and infant birth year. Specifically, census-tract level data from the 2000 US Decennial Census, 2005–2009 ACS, and 2010–2014 ACS were linked to infants born between 1997–2004, 2005–2009, and 2010–2011, respectively.

Among the 12,243 NBDPS participants in our study population with at least one geocoded address, 97% were assigned a maternal neighborhood during the periconceptional period, as described above. Geocoding at the census tract level was successful for 93% of the interviewed cases and 94% of the controls. Overall, 6315 census tracts were represented in our study sample.

2.4 | Assessing neighborhood-level socioeconomic position

Neighborhood-level SEP was characterized using the neighborhood deprivation index (NDI) developed by Messer et al. (Messer et al., 2006). The NDI is a standardized index that represents five socioeconomic domains including income/poverty, education, employment, housing, and occupation, and has been commonly used to examine the relationships between neighborhood socioeconomic deprivation and pregnancy outcomes (Elo et al., 2009; Janevic et al., 2010; O'Campo et al., 2008). The NDI is comprised of eight census-tract level indicators including percent of crowded housing, percent of males in management and professional occupations, percent of households in poverty, percent of households on public assistance, percent of female-headed households with dependents, percent of unemployed residents, percent of households earning < $30,000 per year, and percent of residents with less than a high school education (Table SS1). To create this index, census tract-level geocoded data from NBDPS centers were pooled and reduced using principal component analysis (PCA). The component loadings of the first principal component were used to weight each census variable's contribution to the index score. The index score was standardized to have a mean of 0 and a standard deviation of 1 (Range: −1.7, 5.6), with high values indicating higher levels of neighborhood deprivation and low values indicating lower levels of neighborhood deprivation. The continuous index score was categorized into tertiles based on the distribution among controls to represent low (reference), moderate, or high neighborhood deprivation and subsequently linked to NBDPS participants based on the periconceptional residence, as described above (Rothman et al., 2014).

2.5 | Individual-level variables

Maternal characteristics were obtained from the NBDPS interview. Self-reported maternal age at conception was dichotomized at 20 years (<20 vs. ≥20 years), since epidemiologic studies of gastroschisis have identified a definitive change in risk at this age threshold (Carmichael et al., 2017; Mac Bird et al., 2009; Reefhuis & Honein, 2004). Maternal pre-pregnancy BMI was calculated using self-reported weight and height (kg/m^2) and subsequently categorized into three groups, representing underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), and overweight/obese (≥25.0 kg/m^2) (Draper et al., 2008).

We developed directed acyclic graphs (DAG) (Greenland et al., 1999) to identify minimally sufficient adjustment sets to mitigate confounding in our analysis of the associations between (1) maternal age and gastroschisis (Figure SS1) and (2) maternal BMI and gastroschisis (Figure S2) with potential effect measure modification by nSEP. Based on our DAGs, the adjustment set for our analyses of maternal age included iSEP characterized by years of education (0–11, 12, >12 years) and household income (<$10,000, $10,000–$50,000, >$50,000); and the adjustment set for analyses of BMI included iSEP similarly characterized by years of education (0–11, 12, >12 years) and household income (<$10,000, $10,000–$50,000, >$50,000), maternal age at conception modeled as a quadratic term to allow for flexible adjustment, smoking (yes, no), alcohol (yes, no), and recreational drug use (yes, no) during the periconceptional period.

2.6 | Statistical analysis

Missing values for the following covariates were imputed using 10 cycles of multiple imputation: household income (9%), pre-pregnancy BMI (3.8%), education (2%), alcohol use (2%), recreational drug use (1.8%), smoking (1.7%), and census-tract SEP indicators (0.01%). For each of the 10 imputation datasets, a PCA was performed to construct the NDI. In addition, to account for potential correlation and non-independence among mothers clustered within the same neighborhood, generalized estimating equations (GEEs) with logistic links and robust errors were conducted on each imputation dataset to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs). All imputation datasets were analyzed separately and the results were combined for inference using the *proc mianalyze* procedure in SAS (SAS/STAT® 13.1 User's Guide, 2013).

To assess potential effect measure modification by nSEP, we compared results within strata of NDI, adjusting for the appropriate minimally sufficient adjustment set. Effect measure modification was evaluated on the additive scale for public health relevance. The additive scale is recommended to indicate whether the effect of a risk factor is greater in a specific sub-population to help target potential interventions and resource allocations. Thus, we calculated the relative excess risk due to interaction (RERI) with 95% CIs based on standard errors obtained using the delta method (Hosmer & Lemeshow, 1992). All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA) and independently replicated (by co-author SE).

