Title
Prenatal Environmental Exposures and Teen Births Around the New Bedford Harbor Superfund Site (USA)

Author
DeVille, Nicole

Publication Date
2019

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA,
IRVINE

Prenatal Environmental Exposures and Teen Births around the New Bedford Harbor Superfund Site (USA)

DISSERTATION

submitted in partial satisfaction of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

in Public Health

by

Nicole Victoria DeVille

Dissertation Committee:
Scott M. Bartell, Public Health
Miryha G. Runnerstrom, Public Health
Verónica M. Vieira, Public Health (*Chair*)

2019

DEDICATION

To

my parents, my sister, my partner,

and all my family and friends

in recognition of their unconditional love and support

on this incredible journey

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ACKNOWLEDGMENTS

I would like to express the deepest appreciation to my committee chair, Professor Verónica Vieira, who reignited in me excitement towards research and scholarship. Without her guidance, support and encouragement, this dissertation and completion of my degree would not have been possible. Thank you for believing in me.

I would like to thank my committee members, Professor Scott Bartell and Professor Miryha Runnerstrom, whose interesting research and dedication to their students inspires me. I feel so fortunate to have learned from and worked with you both.

Financial support was provided by the University of California, Irvine, and National Institute of Environmental Health Sciences Grant P42 ES007381.

CURRICULUM VITAE

NICOLE VICTORIA DEVILLE

EDUCATION

2012 B.A. in International Relations, Stanford University

2014 M.P.H. in Epidemiology, University of Hawai'i at Manoa

2019 Ph.D. in Public Health, University of California, Irvine

FIELD OF STUDY

Environmental Epidemiology, Maternal and Child Health

PUBLICATIONS

DeVille N, Franceschini R, George A, Ghadiri M, Grzebyk K. (2016). *Report on the Emerging Leaders in Science and Society (ELISS) National Forum on Drinking Water Safety in the United States*. Washington, D.C.: American Association for the Advancement of Science.

GRANTS

2017 "Empowering Students for Success in Public Health," $5,000
Office of the Vice Provost for Teaching and Learning,
University of California, Irvine

RESEARCH PRESENTATIONS, PANEL PRESENTATION, AND INVITED TALKS

DeVille N, Khalili R, Bartell S, Fabian MP, Levy JI, Korrick SA, Vieira VM. (2019). Prenatal Mixtures of Environmental Exposures and Associations with Subsequent Teen Births. Thematic Poster Presentation for the 31st Annual Conference of the International Society for Environmental Epidemiology, Utrecht, The Netherlands, 8/2019.

Runnerstrom M, DeVille N, DeLeon M. (2019). Empowering first-generation and low-income students for academic and professional success. Oral Presentation for 2019 Lilly Conference on Teaching for Active and Engaged Learning, Anaheim, CA, 3/2019.

RESEARCH PRESENTATIONS, PANEL PRESENTATIONS, AND INVITED TALKS

Bersola S, DeVille N, Nguyen T. (2018). The relationship of the Master's degree to the PhD. Panel Presentation for the Southern California Forum for Diversity in Graduate Education at University of San Diego, San Diego, CA, 10/2018.

DeVille N, Robinson Anthony J, Zuniga M. (2018). Discipline based session: Health and human services. Panel Presentation for the Southern California Forum for Diversity in Graduate Education at University of San Diego, San Diego, CA, 10/2018.

DeVille N, Labe Z, Woods W. (2018). The current student perspective. Panel Presentation for the UCI Graduate Welcome and Orientation, University of California, Irvine, CA, 9/2018.

Runnerstrom M, DeVille N, DeLeon M, Chairez S. (2018). Empowering students for success in public health: A program for first-generation and low-income students. Poster Presentation for 2018 Undergraduate Public Health and Global Health Education Summit, Arlington, VA, 3/2018.

Grijalva C, DeVille N, Romero A. (2017). The relationship of the Master's degree to the PhD. Panel Presentation for the Southern California Forum for Diversity in Graduate Education at California State University, Channel Islands, Camarillo, CA, 11/2017.

DeVille N, Guillian R, Hagen T. (2017). Discipline based session: Health and human services. Panel Presentation for the Southern California Forum for Diversity in Graduate Education at California State University, Channel Islands, Camarillo, CA, 11/2017.

Runnerstrom M, DeVille N, DeLeon M, Chairez S. (2017). Empowering students for success in public health: A pilot program. Poster Presentation for Transforming STEM Higher Education: Discovery, Innovation, and the Value of Evidence Conference, San Francisco, CA, 11/2017.

DeVille N. (2017). Maternal mortality in the United States, 1960-2015. Speed Oral Presentation and Poster Presentation for Women in Statistics and Data Science Conference, San Diego, CA, 10/2017.

DeVille N, Lem H, Magnus A, Sameni S. (2017). Embracing your new graduate life. Panel Presentation for 9th Graduate Welcome and Orientation, University of California, Irvine, CA, 9/2017.

Tarleton H, Brown K, DeVille N. (2016). Discipline based session: Health and human services. Panel Presentation for the Southern California Forum for Diversity in Graduate Education at Loyola Marymount University, Los Angeles, CA, 11/2016.

Chai J, DeVille N. (2016). New women's health data resources for Orange County. Oral Presentation for 4th Orange County Women's Health Summit, Fullerton, CA, 10/2016.

RESEARCH PRESENTATIONS, PANEL PRESENTATIONS, AND INVITED TALKS

DeVille N. (2015). Evolution of the 5-minute Apgar score in the United States, 1978-2013. Poster Presentation for 2015 Population Association of America Annual Meeting, San Diego, CA, 4/2015.

DeVille N. (2014). Evolution of the 5-minute Apgar score in the United States, 1978-2012. Oral Presentation for the Summer Research Symposium, Graduate Division, University of California, Irvine, 8/2014.

DeVille N, Helm S, Hishinuma E, Lauricella M. (2014). The need for underage drinking prevention among Indigenous and Pacific youth in rural Hawai`i. Poster Presentation for the Biomedical Sciences Symposium of the John A. Burns School of Medicine, University of Hawai`i, 4/2014.

McCarthy K, Helm S, Lee W, Hanakahi V, Haumana, Uemoto MH, Lawler A, DeVille N. (2014). Historical cultural trauma. Influence of colonialism discussed by Native Hawaiian haumana. Poster presentation for the Biomedical Sciences Symposium, John A. Burns School of Medicine, University of Hawai`i, 4/2014.

Uemoto MH, Helm S, Lee W, Hanakahi V, Haumana, McCarthy K, Lawler A, DeVille N. (2014). Lōkāhi Triangle: a concept of well-being as discussed by Native Hawaiian youth. Poster presentation for the Biomedical Sciences Symposium, John A. Burns School of Medicine, University of Hawai`i, 4/2014.

Helm S, Okamoto L, Lee W, Hanakahi V, McCarthy K, DeVille N, Khil J, Haumana, et al. (2013). Social justice research and action. Hawaiian epistemology and youth drug prevention. Oral Presentation for European Congress of Community Psychology Annual Meeting, Napoli, IT, 11/2013.

Helm S, Lee W, Hanakahi V, Lee A, Haumana, McCarthy K, Khil J, Emhoff D, DeVille N. (2013). Puni Ke Ola. Life flourishes in a healthy community. Paper Presentation for The Native Children’s Research Exchange. Denver, CO, 9/2013.

Jost B, DeVille N, Skotheim JM, Wang SC, Payne JL. (2010). No consistent association between test size and extinction risk in Foraminifera. Oral Presentation for Geological Society of American Annual Meeting, Denver, CO, 11/2010.

DeVille N. (2010). Size as a risk factor for extinction: a case study of the fossil record of Foraminifera. Poster Presentation for Stanford Symposium for Undergraduate Research and Public Service. Palo Alto, CA, 10/2010.

TEACHING AND COURSE DESIGN EXPERIENCE

Co-Instructor/Teaching Assistant, Program in Public Health, University of California, Irvine

Fall 2017-Spring 2018	PUBHLTH 198 Empowering Students for Success in Public Health

Teaching Assistant, Program in Public Health, University of California, Irvine

Winter 2016	PUBHLTH 1 Principles of Public Health
Summer 2016, Summer 2017	PUBHLTH 10 Stress Management Essentials
Winter 2018	PUBHLTH 60 Environmental Quality and Health
Summer 2015	PUBHLTH 122 Health Policy
Spring 2016	PUBHLTH 126 Public Health Law: Fundamentals in Action
Spring 2016	PUBHLTH 139 Public Health Management
Fall 2017	PUBHLTH 150 Public Health and Wellness
Fall 2015, Fall 2016, Summer 2016	PUBHLTH 170 Introduction to Global Health
Summer 2018	PUBHLTH 172 Climate Change and Disaster Management
Summer 2016	PUBHLTH 195W Public Health Practicum and Culminating Experience

Course Design Assistant, Program in Public Health, University of California, Irvine

Spring 2016 - Summer 2016	PUBHLTH 1 Principles of Public Health (Online)
Spring 2016 - Summer 2016	PUBHLTH 2 Case Studies in Public Health Practice (Online)
Summer 2017 - Spring 2018	PUBHLTH 172 Climate Change and Disaster Management (Online)

Reader, Program in Public Health, University of California, Irvine

Spring 2015	PUBHLTH 195W Public Health Practicum and Culminating Experience

FELLOWSHIPS AND AWARDS

2019	UCI Program in Public Health Departmental Award of Excellence in Writing
2019	UCI Program in Public Health Departmental Award of Academic Excellence
2019	NIH Travel Award for International Society for Environmental Epidemiology Annual Meeting
2019	UCI Program in Public Health Dissertation Writing Fellowship
2018	International Teaching & Learning Cooperative Graduate Student Grant
2017	Women Leaders in Global Health at Stanford Conference Scholar
2016	California Water Policy Conference Scholarship
2016	UC Global Health Institute Student Ambassador
2015-2016	AAAS Emerging Leaders in Science and Society Fellow
2015	UC Irvine Data Science Initiative Summer Research Fellow
2014-2015	Liko A’e Native Hawaiian Leadership Program Scholar
2014-2016	‘Imi Na’auao Scholarship
2014-2015	George Hi’ilani Mills Scholarship
2014	UCI Competitive Edge Scholar
2014	Na Pua No`eau Ke Ola Mau Scholar
2014	University of Hawai’i Graduate Division Achievement Scholarship
2012-2016	Dr. Hans and Clara Zimmerman Foundation Health Scholarship
2010	Stanford University School of Earth Sciences Summer Fellow
2010-2011	Mildred Towle Scholarship for Study Abroad
2013-2014	Mānoa Opportunity Grant
2009-2012	Henry A. Zuberano Scholarship
2008-2014	Na Ho`okama A Pauahi Scholarship

FELLOWSHIPS AND AWARDS

2008-2010 Kai'ulani Home for Girls Trust Scholarship

2008-2014 Hawai'i Community Scholarship

UNIVERSITY, DEPARTMENT, AND PROFESSIONAL SERVICE

2018-2019 *Peer Mentor*, Public Health Diverse Educational Community and Doctoral Experience (DECADE) Council
Program in Public Health, University of California, Irvine

Summer 2017, Summer 2018 *Peer Mentor*, Competitive Edge Summer Program
Graduate Division, University of California, Irvine

2017 *Graduate Mentor*, Women and Minorities in STEM Mentorship Program, University of California, Irvine

2017-2018 *Member*, Physical Activity Working Group
Healthy Campus Initiative, University of California, Irvine

2017-2018 *Graduate Student Representative*, Advisory Board
Bren Events Center, University of California, Irvine

2016-2019 *Graduate Mentor*, Diverse Educational Community and Doctoral Experience Partnering in Leadership with Undergraduate Students (DECADE PLUS)
Graduate Division, University of California, Irvine

2016-2017 *Project Management Intern*, UCI Graduate Welcome and Orientation
Graduate Division, University of California, Irvine

2016-2017 *Planning Committee Member*, 2017 Orange County Early Childhood STEM Symposium
First 5 Orange County

2016-2018 *Medical Academics Representative*, Associated Graduate Students
University of California, Irvine

2015-2017 *Assistant Coach*, UCI Women's Rugby Team
Anteater Club Sports, Campus Recreation, University of California, Irvine

2015-2017 *Graduate Student Representative*, Student Health Insurance Advisory Committee (SHIAC), University of California, Irvine

UNIVERSITY, DEPARTMENT, AND PROFESSIONAL SERVICE

2015-2017 *Mentor*, Global Health Research Education and Translation Peer Mentor Program
Program in Public Health, University of California, Irvine

2015-2016 *Planning Committee Member*, 2016 Learners Today, Leaders Tomorrow Summit
First 5 Orange County, Children and Families Commission of Orange County

ABSTRACT OF THE DISSERTATION

Prenatal Environmental Exposures and Teen Births around the New Bedford Harbor Superfund Site (USA)

By

Nicole Victoria DeVille

Doctor of Philosophy in Public Health

University of California, Irvine, 2019

Dr. Verónica M. Vieira, Chair

While widescale public health prevention efforts have significantly decreased national teen birth rates, disparities in teen births persist at local levels. The aims of this dissertation were to conduct a spatial analysis of maternal teen birth status in all births surrounding the New Bedford Harbor Superfund site (MA, USA) over two distinct time periods (1992-1998 and 2002-2008); to assess whether joint exposures of modeled prenatal chemical exposures elevate risk of subsequent teen birth in infant females born between 1992-1998 near NBH (MA Birth Record Cohort); and, to ascertain whether similar or different combinations of joint exposures affect subsequent teen birth in New Bedford Cohort (NBC) females. The spatial analyses in Chapter 2 demonstrated a statistically significant hot spot of elevated risk of teen birth west of the NBH only for the later time period (2002-2008). Chapter 3 employed predictive exposure models built from measured biomarkers in the NBC to estimate prenatal exposures for cord serum DDE, cord serum HCB, maternal hair Hg, cord blood Pb, and cord serum PCB_4 for all births in four towns surrounding the NBH from 1992-1998. Epidemiologic models, using

an innovative extension of generalized additive models, for both MBRC (Chapter 3) and the NBC (Chapter 4) demonstrated higher risk for subsequent teen birth across low levels of DDE and higher levels of the remaining chemical exposures. In Chapter 4, the apparent protective effect of DDE persisted even after adjustment for maternal dietary factors. Although this research has its limitations, it provides a novel approach to analyzing mixtures of chemical and non-chemical exposures and makes a significant contribution to the literature on the effects of joint chemical exposures on maternal, child, and adolescent health.

CHAPTER 1:

RISKY BEHAVIOR IN THE NEW BEDFORD HARBOR COMMUNITY

Chemical Exposures and Risk-Taking

Full development of the prefrontal cortex and its associated inhibitory functions extends past adolescence into early adulthood (Diamond 2002). Impulsive and reward-driven areas of the brain may dominate adolescents' and young adults' decision-making processes and actions, increasing susceptibility to engage in high-risk, sensation-seeking activities (Charnigo et al. 2013; Goldenberg et al. 2013; Romer 2010; Steinberg 2007). Manifestations of risk-taking behavior in these age groups, such as risky sexual behavior and teen births, typify major public health problems with high economic and social costs (Kearney and Levine 2012). Early age at first sexual intercourse is associated with an increased risk of teen pregnancy, sexually transmitted disease, and poor psychosocial and physical health in adulthood (Heywood et al. 2015; Skinner et al. 2015). In 2010, teen pregnancy and childbirth in the U.S. cost over $9 billion in medical and foster care expenses, lost tax revenues (because of failure of teen mothers to complete high school), and expenses from increased incarceration rates among children of teen mothers. Further, children of teenage mothers are at a greater risk for a cadre of negative social and health outcomes, including lower educational achievement, high school dropout, higher morbidity, incarceration during adolescence, teenage pregnancy, and unemployment as a young adult (Jaffee et al. 2001; Jutte et al. 2010).

Adolescent risk-taking is influenced by a complex array of factors including sex, sociodemographic characteristics, peer behavior, and community characteristics (e.g.

neighborhood crime and safety) (Wiehe et al. 2013). Although environmental levels of polychlorinated biphenyls (PCBs) and organochlorine pesticides, such as hexachlorobenzene (HCB), dichlorodiphenyl trichloroethane (DDT) and its primary metabolite, dichlorodiphenyl dicloroethene (DDE), are generally on the decline, early-life exposures to these prevalent environmental contaminants persist (Korrick and Sagiv 2008). A growing body of literature provides mechanistic insight on the neurotoxic effects of both individual and mixtures of environmental exposures (Liu and Lewis 2013; Wu et al. 2016). Animal models and epidemiologic studies support associations of early life exposures to PCBs, lead (Pb), and mercury (Hg) with subsequent impairment of impulse control, a core function of the prefrontal cortex and a correlate of risk-taking (Cory-Slechta et al. 2002; Stewart et al. 2005, 2006). Pb, even at low exposures, is also associated with long-term high-risk behaviors, such as delinquency (Needleman 2009; Needleman et al. 1979; Needleman et al. 1990; Needleman et al. 1996). Attention and behavioral deficits have been reported for children exposed to PCBs and dioxins, although such deficits have not been as extensively or systematically studied as for lead exposure (Schantz et al. 2003). A systematic review of several national and international cohorts indicates that there is limited published human data regarding potential neurodevelopmental toxicities of early-life exposures to DDT, DDE and HCB (Korrick & Sagiv, 2008).

The New Bedford Harbor Superfund Site

The New Bedford Harbor consists of 18,000 acres of urban estuary surrounded by four towns: Acushnet, Dartmouth, Fairhaven and New Bedford. In 1982, the harbor was designated as a Superfund site by the Environmental Protection Agency (EPA) because of extensive PCB contamination due to emissions by local electronics manufacturing facilities (United States Environmental Protection Agency 2019). Historically, the harbor also had previous contamination from copper, lead, polycyclic aromatic hydrocarbons (PAHs) and other industrial discharges from the whaling period in the 1700's through the textile period in the early 1900's. Organochlorines, including DDE and HCB, have also been found in the harbor. The lipophilic properties of PCBs and organochlorines allow these compounds to persist in the environment and to bioaccumulate within the marine food chain (Chopra et al. 2011; Pelletier et al. 2003). DDE, HCB, Hg, Pb and PCBs have all been detected in prenatal biomarker samples collected from the New Bedford Cohort, a cohort of mothers and infants residing near the New Bedford Harbor (NBH) Superfund Site (Korrick et al. 2000; Korrick 2010; Sagiv et al. 2010; Sagiv et al. 2012). As a heavily industrialized area, the New Bedford community contains a number of other hazardous waste sites, increasing the potential for multiple exposures in this population.

Risky Behavior in the New Bedford Harbor Community

New Bedford, Massachusetts (MA) is a diverse low-income city with approximately 95,000 residents in 2010. Approximately 22% of residents live below the poverty level, and 70% of the population lives in census blocks meeting one of the MA environmental justice criteria (Commonwealth of Massachusetts 2019). New Bedford contains a number of other hazardous waste sites and industrial sources of pollutants. Although individuals are continuously exposed to multiple chemicals, pregnant women and children may exhibit higher susceptibility and sensitivity to such exposures (Kalloo et al. 2018; Thompson and Boekelheide 2013; Wigle et al. 2007). Further, residing near a hazardous waste site or a Superfund site may exacerbate risk for adverse health outcomes from joint chemical exposures. Teen birth rates in the New Bedford area consistently rank among the highest in Massachusetts (Massachusetts Department of Public Health 2014). Thus, this research focuses on a community in which the potential for multiple exposures is high and risk-taking behaviors have a considerable public health impact.

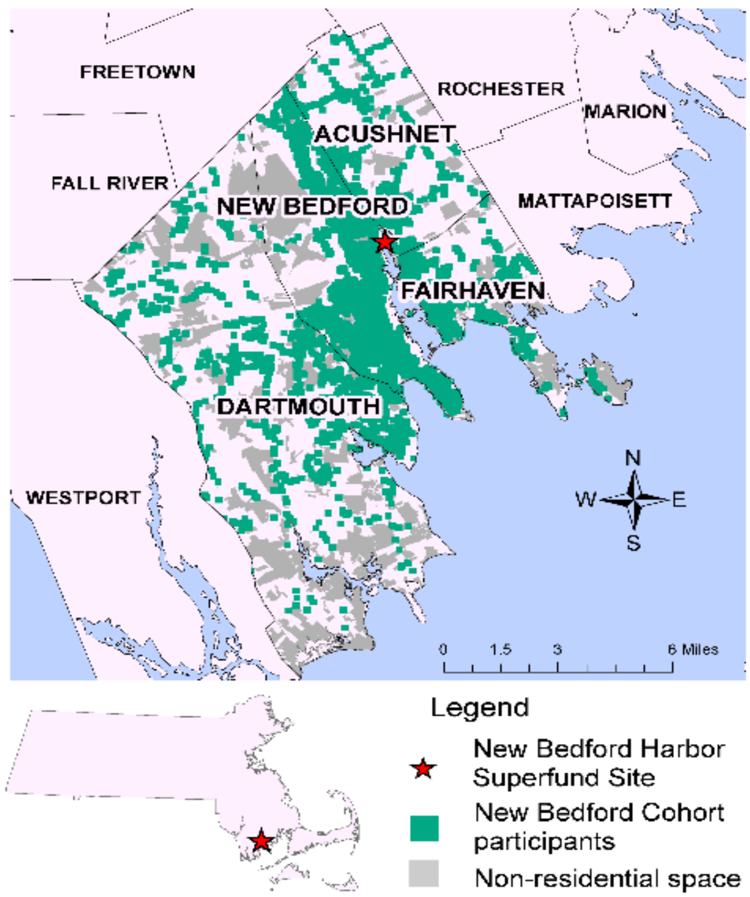

Figure 1.1. Map of New Bedford Harbor Superfund Site, Surrounding Towns, and New Bedford Cohort Participants.

CHAPTER 2:

SPATIAL VARIABILITY OF TEEN BIRTHS IN FOUR TOWNS SURROUNDING THE NEW BEDFORD HARBOR SUPERFUND SITE, 1992-1998 AND 2002-2008

Objective

Teen birth is a significant public health concern. While widescale public health prevention efforts have drastically lowered national teen birth rates, disparities in teen births persist. Although some studies have been conducted on geographic variability of teen births nationally and in other states, no study to date has assessed spatial variation of teen births and potential risk factors in the New Bedford community. The objectives of this study were to explore geographic variation in teen births in four towns (Acushnet, Dartmouth, Fairhaven, New Bedford) surrounding the New Bedford Harbor (NBH) Superfund site over two separate time periods 1992-1998 and 2002-2008 and to determine whether sociodemographic risk factors account for any observed geographic variability.

Methods

MADPH Birth Records

We examined the association between location of maternal birth residence and maternal teen birth status using birth record data from the Massachusetts Department of Public Health (MADPH). Birth records included location of maternal residence at birth and other maternal and infant sociodemographic variables for all births in four towns surrounding NBH (Acushnet, Dartmouth, Fairhaven, New Bedford) from 1992-1998 (N=12,178) and 2002-2008 (N=12,426). Using geographic information systems (GIS), median block-group household income level from 2000 United States Census Bureau data was assigned to geocoded birth addresses. An indicator for maternal teen birth status was assigned based on maternal age provided in the birth records.

Covariates

Sociodemographic risk factors may contribute to spatial patterns in teen birth, particularly when distribution of factors is disparate across the study area. The spatial analyses included covariates available in the MADPH birth records. Covariate adjustment was determined by assessing associations with maternal teen birth status using univariate logistic regression models; variables were included in the adjusted models if statistically significant ($p<0.05$) or if the variable yielded a change in effect size of at least 10%. The parametrically modeled categorical covariates were household income less than 20,000, maternal education less than high school, paternal education less than high school, maternal marital status (married, other), prenatal care payment source (private insurance, other), parity (1, 2, 3, ≥4), maternal race (Non-Hispanic White, Non-Hispanic African American, Hispanic, Non-Hispanic Other), adequacy of prenatal care (Adequate on Kessner Index, other), and maternal smoking during pregnancy (any, none), maternal country of birth (Azores/Portugal, Cape Verde, other), and maternal alcohol consumption during pregnancy (any, none). Due to a large proportion of missing data for paternal education (15%), we imputed five data sets using fully conditional specification with the “mice” package in R (Fichman & Cummings, 2003; Rubin, 1996). We present results for one imputation, although results for the five imputed data sets were similar. Covariate correlation coefficients and charts for both time periods are presented in Appendix A Tables A.1-A.2 and Figures A.2-A.3.

Spatial Analysis

Generalized additive models (GAMs) are a type of semi-parametric statistical model that allows for simultaneous smoothing and adjustment of covariates (Hastie & Tibshirani, 1995; Vieira, Webster, Weinberg, Aschengrau, & Ozonoff, 2005; Webster, Vieira, Weinberg, & Aschengrau, 2006). To predict teen births in the four study towns, we employed GAMs to smooth maternal address at time of birth and adjustment for other maternal characteristics. Latitude and longitude of maternal address were included in a bivariate *loess* smooth, which adapts to changes in population density while allowing for observation of localized patterns, and employed as a proxy for spatially varying risk factors for teen birth (Hastie & Tibshirani, 1995). Span size selection was determined by minimizing Akaike Information Criteria (AIC) and examining AIC curve plots when the optimal span was 0.05 (Appendix A Figure A.4). The models were used to predict teen births across a grid of evenly spaced points covering the study area, and individuals with missing data were not included in the final models. This criterion did not apply to missing paternal education, which was imputed; the proportion of missing data for all other covariates was less than one percent. Covariates were held fixed so that the spatial surface represented predictions at the referent level (Tables 2.1 and 2.2). We used permutation tests to assess the statistical significance of location and produce a global P value under the null hypothesis that teen birth does not depend on geographic location of residence at birth, adjusting for other sociodemographic risk factors (Vieira, Webster, Weinberg, & Aschengrau, 2009; Vieira et al., 2005; Webster et al., 2006). Contour lines were drawn on maps to indicate areas of significantly elevated (hot spot) or decreased (cold spot) risk.

ArcGIS and R (version 3.3.3) were utilized for data management. For spatial analyses and map creation, we used the R MapGAM package (Vieira et al. 2018). The institutional review board of the University of California, Irvine (Irvine, California) approved this research.

Results

Population Characteristics

Selected study population characteristics and their univariate associations with maternal teen birth status are presented in Tables 2.1 and 2.2. Of the 12,178 infants born in the study area between 1992-1998, 1,874 infants (15.4%) were maternal teen birth cases (infant's mother gave birth at less than 20 years of age). Between 2002 and 2008, 1,457 (11.7%) infants born in the study were maternal teen birth cases. For births in the study area between 1992 and 1998, the proportion of teen birth cases decreased from 15.6% (1992) to 13.4% (1998), with a peak in teen birth cases observed in 1994 (16.3%). Although teen birth cases fluctuated across the 2002-2008 period, the same number of teen birth cases (199, 13.7%) was observed at the start and end of the study period.

Mean maternal age was similar for teen mothers in both time periods, 17.7 years and 17.8 years, respectively. A slightly larger difference in mean maternal age was observed for non-teen mothers, 27.5 years and 28.1 years, respectively. Distributions of maternal race and ancestry were similar across both study periods; the majority of both cases and non-cases were of non-Hispanic White maternal race and Other maternal ancestry. For both time periods, any smoking during pregnancy was more prevalent in teen birth cases, although any alcohol consumption during pregnancy was more prevalent in the non-teen birth mothers. The proportion of teen mothers who did not attain high school education decreased over time (64.6% compared to 57.2%). More teen moms were married in the earlier study period (11.4% compared to 5.7%). While the majority of mothers received adequate prenatal care, the proportion of those who received less than adequate or no prenatal care was nearly double among maternal teen birth cases for both time periods. Private insurance comprised the majority of prenatal care source of payment in non-cases for both time periods (55.9% and 50.8%, respectively); the proportion of teen mothers whose prenatal care was paid by private insurance increased across the two study periods (18.8% compared to 23.9%). The majority of teen birth cases were primiparous; parity was higher in non-cases for both time periods. Greater proportions of lower household income and lower partner educational attainment were observed in teen birth cases compared to non-cases across both study periods.

1992-1998 Spatial Analysis

Spatial analysis results for 1992-1998 are presented in Figure 2.1. The optimal span for the unadjusted model was 0.05; however, the model was fit at a span of 0.20, based on a local minimum in the AIC curve, to address potential edge effects. The unadjusted analysis indicated a statistically significant hot spot and several cold spots for teen births west of the New Bedford Harbor ($p<0.001$) (Figures 2.1.A & 2.1.C). Individual adjustment for maternal race, maternal ancestry, smoking during pregnancy, alcohol consumption during pregnancy, maternal education, marital status, adequacy of prenatal care, prenatal care payment source, household income, parity, and paternal education produced changes in the spatial variability of teen birth risk (Appendix A Figures A.5-A.15). All of the tested covariates had statistically significant effect sizes of at least 10% in univariate analyses and were included in the fully adjusted model (Figure 2.1.B). After stepwise adjustment (Appendix A Figure A.16), location was no longer a significant predictor of teen birth after covariate adjustment (p=0.469).

2002-2008 Spatial Analysis

The 2002-2008 spatial analysis results are presented in Figure 2.2. Similar to the unadjusted model including only location for 1992-1998, the optimal span size was 0.05. The unadjusted model was fit at a span of 0.20 and displayed a statistically significant area of increased risk of teen birth west of the NBH (p<0.001) (Figure 2.2.A & 2.2.C). We individually tested the same covariates from the 1992-1998 spatial analysis and found maternal race, maternal ancestry, smoking during pregnancy, alcohol consumption during pregnancy, maternal education, marital status, adequacy of prenatal care, prenatal care payment source, household income, parity, and paternal education yielded changes in the spatial variation of teen birth risk (Appendix A Figures A.17-A.27); stepwise covariate adjustment is presented in Appendix A Figure A.28. All covariates were included in the fully adjusted model fit at an optimal span of 0.70 (Figure 2.2.B), and the geographic hot spot for increased risk of teen birth remained after adjustment (p<0.001). Figure 2.3 displays the results of the 1992-1998 and 2002-2008 spatial analyses on a scale overlapping the predicted odds ratios ranges. When mapped on the same scale and adjusted for the same covariates, only the 2002-2008 analysis indicates location as a significant predictor of teen births.

Discussion

Spatial analyses are useful in elucidating risk factors and highlighting health disparities not easily identifiable via traditional epidemiologic design and analysis (Graves, 2008). Recent work has explored spatiotemporal patterns at the state and county levels across the United States and provides support that teen birth rates demonstrate some dependence on spatially varying risk factors (Callaghan, 2014; Khan, Rossen, Hamilton, Dienes, & Wei, 2018; Khan et al., 2017). In our study, even after adjustment for two known strongly associated variables, educational attainment and income level (Abma, Martinez, & Copen, 2010; Lou & Thomas, 2015; Penman-Aguilar, Carter, Snead, & Kourtis, 2013; Shoff & Yang, 2012), a statistically significant hot spot of elevated risk of teen birth remained during the 2002-2008 time period. Although spatial distribution of cases and non-cases of teen birth was similar across the two study periods (Appendix A Figure A.1), individual-level sociodemographic factors did not appear to explain the spatial patterns in the 2002-2008 period as they did in the 1992-1998 period. Attenuation of observed spatial patterns in the 1992-1998 period after additional adjustment for marital status, maternal race, and socioeconomic proxies (i.e. adequacy of prenatal care, prenatal care source of payment) was expected and provides further support for the importance of such sociodemographic risk factors for teen birth (Shoff & Yang, 2012).

Previous research in this community has established links between other environmental and sociodemographic factors and neurodevelopmental and behavioral outcomes, such as ADHD-related behaviors, in a subset of the study population (Korrick & Sagiv, 2008; Sagiv et al., 2012, 2010). This study was limited to variables available in MADPH birth records and further research in this population should explore whether other stressors, such as environmental exposures or other sociodemographic and lifestyle factors, may be contributing to the observed hot spot west of the New Bedford Harbor in the 2002-2008 analysis.

Using MADPH birth record data from all live births over two distinct time periods (1992-1998 and 2002-2008), we assessed spatiotemporal patterns of teen birth events near a Superfund site. A strength of this study is that it is the first to explore spatiotemporal variation in teen births at a community level (versus county level) in a state with comparatively low teen birth rates (Khan et al., 2018; Shoff & Yang, 2012). Another strength of the study was the imputation of missing data for paternal education, which in combination with low proportions of missingness (<2%) amongst all other variables, allowed us to retain a relatively large sample size across both time periods.

Our study has several limitations. Use of the MADPH birth record data likely presents a slight underestimate of teen birth events over both time periods as some births may not be registered with MADPH. Additionally, we were limited to maternal demographic characteristics available in the birth records, and these individual-level sociodemographic characteristics appeared to explain spatial heterogeneity only for the earlier time period. We were limited in the proxies we could utilize for other social and lifestyle factors that are associated with teen birth and were unable to adjust for some individual-level confounders at all (e.g. risk factors before pregnancy and birth). We employed adequacy of prenatal care and prenatal care payment source as proxies for access to healthcare and socioeconomic status. Further, we employed substance use (smoking or alcohol consumption) during pregnancy as a proxy since positive associations between substance use and premarital teen pregnancy are well established in the literature (Grossman et al., 2004; Mensch & Kandel, 1992; Salas-Wright, Vaughn, Ugalde, & Todic, 2015). Another limitation is the use of maternal address at birth and limited information on residential history prior to or during pregnancy, which could affect spatial distribution of teen birth cases over time. One review found that residential mobility during pregnancy ranged from approximately 10-30% and that younger maternal age was correlated with higher residential mobility during pregnancy (Miller, Siffel, & Correa, 2010).

Conclusion

Our spatial analyses employed generalized additive models to assess the importance of location as a predictor of teen birth in communities surrounding the New Bedford Harbor over two distinct periods of time. Our results suggest social and demographic variables accounted for the geographic hot spot of teen births in the 1992-1998 analysis. Results from the 2002-2008 analysis indicate that location, as a proxy for spatially-varying risk factors, is a significant predictor of teen births. Further exploration of environmental and sociodemographic factors contributing to elevated risk of teen births west of the NBH Superfund site observed during the later study period is warranted.

Table 2.1. Characteristics of, univariate associations with, and adjusted odds ratios for teen birth for mothers of children born in the New Bedford Harbor study area, 1992-1998 (N=12,178).

Selected Characteristics	Teen Birth (n=1,874)	No Teen Birth (n=10,304)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Infant Year of Birth (continuous)			0.98 (0.96, 1.01)	N/A
1992	293 (15.6)	1,624 (15.8)		
1993	294 (15.7)	1,517 (14.7)		
1994	305 (16.3)	1,493 (14.5)		
1995	233 (12.4)	1,390 (13.5)		
1996	253 (13.5)	1,385 (13.4)		
1997	245 (13.1)	1,385 (13.4)		
1998	251 (13.4)	1,510 (14.7)		
Maternal Characteristics				
Age (mean ± sd)	17.7 ± 1.27	27.5 ± 5.06	N/A	N/A
Race/Ethnicity				
White, non-Hispanic	1,189 (63.4)	8,358 (81.1)	referent	
Black, non-Hispanic	135 (7.2)	411 (4.0)	2.31 (1.88, 2.83)	1.27 (0.92, 1.76)
Hispanic	377 (20.1)	874 (8.5)	3.03 (2.65, 3.47)	1.47 (1.20, 1.80)
Other, non-White	170 (9.1)	630 (6.1)	1.90 (1.58, 2.27)	1.02 (0.72, 1.45)
Missing	3 (0.2)	31 (0.3)		
Country of Birth				
Azores/Portugal	412 (22.0)	2,670 (25.9)	0.86 (0.76, 0.97)	0.94 (0.80, 1.11)
Cape Verde	233 (12.4)	763 (7.4)	1.70 (1.45, 2.00)	1.01 (0.73, 1.40)
Other	1,226 (65.4)	6,840 (66.4)	referent	
Missing	3 (0.2)	31 (0.3)		
Any Smoking During Pregnancy				
Yes	504 (26.9)	2,317 (22.5)	1.27 (1.13, 1.41)	0.70 (0.60, 0.81)
No	1,367 (72.9)	7,958 (77.2)	referent	
Missing	3 (0.2)	29 (0.3)		
Any Alcohol Consumption During Pregnancy				
Yes	16 (0.8)	208 (2.0)	0.42 (0.25, 0.69)	0.29 (0.15, 0.56)
No	1,854 (99.0)	10,046 (97.5)	referent	
Missing	4 (0.2)	50 (0.5)		
Maternal Education at Birth				
<HS education	1,210 (64.6)	2,338 (22.7)	6.20 (5.58, 6.89)	4.82 (4.18, 5.55)
≥HS education	661 (35.2)	7,921 (76.9)	referent	
Missing	3 (0.2)	45 (0.4)		
Marital Status at Birth				
Married	214 (11.4)	6,839 (66.4)	0.07 (0.06, 0.08)	0.14 (0.11, 0.16)
Unmarried	1,660 (88.6)	3,465 (33.6)	referent	
Missing	0 (0.0)	0 (0.0)		

Table 2.1 continued. Characteristics of, univariate associations with, and adjusted odds ratios for teen birth for mothers of children born in the New Bedford Harbor study area, 1992-1998 (N=12,178).

	Teen Birth (n=1,874)	No Teen Birth (n=10,304)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Maternal Characteristics (continued)				
Adequate Prenatal Care (Kessner Index)				
Yes	1,171 (62.5)	8,069 (78.3)	0.45 (0.40, 0.50)	0.67 (0.58, 0.77)
No	687 (36.6)	2,114 (20.5)	referent	
Missing	16 (0.9)	121 (1.2)		
Prenatal Care Source of Payment				
Private Insurance	353 (18.8)	5,757 (55.9)	0.18 (0.16, 0.21)	0.56 (0.48, 0.66)
Other Payment	1,512 (80.7)	4,488 (43.6)	referent	
Missing	9 (0.5)	59 (0.5)		
Annual Household Income at Birth				
<20K/year	630 (33.6)	2,053 (19.9)	2.04 (1.83, 2.27)	1.00 (0.86, 1.15)
≥20K/year	1,244 (66.4)	8,251 (80.1)	referent	
Missing	0 (0.0)	0 (0.0)		
Parity				
1 child	1,501 (80.1)	3,826 (37.1)	referent	
2 children	286 (15.3)	3,735 (36.2)	0.20 (0.17, 0.22)	0.17 (0.15, 0.20)
3 children	68 (3.6)	1,714 (16.6)	0.10 (0.08, 0.13)	0.06 (0.04, 0.08)
≥4 children	15 (0.8)	978 (9.5)	0.04 (0.02, 0.07)	0.02 (0.01, 0.03)
Missing	4 (0.2)	51 (0.5)		
Paternal Education at Birth				
<HS education	1,007 (53.7)	2,990 (29.0)	2.84 (2.57, 3.14)	1.28 (1.12, 1.47)
≥HS education	867 (46.3)	7, 314 (71.0)	referent	

Note: OR, odds ratio; CI, confidence interval; sd, standard deviation; HS, high school.
[a] Missing values were excluded from the analyses.

Table 2.2. Characteristics of, univariate associations with, and adjusted odds ratios for teen birth for mothers of children born in the New Bedford Harbor study area, 2002-2008 (N=12,426).

Selected Characteristics	Teen Birth (n=1,457)	No Teen Birth (n=10,969)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Infant Year of Birth (continuous)			1.01 (0.98, 1.04)	N/A
2002	199 (13.7)	1,528 (13.9)		
2003	193 (13.2)	1,570 (14.3)		
2004	211 (14.5)	1,579 (14.4)		
2005	203 (13.9)	1,599 (14.6)		
2006	231 (15.8)	1,623 (14.8)		
2007	221 (15.2)	1,537 (14.0)		
2008	199 (13.7)	1,533 (14.0)		
Maternal Characteristics				
Age (mean ± sd)	17.8 ± 1.22	28.1 ± 5.35	N/A	N/A
Race/Ethnicity				
White, non-Hispanic	784 (53.8)	7,973 (72.7)	referent	
Black, non-Hispanic	82 (5.6)	584 (5.3)	1.43 (1.12, 1.82)	0.82 (0.59, 1.15)
Hispanic	486 (33.4)	1,603 (14.7)	3.08 (2.72, 3.49)	1.31 (1.08, 1.59)
Other, non-White	103 (7.1)	795 (7.2)	1.32 (1.06, 1.64)	0.61 (0.41, 0.91)
Missing	2 (0.1)	14 (0.1)		
Country of Birth				
Azores/Portugal	212 (14.6)	2,406 (22.0)	0.61 (0.53, 0.72)	0.79 (0.65, 0.96)
Cape Verde	124 (8.5)	750 (6.8)	1.15 (0.94, 1.41)	1.30 (0.89, 1.90)
Other	1,119 (76.8)	7,799 (71.1)	referent	
Missing	2 (0.1)	14 (0.1)		
Any Smoking During Pregnancy				
Yes	403 (27.7)	2,992 (27.3)	1.02 (0.90,1.15)	0.66 (0.56, 0.77)
No	1,052 (72.2)	7,966 (72.6)	referent	
Missing	2 (0.1)	11 (0.1)		
Any Alcohol Consumption During Pregnancy				
Yes	12 (0.8)	187 (1.7)	0.48 (0.27, 0.86)	0.65 (0.32, 1.31)
No	1,443 (99.1)	10,769 (98.2)	referent	
Missing	2 (0.1)	13 (0.1)		
Maternal Education at Birth				
<HS education	833 (57.2)	2,104 (19.2)	5.65 (5.03, 6.33)	3.98 (3.43, 4.63)
≥HS education	620 (42.6)	8,845 (80.6)	referent	
Missing	4 (0.3)	20 (0.2)		
Marital Status at Birth				
Married	83 (5.7)	5,906 (53.8)	0.05 (0.04, 0.06)	0.10 (0.07, 0.13)
Unmarried	1,374 (94.3)	5,063 (46.2)	referent	
Missing	0 (0.0)	0 (0.0)		

Table 2.2 continued. Characteristics of, univariate associations with, and adjusted odds ratios for teen birth for mothers of children born in the New Bedford Harbor study area, 2002-2008 (N=12,426).

	Teen Birth (n=1,457)	No Teen Birth (n=10,969)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Maternal Characteristics (continued)				
Adequate Prenatal Care (Kessner Index)				
Yes	846 (58.1)	8,030 (73.2)	0.51 (0.45, 0.57)	0.68 (0.59, 0.79)
No	584 (40.1)	2,801 (25.5)	referent	
Missing	27 (1.8)	138 (1.3)		
Prenatal Care Source of Payment				
Private Insurance	348 (23.9)	5,572 (50.8)	0.18 (0.16, 0.21)	0.84 (0.71, 0.99)
Other Payment	1,095 (75.1)	5,328 (48.6)	referent	
Missing	14 (1.0)	69 (0.6)		
Annual Household Income at Birth				
<20K/year	347 (23.8)	1,634 (14.9)	1.79 (1.57, 2.04)	1.08 (0.90, 1.28)
≥20K/year	1,089 (74.8)	9,173 (83.6)	referent	
Missing	21 (1.4)	162 (1.5)		
Parity				
1 child	1,204 (82.6)	3,899 (35.5)	referent	
2 children	220 (15.1)	4,025 (36.7)	0.18 (0.15, 0.21)	0.16 (1.37, 1.94)
3 children	23 (1.6)	1,927 (17.6)	0.04 (0.03, 0.05)	0.03 (0.02, 0.04)
≥4 children	1 (0.1)	1,070 (9.8)	0.003 (0.004, 0.02)	0.001 (0.002, 0.01)
Missing	9 (0.6)	48 (0.4)		
Partner Education at Birth				
<HS education	752 (51.6)	2,851 (26.0)	3.08 (2.75, 3.44)	1.54 (1.33, 1.78)
≥HS education	690 (47.4)	8,058 (73.5)	referent	
Missing	15 (1.0)	60 (0.5)		

Note: OR, odds ratio; CI, confidence interval; sd, standard deviation; HS, high school.
[a] Missing values were excluded from the analyses.

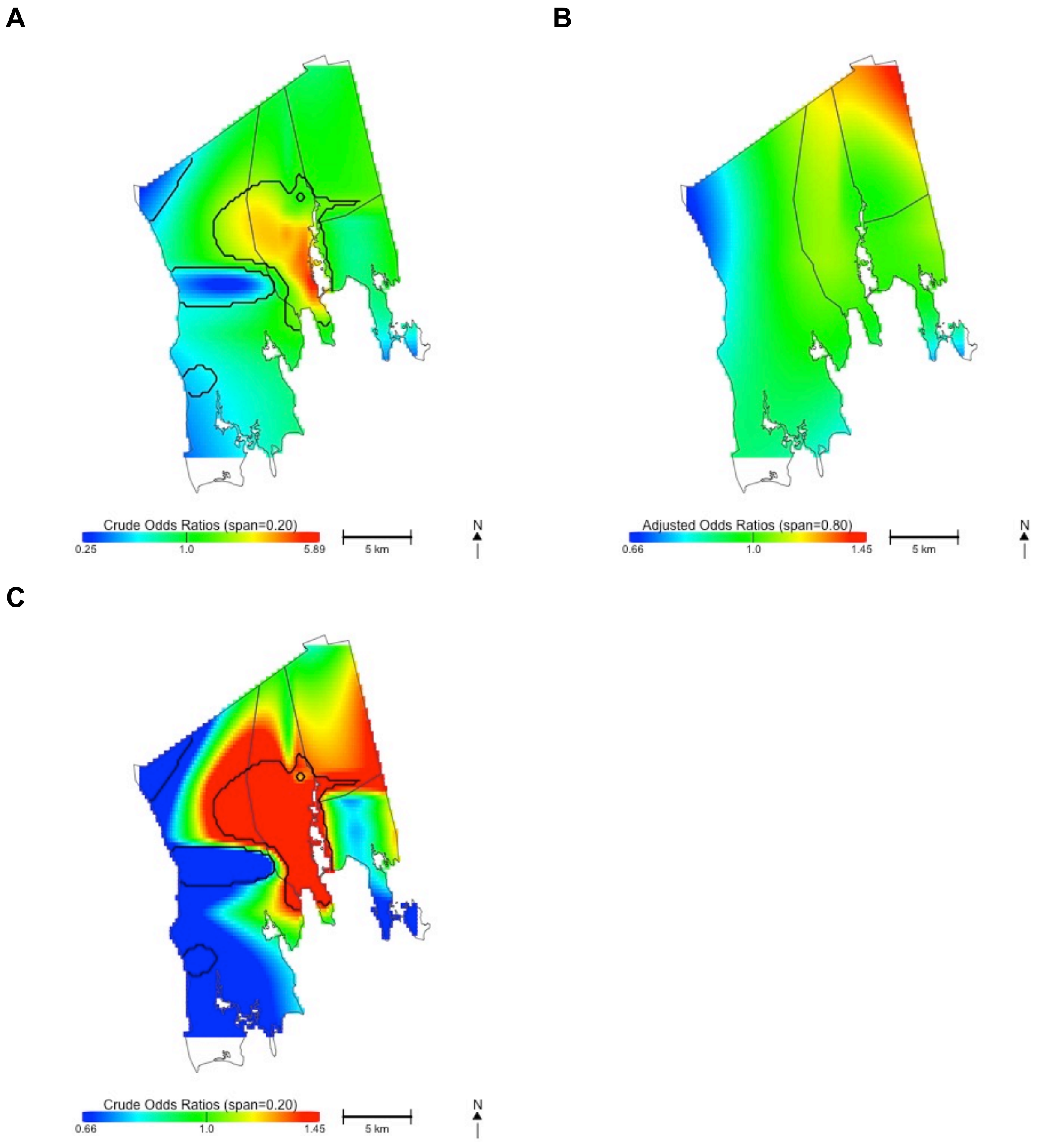

Figure 2.1. Crude and adjusted teen birth spatial analysis results for 1992-1998. Odds ratios are relative to the area of the study towns. (A) Crude, fit to span of 0.20 to address edge effects (global $p<0.001$). (B) Adjusted, optimal span of 0.80 (global $p=0.469$). (C) Crude, fit to span of 0.20 and mapped on adjusted odds scale. Black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. Location is no longer significant after adjustment for maternal education, maternal race/ancestry, marital status, smoking/alcohol consumption during pregnancy, parity, household income, adequacy of prenatal care, prenatal care payment source, and paternal education.

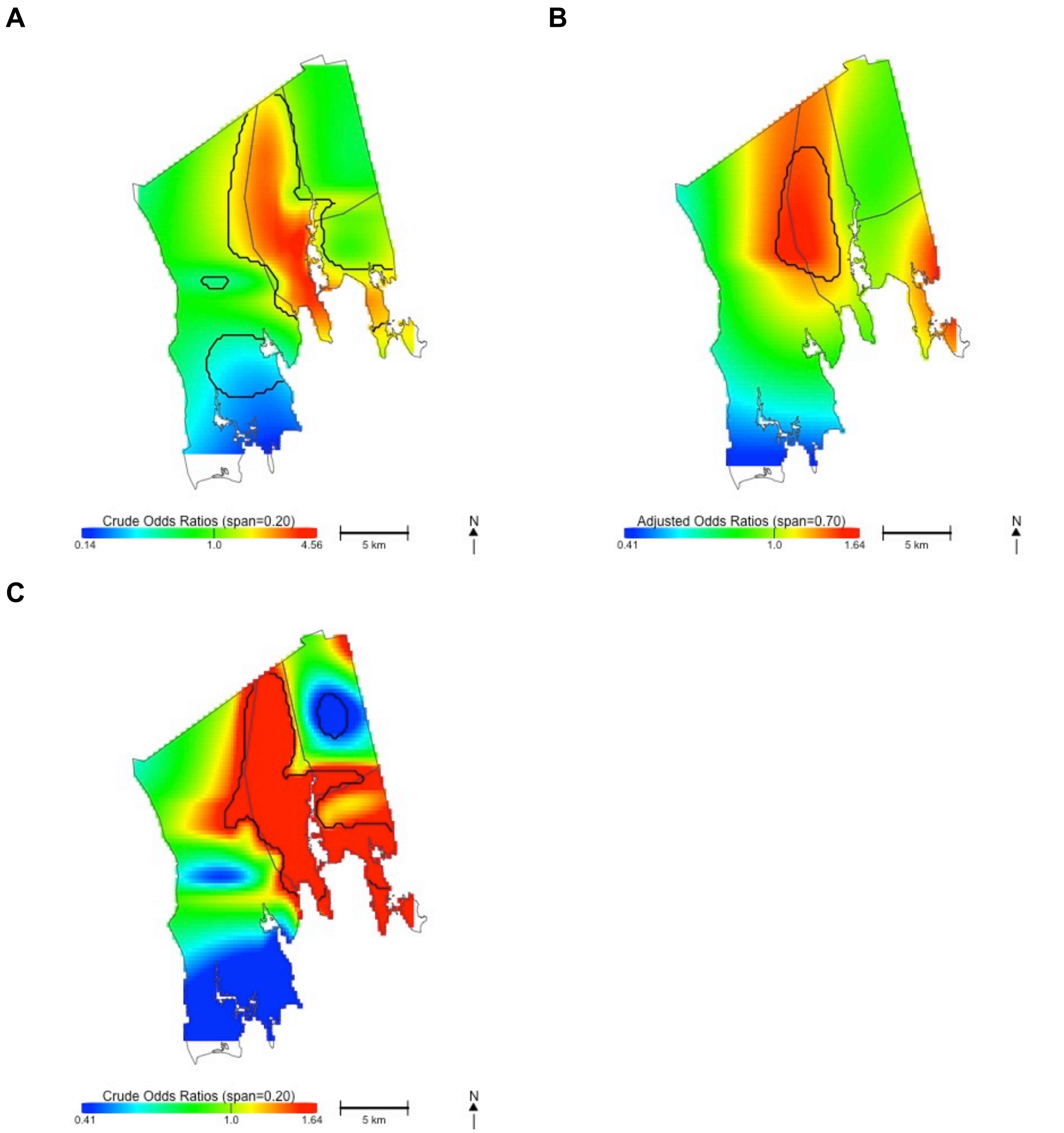

Figure 2.2. Crude and adjusted teen birth spatial analysis results for 2002-2008. Odds ratios are relative to the area of the study towns. (A) Crude, fit to span of 0.20 to address edge effects (global $p<0.001$). (B) Adjusted, optimal span of 0.70 (global $p<0.001$). (C) Crude, span of 0.20 and mapped on adjusted odds scale. Black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A significant geographic hotspot remained after adjustment maternal education, maternal race/ancestry, marital status, smoking/alcohol consumption during pregnancy, parity, household income, adequacy of prenatal care, prenatal care payment source, and paternal education.

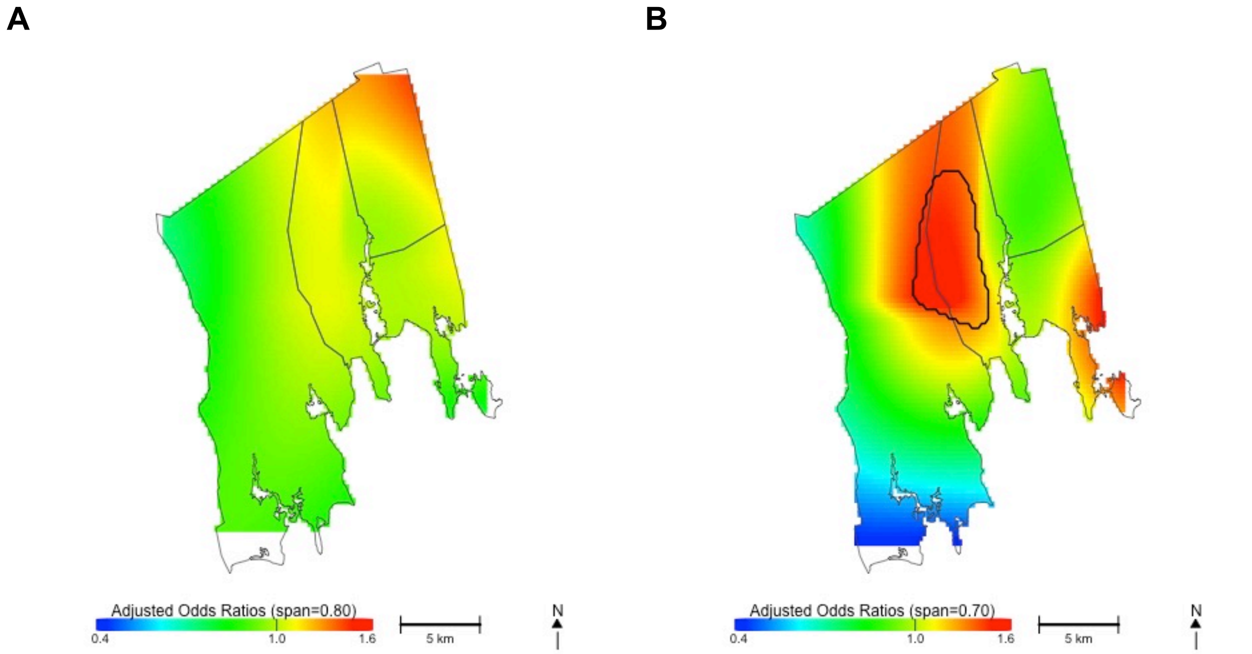

Figure 2.3. Adjusted teen birth spatial analysis results for 1992-1998 and 2002-2008 on overlapping scale. Odds ratios are relative to the area of the study towns and mapped on a scale that overlaps the adjusted models' OR ranges. (A) 1992-1998 adjusted, optimal span of 0.80 (global p=0.469). (B) 2002-2008 adjusted, optimal span of 0.70 (global p<0.001). Black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. Both models were adjusted for maternal education, maternal race/ancestry, marital status, smoking/alcohol consumption during pregnancy, parity, household income, adequacy of prenatal care, prenatal care payment source, and paternal education. A significant hotspot was apparent only in the 2002-2008 analysis.