3 | RESULTS

3.1 | Description of study population

We analyzed data from 1269 case infants with gastroschisis and 10,217 control infants. Compared to mothers of controls, mothers of case infants were younger (≤20 years) and more likely to be nulliparous; Hispanic; have normal weight or underweight BMI; complete 12 or fewer years of education; have a household income of less than or equal to $50,000;

and to self-report smoking, alcohol and recreational drug use during the periconceptional period (Table 1). Case infants were more likely to be born preterm (32–36 gestational weeks) or very preterm (<32 gestational weeks); and more likely born to residents of California. In our study population, mothers of case infants were more likely to reside in highly deprived ("low" SEP) neighborhoods (45%) (Table 2) and have a shorter mean duration of residence at their periconceptional neighborhood (~2.6 years) compared with mothers of control infants (~3.5 years) (Table 1).

The first principal component of the NDI explained 57% of the total variability among the component measures. The top three indicators most strongly associated with the first principal component were low education, households earning <$30,000 per year, and poverty (Table SS1).

3.2 | Does nSEP modify the association between maternal age at conception and gastroschisis?

Within each stratum of neighborhood socioeconomic deprivation, young maternal age at conception (<20 years) was strongly associated with a higher risk of gastroschisis, and the effect size varied by strata. The magnitude of the association with young maternal age was higher among mothers residing in low deprivation ("high" SEP) neighborhoods (aOR: 6.6; 95% CI: 4.6, 9.4) than among mothers residing in high deprivation ("low" SEP) neighborhoods (aOR: 3.1, 95% CI: 2.6, 3.8). Furthermore, we observed evidence of antagonistic effect measure modification, on the additive scale, by high deprivation neighborhoods (RERI: −2.8; 95% CI: −5.0, −0.6) for the association between young maternal age at conception and gastroschisis. In other words, residing in high deprivation neighborhoods diminishes the effect of young maternal age at conception on the risk of gastroschisis. However, no modification was observed for moderate deprivation neighborhoods (RERI: −2.0; 95% CI: −4.1, 0.2).

Overall, though maternal age remained associated with an elevated odds of gastroschisis across strata of nSEP, the magnitude of the association between young maternal age at conception and gastroschisis decreased as neighborhood deprivation increased (Table 3).

3.3 | Does nSEP modify the association between maternal pre-pregnancy BMI and gastroschisis?

Normal (18.5 kg/m^2 ≤ BMI < 25 kg/m^2) or underweight BMI (<18.5 kg/m^2) were consistently associated with an increased risk of gastroschisis compared to overweight/obese BMI (≥25 kg/m^2), irrespective of the neighborhood socioeconomic deprivation level. Specifically, within each stratum of NDI, mothers with underweight (aOR range: 1.5–2.1) and normal (aOR range: 2.2–2.3) BMI had approximately two times the odds of having an infant with gastroschisis compared to mothers with overweight/obese BMI. The RERI estimates indicated that residing in moderate or high deprivation neighborhoods did not modify the odds of gastroschisis for mothers with normal (moderate deprivation RERI: 0.03, 95% CI: −0.6, 0.6; high deprivation RERI: −0.2, −0.9, 0.4) or underweight (moderate deprivation RERI: 0.6, 95% CI: −0.5, 1.7; high deprivation RERI: 0.4, 95% CI: −0.7, 1.5) BMI (Table 4).

4 | DISCUSSION

In our study, young maternal age and low/normal maternal BMI were consistently associated with elevated odds of gastroschisis regardless of nSEP. We observed that neighborhood deprivation sub-additively modified the association between maternal age at conception and gastroschisis, such that young mothers in low deprivation ("high" SEP) neighborhoods had nearly double the risk of having an infant with gastroschisis than young mothers in high deprivation ("low" SEP) neighborhoods. In other words, the association between young maternal age and gastroschisis among mothers residing in low deprivation ("high" SEP) neighborhoods was nearly double the association of young maternal age and gastroschisis among mothers residing in high deprivation ("low" SEP) neighborhoods. Neighborhood socioeconomic deprivation was not found to modify the association between maternal pre-pregnancy BMI and gastroschisis.

Prior studies have consistently reported associations of gastroschisis with maternal age and BMI, yet we are unaware of any other studies that have evaluated the potential influence of contextual socioeconomic factors on these unique associations. In a previous analysis of this same NBDPS population (Neo et al., 2023), we observed a monotonic increase in the odds of gastroschisis among mothers residing in moderate and high deprivation areas, after adjustment for maternal race/ethnicity, education, household income, length of residency, and birth year. Since neighborhood deprivation may differentially affect women depending on factors such as race/ethnicity, age, and others, this indicates the importance of examining how contextual factors may impact the relationships between individual-level risk factors and gastroschisis.

Our results are consistent with the strong evidence in the existing literature that mothers younger than 20 years are at a higher risk of having an infant with gastroschisis relative to mothers older than 20 years (Kazaura et al., 2004; Mac Bird et al., 2009; Torfs et al., 1994). The reasons that young mothers are at higher risk remain unknown. It is suspected that lifestyle behaviors, environmental exposures, and other risk factors known to be more prevalent among younger mothers likely play a role in the risk of gastroschisis (Draper et al., 2008; Feldkamp et al., 2019; Fisher et al., 2022). In addition, to some degree, it is plausible that these risk factors are in some ways influenced by the contextual characteristics closely related to the SEP of a mother's residing neighborhood. Although we observed that nSEP modifies the association between maternal age at conception and gastroschisis, young mothers consistently had a higher risk than older mothers, across all strata of nSEP, suggesting that the underlying etiology of gastroschisis among adolescent mothers is partly driven by biologic or social factor(s) unrelated to our measure of nSEP.

It is unclear why young mothers residing in low deprivation neighborhoods have a substantially higher risk of gastroschisis relative to young mothers in high deprivation neighborhoods. One possible explanation leans on the relative social deprivation hypothesis, which suggests that inequality between a mother's social experience relative to her peer community may cause additional psychological strain leading to higher levels of psychosocial stress (Ganahl et al., 1980; Smith & Huo, 2014). Although adolescent mothers tend to be more socially disadvantaged irrespective of the level of neighborhood deprivation

(Singh et al., 2001), residing in low deprivation areas may cause increased levels of psychosocial stress associated with relative social standing comparisons, lack of social support during pregnancy, and a sense of relative deprivation. This may potentially explain, at least in part, why the risk of gastroschisis among young mothers in low deprivation areas was nearly double that of young mothers in high deprivation areas.

Our results for the association between maternal BMI and gastroschisis are also consistent with prior literature demonstrating that mothers with low/normal BMI have an increased risk of having an infant with gastroschisis. Although neighborhood socioeconomic factors have been shown to be associated with BMI through access to physical activity opportunities (Lee et al., 2007) or access to healthy foods (Larson et al., 2009), our results indicated that neighborhood deprivation did not modify the association between maternal BMI and gastroschisis given that the effect estimates remained similar regardless of nSEP. This suggests that individual-level factors associated with BMI may play a more important role in the development of gastroschisis.

This study has some limitations. First, non-differential exposure misclassification may have resulted from two sources. The first is the use of census tracts to define maternal neighborhoods. Though based on reported residence during early pregnancy, this geographical unit may not accurately represent the "neighborhood" to which a mother perceives she belongs. However, census tracts have been used in prior neighborhood-level studies and have been shown to be meaningfully useful in the context of adverse birth outcomes (Krieger et al., 2003). The second potential source of non-differential exposure misclassification is due to the lack of data regarding the amount of time and interaction mothers may have with their residential environment. Mothers who do not often interact with their neighborhoods may be misclassified with respect to the level of neighborhood socioeconomic deprivation to which they are exposed. However, the impact of this potential misclassification cannot be determined with the data available. Another limitation of this study is selection bias that may have been introduced at two levels. The first is factors associated with non-participation in the NBDPS, since participation was 65% for both case and control mothers, respectively. However, a previous study reported that participants and non-participants had similar demographic characteristics (Cogswell et al., 2009). The second is if maternal characteristics differed between mothers with and without a geocoded address. In our data, mothers who were excluded due to missing geocodes were more likely to be younger than 20 years and of non-Hispanic Black or Hispanic race and ethnicity. However, given only 3% of NBDPS participants were excluded due to missing geocoded addresses, the potential impact of this selection bias is likely to be minimal. Lastly, the potential for residual confounding should be noted. Although we adjusted for several covariates identified by our DAG, it is possible that residual confounding from unknown confounders, such as environmental or occupational exposures, or mis-specified variables contributed to our results.