CHAPTER 3:

PRENATAL EXPOSURE MIXTURES AND SUBSEQUENT TEEN BIRTHS AROUND THE NEW BEDFORD HARBOR, 1992-1998

Objective

This study examines associations between prenatal environmental exposures and subsequent teen birth among a cohort of New Bedford-area female births. Identification of environmental factors that contribute to increased risk-taking behavior is a public health priority, especially in communities exposed to multiple chemical and non-chemical stressors, as is prevalent near Superfund sites. This research will begin to address the limited understanding of this critical, but inadequately studied, area and to inform targeted public health interventions in such communities.

Methods

MADPH Birth Records

Massachusetts Department of Public Health (MADPH) birth record data was utilized to construct a birth cohort of all children born in the four towns (Acushnet, Dartmouth, Fairhaven, New Bedford) surrounding the New Bedford Harbor Superfund site between January 1992 and December 1998. The MADPH birth records include covariate information collected at birth, including parent demographics (birth place, maternal/paternal/infant race/ethnicity), socioeconomic status proxies (educational attainment, marital status), pregnancy exposures (smoking, alcohol), birth weight, gestational age, pregnancy weight gain, adequacy of prenatal care, and breastfeeding status at birth.

Using geographic information systems (GIS), median household income level, year maternal residence was built, and residential distances (in meters) to the New Bedford Harbor and to the nearest major roadway were assigned to geocoded birth addresses. Median block-group household income was obtained through 2000 United States Census Bureau data. Proximity to a major road was assigned using Massachusetts Department of Transportation (MassDOT) road segments of Class 1-4, which include limited access highways, multi-lane highways, numbered routes, and other major roadways. Property information from the Massachusetts Assessor database was used to assign year maternal residence was built.

The MADPH cohort was followed through age 19 to identify any subsequent cases of teen birth via birth record linkage between the female infant and her child. Between 1992-1998, there were 5,865 female births in the four study towns of Acushnet, Dartmouth, Fairhaven, and New Bedford.

Exposures Measures

Predictive prenatal exposure models were previously constructed for the sum of four prevalent PCB congeners (118, 138, 153, 180) (ΣPCB_4), DDE, HCB, Hg and Pb by fitting generalized additive models (GAMs) to data collected from the New Bedford Cohort (NBC) (Khalili et al., 2019). Biomarkers for these chemical exposures were measured in umbilical cord serum and maternal peripartum hair samples collected from 788 mother-infant pairs in the NBC residing in the New Bedford study area (Acushnet, Dartmouth, Fairhaven, New Bedford) (Sagiv et al. 2010; Sagiv et al. 2012). GAMs were employed, instead of predictive mean matching, in order to apply a multivariate loess (locally weighted scatter plot smoothing) term for maternal address at birth, infant year of birth, and maternal age. The loess term captures potential residual effects from unmeasured or inadequately measured covariates with a spatiotemporal component. All epidemiologic analyses included log-transformed measures of DDE, HCB, ΣPCB_4, Pb, and Hg.

Covariates

The epidemiologic analyses include covariates from the birth records. Covariate adjustment was determined by assessing which variables were associated with teen pregnancy using univariate logistic regression models; variables were included in the epidemiologic models if statistically significant ($p<0.05$) or if the variable yielded a change in effect size of at least 10%. The selected categorical covariates were household income less than 20,000, maternal education less than high school, paternal education less than high school, maternal marital status (married, other), prenatal care payment source (private insurance, other), parity (1, 2, 3, ≥4), maternal race (Non-Hispanic White, Non-Hispanic African American, Hispanic, Non-Hispanic Other), adequacy of prenatal care (Adequate on Kessner Index, other), breastfeeding initiated at hospital (yes, no), year maternal residence built (before 1951, 1951-1970, after 1970), and maternal smoking during pregnancy (any, none). Additional categorical variables tested but not retained in the final mixture model were maternal country of birth (Azores/Portugal, Cape Verde, other), maternal alcohol consumption during pregnancy (any, none), delivery payment source (private insurance, other), and teen birth status of the infant's mother. Continuous variables included in the final epidemiologic models were maternal age at birth and infant year of birth. We also tested infant birthweight, weight gain during pregnancy, residential distance to New Bedford Harbor (in meters), and residential distance to nearest major roadway (in meters), although they did not improve the fit of the final mixture model. A correlation chart for continuous covariates is presented in Appendix B Figure B.1.

Epidemiologic Models

After applying the NBC exposure models, we fit epidemiologic models of teen birth for all female births in the MADPH cohort. Only children with complete data were included in epidemiologic analyses (Table 3.1). Information on the infants born between 1992-1998 from vital records were linked by MADPH to maternal information in subsequent vital records to identify teen mothers younger than 20 years old. Exposure effects were examined in both single and multiple-exposure models. We used logistic regression to assess independent prenatal exposure effects on the risk for teen birth. To analyze the effects of mixtures of exposures and continuous covariates, GAMs with a multivariate smooth term for joint exposures was used and odds ratios with 95% confidence intervals estimated. The following model was utilized for teen birth:

$$\boldsymbol{logit}\ [\boldsymbol{p}(\boldsymbol{x1}, \dots, \boldsymbol{xN})] = \boldsymbol{S}(\boldsymbol{x1}, \dots, \boldsymbol{xN}) + \boldsymbol{b'z}$$

where $logit\ [p(x1, \dots, xN)]$ is the log odds of teen birth at a mixture of multiple continuous exposures and covariates $(x1, \dots, xN)$; $S(x1, \dots, xN)$ represents a multivariate *loess* (locally weighted scatter plot smoothing) term; b denotes the vector of parameters; and, z comprises the vector of covariates. The optimal span size, which determines the amount of smoothing, was selected by minimizing the Akaike

Information Criteria (AIC) (Hastie and Tibshirani 1995; Vieira et al. 2005; Webster et al. 2006).

The final mixture model was used to map odds ratios for teen birth by predicting combinations of two exposures on an X-Y axis, where X-coordinates represent levels of one continuous chemical exposure (e.g. HCB) and Y-coordinates represent levels of another continuous exposure (e.g. ΣPCB_4). The smoothed surface illustrates the odds ratios (ORs) at varying levels of the two exposures on the axes, while holding the remaining continuous predictors included in the *loess* and other covariates constant. Chemical exposure distributions exhibited skewedness; therefore, predictions were restricted from the 5^{th} to 95^{th} percentiles of the chemical distribution exposures on the axes to limit the impact of edge effects (Vieira et al. 2017). Each map is predicted at the level of highest OR for the categorical covariates and either the maximum or minimum value for the remaining continuous predictors not assigned to an axis. For example, each map is predicted for a single mother (versus “married”) because higher risk was observed in that category during multivariate logistic regression analyses. Maps are predicted at the following levels for the other categorical covariates: maternal/paternal education less than high school; non-White, Other maternal race; any smoking during pregnancy; non-initiation of breastfeeding at hospital; multiparous mothers of three (parity=3); inadequate prenatal care; other (non-private insurance) prenatal care source of payment; maternal residence at birth built after 1970; and, annual household income less than $20,000. Permutation tests provided a global p-value for statistical significance. A distribution of deviance statistics was generated under the null hypothesis that the smooth term for the mixture is not significant by permuting the variables in the smooth and refitting the model (Vieira et al. 2005; Webster et al. 2006).

R (version 3.3.3) and ArcGIS were utilized for data management. For spatial analyses and map creation, we used the R MapGAM package (Vieira et al. 2018). This research is approved by the institutional review boards of University of California, Irvine and the Massachusetts Department of Public Health.

Results

Population Characteristics and Predicted Chemical Exposures

The distribution of predicted prenatal exposures and selected study population characteristics and their univariate associations with subsequent teen birth are presented in Tables 3.1 and 3.2. Each of the predicted chemical exposures was significantly associated with teen birth. HCB and Pb were negatively associated with teen birth, while ΣPCB_4, DDE, and Hg were protective in the univariate associations. All infants in the study population were female. Of the 5,865 infant females born in the study area between 1992-1998, 291 (4.96%) cases (female infant subsequently gave birth at less than 20 years of age) were identified. For births in the study area between 1992 and 1998, the proportion of females who eventually gave birth as teens decreased steadily from 24.4% (1992) to 7.6% (1998).

Female infants who eventually gave birth as teens had a slightly lower birthweight on average than their counterparts. Mothers of female infants who eventually became pregnant were slightly younger on average than mothers of female infants who did not become pregnant, 23.4 versus 26.1 years old, respectively. The percentage of mothers who were teenagers themselves when they gave birth in 1992-1998 was nearly double for female infants with a subsequent teen birth (25.1%) compared to those without (14.1%). Parity was slightly higher for mothers of teen birth cases, particularly for three or more children (29.2% compared to 22.9%). Female infants who gave birth as teens had higher proportions of lower maternal (54.3% compared to 27.4%) and paternal (52.9% compared to 32.3%) educational attainment, unmarried mothers (64.6% compared to 40.9%), and lower annual household income (39.2% compared to 32.3%). Distributions of maternal ancestry were similar among cases and non-cases; while the majority of both cases and non-cases were of non-Hispanic White maternal race, the proportion with Hispanic maternal race was more than double amongst teen birth cases (24.1% versus 9.9%). Smoking was more prevalent among mothers of cases (32.3% compared to 22.6%), while any alcohol consumption was slightly higher amongst non-cases (1.8% compared to 1.0%). While the majority of mothers received adequate prenatal care, the proportion of those who didn’t was nearly double among cases of teen birth (7.2% compared to 4.4%); private insurance comprised the majority of prenatal care source of payment in non-cases (51.9%), while only 22% of prenatal care for cases was paid by private insurance. A greater proportion of mothers of non-cases initiated breastfeeding at the hospital (40.7% compared to 27.8%). On average, female infants who did not give birth as teens had a greater proportion of newer maternal residences and lived further from a major roadway and the New Bedford Harbor.

Exposure Mixture Models and Maps

Five chemical exposures and two non-chemical continuous predictors were included in the final mixture model in two multivariate smooth terms:

$$\begin{aligned}&\textbf{log odds of teen birth}\\&= \mathbf{S}(\textbf{log cord serum HCB}, \textbf{log maternal hair Hg}, \textbf{log cord blood Pb}, \textbf{log cord serum }\boldsymbol{\Sigma}\textbf{PCB4})\\&+ \mathbf{S}(\textbf{log cord serum DDE}, \textbf{maternal age at birth}, \textbf{infant year of birth})\\&+ \ \textbf{vector}(\textbf{parameters})'\textbf{vector}(\textbf{covariates})\end{aligned}$$

The first loess smooth term included log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum ΣPCB_4; the second loess smooth term included log cord serum DDE, maternal age at birth, and infant year of birth. The continuous variables in the smooths were grouped to minimize correlation between the exposures and other continuous predictors (Appendix B Figure B.1). The GAM was not stable when the exposures and continuous predictors were included in a single loess smooth. The final mixture model included adjustment for the following categorical covariates: household income less than $20,000, maternal education less than high school, paternal education less than high school, maternal marital status, prenatal care payment source, parity, maternal race, adequacy of prenatal, breastfeeding initiated at hospital, year maternal residence built, and maternal smoking during pregnancy. Results from the final mixture model suggest that female infants born earlier in the study period (i.e. 1992) to younger mothers have an increased risk of teen birth across different combinations of prenatal chemical exposures (global $p<0.001$). Table 3.3 presents a summary of teen birth odds ratio ranges for selected combinations of chemical exposures on the map axes.

Figure 3.1 presents the distribution of teen birth cases across varying levels of exposure for log cord serum HCB (as a fixed X-axis) and the other four chemical exposures on the Y-axis. Values on each axis are restricted from the 5th to the 95th percentile. Births appear to be distributed generally at middle exposure combinations, but there are some data points at higher exposure combinations. For female infants born earlier in the study period to younger mothers, higher levels of cord serum HCB and maternal hair Hg resulted in higher risk for subsequent teen birth (Figure 3.2A). The observed pattern persisted for combinations of cord serum HCB and cord blood Pb (Figure 3.2B) and cord serum HCB and log cord serum ΣPCB_4 (Figure 3.2C). However, higher levels of cord serum HCB and lower levels of cord serum DDE yielded higher risk of teen birth (Figure 3.2D).

Predicting at minimum levels of log cord serum DDE (Figure 3.3) yielded nearly identical map patterns to maximum levels (Figure 3.2); however, ORs for teen birth increased approximately threefold across the different exposure combinations of cord serum HCB and maternal hair Hg (Figure 3.3A), cord serum HCB and cord blood Pb (Figure 3.3B), and cord serum HCB and cord serum ΣPCB_4 (Figure 3.3C). Figure 3.4 depicts the distribution of teen birth cases at varying levels of cord serum DDE and the other four chemical exposures. For each of the exposure axis combinations, the majority of data is generally in the mid-to-lower value range but again, there is some data at higher exposure combinations. The protective pattern for DDE remains consistent when predicting and mapping adjusted odds ratios at varying levels of cord serum DDE with cord serum HCB (Figure 3.5A), maternal hair Hg (Figure 3.5B), cord blood Pb (Figure 3.5C), and cord serum ΣPCB_4 (Figure 3.5D).

Discussion

The purpose of this study was to assess associations between mixtures of prenatal environmental exposures and subsequent teen birth among infant females born near the New Bedford Harbor Superfund site. A mixture of HCB, Hg, Pb, ΣPCB_4, DDE, maternal age at birth, and infant year of birth was associated with teen birth. For all exposure axis combinations, maternal age at birth and infant year of birth were included in a multivariate smooth at minimum levels. We found risk of subsequent teen birth was greater for female infants with younger mothers, which is well-documented in previous research (Bonell et al. 2006; Coyne and D'onofrio 2012; East et al. 2007; Hardy et al. 1998; Pogarsky et al. 2006). We used infant year of birth as a temporal proxy to control for policies and interventions aimed at reducing teen pregnancy that may have been implemented over the study period (Colen et al. 2006; Santelli and Melnikas 2010). Since the female infants were born between 1992 and 1998, the eldest would reach child-bearing age during the mid-2000's, when teen birth rates were at historic lows (Hamilton and Ventura 2012; Ventura et al. 2014). Consistent with the literature, we observed elevated risk of subsequent teen birth for female infants born earlier in the study period (i.e. 1992).

Maternal substance use (e.g. tobacco, alcohol, cannabis) during pregnancy, even at low levels, is associated with neurodevelopmental deficits (Huizink and Mulder 2006; Polańska et al. 2015). While any smoking during pregnancy was associated with higher risk of subsequent teen birth in the study's female infants, any alcohol consumption showed a protective effect in the univariate analysis. Some maternal underreporting of substance use during pregnancy is likely due to social desirability bias

(Garg et al., 2016; Krumpal 2013). Directional associations between teen births and prenatal chemical exposures were generally as expected in the adjusted model, with the exception of cord serum DDE, which appeared to have a protective effect. Previous research in the NBC demonstrated a modest to strong correlation between DDE and maternal diet during pregnancy (Korrick et al., 2000). The neurotoxic effects of DDE may be overpowered by the protective effects of maternal fish consumption during pregnancy (Myers and Davidson 2007; Sagiv et al. 2012). Additionally, maternal diets high in fresh fruit and vegetable consumption may result in increased risk of exposure to pesticides (e.g. DDE); however, healthy prenatal diet, and other healthy lifestyle factors, may confound the relationship between prenatal DDE exposure and teen birth.

Despite mechanistic support for a role of chemical exposures in risk-taking, there is a paucity of epidemiologic studies on prenatal chemical exposure mixtures and manifestation of risk-taking behaviors during adolescence. Much of the epidemiologic literature focuses on early life individual and combined exposures and associations with early childhood neurodevelopment and neurobehavioral outcomes (Bellinger, 2013; González-Alzaga et al. 2014; Henn et al. 2014; Sanders et al. 2015); thus, this research adds to a critical but understudied area. A strength of this research is the large sample size achieved via exposure modeling, which gives the statistical power to study the relationship of a rare outcome in a larger population (N=5,865) than the New Bedford Cohort (N=371).

Various statistical approaches to characterizing and assessing chemical (and non-chemical) mixtures exist (Braun et al. 2016; Hamra and Buckley 2018; Huang et al. 2018; Kalloo et al. 2018; Taylor et al. 2016); however, the extension of generalized additive models employed in our research has several strengths. GAMs are flexible; however, they are limited by the number of terms in a single smooth before destabilizing. Thus, our final mixture model allowed for smoothing of five log-transformed chemical exposures and two continuous covariates across two *loess* terms while concurrently adjusting for additional categorical covariates. Inclusion of two loess smooth terms permitted us to separate the continuous exposures and covariates to minimize correlation between the exposures. Furthermore, utilization of the MapGAM package in R allowed us to map cross-sections of odds ratios based on varying levels of two continuous exposures in the mixture, while holding all other exposures and covariates constant at their riskiest level for interpretation of results. Finally, permutation tests were used to evaluate the statistical significance of the loess mixture term(s).

Linkage of birth records to hospitalization records for the outcome of teen birth restricts the case count to those females who had a live birth registered through MADPH; thus, it is probable that rates of engagement in risky sexual activity and subsequent intended or unintended teen pregnancy may be underestimated in our study population. Covariate adjustment in our analyses was restricted primarily to maternal and infant demographic variables available in the MADPH birth records; therefore, we were unable to adjust for some potential confounders at the individual (mother-infant pair) level (e.g. household income) or at all (e.g. maternal prenatal diet). Further, we did not have information on whether the female infant gave birth more than one time during adolescence or if the indicated birth was a first or later birth, which may help identify sub-populations potentially at-risk for repeat teen births. The chemical exposure models employed in this study were constructed from a subset of the study population (i.e. the NBC), which limits the generalizability of study results to females born in different time periods or geographic regions. Further prospective studies examining the prenatal window of exposure are warranted to elucidate the effects of mixtures of chemical exposures and non-chemical stressors on neurodevelopment and manifestation of risky behaviors, such as teen birth, in vulnerable and understudied populations.

Conclusion

Our analyses utilized an innovative extension of generalized additive models to characterize and to assess the statistical significance of exposure mixtures, and our results suggest that prenatal chemical exposures may interact with other social and demographic variables to contribute to elevated risk of subsequent teen births in female infants born near the New Bedford Harbor. Infants born earlier in the study period to younger mothers demonstrated higher risk of subsequent teen birth at minimum levels of cord serum DDE and maximum levels of HCB, Hg, Pb, and ΣPCB_4. Identification of environmental and social factors that contribute to increased risk-taking behavior is a public health priority, especially among communities exposed to multiple chemical and non-chemical stressors, as is prevalent near Superfund sites.

Table 3.1. Distributions of log-transformed predicted prenatal exposures and univariate associations between log-transformed predicted exposures and teen birth in females born in the New Bedford Harbor study area between 1992-1998 (N=5,865).

Prenatal Exposure	Teen Birth (n=291)			No Teen Birth (n=5,574)			OR (95% CI)
	5th Percentile	Median	95th Percentile	5th Percentile	Median	95th Percentile	
Cord Serum ΣPCB_4 (ng/g)	-2.32	-1.76	-0.68	-2.29	-1.58	-0.49	0.58 (0.39, 0.87)
Cord Serum DDE (ng/g)	-1.97	-1.30	0.42	-1.80	-1.05	0.21	0.61 (0.40, 0.92)
Cord Serum HCB (ng/g)	-4.03	-3.58	-3.05	-4.23	-3.61	-3.07	1.70 (1.15, 2.53)
Cord Blood Pb (μg/dL)	0.03	0.44	1.13	-0.20	0.35	0.99	3.33 (2.27, 4.89)
Maternal Hair Hg (μg/g)	5.48	6.06	6.93	5.54	6.23	7.08	0.64 (0.44, 0.94)

Note: DDE, ρ,ρ′-dichlorodiphenyl dichloroethylene; HCB, hexachlorobenzene; Hg, mercury; OR, unadjusted odds ratio for change from 5th to 95th percentile; Pb, lead; PCB, polychlorinated biphenyl; ΣPCB_4, sum of four prevalent PCB congeners (118, 138, 153, and 180) in cord serum; CI, confidence interval.

Table 3.2. Infant and maternal characteristics of the MBRC, univariate associations with, and final mixture model estimates for teen birth in females born in the New Bedford Harbor study area, 1992-1998 (N=5,865).

	Teen Birth (n=1,874)	No Teen Birth (n=10,304)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Female Infant Characteristics				
Birthweight (g) (mean ± sd)	3,263 ± 508	3,303 ± 511	0.99 (0.99, 1.00)	N/A
Infant Year of Birth (continuous)			0.82 (0.77, 0.87)	N/A
1992	71 (24.4)	846 (15.2)		
1993	56 (19.2)	809 (14.5)		
1994	60 (20.6)	837 (15.0)		
1995	31 (10.7)	739 (13.3)		
1996	24 (8.2)	750 (13.5)		
1997	27 (9.3)	765 (13.7)		
1998	22 (7.6)	828 (14.8)		
Maternal Characteristics				
Age (mean ± sd)	23.4 ± 5.4	26.1 ± 5.8	0.91 (0.89, 0.94)	N/A
Weight Gain (lbs) (mean ± sd)	27.5 ± 12.6	29.6 ± 12.2	0.98 (0.97, 0.99)	N/A
Race/Ethnicity				
White, non-Hispanic	181 (62.2)	4,386 (78.7)	referent	
Black, non-Hispanic	18 (6.2)	248 (4.4)	1.76 (1.06, 2.90)	1.12 (0.24, 2.94)
Hispanic	70 (24.1)	553 (9.9)	3.07 (2.30, 4.10)	1.54 (0.87, 2.73)
Other, non-White	22 (7.5)	367 (6.6)	1.45 (0.92, 2.29)	1.77 (0.66, 4.73)
Missing	0 (0.0)	20 (0.4)		
Country of Birth				
Azores/Portugal	70 (24.0)	1,370 (24.6)	0.98 (0.74, 1.30)	N/A
Cape Verde	27 (9.3)	463 (8.3)	1.12 (0.74, 1.69)	N/A
Other	194 (66.7)	3,721 (66.7)	referent	
Missing	0 (0.0)	20 (0.4)		
Any Smoking During Pregnancy				
Yes	94 (32.3)	1,261 (22.6)	1.63 (1.26, 2.09)	1.17 (0.74, 1.85)
No	197 (67.7)	4,295 (77.1)	referent	
Missing	0 (0.0)	18 (0.3)		
Any Alcohol Consumption During Pregnancy				
Yes	3 (1.0)	102 (1.8)	0.56 (0.18, 1.76)	N/A
No	288 (99.0)	5,447 (94.3)	referent	
Missing	0 (0.0)	25 (8.6)		
Maternal Education at Birth				
<HS education	158 (54.3)	1,529 (27.4)	3.15 (2.48, 4.00)	1.49 (0.73, 1.70)
≥HS education	132 (45.4)	4,023 (72.2)	referent	
Missing	1 (0.3)	22 (0.4)		

Table 3.2 continued. Infant and maternal characteristics of the MBRC, univariate associations with, and final mixture model estimates for teen birth in females born in the New Bedford Harbor study area, 1992-1998 (N=5,865).

	Teen Birth (n=1,874)	No Teen Birth (n=10,304)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Maternal Characteristics (continued)				
Adequate Prenatal Care (Kessner Index)				
Yes	270 (92.8)	5,260 (94.4)	0.60 (0.52, 0.87)	0.91 (0.61, 1.36)
No	21 (7.2)	244 (4.4)	referent	
Missing	0 (0.0)	70 (1.3)		
Prenatal Care Source of Payment				
Private Insurance	65 (22.3)	2,891 (51.9)	0.26 (0.20, 0.35)	0.66 (0.41, 1.07)
Other Payment	226 (77.7)	2,647 (47.5)	referent	
Missing	0 (0.0)	36 (0.6)		
Annual Household Income at Birth				
<20K/year	114 (39.2)	1,192 (21.4)	2.37 (1.86, 3.02)	1.48 (0.96, 2.28)
≥20K/year	177 (60.8)	4,382 (78.6)	referent	
Missing	0 (0.0)	0 (0.0)		
Parity				
1 child	110 (37.8)	2,421 (43.4)	referent	
2 children	96 (33.0)	1,848 (33.2)	1.14 (0.86, 1.51)	1.39 (0.86, 2.24)
3 children	54 (18.6)	825 (14.8)	1.44 (1.03, 2.01)	1.61 (0.89, 2.89)
≥4 children	31 (10.6)	452 (8.1)	1.51 (1.00, 2.28)	1.26 (0.53, 3.01)
Missing	0 (0.0)	28 (0.5)		
Year Maternal Residence Built				
≤1950	211 (72.5)	3,811 (68.4)	1.69 (1.16, 2.46)	0.90 (0.44, 1.84)
1951-1970	36 (12.4)	604 (10.8)	1.82 (1.12, 2.96)	0.90 (0.51, 1.60)
>1970	32 (11.0)	975 (17.5)	referent	
Missing	12 (4.1)	184 (3.3)		
Marital Status at Birth				
Married	103 (35.4)	3,296 (59.1)	0.38 (0.29, 0.48)	0.82 (0.49, 1.38)
Unmarried	188 (64.6)	2,278 (40.9)	referent	
Missing	0 (0.0)	0 (0.0)		
Partner Education at Birth				
<HS education	154 (52.9)	1,798 (32.3)	2.36 (1.86, 2.99)	1.12 (0.73, 1.70)
≥HS education	137 (47.1)	3,776 (67.7)	referent	
Distance to Harbor (m) (mean±sd)	1,182 ± 1,329	1,633 ± 3,301	0.99 (0.99, 0.99)	N/A
Distance to Major Road (m) (mean±sd)	111 ± 147	194 ± 391	0.99 (0.99, 0.99)	N/A

Table 3.2 continued. Infant and maternal characteristics of the MBRC, univariate associations with, and final mixture model estimates for teen birth in females born in the New Bedford Harbor study area, 1992-1998 (N=5,865).

	Teen Birth (n=1,874)	No Teen Birth (n=10,304)	Univariate OR (95% CI)	Adjusted OR[a] (95% CI)
Maternal Characteristics (continued)				
Initiated Breastfeeding at Hospital				
Yes	81 (27.8)	2,271 (40.7)	0.56 (0.43, 0.72)	0.64 (0.41, 0.99)
No	210 (72.2)	3,272 (58.7)	Referent	
Missing	0 (0.0)	31 (0.6)		
Maternal Teen Birth Status				
Mom is teen at birth	73 (25.1)	786 (14.1)	2.04 (1.55, 2.69)	N/A
Mom not teen at birth	218 (74.9)	4,788 (85.9)	Referent	

Note: MBRC, Massachusetts Birth Record Cohort; OR, odds ratio; CI, confidence interval; sd, standard deviation; HS, high school. [a] Missing values were excluded from the analyses.

Table 3.3. Summary of odds ratio ranges for selected exposure axes combinations of the final teen birth mixture model for females born in the New Bedford Harbor study area, 1992-1998 (N=5,865).

Map Axes	Figure	Odds Ratio Range	Fixed Levels of Other Continuous Variables in Smooth
Log HCB, Log Hg	3.2A	0.58-3.94	max(Log Pb), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth), max(Log DDE)
Log HCB, Log Pb	3.2B	0.32-2.29	max(Log Hg), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth), max(Log DDE)
Log HCB, Log ΣPCB_4	3.2C	0.07-1.67	max(Log Hg), max(Log Pb), min(Maternal Age), min(Year of Birth), max(Log DDE)
Log HCB, Log DDE	3.2D	4.73-13.5	max(Log Hg), max(Log Pb), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth)
Log HCB, Log Hg	3.3A	4.17-27.9	max(Log Pb), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth), min(Log DDE)
Log HCB, Log Pb	3.3B	2.27-16.1	max(Log Hg), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth), min(Log DDE)
Log HCB, Log ΣPCB_4	3.3C	0.58-12.4	max(Log Hg), max(Log Pb), min(Maternal Age), min(Year of Birth), min(Log DDE)
Log HCB, Log DDE	3.3D	10.5-28.5	max(Log Hg), max(Log Pb), max(Log ΣPCB_4), min(Maternal Age), min(Year of Birth)
Log DDE, Log HCB	3.5A	10.5-28.5	max(Log Hg), max(Log Pb), max(Log ΣPCB_4), min(Maternal Age at Birth), min(Year of Birth)
Log DDE, Log Hg	3.5B	15.2-34.0	max(Log HCB), max(Log Pb), max(Log ΣPCB_4), min(Maternal Age at Birth), min(Year of Birth)
Log DDE, Log Pb	3.5C	2.13-17.0	max(Log HCB), max(Log Hg), max(Log ΣPCB_4), min(Maternal Age at Birth), min(Year of Birth)
Log DDE, Log ΣPCB_4	3.5D	1.14-14.5	max(Log HCB), max(Log Hg), max(Log Pb), min(Maternal Age at Birth), min(Year of Birth)

Note: DDE, ρ,ρ′-dichlorodiphenyl dichloroethylene; HCB, hexachlorobenzene; Hg, mercury; Pb, lead; PCB, polychlorinated biphenyl; ΣPCB_4, sum of four prevalent PCB congeners (118, 138, 153, and 180) in cord serum.

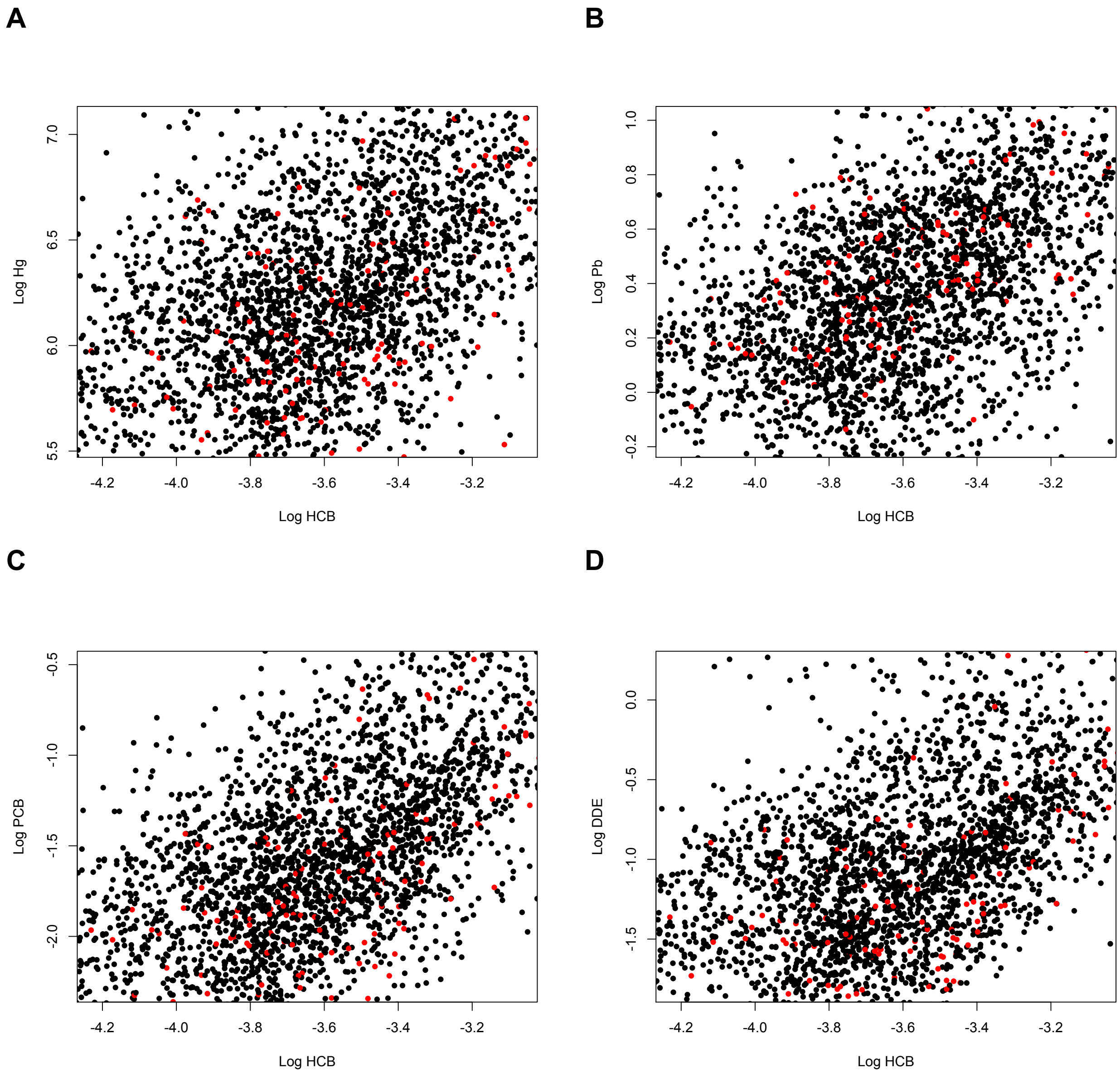

Figure 3.1. Distributions of log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum ΣPCB_4, log cord serum DDE exposure values among MADPH female infants born between 1992-1998 by teen birth case status (291 cases and 5,574 non-cases). Point maps illustrate the distribution of varying levels of exposure for log cord serum HCB on the x-axis and log maternal hair Hg (A); log cord blood Pb (B); log cord serum ΣPCB_4 (C); and log cord serum DDE (D) on the y-axis for teen birth cases (red circles) and non-cases (black circles). Each axis is restricted to the 5^{th} and 95^{th} percentile of the final mixture model distribution of the variable.

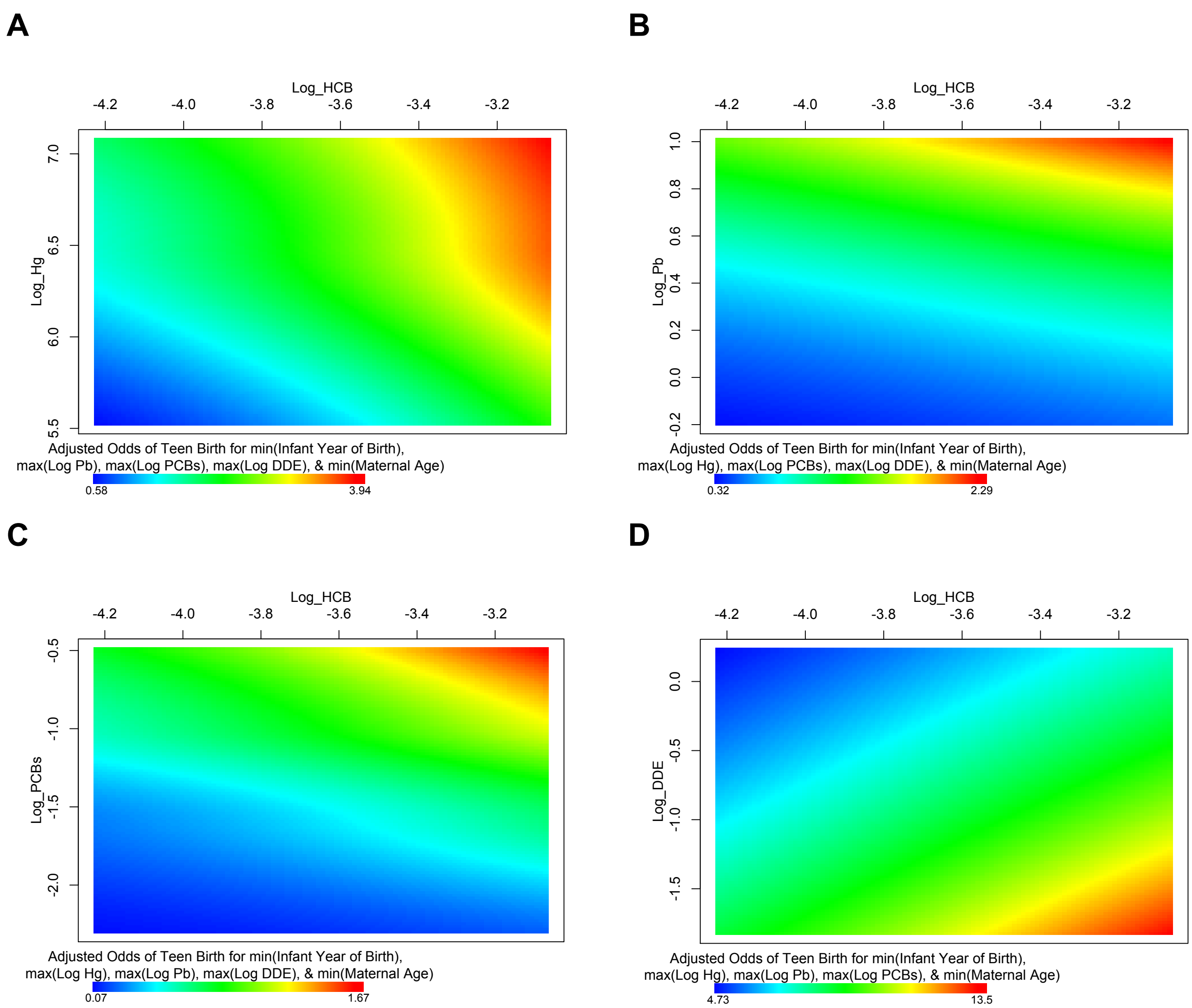

Figure 3.2. Association between teen birth and mixture of log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum ΣPCB_4, log cord serum DDE, maternal age at birth, and infant year of birth in MADPH female births from 1992-1998. Odds ratios for teen birth were predicted for a girl born to an 18-year-old mother in 1992 at varying log cord serum HCB levels on the x-axis and varying log maternal hair Hg (A); log cord blood Pb (B); log cord serum ΣPCB_4 (C); and log cord serum DDE (D) on the y-axis. For each map, exposures not on the axes were held constant at the maximum value, hypothesized to be the greatest risk. Analyses were further adjusted for household income less than \$20,000, parental education less than high school, maternal marital status, prenatal care payment source, parity, maternal race, adequacy of prenatal care, breastfeeding initiated at hospital, year maternal residence built, and maternal smoking during pregnancy.

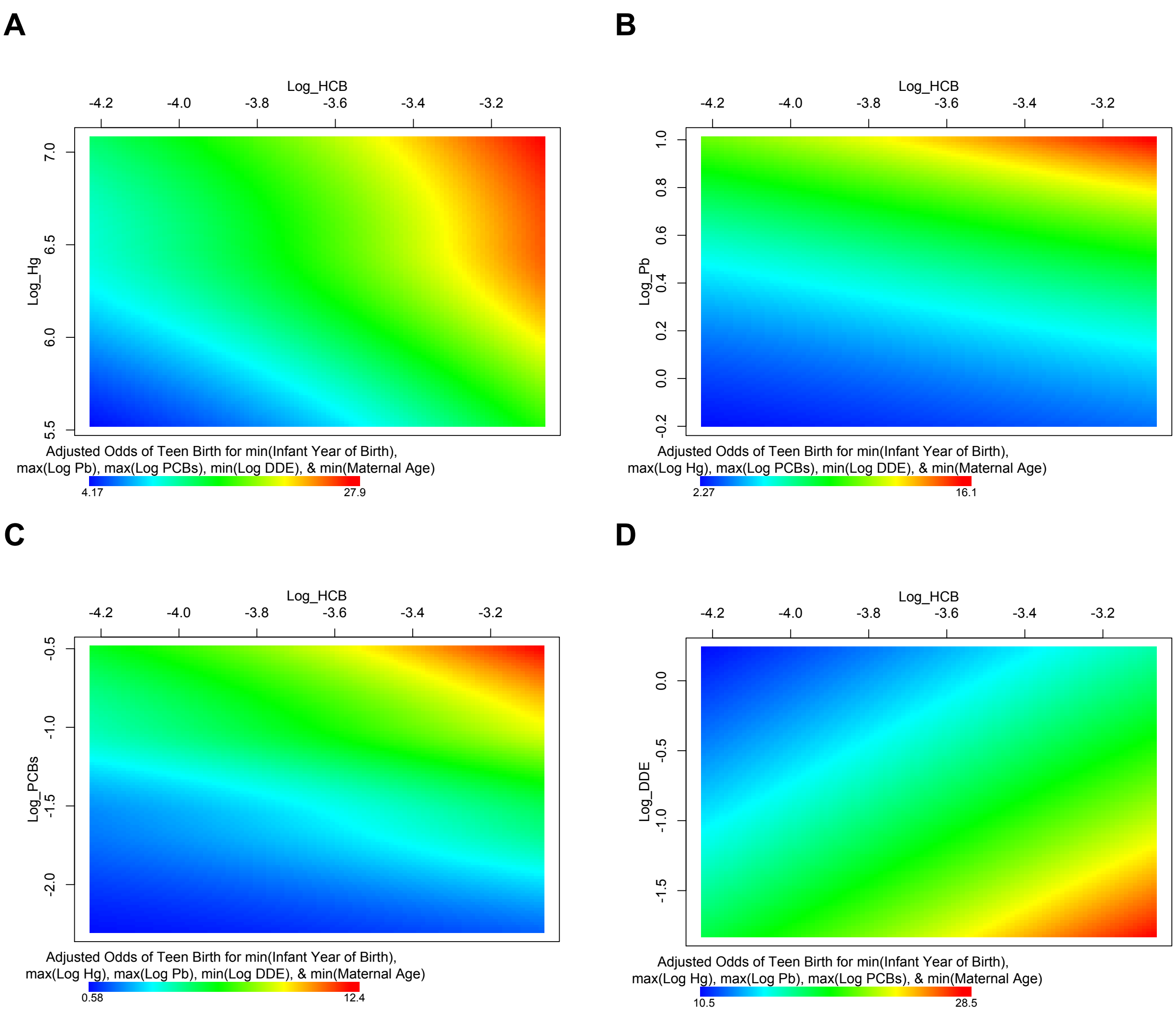

Figure 3.3. Association between teen birth and mixture of log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum ΣPCB_4, log cord serum DDE, maternal age at birth, and infant year of birth in MADPH female births from 1992-1998. Odds ratios for teen birth were predicted for a girl born to an 18-year-old mother in 1992 at varying log cord serum HCB levels on the x-axis and varying log maternal hair Hg (A); log cord blood Pb (B); log cord serum ΣPCB_4 (C); and log cord serum DDE (D) on the y-axis. For each map, exposures not on the axes were held constant at the maximum value, except for DDE, which was predicted at the minimum value. Analyses were further adjusted for household income less than $20,000, parental education less than high school, maternal marital status, prenatal care payment source, parity, maternal race, adequacy of prenatal care, breastfeeding initiated at hospital, year maternal residence built, and maternal smoking during pregnancy.

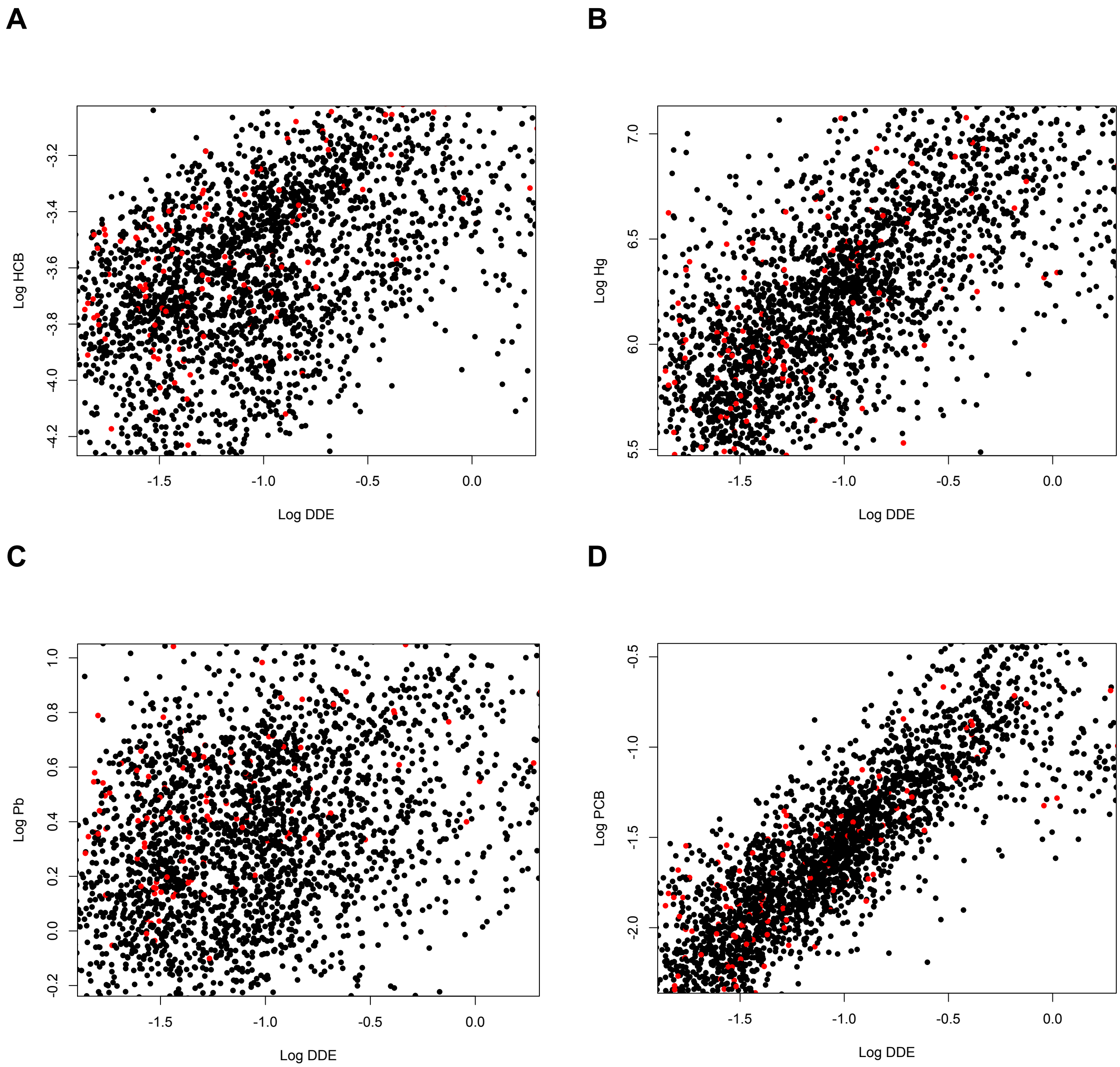

Figure 3.4. Distributions of log cord serum DDE, log cord serum HCB, log maternal hair Hg, log cord blood Pb, and log cord serum ΣPCB$_4$ exposure values among MADPH female infants born between 1992-1998 by teen birth case status (291 cases and 5,574 non-cases). Point maps illustrate the distribution of varying levels of exposure for log cord serum DDE on the x-axis and log cord serum HCB (A), log maternal hair Hg (B); log cord blood Pb (C); and log cord serum ΣPCB$_4$ (D) on the y-axis for teen birth cases (red circles) and non-cases (black circles). Each axis is restricted to the 5th and 95th percentile of the final mixture model distribution of the variable.

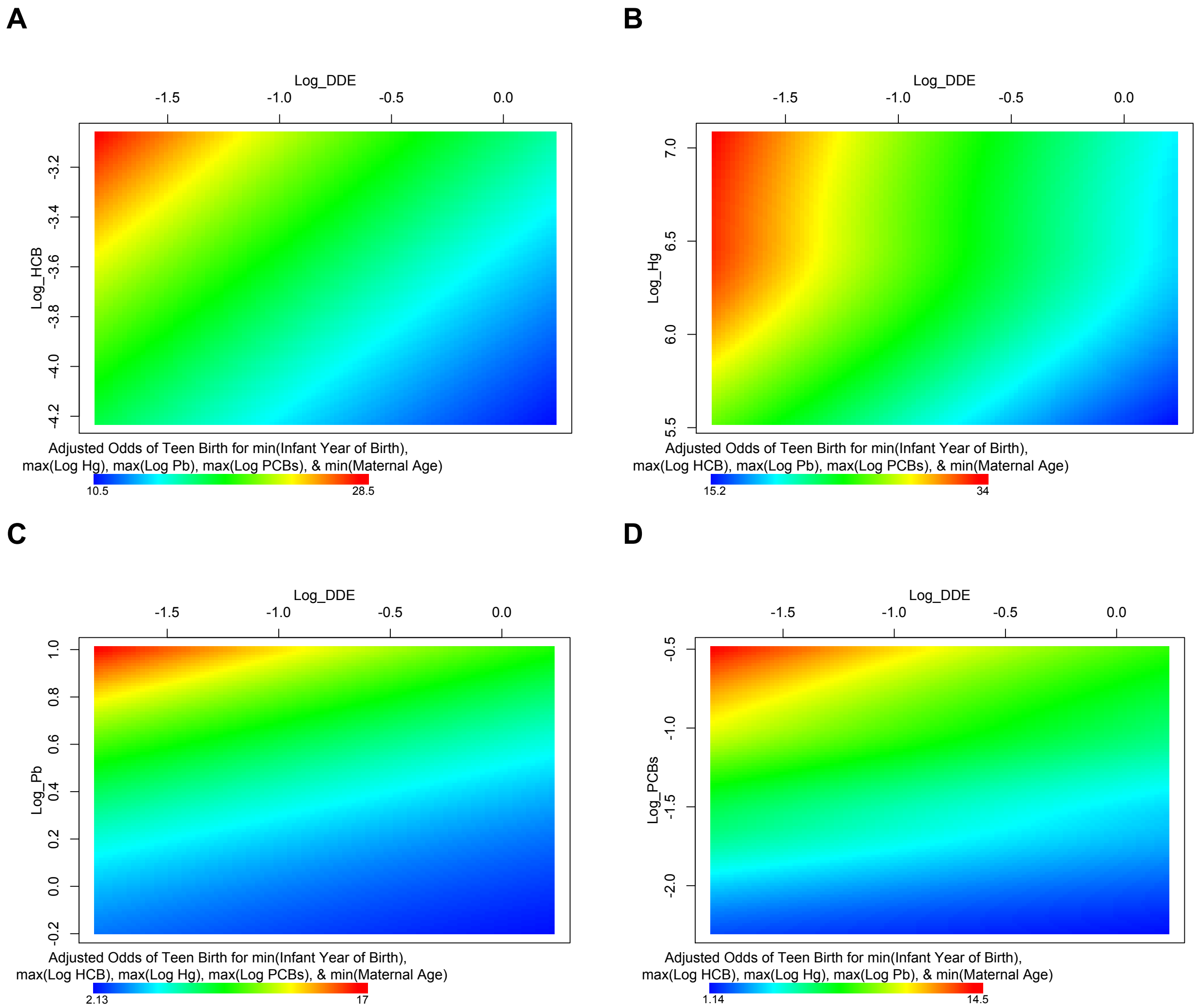

Figure 3.5. Association between teen birth and mixture of log cord serum DDE, log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum ΣPCB_4, maternal age at birth, and infant year of birth in MADPH female births from 1992-1998. Odds ratios for teen birth were predicted for a girl born to an 18-year-old mother in 1992 at varying log cord serum DDE levels on the x-axis and varying log cord serum HCB (A); log maternal hair Hg (B); log cord blood Pb (C); and log cord serum ΣPCB_4 (D) on the y-axis. For each map, exposures not on the axes were held constant at the maximum value. Analyses were further adjusted for household income less than $20,000, parental education less than high school, maternal marital status, prenatal care payment source, parity, maternal race, adequacy of prenatal care, breastfeeding initiated at hospital, year maternal residence built, and maternal smoking during pregnancy.

CHAPTER 4:

PRENATAL EXPOSURE MIXTURES AND TEEN BIRTHS IN THE NEW BEDFORD COHORT

Objective

This study examines associations between prenatal environmental exposures and subsequent teen birth among the New Bedford Cohort (NBC), a subset of the Massachusetts Birth Record Cohort (MBRC). We assessed whether patterns of predicted prenatal exposure mixtures observed in the larger MBRC were also present using measured biomarker data in the smaller NBC, with adjustment for additional covariates included in the NBC data.

Methods

The New Bedford Cohort

New Bedford is a racially diverse low-income city with approximately 95,000 residents, 23% of whom live below the poverty level and 70% of whom live in census blocks meeting at least one of the Massachusetts environmental justice criteria. The New Bedford Cohort is a prospective cohort of 788 mother-infant pairs, with children born 1993–1998 to mothers residing in one of four towns (New Bedford, Acushnet, Fairhaven, Dartmouth) surrounding the New Bedford Harbor Superfund site in Massachusetts. Extensive biomarker data was gathered for mother-infant pairs; details on the collection of biomarker data and analytical methods are described elsewhere (Korrick et al., 2000; Sagiv et al., 2012, 2010). Umbilical cord serum samples were analyzed for dichlorodiphenyldichloroethylene (DDE), hexachlorobenzene (HCB), and 51 individual PCB congeners. The sum of four prevalent PCB congeners (118, 138, 153, 180) (ΣPCB_4) is used in analyses. In addition, cord blood lead (Pb); maternal toenail arsenic (As), selenium (Se), and manganese (Mn); and peripartum maternal total hair mercury (Hg) levels were measured. Children in the NBC completed periodic neurodevelopmental assessments from birth through their teenage years; questionnaires, psychometric tests, and medical record reviews were used to determine non-chemical, sociodemographic covariates for mothers and children in the NBC.

We linked the NBC females to MADPH birth records used in the MBRC analysis (Chapter 3) to determine any subsequent cases of teen birth. Between 1993-1998, the NBC included 371 female births from one of the four study towns of Acushnet, Dartmouth, Fairhaven, and New Bedford.

Covariates

The epidemiologic analyses include covariate information gathered from the NBC study. Covariate adjustment was determined by testing which variables were associated with teen birth using univariate logistic regression models; variables were included in the epidemiologic models if statistically significant ($p<0.05$) or if the variable produced a change in effect size of at least 10%. Categorical covariates tested in univariate analyses were household income greater/less than 20,000, maternal education greater/less than high school, paternal education greater/less than high school, maternal marital status (married, other), infant and maternal race/ethnicity (Non-Hispanic White, Non-Hispanic African American, Hispanic, Non-Hispanic Other), ever breastfed child (yes, no), maternal ancestry (foreign-born or not), maternal smoking during pregnancy (any, none), and illicit drug use in year prior to birth (any, none). Continuous variables tested in univariate analyses included infant birthweight, Hobel pregnancy risk score, gestational age, maternal age at child's birth, maternal IQ, maternal depression score on Beck Depression Index (BDI), and Home Observation for Measurement of the Environment (HOME) score. The final models were adjusted for the following covariates pertaining to the mother of the teen: maternal depression, maternal age at teen's birth, quality of the home environment, maternal race/ethnicity, maternal ancestry, and annual household income at teen's birth. Information on maternal dietary factors, such as consumption of organ meat, seafood, local produce, and grains and vitamin use during pregnancy, was available and included in an adjusted analysis.