Despite these limitations, this study also has several strengths. This is the first known study to examine if nSEP modifies the associations between maternal age, pre-pregnancy BMI, and the risk of gastroschisis. Our findings build upon our previous research in this study population, which showed that high deprivation/low nSEP was associated with an increased risk of gastroschisis (Neo et al., 2023). Another strength of this study is the use of NBDPS data. The NBDPS provided population-based ascertainment of cases and controls, extensive covariate information, standardized case classification verified by clinical geneticists, and a large sample size. In addition, maternal residential addresses were centrally geocoded at the CDC increasing data consistency and improving quality control of geocoded addresses used to characterize nSEP. Lastly, our study was strengthened by defining maternal neighborhood based on addresses during the periconceptional period, which closely aligns with the critical period of gastroschisis development.

In our study, the well-established association between young maternal age and risk of gastroschisis was modified by neighborhood socioeconomic position, suggesting that neighborhood-level characteristics may play a partial role in the relationship between maternal age and gastroschisis for some women. This is the first study to evaluate the potential influence of nSEP on these individual-level risk factors for gastroschisis, and more studies may help corroborate our findings as well as to further investigate why young mothers in high nSEP/low deprivation neighborhoods have a higher risk of having an infant with gastroschisis compared with young mothers in low nSEP/high deprivation neighborhoods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding information

This work was supported by a cooperative agreement from the Centers for Disease Control and Prevention (CDC; U50CCU422096) to the North Carolina Center for Birth Defects Research and Prevention, and through cooperative agreements under PA 96043, PA 02081, and FOA DD09-001 from the CDC to other Centers for Birth Defects Research and Prevention participating in the National Birth Defects Prevention Study. This work was also supported in part by an institutional training grant from the National Institute of Child Health and Development (T32 HD 52468).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

REFERENCES

Bhatt P, Poku FA, Umscheid J, Ayensu M, Parmar N, Vasudeva R, Donda K, Doshi H, & Dapaah-Siakwan F (2022). Trends in prevalence and mortality of gastroschisis and omphalocele in the United States from 2010 to 2018. World Journal of Pediatrics, 18(7), 511–514. 10.1007/s12519-022-00544-2 [PubMed: 35294711]

Carmichael SL, Ma C, & Shaw GM (2009). Socioeconomic measures, orofacial clefts, and conotruncal heart defects in California. Birth Defects Research Part A: Clinical and Molecular Teratology, 85, 850–857. 10.1002/bdra.20614 [PubMed: 19645048]

Carmichael SL, Ma C, Tinker S, & Shaw GM (2017). Original contribution maternal stressors and social support and risks of delivering babies with gastroschisis or hypospadias, 185, 1240–1246. 10.1093/aje/kww121

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]

Cogswell ME, Bitsko RH, Anderka M, Caton AR, Feldkamp ML, Sherlock SMH, Meyer RE, Ramadhani T, Robbins JM, Shaw GM, Mathews TJ, Royle M, Reefhuis J, & the National Birth Defects Prevention Study. (2009). Control selection and participation in an ongoing, population-based, case-control study of birth defects. American Journal of Epidemiology, 170(8), 975–985. 10.1093/aje/kwp226 [PubMed: 19736223]

Culhane JF, & Elo IT (2005). Neighborhood context and reproductive health. American Journal of Obstetrics and Gynecology, 192, S22–S29. 10.1016/j.ajog.2005.01.071 [PubMed: 15891708]

Draper ES, Rankin J, Tonks AM, Abrams KR, Field DJ, Clarke M, & Kurinczuk JJ (2008). Recreational drug use: A major risk factor for gastroschisis? American Journal of Epidemiology, 167(4), 485–491. 10.1093/aje/kwm335 [PubMed: 18063593]

Elo IT, Culhane JF, Kohler IV, O'Campo P, Burke JG, Messer LC, Kaufman JS, Laraia BA, Eyster J, & Holzman C (2009). Neighbourhood deprivation and small-for-gestational term births in the United States. Paediatric and Perinatal Epidemiology, 23(1), 87–96. 10.1111/J.1365-3016.2008.00991.X [PubMed: 19228318]

Facts about Gastroschisis j CDC. Accessed August 15, 2020. https://www.cdc.gov/ncbddd/birthdefects/gastroschisis.html