Epidemiologic Models

Using measured NBC exposure data, we fit epidemiologic models of teen birth for all female births in the NBC cohort. Mother-infant pairs with incomplete data were excluded from the epidemiologic analyses (Table 4.2). Exposure effects were examined in both single and multiple-exposure models. We used logistic regression to assess independent prenatal exposure effects on the risk for teen birth in the NBC. To analyze the effects of mixtures of exposures and continuous covariates, GAMs with a multivariate smooth term for joint exposures was used and odds ratios with 95% confidence intervals estimated. The following model was employed for teen birth:

$$\boldsymbol{logit\ [p(x1, \dots, xN)] = S(x1, \dots, xN) + b'z}$$

where $logit\ [p(x1, \dots, xN)]$ is the log odds of teen birth at a combination of continuous exposures $(x1, \dots, xN)$; $S(x1, \dots, xN)$ represents a bivariate *loess* (locally weighted scatter plot smoothing) term; b denotes the vector of parameters; and, z comprises the vector of covariates. The optimal span size was selected by minimizing the Akaike Information Criteria (AIC) (Hastie and Tibshirani 1995; Vieira et al. 2005; Webster et al. 2006).

The adjusted model was used to map odds ratios for teen birth by predicting combinations of two exposures on an X-Y axis, where X-coordinates represent levels of one continuous chemical exposure (e.g. HCB) and Y-coordinates represent levels of another continuous exposure (e.g. ΣPCB_4). The smoothed surface illustrates the odds ratios (ORs) at varying levels of the two exposures on the axes, while holding the remaining covariates constant. Chemical exposure distributions exhibited skewedness; therefore, predictions were restricted from the 5^{th} to 95^{th} percentiles of the chemical distribution exposures on the axes to limit the impact of edge effects (Vieira et al. 2017). Each map is predicted at the level of highest risk for the categorical covariates and either the maximum or minimum value for the continuous covariates included in the model. For example, each map is predicted for the minimum age of the mother at birth (versus the mean or maximum age) because highest risk was observed at that level during multivariate logistic regression analyses. Maps are predicted at the following levels for the other covariates: maximum maternal depression score on BDI; minimum quality of the home environment (minimum HOME score); non-Hispanic White maternal race; whether mother is foreign-born; and, annual household income less than $20,000 at birth. Permutation tests provided a global p-value for statistical significance. A distribution of deviance statistics was generated under the null hypothesis that the smooth term for the mixture is not significant by permuting the variables in the smooth and refitting the model (Vieira et al. 2005; Webster et al. 2006).

R (version 3.3.3) and ArcGIS were utilized for data management. For spatial analyses and map creation, we used the R MapGAM package (Vieira et al. 2018). This research is approved by the institutional review boards of University of California, Irvine and the Massachusetts Department of Public Health.

Results

Population Characteristics and Measured Chemical Biomarkers

The distribution of log-transformed measured prenatal biomarker exposures and selected study population characteristics and their univariate associations with subsequent teen birth are presented in Tables 4.1 and 4.2. In the univariate analyses, ΣPCB_4, DDE, and Hg were protective and significantly associated with subsequent teen birth. HCB, Pb, and As were also protective although the confidence intervals included the null. Se and Mn were negatively associated with subsequent teen birth and exhibited particularly wide confidence intervals due to the large number of cases missing biomarker data for those particular exposures. All infants in the study population were female. Of the 371 infant females born in the study area between 1993-1998, 19 (5.12%) cases (female infant subsequently gave birth between 13-19 years of age) were identified.

Female infants who eventually gave birth as teens had a slightly higher birthweight on average than their counterparts. Average gestational age was comparable amongst cases and non-cases of subsequent teen birth, although cases exhibited a slightly higher Hobel pregnancy risk score than non-cases. Mothers of female infants who eventually became pregnant were slightly younger on average than mothers of female infants who did not become pregnant, 23.6 versus 26.6 years old, respectively. Female infants who gave birth as teens had higher proportions of lower maternal (36.8% compared to 15.6%) and paternal (36.8% compared to 22.7%) educational attainment (less than 12th grade), unmarried mothers (57.9% compared to 38.1%), and lower annual household income (63.2% compared to 31.5%). Distributions of maternal ancestry were similar among cases and non-cases; while the majority of both cases and non-cases were of non-Hispanic White maternal race, the proportion with Hispanic maternal race was more than double amongst teen birth cases (15.8% versus 5.7%). Smoking was more prevalent among mothers of non-cases (26.1% compared to 21.1%), and illicit drug use in the year prior to birth was also slightly higher for mothers of non-cases (11.4% compared to 10.5%). A greater proportion of mothers of non-cases ever breastfed the study child (44.0% compared to 31.6%). On average, mothers of female infants who subsequently gave birth as teens had a lower IQ and higher maternal depression score. HOME scores were higher, indicative of higher quality home environment, on average for non-cases of subsequent teen birth.

Exposure Mixture Models and Maps

We created six final mixture models, each of which included a bivariate smooth term with two *measured* chemical exposures:

$$\textbf{log odds of teen birth} = \mathbf{S}(\textbf{exposures}) + \ \textbf{vector}(\textbf{parameters})'\textbf{vector}(\textbf{covariates})$$

Six exposure combinations were tested in the smooth term: (1) HCB and ΣPCB_4, (2) HCB and Pb, (3) HCB and DDE, (4) ΣPCB_4 and Pb, (5) ΣPCB_4 and DDE, and (6) Pb and DDE .Each model was adjusted for maternal depression, maternal age at birth, quality of the home environment, maternal race/ethnicity, whether mother was foreign born, and household income less than $20,000.

Figure 4.1 presents the distribution of females in the NBC across varying levels of exposure combinations, represented as black dots on the color map surface. Values on each axis are restricted from the 5^{th} to the 95^{th} percentile. The majority of participants appear to be distributed generally at middle exposure combinations, but there are data points at higher exposure combinations. For female infants born to younger foreign-born mothers with higher maternal depression, lower quality of home environment and lower household income, higher levels of cord serum HCB and cord serum ΣPCB_4 resulted in elevated risk for subsequent teen birth (Figure 4.1A). The observed pattern remained for combinations of cord serum HCB and cord blood Pb (Figure 4.1B) and cord serum ΣPCB_4 and cord blood Pb (Figure 4.1D). However, higher levels of cord serum HCB and lower levels of cord serum DDE yielded higher risk of teen birth (Figure 4.1C). The apparent protective effect of cord serum DDE persisted when mapped in combination with cord serum ΣPCB_4 (Figure 4.1E) and cord blood (Figure 4.1F). The protective pattern for DDE remains consistent when predicting and mapping adjusted odds ratios at varying levels of cord serum DDE with cord serum ΣPCB_4 (Figure 4.1E) and cord blood Pb (Figure 4.1F). None of the mixture models were statistically significant, likely due to small sample size.

Figure 4.2 presents associations for a mixture of cord serum DDE and cord blood Pb and subsequent teen birth with further adjustment for maternal dietary factors available in NBC. We adjusted for organ meat consumption (Figure 4.2A), seafood consumption (Figure 4.2B), local produce consumption (Figure 4.2C), consumption of grains (Figure 4.2D), vitamin use during pregnancy (Figure 4.2E), and both consumption of local produce and vitamin use (Figure 4.2F). After adjustment for maternal dietary factors, the general pattern of elevated risk at lower levels of cord serum DDE and higher levels of cord blood Pb persisted. Individual adjustment (Figures 4.2C & 4.2E) and co-adjustment (Figure 4.2F) for consumption of local produce and vitamin use during pregnancy shifted the highest risk of subsequent teen birth to levels of cord serum DDE slightly higher than the minimum (i.e. up the y-axis) yet still at the highest levels of cord blood Pb.

Discussion

The purpose of this study was to assess associations between mixtures measured of prenatal environmental exposures and subsequent teen birth among infant females enrolled in the New Bedford Cohort study. Combinations of measured biomarkers (i.e. DDE, HCB, Pb, and ΣPCB_4) resulted in increased risk of subsequent teen birth. Consistent with the analysis of the MADPH cohort, we found risk of subsequent teen birth was greater for female infants with younger mothers, which is documented extensively in previous research (Bonell et al., 2006; Coyne & D’onofrio, 2012; East et al., 2007; Hardy et al., 1998; Pogarsky et al., 2006). Low-level substance use (e.g. tobacco, alcohol, cannabis) prior to or during pregnancy is associated with neurodevelopmental deficits (Huizink and Mulder 2006; Polańska et al. 2015). While illicit substance use in the year prior to birth was associated with higher risk of subsequent teen birth in NBC female infants, any smoking during pregnancy produced a protective effect in the univariate analysis. In both categories, mothers of infants who had a subsequent teen birth indicated lower proportions of substance use. Social desirability bias may contribute to maternal underreporting of substance use prior to or during pregnancy (Garg et al., 2016; Krumpal 2013).

Directional associations between teen births and measured prenatal chemical exposures were generally as expected in the adjusted models, with the exception of cord serum DDE, which appeared to have a protective effect. These results are consistent with the findings in the MADPH cohort of all female births over the study period. Korrick et al. (2000) demonstrated a modest correlation between measured cord serum DDE and maternal diet during pregnancy. Availability of maternal diet information during pregnancy allowed us to assess whether maternal dietary factors may help explain the observed protective effect of DDE observed in both the MADPH and NBC study populations. The neurotoxic effects of DDE may be overpowered by the protective effects of maternal fish consumption during pregnancy (Myers & Davidson 2007; Sagiv et al. 2012). Additionally, maternal diets high in fresh produce consumption may result in increased risk of exposure to pesticides (e.g. DDE) (Winter, 2012); however, healthy prenatal diet, and other healthy lifestyle factors, including vitamin and nutrient supplement use during pregnancy, may affect neurodevelopment and confound the relationship between prenatal DDE exposure and teen birth (Gould et al., 2017; Julvez et al., 2009; Mcgarel, Pentieva, Strain, & Mcnulty, 2015). Our mixture model with DDE and Pb, when adjusted for local produce and vitamin use, suggests confounding by diet and supports a potential link between DDE and healthier diet; however, residual confounding may still exist.

Despite mechanistic support for a role of chemical exposures in risk-taking, there are, to our knowledge, no epidemiologic studies on prenatal chemical exposure mixtures and manifestation of risk-taking behaviors (i.e. teen birth) during adolescence. The initial assessment of *modeled* prenatal exposure mixtures and subsequent teen birth in the MADPH cohort (Chapter 3) and current validation study of mixture patterns with observed biomarkers in a subset of the population (NBC females) adds to this critically understudied area of environmental health. Further, the extension of GAMs employed in our research has several strengths. Our final mixture model allowed for smoothing of log-transformed chemical exposures while concurrently adjusting for additional covariates not available in the larger MADPH cohort. Furthermore, utilization of the MapGAM package in R allowed us to map cross-sections of odds ratios based on varying levels of two exposures in the mixture, while holding the other exposures and covariates constant at their riskiest level for interpretation of results. Finally, permutation tests were used to evaluate the statistical significance of the exposure mixtures.

Despite its strengths, the study has several limitations. Linkage of birth records to hospitalization records for the outcome of teen birth restricts the case count to those females who had a live birth registered through MADPH; thus, it is probable that engagement in risky sexual activity and rates of subsequent intended or unintended teen pregnancy may be underestimated in the NBC. Our analyses were limited by a small overall sample size (N=371) and low teen birth case count (n=19). For both cases and non-cases, missing data was an issue for several covariates and particularly for four of the eight measured exposures (maternal hair Hg, maternal toenail As, maternal toenail Se, and maternal toenail Mn). We were unable to assess exposure combinations that included Hg, As, Se, and Mn. Finally, the generalizability of study results is limited to females born in the NBC. Future research in prospective cohort settings is warranted to ascertain whether the joint exposures examined in this study and others not examined elevate teen birth risk in other geographic settings and time periods.

Conclusion

Our analyses utilized an innovative extension of generalized additive models to assess the relationship between *measured* chemical exposure mixtures and subsequent teen birth. Our results suggest that prenatal chemical exposures may interact with sociodemographic variables to contribute to elevated risk of subsequent teen births in female infants enrolled in the New Bedford Cohort study. Infants born to younger mothers demonstrated elevated risk of subsequent teen birth at minimum levels of cord serum DDE and maximum levels of HCB, Pb, and ΣPCB_4. Although limited by relatively small sample of teen birth cases, this confirmatory analysis demonstrates the advantage of utilizing predictive chemical exposure models, derived from a subset of the population, to assess health outcomes.

Table 4.1. Distributions of log-transformed measured prenatal biomarker exposures and univariate associations between log-transformed exposures and teen birth events among females in the New Bedford Harbor Cohort study, 1993-1998 (N=371).

	Teen Births (n=19)				No Teen Births (n=352)				
	Missing (n)	5th percentile	Median	95th percentile	Missing (n)	5th percentile	Median	95th percentile	OR (95% CI)
Cord Serum ΣPCB_4 (ng/g)	0	-3.32	-1.92	-1.07	16	-2.87	-1.69	-0.29	0.17 (0.03, 0.83)
Cord Serum DDE (ng/g)	0	-2.39	-1.32	-0.72	16	-2.20	-1.19	0.29	0.14 (0.02, 0.79)
Cord Serum HCB (ng/g)	0	-4.93	-3.87	-3.42	16	-4.88	-3.74	-2.90	0.48 (0.12, 1.90)
Cord Blood Pb (µg/dL)	0	-1.33	0.43	1.31	21	-0.78	0.12	1.42	0.92 (0.31, 2.78)
Maternal Hair Hg (µg/g)	7	4.90	5.54	6.50	117	4.84	6.10	7.50	0.13 (0.02, 0.97)
Maternal Toenail As (µg/g)	11	-3.10	-2.72	-2.24	165	-3.60	-2.70	-1.54	0.48 (0.05, 5.14)
Maternal Toenail Se (µg/g)	11	-0.22	-0.03	0.42	165	-0.19	0.03	0.33	1.13 (0.12, 10.8)
Maternal Toenail Mn (µg/g)	11	-1.77	-0.85	0.02	165	-2.60	-1.31	0.09	5.98 (0.50, 49.8)

Note: As, arsenic; CI, confidence interval; DDE, ρ,ρ′-dichlorodiphenyl dichloroethylene; HCB, hexachlorobenzene; Hg, mercury; Mn, manganese; OR, unadjusted odds ratio for change from 5^{th} to 95^{th} percentile; Pb, lead; PCB, polychlorinated biphenyl; ΣPCB_4, sum of four prevalent PCB congeners (118, 138, 153, and 180) in cord serum; Se, selenium.

Table 4.2. Characteristics of 371 New Bedford Cohort mother-female infant pairs (born 1993-1998) by teen birth case status and their univariate odds ratios (OR) and 95% confidence intervals (CI).

Selected Characteristics	Cases n (%)	Non-cases n (%)	OR (95% CI) [a]
Child Characteristics			
Race/ethnicity			
Non-Hispanic White	12 (63.2)	240 (68.2)	referent
Non-Hispanic African American	2 (10.5)	28 (8.0)	1.43 (0.30, 6.71)
Hispanic	4 (21.1)	36 (10.2)	2.22 (0.68, 7.27)
Non-Hispanic Other	1 (5.3)	47 (13.4)	0.43 (0.05, 3.35)
Missing	0 (0)	1 (0.3)	
Ever breastfed study child			
Yes	6 (31.6)	155 (44.0)	0.57 (0.21, 1.59)
No	11 (57.9)	163 (46.3)	referent
Missing	2 (10.5)	34 (9.7)	
Hobel pregnancy risk score (mean (sd))	15.6 (14.3)	14.7 (10.8)	1.27 (0.31, 5.24)
Birthweight, grams (mean (sd))	3459 (510)	3386 (665)	1.22 (0.54, 2.75)
Gestational age, weeks (mean (sd))	40.0 (1.0)	39.8 (1.3)	1.70 (0.34, 8.53)
Missing	0 (0)	2 (0.6)	
Maternal Characteristics			
Age at child's birth, years (mean (sd))	23.6 (4.9)	26.6 (5.4)	0.13 (0.02, 0.75)
Marital status at child’s birth			
Never married/divorced/widowed	11 (57.9)	134 (38.1)	2.67 (0.96, 7.39)
Married	6 (31.6)	195 (55.4)	referent
Missing	2 (10.5)	23 (6.5)	
Education at child’s birth			
Less than 12th grade	7 (36.8)	55 (15.6)	3.47 (1.27, 9.52)
High school graduation or higher	10 (52.6)	273 (77.6)	referent
Missing	2 (10.5)	24 (6.8)	
Smoking during pregnancy			
Yes	4 (21.1)	92 (26.1)	0.96 (0.29, 3.13)
No	10 (52.6)	220 (62.5)	referent
Missing	5 (26.3)	40 (11.4)	
Illicit drug use in year prior to birth			
Yes	2 (10.5)	40 (11.4)	1.26 (0.27, 5.94)
No	10 (52.6)	251 (71.3)	referent
Missing	7 (36.8)	61 (17.3)	
Foreign-born			
Yes	1 (5.3)	55 (15.6)	0.39 (0.05, 3.11)
No	11 (57.9)	238 (67.6)	referent
Missing	7 (36.8)	59 (16.8)	

Table 4.2 Continued. Characteristics of 371 New Bedford Cohort mother-female infant pairs (born 1993-1998) by teen birth case status and their univariate odds ratios and 95% confidence intervals.

Maternal Characteristics (continued)	Cases n (%)	Non-cases n (%)	OR (95% CI) [a]
Race/ethnicity			
Non-Hispanic White	9 (47.4)	257 (73.0)	referent
Non-Hispanic African American	0 (0)	14 (4.0)	
Hispanic	3 (15.8)	20 (5.7)	4.28 (1.07, 17.1)
Non-Hispanic Other	3 (15.8)	27 (7.7)	2.09 (0.54, 8.04)
Missing	4 (21.1)	34 (9.7)	
IQ (mean (sd))	94.4 (8.6)	97.7 (10.4)	0.35 (0.07, 1.83)
Missing	3 (15.8)	59 (16.8)	
Depression (BDI score) (mean (sd))	10.5 (11.5)	7.6 (8.7)	2.31 (0.54, 9.81)
Missing	6 (31.6)	102 (29.0)	
Other Household Characteristics			
Father's education at child's birth			
Less than 12th grade	7 (36.8)	80 (22.7)	2.68 (0.94, 7.62)
High school graduation or higher	8 (42.1)	245 (69.6)	referent
Missing	4 (21.1)	27 (7.7)	
HOME score (mean (sd))	42.6 (5.4)	46.1 (5.0)	0.13 (0.03, 0.64)
Missing	4 (21.1)	83 (23.6)	
Annual household income at child's birth			
<$20,000	12 (63.2)	111 (31.5)	4.69 (1.61, 13.7)
≥$20,000	5 (26.3)	217 (61.6)	referent
Missing	2 (10.5)	24 (6.8)	

Note: OR, odds ratio; CI, confidence interval; BDI, Beck Depression Index; HOME, Home Observation for Measurement of the Environment; sd, standard deviation.
[a] Missing values were excluded from the analyses. OR for Other maternal race includes African American. ORs for continuous variables are for a change from the 5th to 95th percentile. This range is 35 Hobel pregnancy risk score points, 1461 grams birth weight, 4.1 weeks gestational age, 17 years maternal age, 35.4 maternal IQ points, 28 BDI score points, and 17 HOME score points. A higher BDI score indicates more severe depression. A higher HOME score indicates a better home environment.

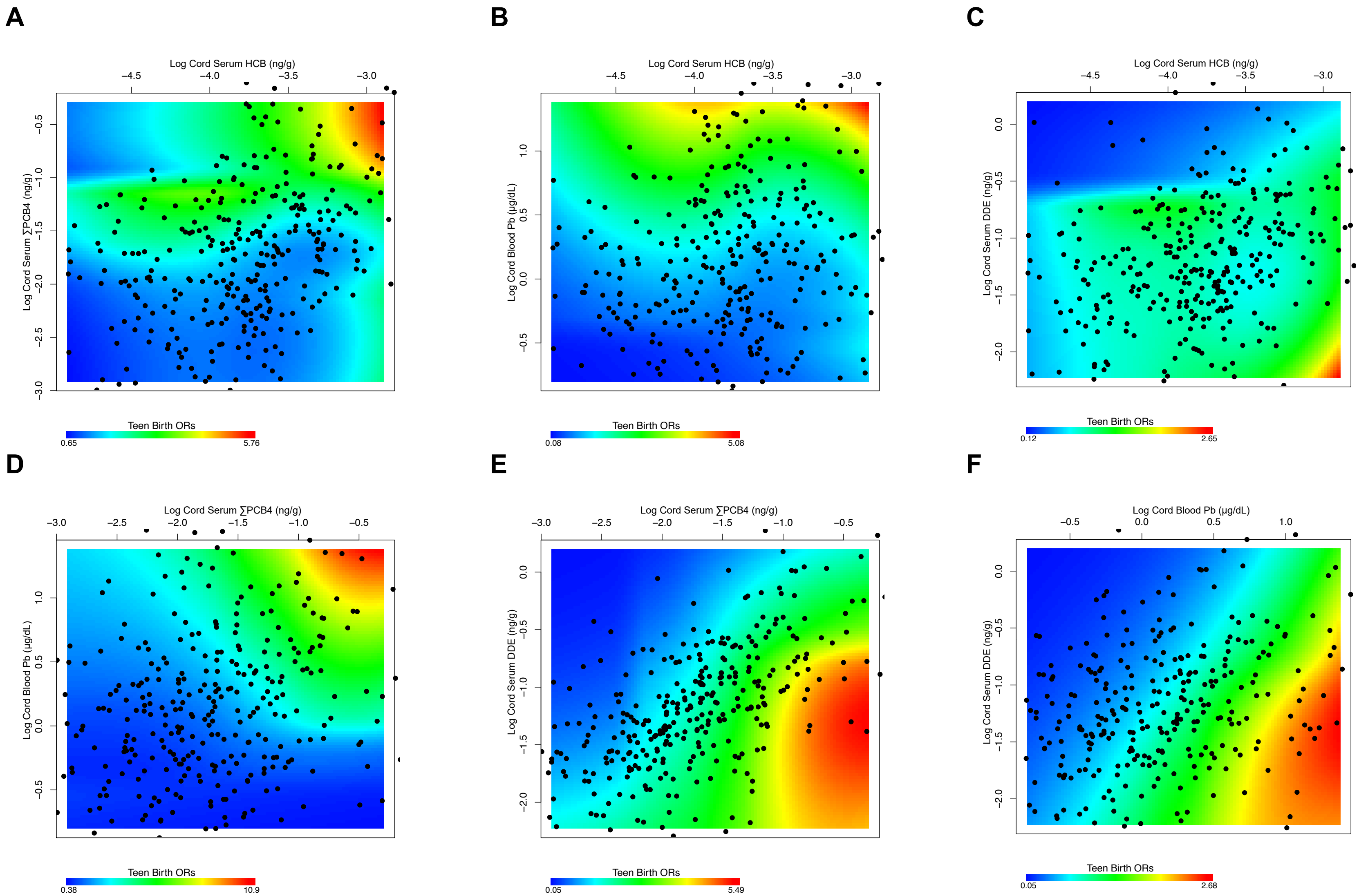

Figure 4.1. Associations between mixtures of measured prenatal biomarker exposures and subsequent teen birth events among females in the New Bedford Harbor Cohort study, 1993-1998 (N=371). Analyses were adjusted for the following characteristics pertaining to the mother of the teen: maternal depression, maternal age at teen's birth, quality of the home environment, maternal race/ethnicity, whether the mother was foreign born, and annual household income at teen's birth.

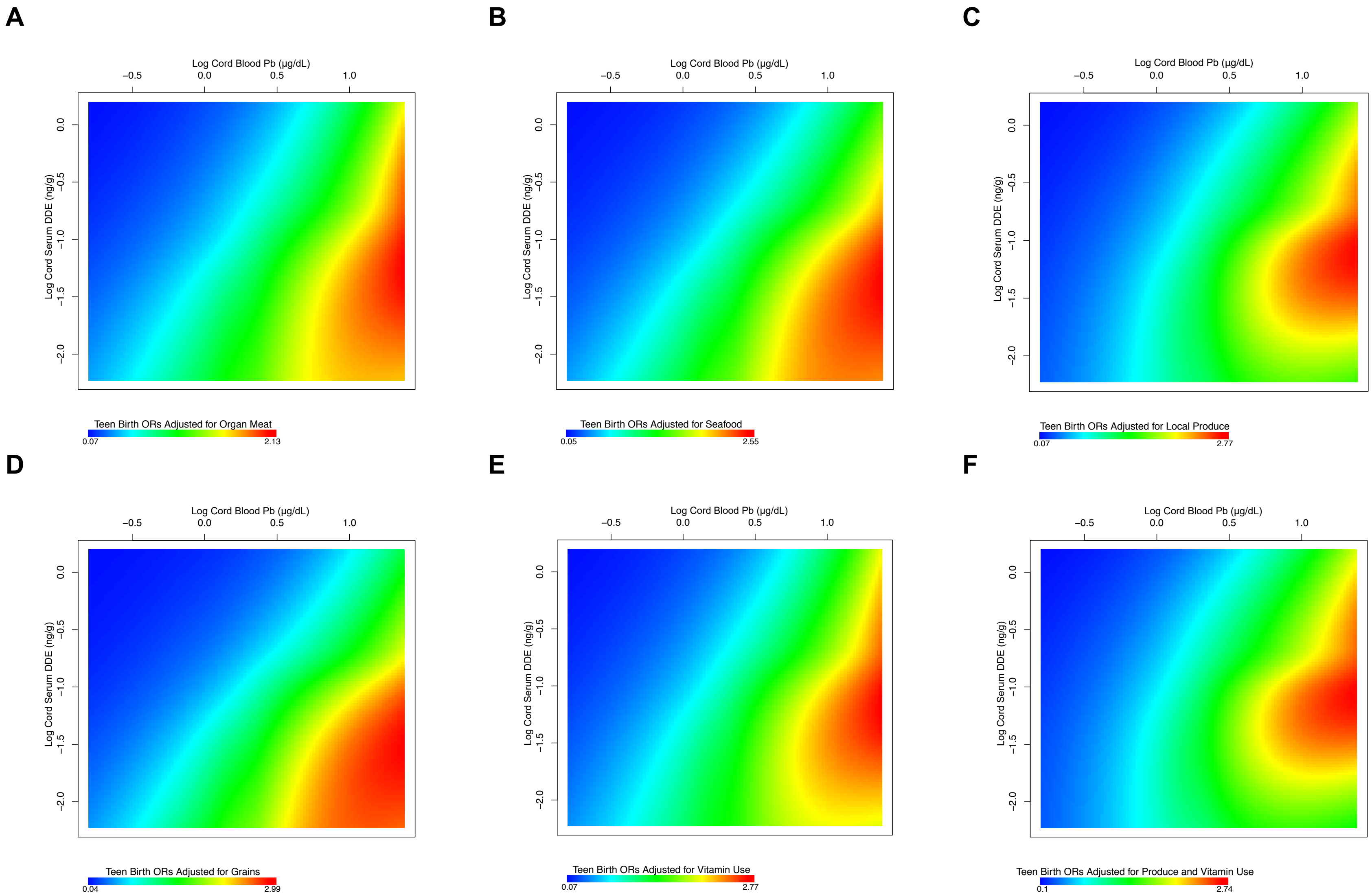

Figure 4.2. Associations between a mixture of measured log cord serum DDE and log cord blood Pb and subsequent teen birth events among females in the New Bedford Harbor Cohort study, 1993-1998 (N=371). Analyses were further adjusted for the following characteristics pertaining to the mother of the teen: maternal depression, maternal age at teen's birth, quality of the home environment, maternal race/ethnicity, whether the mother was foreign born, and annual household income at teen's birth.

CHAPTER 5:

CONCLUSIONS

Mitigating teen birth is a public health priority. While widescale public health prevention efforts have drastically lowered national teen birth rates, disparities in teen births persist at local levels. The aims of this research were three-fold: (1) to conduct a spatial analysis of maternal teen birth status in all births surrounding the New Bedford Harbor (NBH) Superfund site (MA, USA) over two distinct time periods (1992-1998 and 2002-2008); (2) to assess whether joint exposures of modeled prenatal chemical exposures in combination with other sociodemographic maternal and infant factors elevate risk of subsequent teen birth in infant females born between 1992-1998 near NBH (MA Birth Record Cohort); and, (3) to determine whether similar or different combinations of joint exposures affect subsequent teen birth in New Bedford Cohort females, a subset of the MBRC.

The spatial analyses in Chapter 2 indicated a statistically significant hot spot of elevated risk of teen birth west of the NBH only for the later time period (2002-2008) and after adjustment for covariates available in Massachusetts Department of Public Health birth records. Chapter 3 employed predictive exposure models built from measured biomarkers in the NBC to estimate prenatal exposures for cord serum DDE, cord serum HCB, maternal hair Hg, cord blood Pb, and cord serum ΣPCB_4 for all births in four towns surrounding the NBH from 1992-1998. Epidemiologic models were constructed using an innovative extension of generalized additive models (GAMs) to assess the effects of joint chemical exposures on subsequent teen birth risk. All modeled prenatal exposures and two other continuous variables (maternal age at birth and infant year of birth) were included in two loess terms and used to generate a surface of odds ratios for subsequent teen birth across varying levels of two chemical exposures (while holding the other exposures and covariates in the model constant). For infants born earlier in the study period (i.e. 1992) with younger mothers, we found that odds ratios for subsequent teen birth were highest across low levels of DDE and higher levels of the remaining chemical exposures. Chapter 4 utilized GAMs to determine whether similar joint exposures patterns were predictive of increased risk for subsequent teen birth in NBC females. As observed in MBRC females, odds ratios for subsequent teen birth were higher for low levels of DDE and higher levels of HCB, Pb, and ΣPCB_4. The protective effect of DDE remained, although attenuated, after adjustment for maternal dietary factors, including consumption of organ meat, seafood, local produce, and grains and vitamin use during pregnancy.

Although this research has its limitations, it provides an innovative approach to analyzing mixtures of chemical and non-chemical stressors and makes a significant contribution to the literature on the effects of joint chemical exposures on maternal, child, and adolescent health. Further, this research can help identify particularly vulnerable sub-populations and direct teen pregnancy and teen birth prevention efforts to those at greatest risk.

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APPENDIX A: SUPPLEMENTAL MATERIAL FROM CHAPTER 2

Table A.1. Pearson's Correlation Matrix Displayed in List Form for Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 1992-1998.

Pair	Covariate 1	Covariate 2	Pearson's r	p-value
1	Infant Year of Birth	Paternal Education	-0.00009191	9.92E-01
2	Infant Year of Birth	Marital Status	-0.01897180	3.63E-02
3	Paternal Education	Marital Status	-0.23941630	0.00E+00
4	Infant Year of Birth	Alcohol During Pregnancy	-0.01271666	1.61E-01
5	Paternal Education	Alcohol During Pregnancy	0.02135045	1.87E-02
6	Marital Status	Alcohol During Pregnancy	-0.02956744	1.13E-03
7	Infant Year of Birth	Smoking During Pregnancy	-0.04320063	1.91E-06
8	Paternal Education	Smoking During Pregnancy	0.12113210	0.00E+00
9	Marital Status	Smoking During Pregnancy	-0.24858070	0.00E+00
10	Alcohol During Pregnancy	Smoking During Pregnancy	0.11156350	0.00E+00
11	Infant Year of Birth	Maternal Education	-0.02264822	1.26E-02
12	Paternal Education	Maternal Education	0.42398700	0.00E+00
13	Marital Status	Maternal Education	-0.31555100	0.00E+00
14	Alcohol During Pregnancy	Maternal Education	0.01671076	6.60E-02
15	Smoking During Pregnancy	Maternal Education	0.18578420	0.00E+00
16	Infant Year of Birth	Household Income	-0.02808721	1.94E-03
17	Paternal Education	Household Income	0.21155920	0.00E+00
18	Marital Status	Household Income	-0.23111030	0.00E+00
19	Alcohol During Pregnancy	Household Income	-0.00056982	9.50E-01
20	Smoking During Pregnancy	Household Income	0.09031894	0.00E+00
21	Maternal Education	Household Income	0.25195270	0.00E+00
22	Infant Year of Birth	Parity	-0.02630212	3.78E-03
23	Paternal Education	Parity	0.05767160	2.09E-10
24	Marital Status	Parity	0.10612880	0.00E+00
25	Alcohol During Pregnancy	Parity	0.04851053	9.42E-08
26	Smoking During Pregnancy	Parity	0.12029650	0.00E+00
27	Maternal Education	Parity	0.08222658	0.00E+00
28	Household Income	Parity	0.07457817	2.22E-16
29	Infant Year of Birth	Maternal Race	-0.00787568	3.85E-01
30	Paternal Education	Maternal Race	0.14045060	0.00E+00
31	Marital Status	Maternal Race	-0.27385980	0.00E+00
32	Alcohol During Pregnancy	Maternal Race	0.00157416	8.62E-01
33	Smoking During Pregnancy	Maternal Race	-0.00476688	5.99E-01
34	Maternal Education	Maternal Race	0.19527350	0.00E+00

Table A.1 Continued. Pearson's Correlation Matrix Displayed in List Form for Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 1992-1998.

Pair	Covariate 1	Covariate 2	Pearson's r	p-value
35	Household Income	Maternal Race	0.26403840	0.00E+00
36	Parity	Maternal Race	0.09129407	0.00E+00
37	Infant Year of Birth	Maternal Ancestry	-0.04891443	6.93E-08
38	Paternal Education	Maternal Ancestry	0.10017900	0.00E+00
39	Marital Status	Maternal Ancestry	-0.06733771	1.10E-13
40	Alcohol During Pregnancy	Maternal Ancestry	0.00220730	8.08E-01
41	Smoking During Pregnancy	Maternal Ancestry	-0.02403368	8.09E-03
42	Maternal Education	Maternal Ancestry	0.09723805	0.00E+00
43	Household Income	Maternal Ancestry	0.08476078	0.00E+00
44	Parity	Maternal Ancestry	-0.02775424	2.25E-03
45	Maternal Race	Maternal Ancestry	0.28667390	0.00E+00
46	Infant Year of Birth	Adequacy of Prenatal Care	0.00264417	7.72E-01
47	Paternal Education	Adequacy of Prenatal Care	-0.15947740	0.00E+00
48	Marital Status	Adequacy of Prenatal Care	0.21948690	0.00E+00
49	Alcohol During Pregnancy	Adequacy of Prenatal Care	-0.02656960	3.59E-03
50	Smoking During Pregnancy	Adequacy of Prenatal Care	-0.10840760	0.00E+00
51	Maternal Education	Adequacy of Prenatal Care	-0.19593400	0.00E+00
52	Household Income	Adequacy of Prenatal Care	-0.13218640	0.00E+00
53	Parity	Adequacy of Prenatal Care	-0.10544480	0.00E+00
54	Maternal Race	Adequacy of Prenatal Care	-0.17201720	0.00E+00
55	Maternal Ancestry	Adequacy of Prenatal Care	-0.03595193	8.00E-05
56	Infant Year of Birth	Prenatal Care Payment Source	-0.01160802	2.01E-01
57	Paternal Education	Prenatal Care Payment Source	-0.29200030	0.00E+00
58	Marital Status	Prenatal Care Payment Source	0.53544440	0.00E+00
59	Alcohol During Pregnancy	Prenatal Care Payment Source	-0.01536947	9.11E-02
60	Smoking During Pregnancy	Prenatal Care Payment Source	-0.23638770	0.00E+00
61	Maternal Education	Prenatal Care Payment Source	-0.35157260	0.00E+00
62	Household Income	Prenatal Care Payment Source	-0.29284320	0.00E+00
63	Parity	Prenatal Care Payment Source	-0.07901061	0.00E+00
64	Maternal Race	Prenatal Care Payment Source	-0.29886150	0.00E+00
65	Maternal Ancestry	Prenatal Care Payment Source	-0.03190937	4.46E-04
66	Adequacy of Prenatal Care	Prenatal Care Payment Source	0.23244860	0.00E+00

Table A.2. Pearson's Correlation Matrix Displayed in List Form for Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 2002-2008.

Pair	Covariate 1	Covariate 2	Pearson's r	p-value
1	Infant Year of Birth	Paternal Education	-0.0268109	2.88E-03
2	Infant Year of Birth	Marital Status	-0.0545211	1.19E-09
3	Paternal Education	Marital Status	-0.2594298	0.00E+00
4	Infant Year of Birth	Alcohol During Pregnancy	-0.0040514	6.52E-01
5	Paternal Education	Alcohol During Pregnancy	-0.0213008	1.79E-02
6	Marital Status	Alcohol During Pregnancy	0.01170273	1.92E-01
7	Infant Year of Birth	Smoking During Pregnancy	-0.0362389	5.38E-05
8	Paternal Education	Smoking During Pregnancy	0.07489688	0.00E+00
9	Marital Status	Smoking During Pregnancy	-0.2440804	0.00E+00
10	Alcohol During Pregnancy	Smoking During Pregnancy	0.07282101	4.44E-16
11	Infant Year of Birth	Maternal Education	-0.0505934	1.73E-08
12	Paternal Education	Maternal Education	0.3698651	0.00E+00
13	Marital Status	Maternal Education	-0.280945	0.00E+00
14	Alcohol During Pregnancy	Maternal Education	-0.0062346	4.88E-01
15	Smoking During Pregnancy	Maternal Education	0.10358921	0.00E+00
16	Infant Year of Birth	Household Income	0.21713763	0.00E+00
17	Paternal Education	Household Income	0.14588171	0.00E+00
18	Marital Status	Household Income	-0.1840239	0.00E+00
19	Alcohol During Pregnancy	Household Income	-0.0104014	2.50E-01
20	Smoking During Pregnancy	Household Income	0.01583312	8.00E-02
21	Maternal Education	Household Income	0.16343351	0.00E+00
22	Infant Year of Birth	Parity	-0.0138291	1.24E-01
23	Paternal Education	Parity	0.04906572	5.17E-08
24	Marital Status	Parity	0.09881337	0.00E+00
25	Alcohol During Pregnancy	Parity	0.02382075	8.08E-03
26	Smoking During Pregnancy	Parity	0.02936212	1.09E-03
27	Maternal Education	Parity	0.06476305	5.82E-13
28	Household Income	Parity	0.06415308	1.35E-12
29	Infant Year of Birth	Maternal Race	0.02634763	3.33E-03
30	Paternal Education	Maternal Race	0.19252029	0.00E+00
31	Marital Status	Maternal Race	-0.2179464	0.00E+00
32	Alcohol During Pregnancy	Maternal Race	-0.0222657	1.31E-02
33	Smoking During Pregnancy	Maternal Race	-0.1008402	0.00E+00
34	Maternal Education	Maternal Race	0.24853967	0.00E+00
35	Household Income	Maternal Race	0.23779708	0.00E+00
36	Parity	Maternal Race	0.08028741	0.00E+00

Table A.2 Continued. Pearson's Correlation Matrix Displayed in List Form for Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 2002-2008.

Pair	Covariate 1	Covariate 2	Pearson's r	p-value
37	Infant Year of Birth	Maternal Ancestry	0.00728274	4.17E-01
38	Paternal Education	Maternal Ancestry	0.00671023	4.56E-01
39	Marital Status	Maternal Ancestry	-0.0136716	1.28E-01
40	Alcohol During Pregnancy	Maternal Ancestry	0.008409	3.49E-01
41	Smoking During Pregnancy	Maternal Ancestry	0.00763734	3.95E-01
42	Maternal Education	Maternal Ancestry	0.00574157	5.23E-01
43	Household Income	Maternal Ancestry	0.00570021	5.29E-01
44	Parity	Maternal Ancestry	-0.0235474	8.84E-03
45	Maternal Race	Maternal Ancestry	0.17881246	0.00E+00
46	Infant Year of Birth	Adequacy of Prenatal Care	-0.082044	0.00E+00
47	Paternal Education	Adequacy of Prenatal Care	-0.1259579	0.00E+00
48	Marital Status	Adequacy of Prenatal Care	0.18670096	0.00E+00
49	Alcohol During Pregnancy	Adequacy of Prenatal Care	-0.0357982	7.39E-05
50	Smoking During Pregnancy	Adequacy of Prenatal Care	-0.0566268	3.54E-10
51	Maternal Education	Adequacy of Prenatal Care	-0.1857531	0.00E+00
52	Household Income	Adequacy of Prenatal Care	-0.1090106	0.00E+00
53	Parity	Adequacy of Prenatal Care	-0.0880216	0.00E+00
54	Maternal Race	Adequacy of Prenatal Care	-0.1842548	0.00E+00
55	Maternal Ancestry	Adequacy of Prenatal Care	0.0161569	7.37E-02
56	Infant Year of Birth	Prenatal Care Payment Source	0.00531274	5.55E-01
57	Paternal Education	Prenatal Care Payment Source	-0.2937094	0.00E+00
58	Marital Status	Prenatal Care Payment Source	0.50637304	0.00E+00
59	Alcohol During Pregnancy	Prenatal Care Payment Source	0.00260955	7.72E-01
60	Smoking During Pregnancy	Prenatal Care Payment Source	-0.1846132	0.00E+00
61	Maternal Education	Prenatal Care Payment Source	-0.3401547	0.00E+00
62	Household Income	Prenatal Care Payment Source	-0.2049873	0.00E+00
63	Parity	Prenatal Care Payment Source	-0.1108911	0.00E+00
64	Maternal Race	Prenatal Care Payment Source	-0.2833238	0.00E+00
65	Maternal Ancestry	Prenatal Care Payment Source	0.02486385	5.75E-03
66	Adequacy of Prenatal Care	Prenatal Care Payment Source	0.21074617	0.00E+00

A **B**

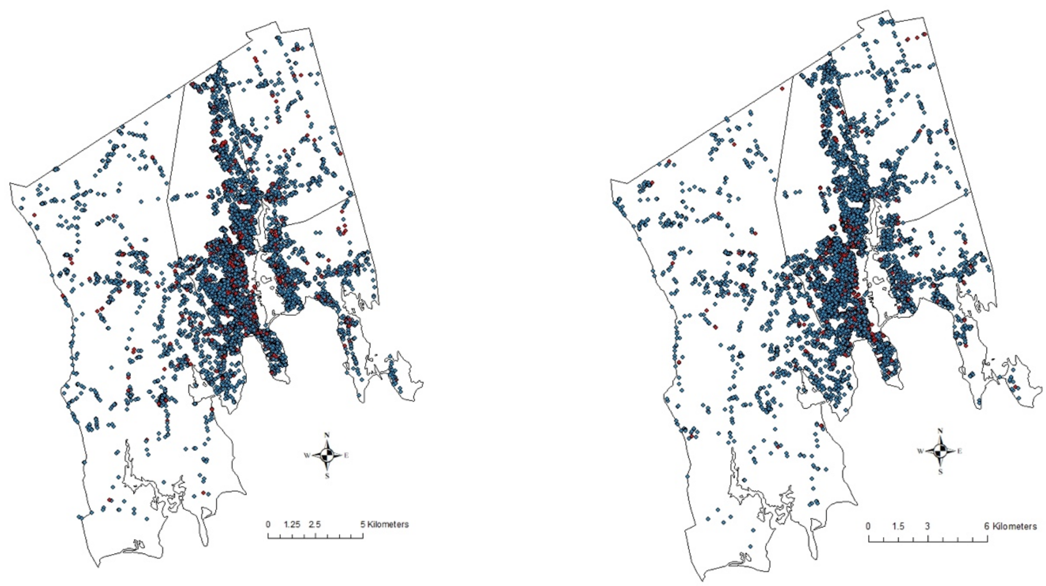


Figure A.1. Spatial Distribution of Teen Births in the four study towns for 1992-1998 and 2002-2008. Red dots represent a case of teen birth; blue dots represent infants with non-teen mothers. (A) Spatial distribution of cases, 1992-1998. (B) Spatial distribution of cases, 2002-2008. Geographic distribution of cases and non-cases was similar across the two study periods.

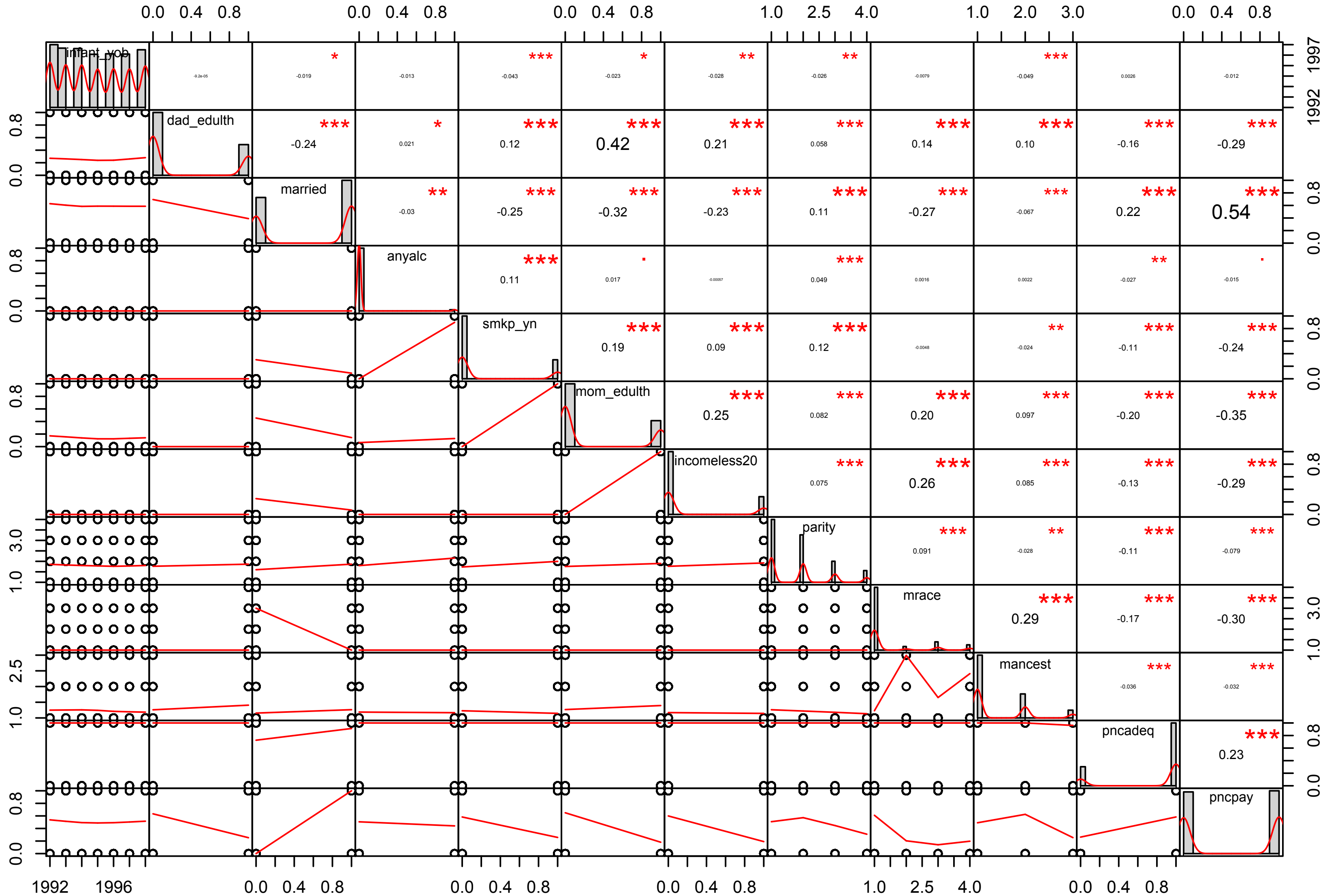


Figure A.2. Correlation Chart for Selected Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 1992-1998.

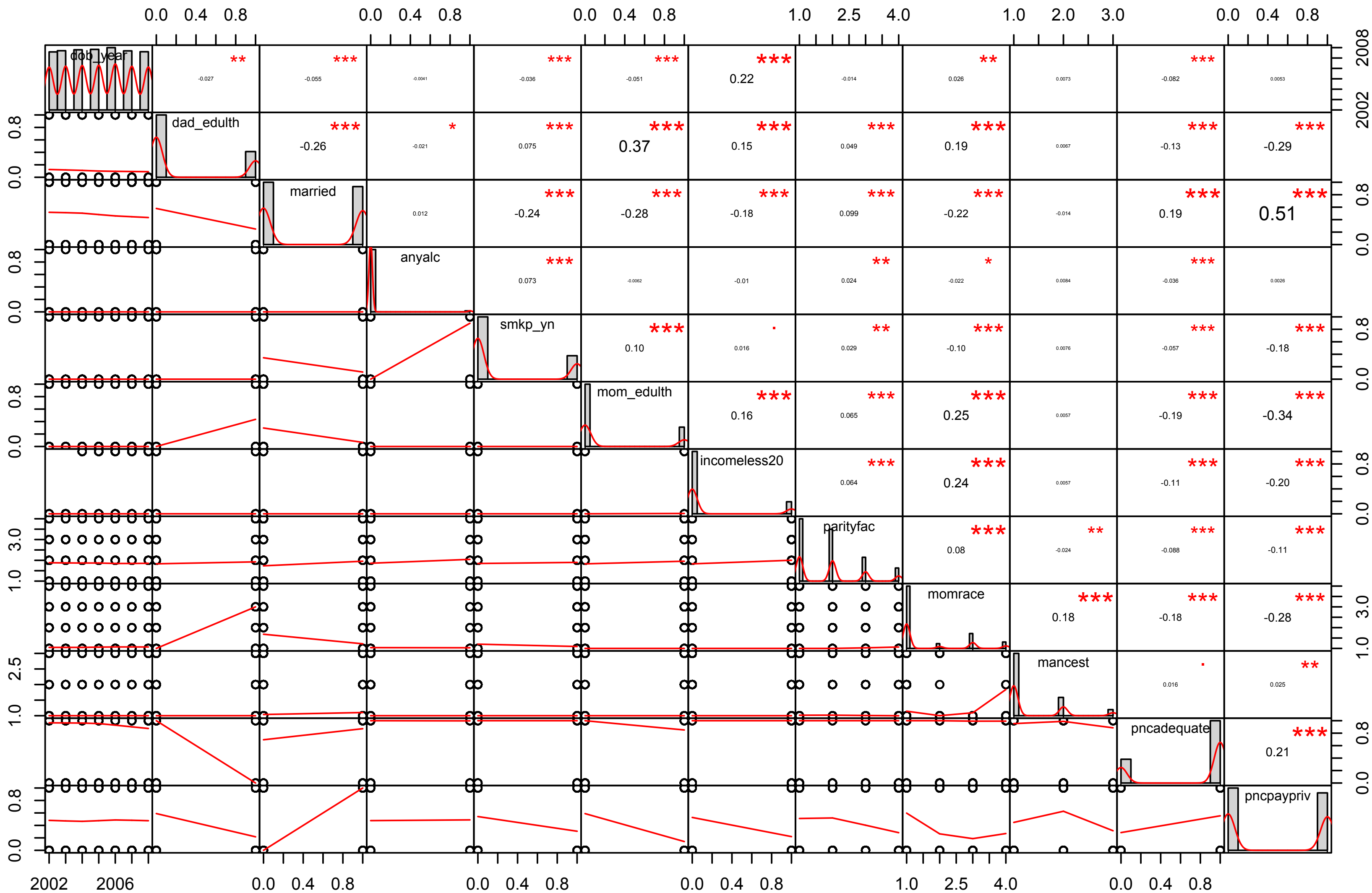


Figure A.3. Correlation Chart for Selected Covariates in the New Bedford Harbor Teen Birth Spatial Analysis, 2002-2008.

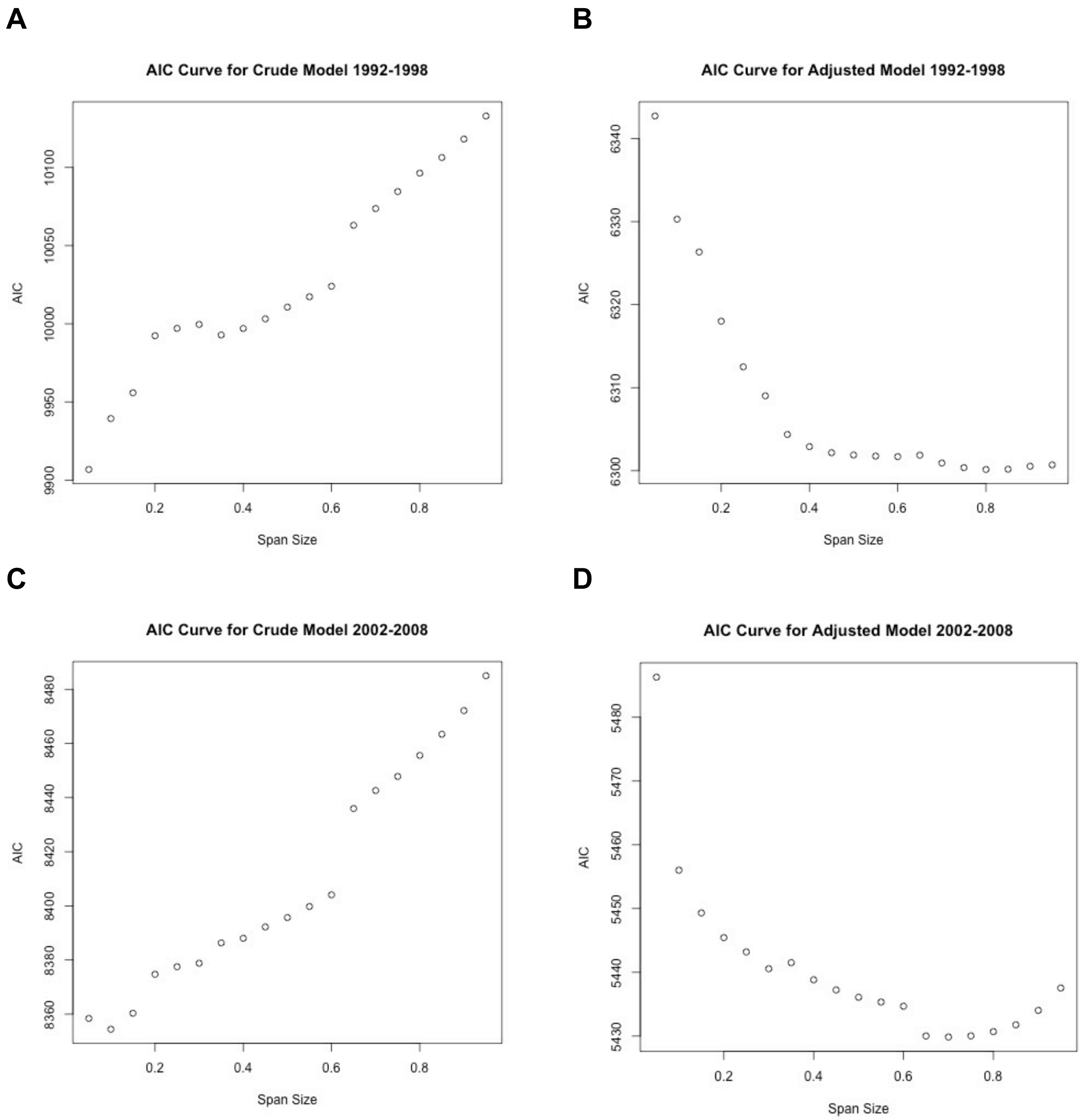


Figure A.4. Akaike Information Criteria (AIC) curves for the crude and adjusted models for both study periods. AIC curves were assessed to determine the optimal span, which minimizes the AIC. (A) Crude curve 1992-1998, optimal span at 0.05, fit at span of 0.20 for greater stability and to minimize edge effects. (B) Adjusted curve 1992-1998, optimal span at 0.80. (C) Crude curve 2002-2008, optimal span at 0.10, fit at span of 0.20 for greater stability and to minimize edge effects. (D) Adjusted curve 2002-2008, optimal span at 0.70.