Feldkamp ML, Arnold KE, Krikov S, Reefhuis J, Almli LM, Moore CA, & Botto LD (2019). Risk of gastroschisis with maternal genitourinary infections: The US National birth defects prevention study 1997–2011. BMJ Open, 9(3), e026297. 10.1136/bmjopen-2018-026297

Feldkamp ML, Carey JC, Pimentel R, Krikov S, & Botto LD (2011). Is gastroschisis truly a sporadic defect? Familial cases of gastroschisis in Utah, 1997 to 2008. Birth Defects Research Part A: Clinical and Molecular Teratology, 91(10), 873–878. 10.1002/bdra.22844 [PubMed: 21987464]

Fisher SC, Howley MM, Romitti PA, Desrosiers TA, Jabs EW, & Browne ML (2022). Maternal periconceptional alcohol consumption and gastroschisis in the National Birth Defects Prevention Study, 1997–2011. Paediatric and Perinatal Epidemiology, 00, 1–10. 10.1111/ppe.12882

Ganahl S, Gonzalez M, & Greenberg J (1980). An empirical examination of relative deprivation, 456, 442–456.

Gill SK, Broussard C, Devine O, Green RF, Rasmussen SA, & Reefhuis J (2012). Association between maternal age and birth defects of unknown etiology—United States, 1997–2007. Birth Defects Research Part A: Clinical and Molecular Teratology, 94(12), 1010–1018. 10.1002/bdra.23049 [PubMed: 22821755]

Greenland S, Pearl J, & Robins JM (1999). Causal diagrams for epidemiologic research. Epidemiology, 10(1), 37–48. 10.1097/00001648-199901000-00008 [PubMed: 9888278]

Hosmer DW, & Lemeshow S (1992). Confidence interval estimation of interaction. Epidemiology, 3(5), 452–456. 10.1097/00001648-199209000-00012 [PubMed: 1391139]

SAS/STAT® 13.1 User's Guide. (2013). The MIANALYZE Procedure. SAS/STAT ® 131 User's Guid. 5172–5231. Accessed April 19, 2022. https://support.sas.com/documentation/onlinedoc/stat/131/mianalyze.pdf

Janevic T, Stein CR, Savitz DA, Kaufman JS, Mason SM, & Herring AH (2010). Neighborhood deprivation and adverse birth outcomes among diverse ethnic groups. Annals of Epidemiology, 20(6), 445–451. 10.1016/j.annepidem.2010.02.010 [PubMed: 20470971]

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. MMWR. 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]

Kirby RS, Marshall J, Tanner JP, Salemi JL, Feldkamp ML, Marengo L, Meyer RE, Druschel CM, Rickard R, Kucik JE, & National Birth Defects Prevention Network. (2013). Prevalence and correlates of gastroschisis in 15 states, 1995 to 2005. Obstetrics and Gynecology, 122(2 Pt 1), 275–281. 10.1097/aog.0b013e31829cbbb4 [PubMed: 23969795]

Kohl M, Wiesel A, & Schier F (2010). Familial recurrence of gastroschisis literature review and data from the population-based birth registry "Mainz model.". Journal of Pediatric Surgery, 45 (9), 1907–1912. 10.1016/j.jpedsurg.2010.05.003 [PubMed: 20850644]

Krieger N, Chen JT, Waterman PD, Soobader MJ, Subramanian SV, & Carson R (2003). Choosing area based socioeconomic measures to monitor social inequalities in low birth weight and childhood lead poisoning: The public health disparities geocoding project (US). Journal of Epidemiology and Community Health, 57(3), 186–199. 10.1136/jech.57.3.186 [PubMed: 12594195]

Lam PK, Torfs CP, & Brand RJ (1999). A low prepregnancy body mass index is a risk factor for an offspring with gastroschisis. Epidemiology, 10(6), 717–721. 10.1097/00001648-199911000-00012 [PubMed: 10535786]

Larson NI, Story MT, & Nelson MC (2009). Neighborhood environments. Disparities in access to healthy foods in the U.S. American Journal of Preventive Medicine, 36(1), 74–81.e10. 10.1016/j.amepre.2008.09.025 [PubMed: 18977112]

Lee RE, Cubbin C, & Winkleby M (2007). Contribution of neighbourhood socioeconomic status and physical activity resources to physical activity among women. Journal of Epidemiology and Community Health, 61(10), 882–890. 10.1136/jech.2006.054098 [PubMed: 17873224]