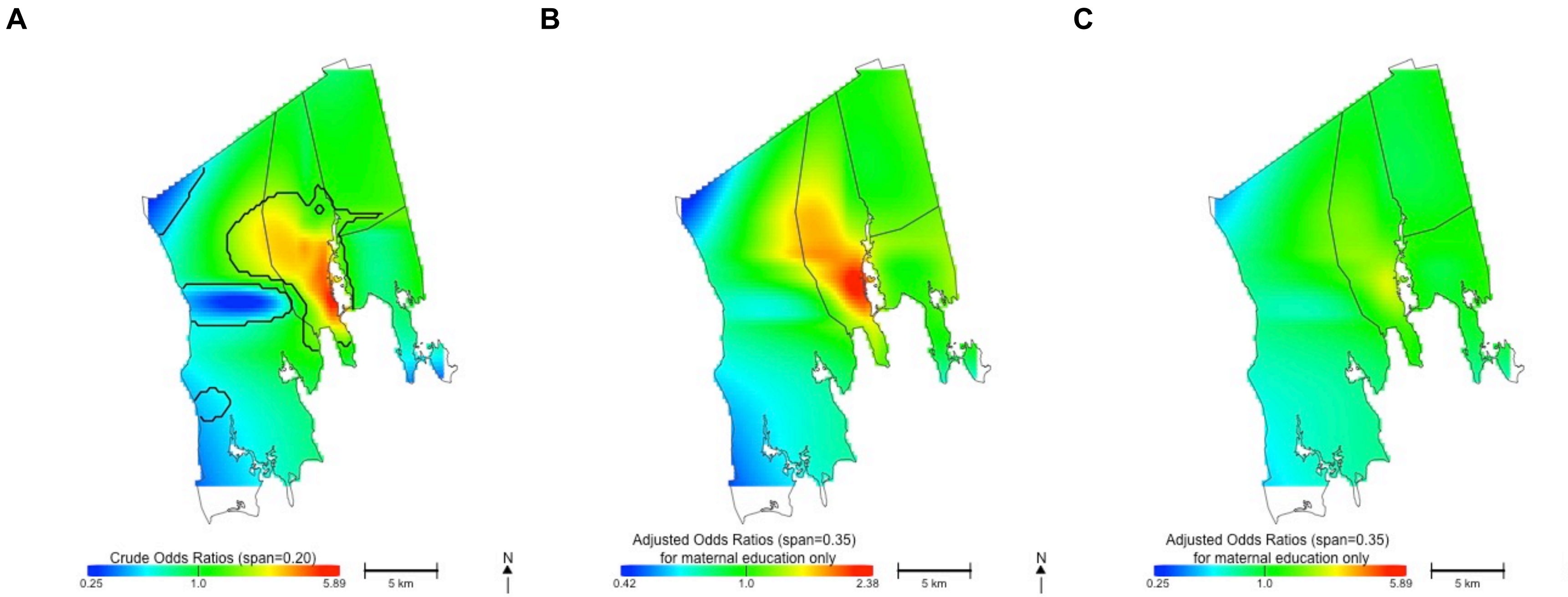


Figure A.5. Univariate adjustment for maternal education, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for maternal education only.

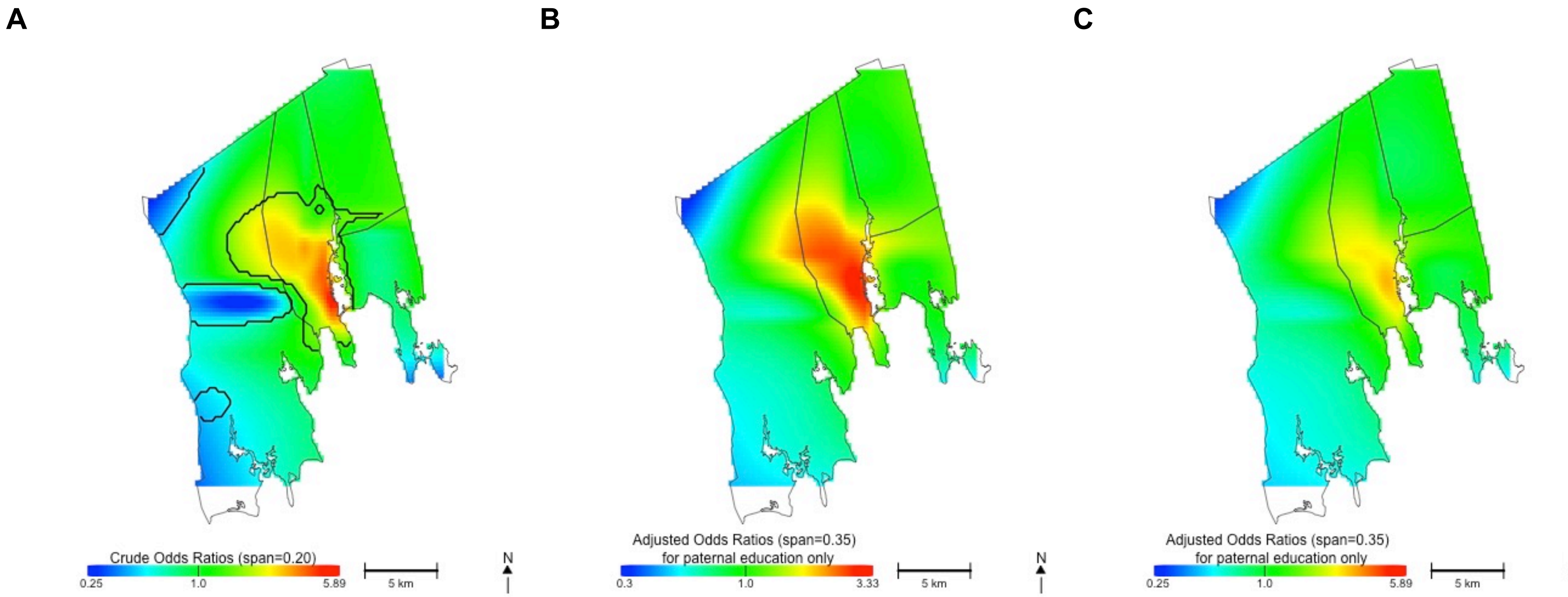


Figure A.6. Univariate adjustment for paternal education, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global $p<0.001$). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for paternal education only.

A **B** **C**

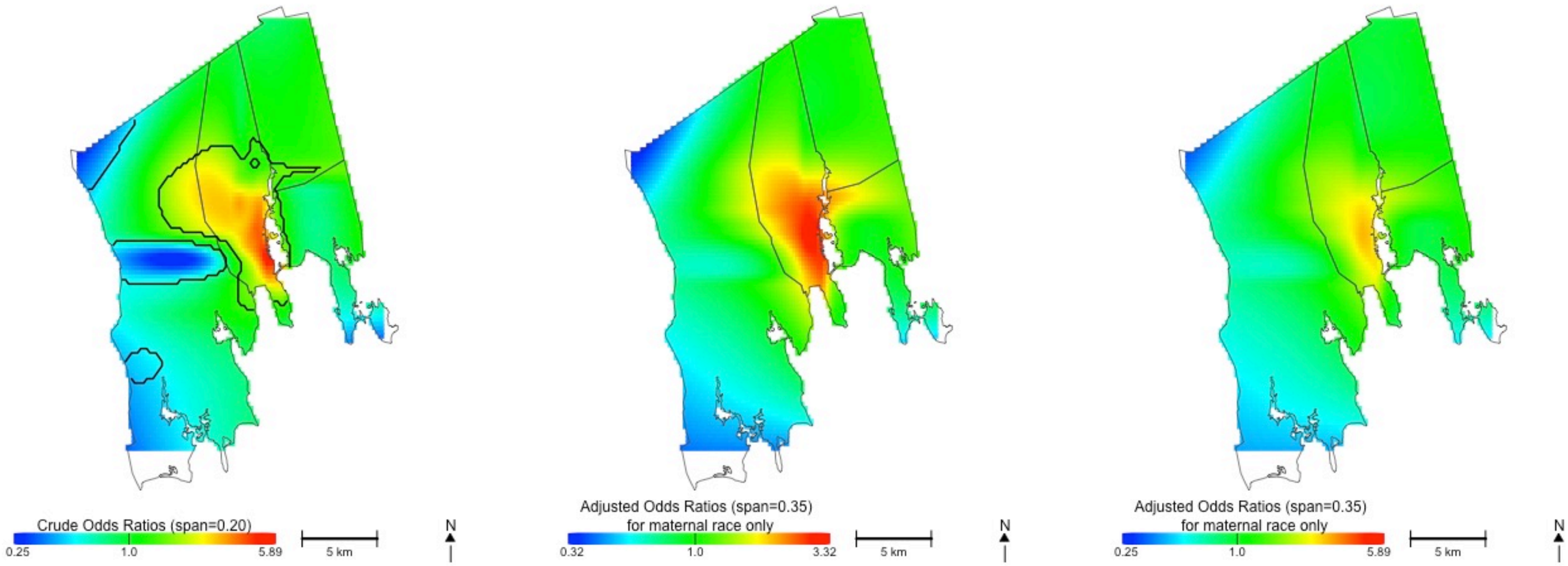


Figure A.7. Univariate adjustment for maternal race, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for maternal race only.

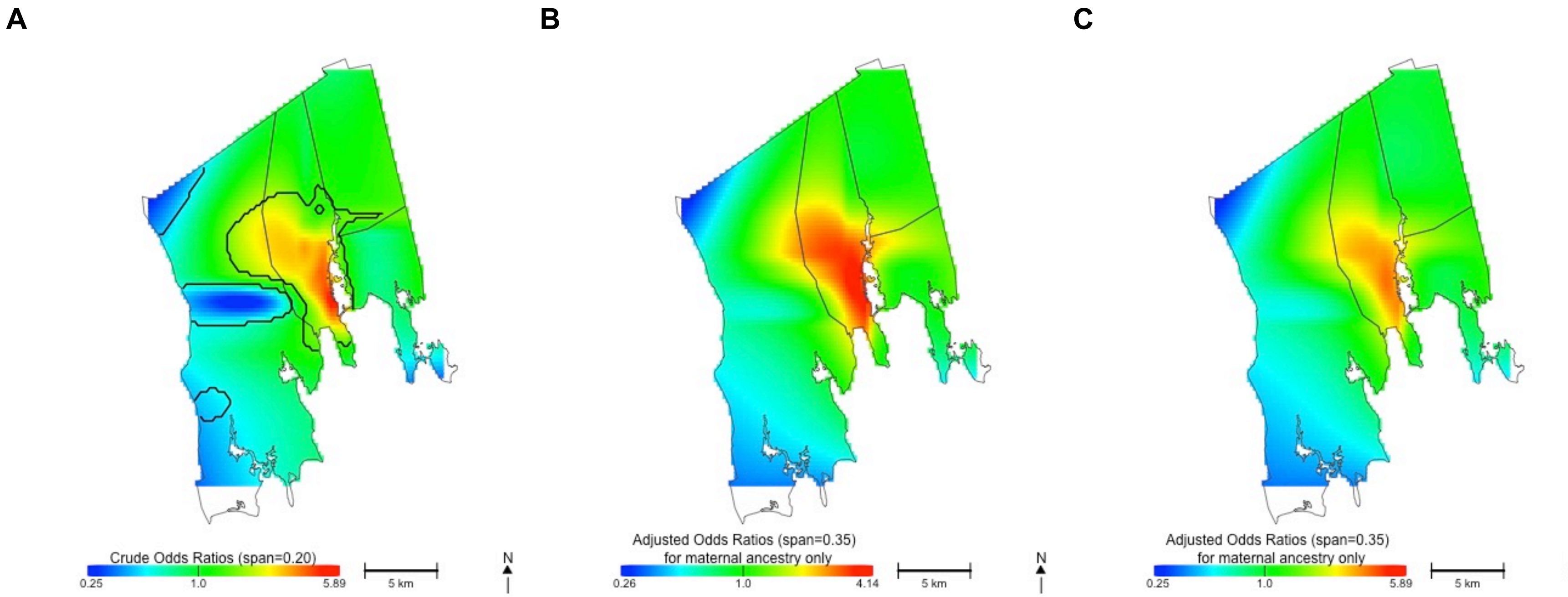


Figure A.8. Univariate adjustment for maternal ancestry, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for maternal ancestry only.

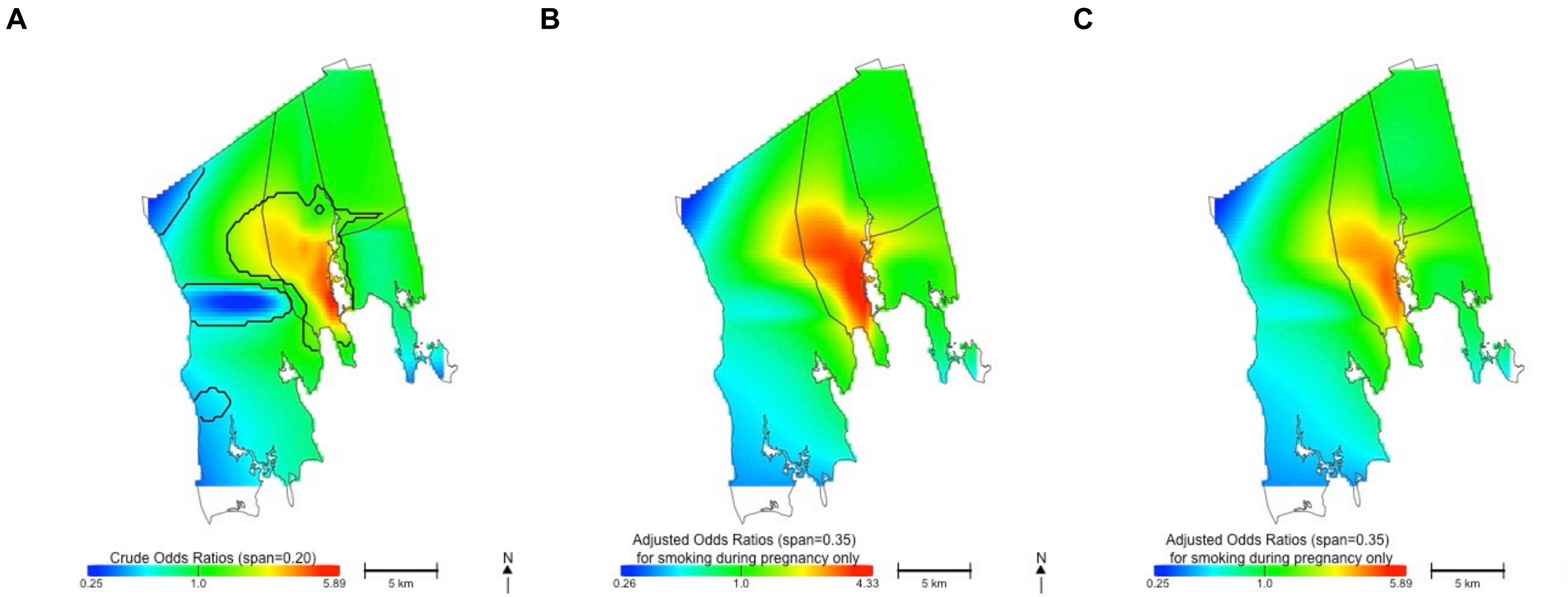


Figure A.9. Univariate adjustment for any smoking during pregnancy, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for any smoking during pregnancy only.

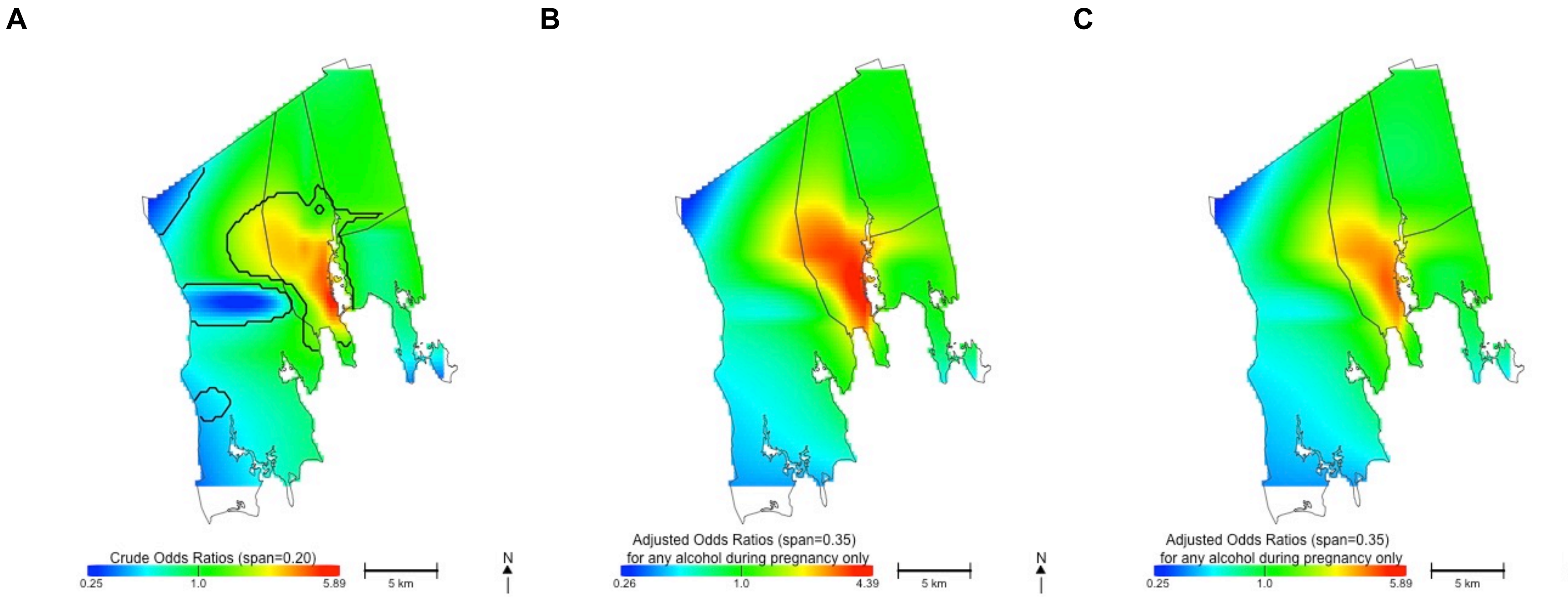


Figure A.10. Univariate adjustment for any alcohol consumption during pregnancy, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global $p<0.001$). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for any alcohol consumption during pregnancy.

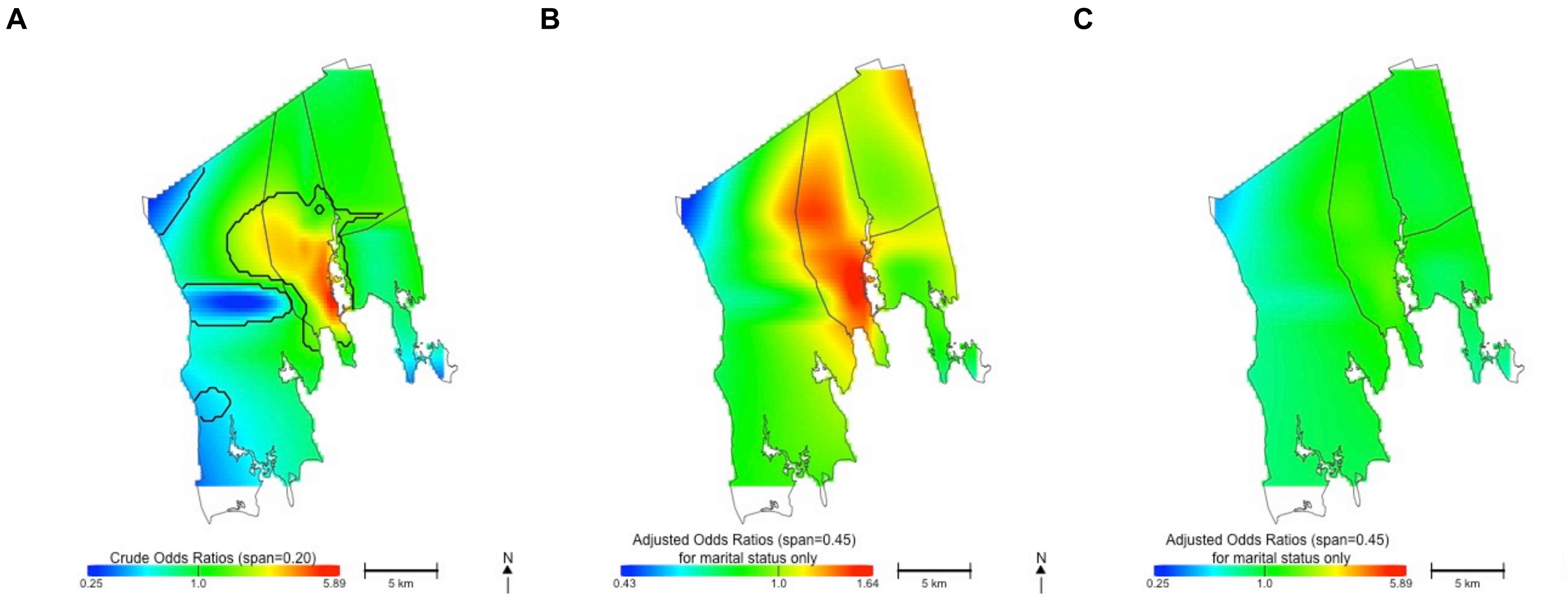


Figure A.11. Univariate adjustment for marital status, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.45. (C) Adjusted, span of 0.45, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for marital status when mapped on the adjusted scale.

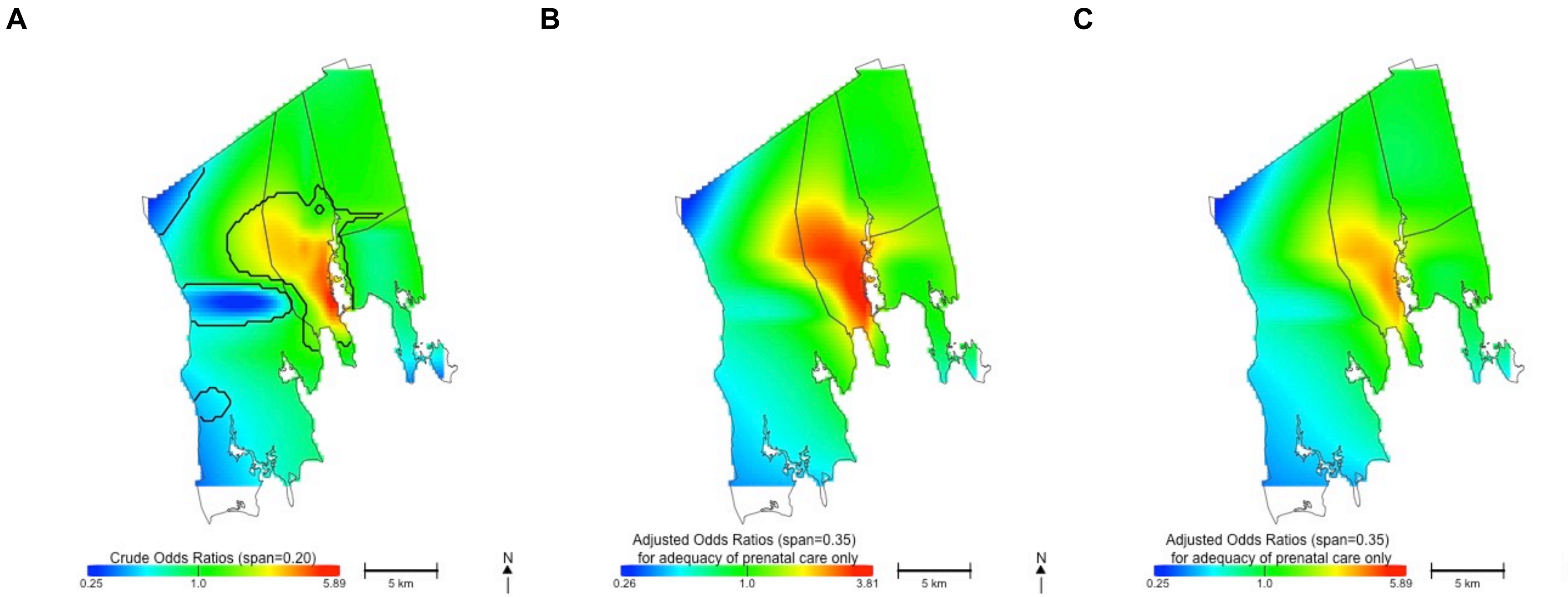


Figure A.12. Univariate adjustment for adequacy of prenatal care, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for adequacy of prenatal care when mapped on both the crude and the adjusted scales.

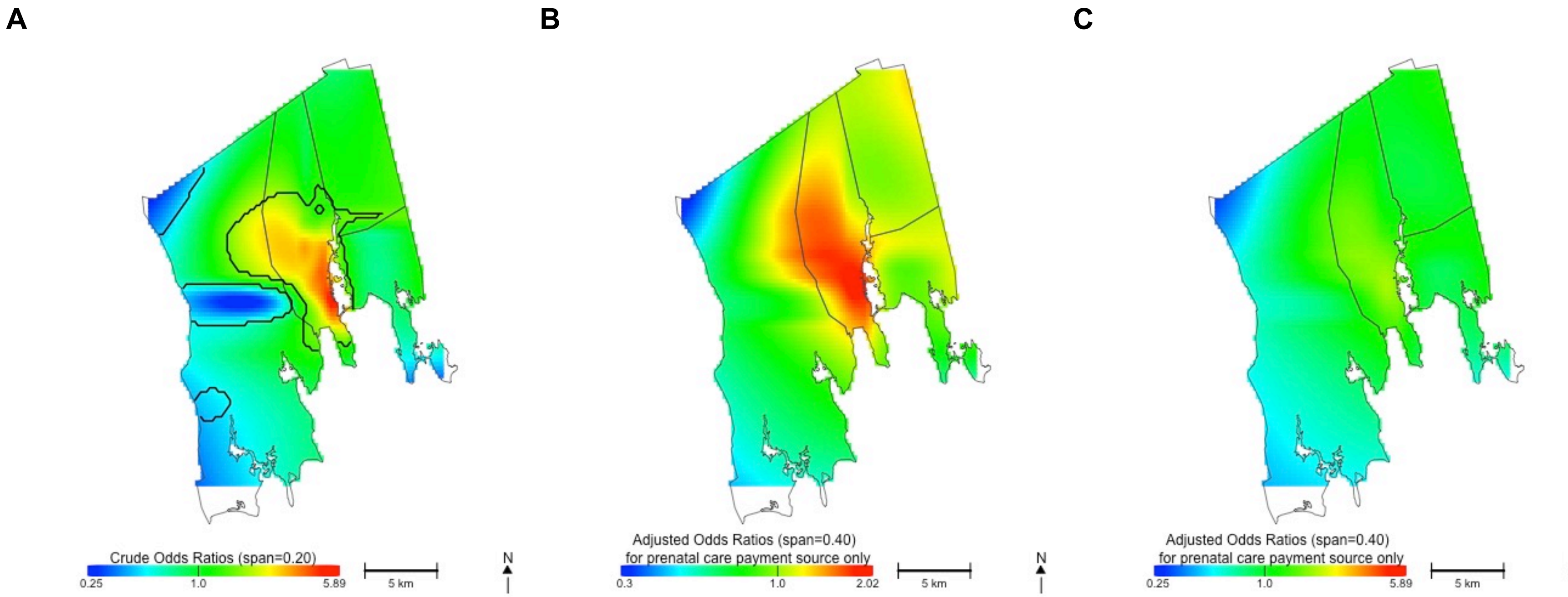


Figure A.13. Univariate adjustment for prenatal care source of payment, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.40. (C) Adjusted, span of 0.40, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for prenatal care source of payment when mapped on the adjusted scale.