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]

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

Messer LC, Laraia BA, Kaufman JS, Eyster J, Holzman C, Culhane J, Elo I, Burke JG, & O'Campo P (2006). The development of a standardized neighborhood deprivation index. Journal of Urban Health, 83(6), 1041–1062. 10.1007/s11524-006-9094-x [PubMed: 17031568]

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]

O'Campo P, Xue X, Wang MC, & Brien Caughy MO (1997). Neighborhood risk factors for low birthweight in Baltimore: A multilevel analysis. American Journal of Public Health, 87(7), 1113–1118. 10.2105/AJPH.87.7.1113 [PubMed: 9240099]

Penman-Aguilar A, Carter M, Christine Snead M, & Kourtis AP (2013). Socioeconomic disadvantage as a social determinant of teen childbearing in the U.S. Public Health Reports, 128(Suppl 1), 5–22. 10.1177/00333549131282s102

Rasmussen SA, Olney RS, Holmes LB, Lin AE, Keppler-Noreuil KM, & Moore CA (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]

Reefhuis J, & Honein MA (2004). Maternal age and nonchromosomal birth defects, Atlanta-1968–2000: Teenager or thirty-something, who is at risk? Birth Defects Research Part A: Clinical and Molecular Teratology, 70(9), 572–579. 10.1002/bdra.20065 [PubMed: 15368555]

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]

Rothman KJ, Greenland S, & Lash TL (2014). Case-control studies: Overview. Wiley StatsRef Stat Ref Online. 29 10.1002/9781118445112.STAT03723

Siega-Riz AM, Herring AH, Olshan AF, Smith J, & Moore C (2009). 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

Singh S, Darroch JE, & Frost JJ (2001). Socioeconomic disadvantage and adolescent women's sexual and reproductive behavior: The case of five developed countries. Family Planning Perspectives, 33(6), 251–258. 10.2307/3030192 [PubMed: 11804434]

Smith HJ, & Huo YJ (2014). Relative deprivation: How subjective experiences of inequality influence social behavior and health, 1, 231–238. 10.1177/2372732214550165

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, & Curry CJR (1993). Familial cases of gastroschisis in a population-based registry. American Journal of Medical Genetics, 45(4), 465–467. 10.1002/ajmg.1320450414 [PubMed: 8465852]

Torfs CP, Velie EM, Oechsli FW, Bateson TF, & Curry CJR (1994). A population-based study of gastroschisis: Demographic, pregnancy, and lifestyle risk factors, 50, 44–53.

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]

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]

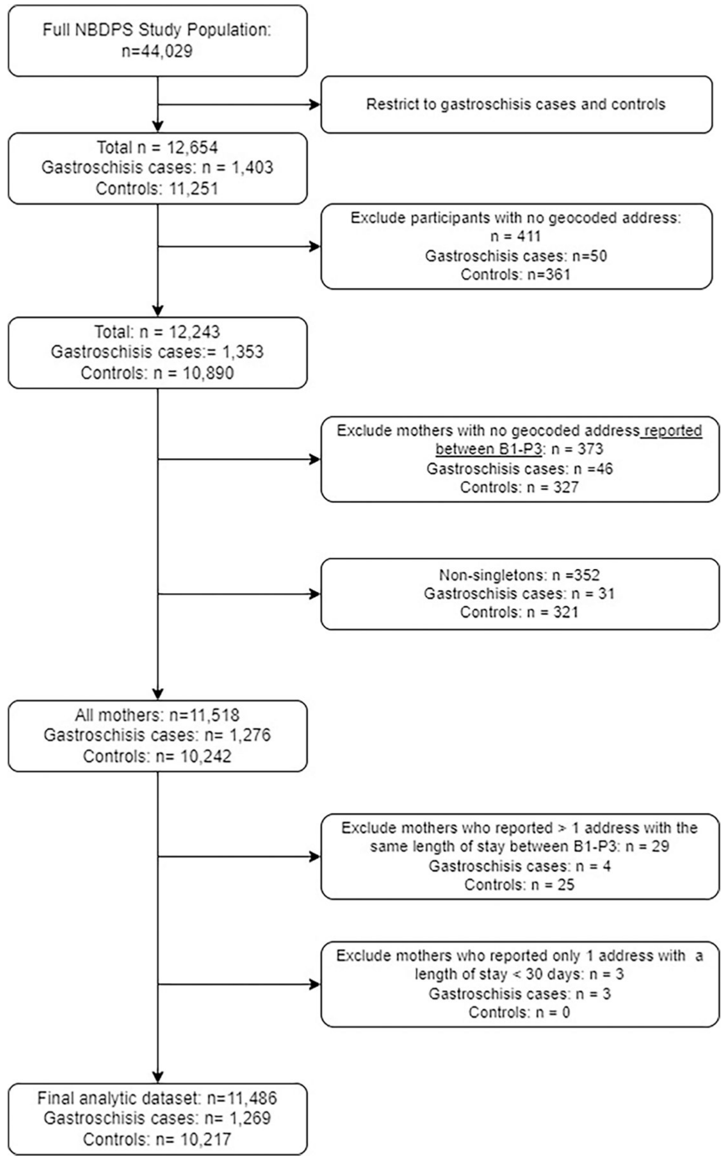

FIGURE 1.
Study population.

TABLE 1

Self-reported maternal characteristics among women who delivered an infant with gastroschisis (cases) or without a birth defect (controls), national birth defects prevention study, 1997–2011.

	Gastroschisis cases *n* = 1269	**Controls *n* = 10,217**
Age at conception (years)		
<20	540 (42.6)	1294 (12.7)
20–25	541 (42.6)	2969 (29.1)
26–35	178 (14.0)	5106 (50.0)
≥36	10 (0.8)	848 (8.3)
Parity		
0	830 (65.4)	3986 (39.0)
1	272 (21.4)	3334 (32.6)
≥2	166 (13.1)	2891 (28.3)
Missing	1 (0.1)	6 (0.1)
Race/ethnicity		
Non-Hispanic White	644 (50.8)	5978 (58.5)
Non-Hispanic Black	107 (8.4)	1089 (10.7)
Hispanic	410 (32.3)	2484 (24.3)
Other	108 (8.5)	660 (6.5)
Missing	0 (0.0)	6 (0.06)
Pre-pregnancy BMI (kg/m^2)		
Low (<18.5)	111 (8.8)	529 (5.2)
Normal (18.5 ≤ BMI < 25)	853 (67.2)	5384 (52.7)
Overweight (25 ≤ BMI < 30)	232 (18.3)	2352 (23.0)
Obese (≥30)	73 (5.8)	1952 (19.1)
Education (years)		
<12	346 (27.3)	1688 (16.5)
12	488 (38.5)	2436 (23.8)
>12	435 (34.2)	6094 (59.6)
Household income ($USD)		
<$10,000	438 (34.5)	2012 (19.7)
$10,000-$50,000	684 (53.9)	4670 (45.7)

	Gastroschisis cases n = 1269	Controls n = 10,217
>$50,000	146 (11.5)	3534 (34.6)
Employment		
Employed	852 (67.1)	7213 (70.6)
Unemployed	376 (29.6)	2839 (27.8)
Unknown	0 (0.0)	5 (0.1)
Missing	41 (3.2)	160 (1.6)
Recreational drug use[a,b]		
Yes	177 (14.0)	465 (4.5)
No	1092 (86.0)	9752 (95.5)
Smokinga		
Yes	450 (35.5)	1839 (18.0)
No	819 (64.5)	8378 (82.0)
Alcohola		
Yes	535 (42.2)	3815 (37.3)
No	734 (57.8)	6402 (62.7)
Gestational age at delivery (weeks)		
Very preterm (<32)	80 (6.3)	107 (1.0)
Preterm (32–36)	710 (55.9)	725 (7.1)
Term (37–45)	478 (37.7)	9384 (91.8)
Missing	1 (0.08)	1 (0.01)
Participating center		
Arkansas	166 (13.1)	1271 (12.4)
California	256 (20.2)	1121 (11.0)
Iowa	119 (9.4)	1220 (11.9)
Massachusetts	113 (8.9)	1263 (12.4)
New York	75 (5.9)	930 (9.1)
Texas	160 (12.6)	1277 (12.5)
CDC/Atlanta	139 (11.0)	1150 (11.3)
North Carolina	99 (7.8)	931 (9.1)
Utah	142 (11.2)	1054 (10.3)
Duration of residence (days)	952 (30–14,152)	1274 (30–14,456)

Note: Data presented as *n* (%) or mean (range).

Abbreviation: BMI, body mass index.

[a]Self-reported use between 1 month prior to conception to the third month of pregnancy.

[b]Recreational drug use includes: marijuana, hash, cocaine, crack, hallucinogens, heroin, hallucinogenic mushrooms.

TABLE 2

Distribution of neighborhood-level socio-economic position (nSEP) associated with maternal residence at conception, as measured by the neighborhood deprivation index, by case–control status, national birth defects prevention study, 1997–2011.

	Gastroschisis cases *n* = 1269	**Controls *n* = 10,217**	**Total *n* = 11,486**
Low deprivation/high nSEP	246 (19.4)	3406 (33.3)	3652 (31.8)
Moderate deprivation/moderate nSEP	454 (35.8)	3405 (33.3)	3860 (33.6)
High deprivation/low nSEP	569 (44.8)	3406 (33.3)	3974 (34.6)

Note: Data presented as *n* (%).

TABLE 3

Association between maternal age at conception and gastroschisis, stratified by neighborhood deprivation index, national birth defects prevention study, 1997–2011.

	T1 (Low deprivation/high nSEP)		T2 (Moderate deprivation/moderate nSEP)		T3 (High deprivation/low nSEP)	
	***N* cases/controls**	**OR (95%CI)**	***N* cases/controls**	**OR (95%CI)**	***N* cases/controls**	**OR (95%CI)**
≥20 years	168/3268	1.0 (Ref)	273/2999	1.3 (1.1–1.6)	288/2656	1.3 (1.0–1.6)
<20 years	78/138	6.6 (4.6–9.4)	181/406	4.9 (3.7–6.5)	281/750	4.1 (3.1–5.3)
ORs (95% CIs) for <20 years within strata of NDI	6.6 (4.6–9.4)		3.7 (3.0–4.7)		3.1 (2.6–3.8)	
RERI (95% CI)			−2.0 (−4.1, 0.2)		−2.8 (−5.0, −0.6)	

Note: Adjusted for household income and maternal education.

Abbreviations: CI, confidence interval; NDI, neighborhood deprivation index; nSEP, neighborhood-level socio-economic position; OR, odds ratio; RERI, relative excess risk due to interaction.

TABLE 4

Association between maternal pre-pregnancy body mass index and gastroschisis, stratified by neighborhood deprivation index, national birth defects prevention study, 1997–2011.

	T1 (Low deprivation/high nSEP)		T2 (Moderate deprivation/moderate nSEP)		T3 (High deprivation/low nSEP)	
	N cases/controls	OR (95%CI)	*N* cases/controls	OR (95%CI)	*N* cases/controls	OR (95%CI)
Overweight/obese	49/1176	1.0 (Ref)	100/1476	1.0 (0.7–1.5)	156/1652	1.1 (0.8–1.6)
Normal	181/2070	2.3 (1.6–3.2)	308/1740	2.3 (1.7–3.2)	365/1574	2.2 (1.5–3.0)
Underweight	16/160	1.5 (0.8–2.7)	47/189	2.1 (1.4–3.4)	59/180	2.0 (1.2–3.2)
ORs (95% CIs) for normal vs. overweight/obese within strata of NDI	2.3 (1.6–3.2)		2.2 (1.7–2.9)		1.9 (1.6–2.4)	
ORs (95% CIs) for underweight vs. overweight/obese within strata of NDI	1.5 (0.8–2.7)		2.1 (1.4–3.1)		1.8 (1.2–2.6)	
RERI (95% CI) for normal weight			0.03 (−0.6, 0.6)		−0.2 (−0.9, 0.4)	
RERI (95% CI) for underweight			0.6 (−0.5, 1.7)		0.4 (−0.7, 1.5)	

Note: Underweight: <18.5 kg/m^2; Normal weight: 18.5 ≤ BMI < 25 kg/m^2; Overweight/obese: ≥25 kg/m^2. T1: Tertile 1 (Low deprivation or high socioeconomic position); T2: Tertile 2 (Moderate deprivation or moderate socioeconomic position); T3: Tertile 3 (High deprivation or low socioeconomic position). Adjusted for household income, maternal education, maternal age at conception, smoking, alcohol, and recreational drug use.

Abbreviations: BMI, body mass index; CI, confidence interval; NDI, neighborhood deprivation index; OR, odds ratio; RERI, relative excess risk due to interaction.