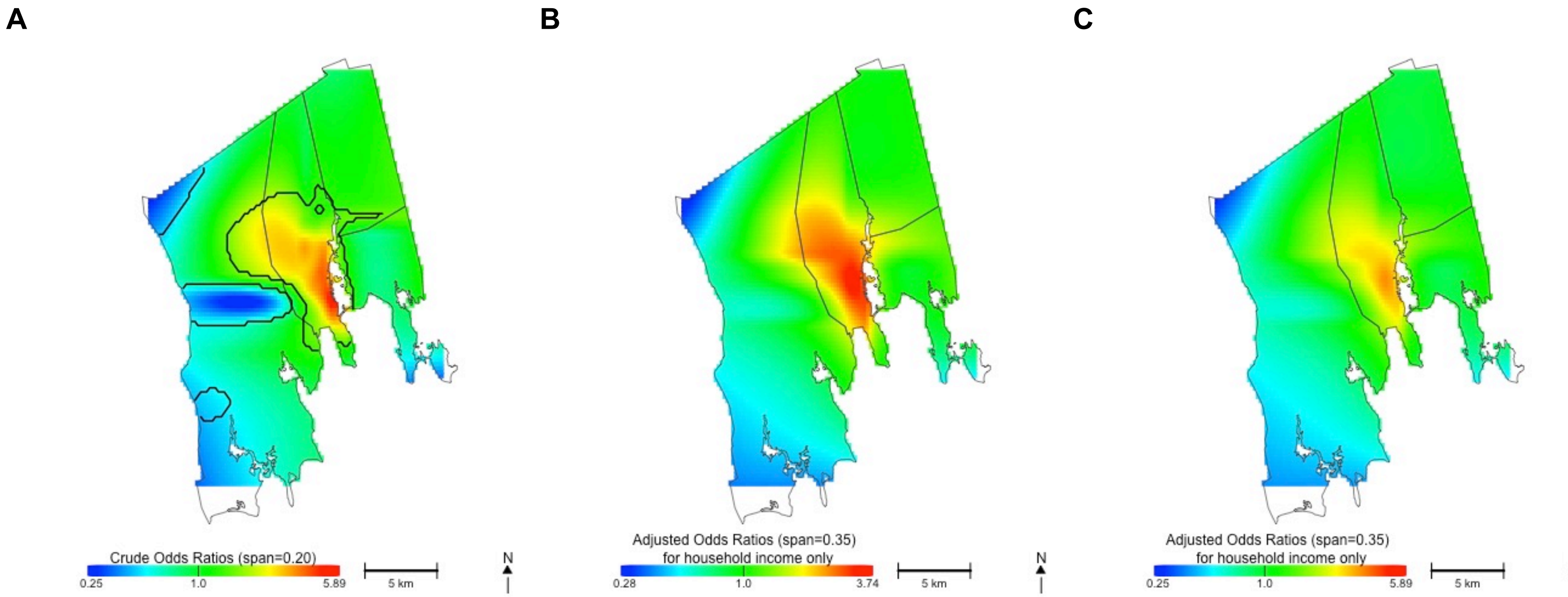


Figure A.14. Univariate adjustment for household income, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for block group median household income on both the crude and adjusted scales.

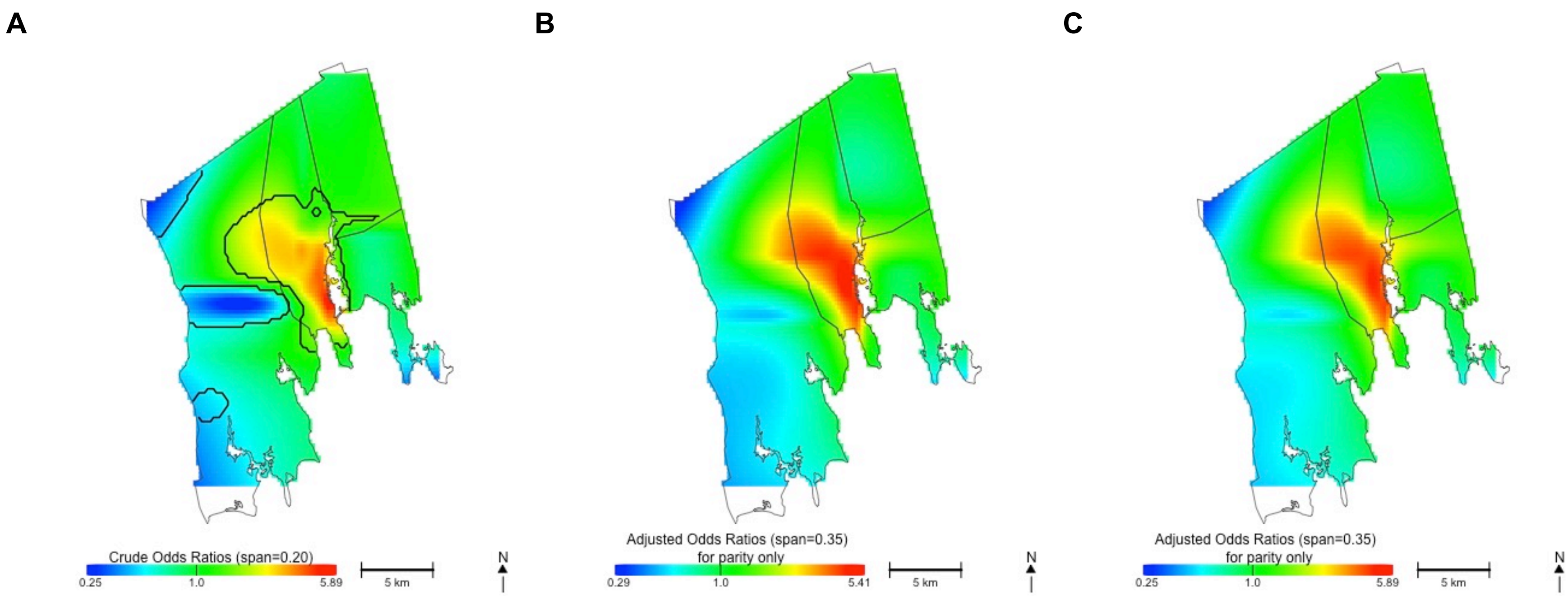


Figure A.15. Univariate adjustment for parity, 1992-1998. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. A non-significant area of increased ORs remains after adjustment for parity on both the crude and adjusted scales.

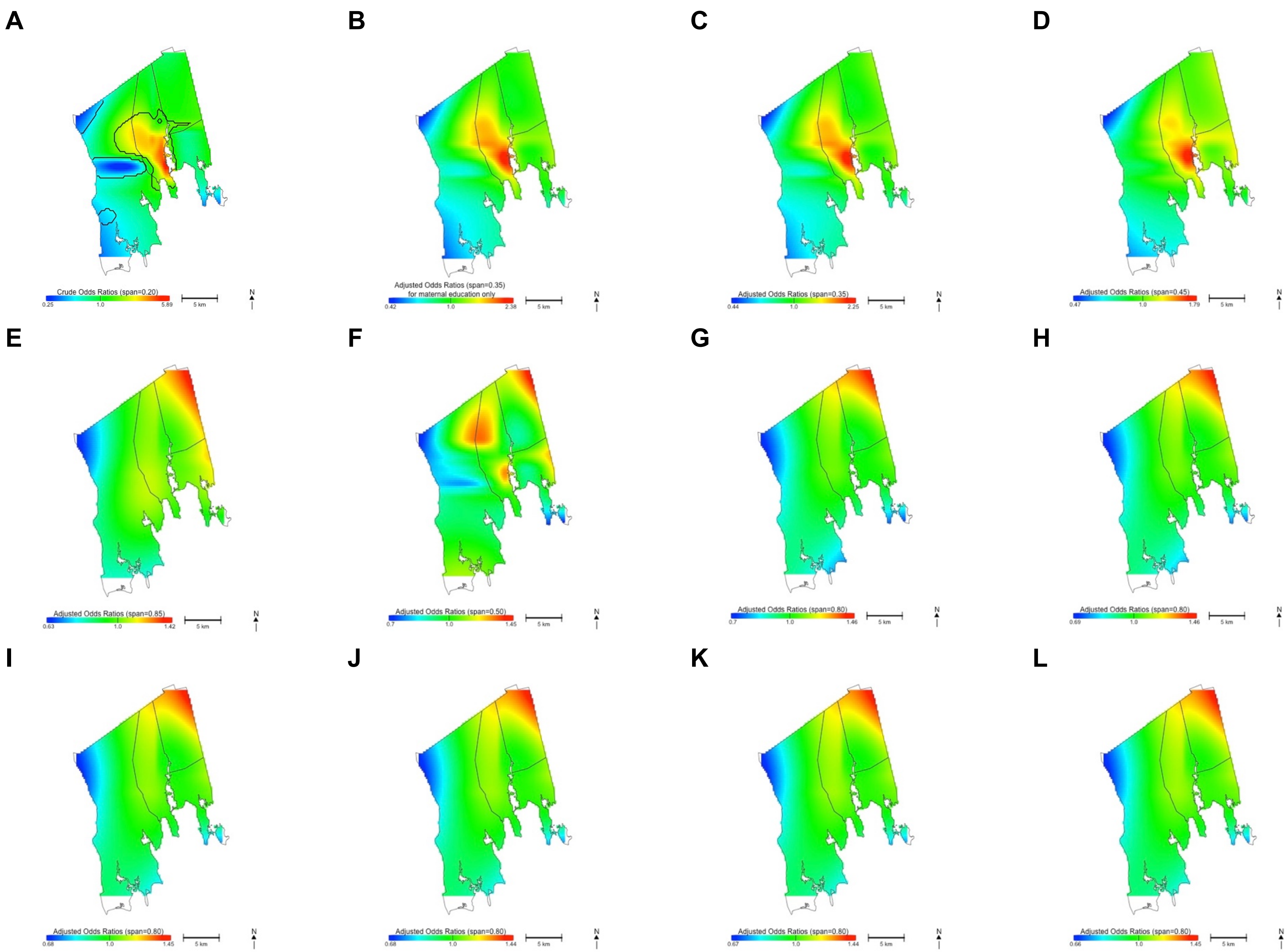


Figure A.16. Stepwise covariate adjustment, 1992-1998. Odds ratios (ORs) are relative to the surface area. (A)

Crude, span of 0.35. (B) Adjusted, for maternal education only. (C) Adjusted, paternal education added. (D) Adjusted, maternal race added. (E) Adjusted, marital status added. (F) Adjusted, parity added. (G) Adjusted, prenatal care payment source added. (H) Adjusted, alcohol consumption during pregnancy added. (I) Adjusted, adequacy of prenatal care added. (J) Adjusted, household income added. (K) Adjusted, maternal ancestry added. (L) Fully adjusted, smoking during pregnancy added. The statistically significant area of increased ORs observed in the crude model is no longer apparent after adjustment for selected covariates (p=0.469).

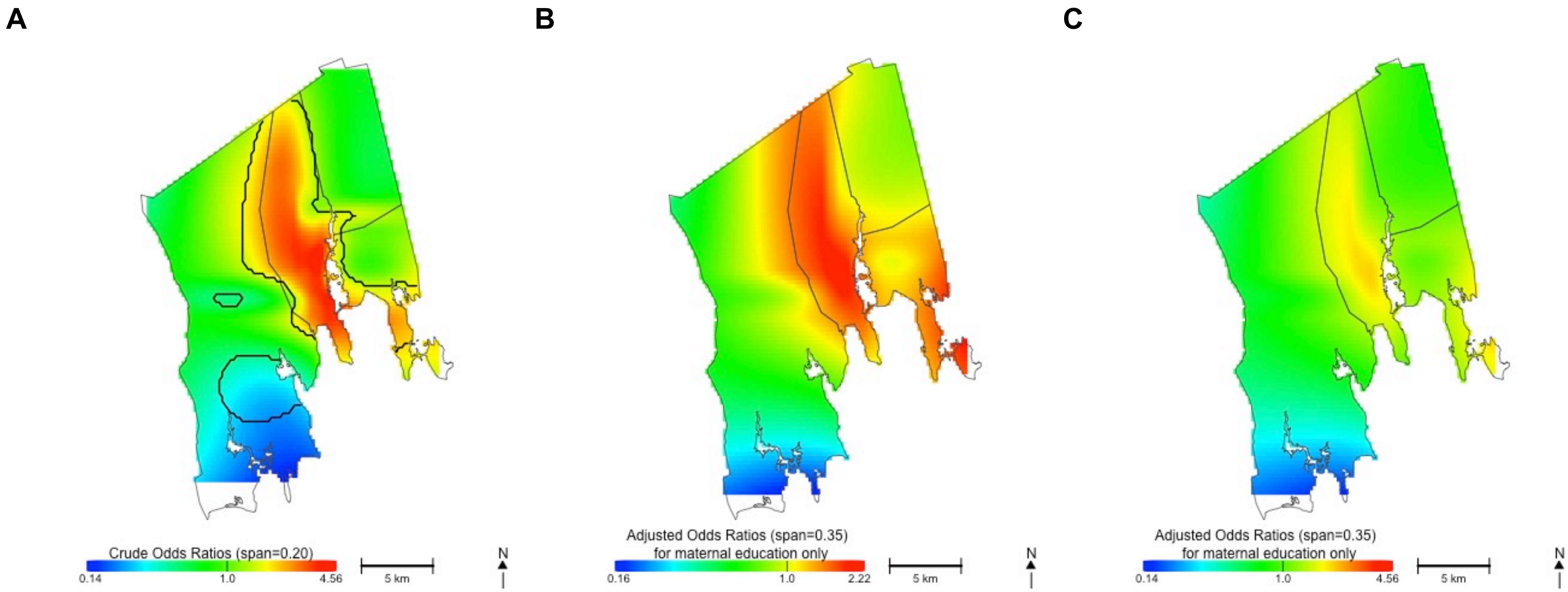


Figure A.17. Univariate adjustment for maternal education, 2002-2008. Odds ratios are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for maternal education only.

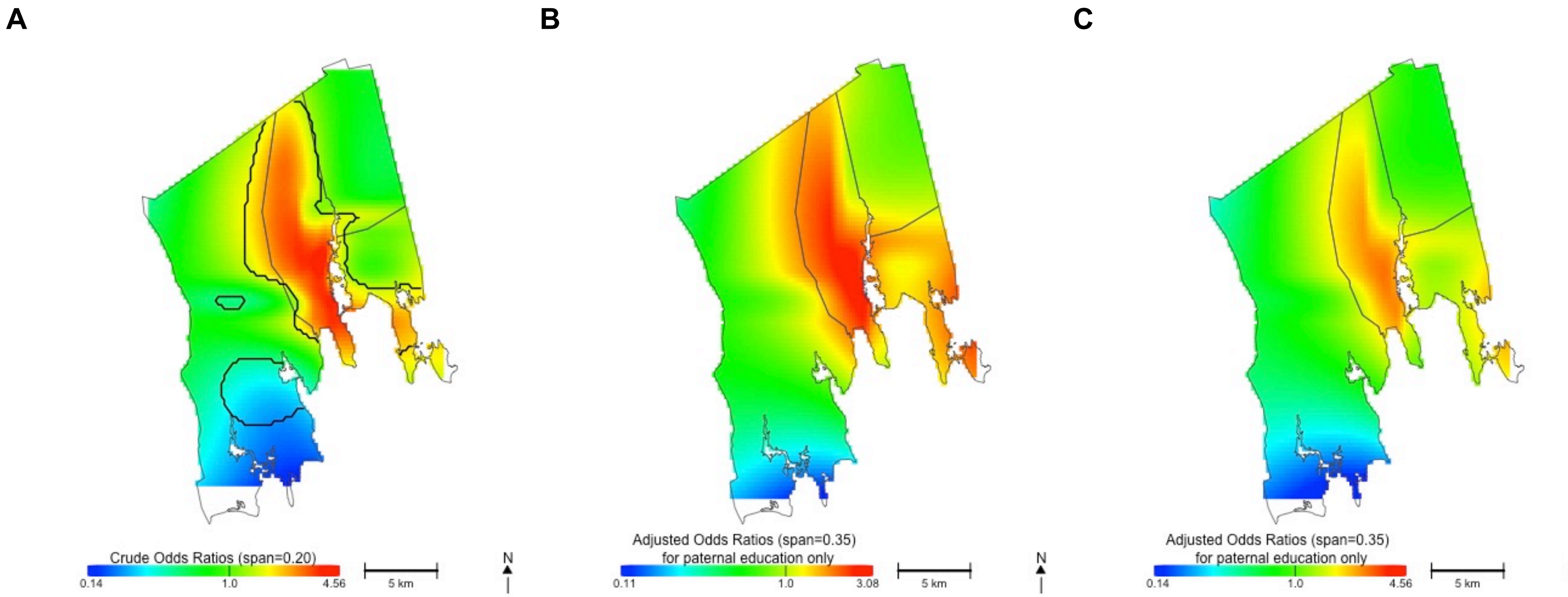


Figure A.18. Univariate adjustment for paternal education, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for paternal education only.

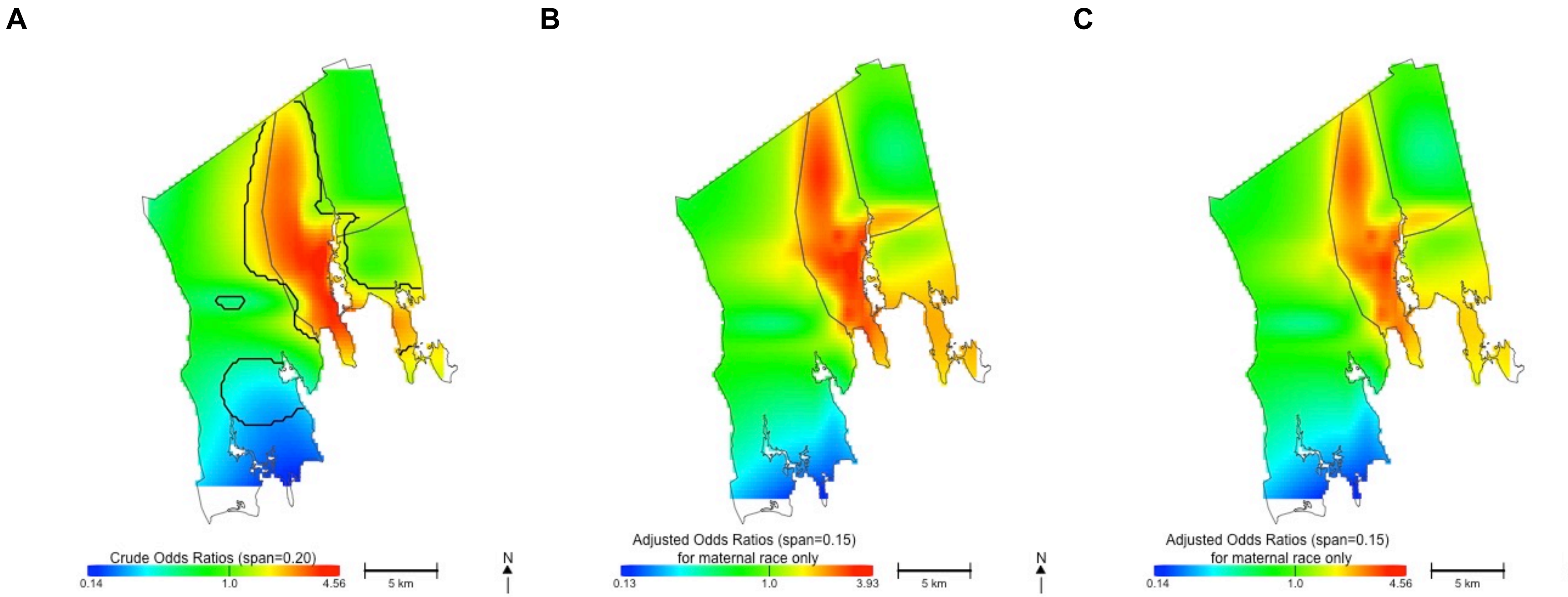


Figure A.19. Univariate adjustment for maternal race, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.15. (C) Adjusted, span of 0.15, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for maternal race only.

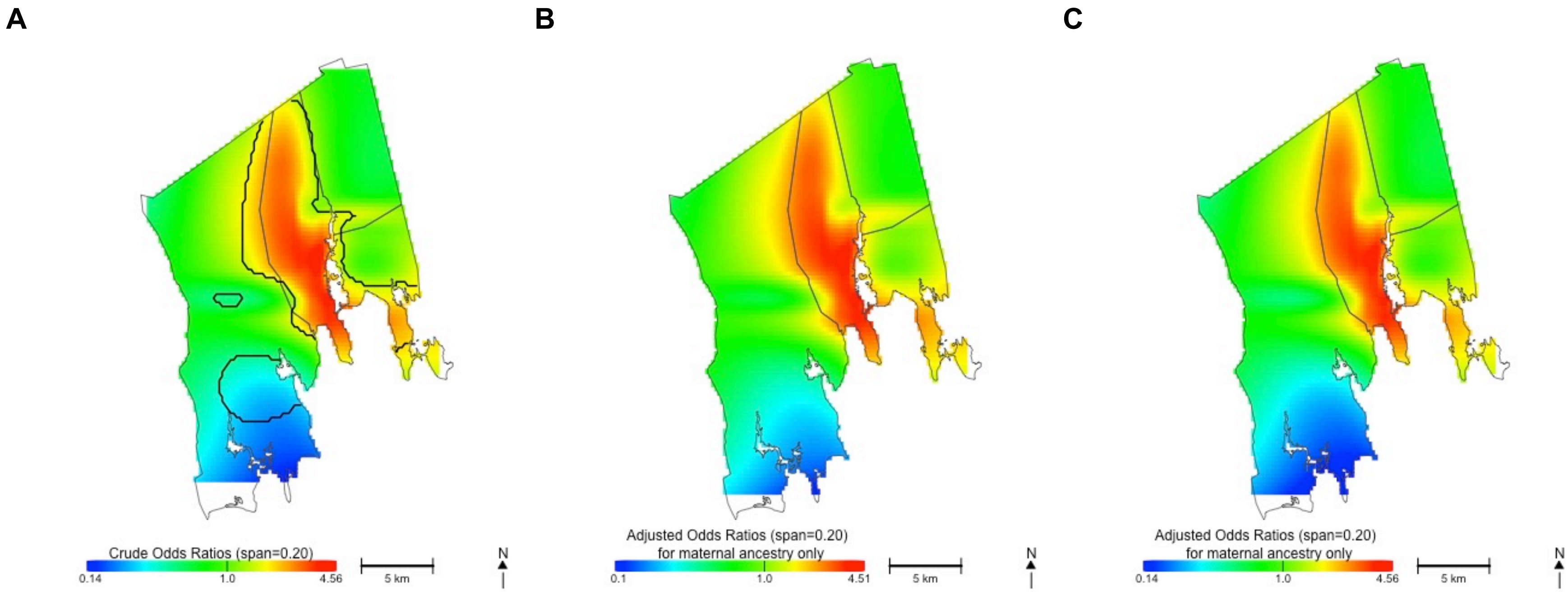


Figure A.20. Univariate adjustment for maternal ancestry, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.20. (C) Adjusted, span of 0.20, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for maternal ancestry.

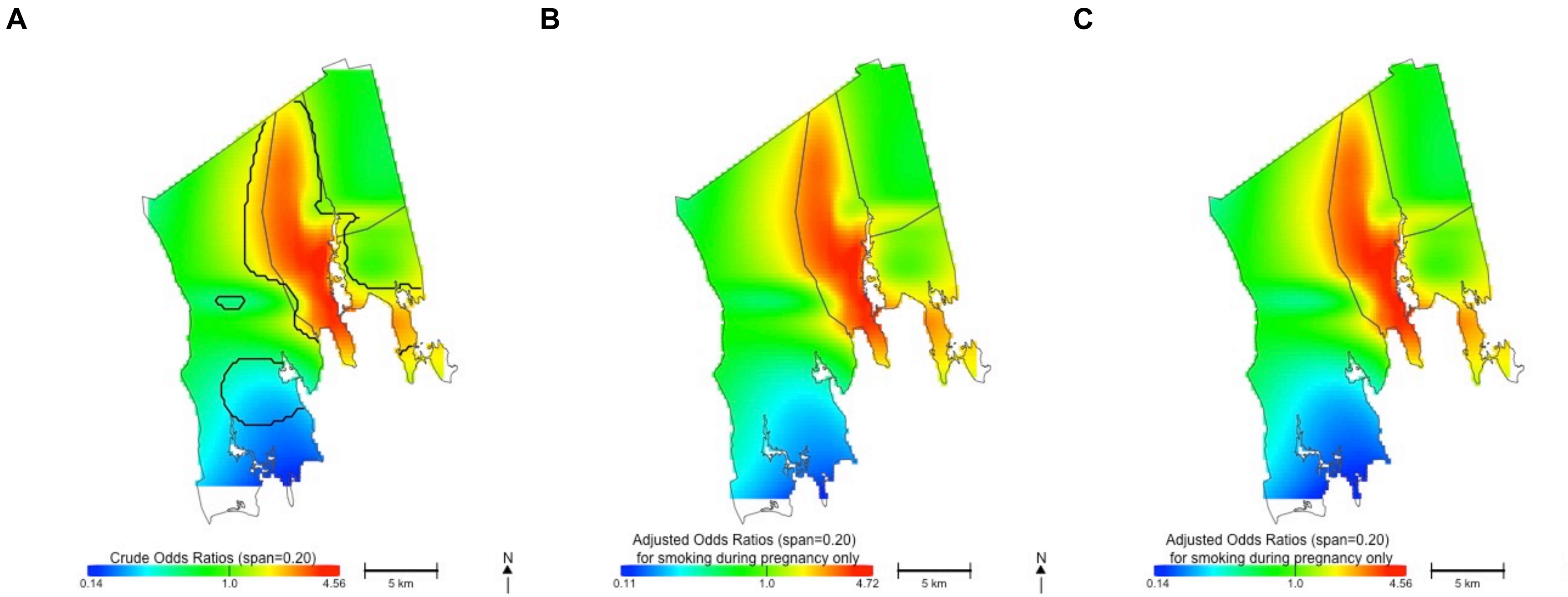


Figure A.21. Univariate adjustment for any smoking during pregnancy, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.20. (C) Adjusted, span of 0.20, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for any smoking during pregnancy.

A B C

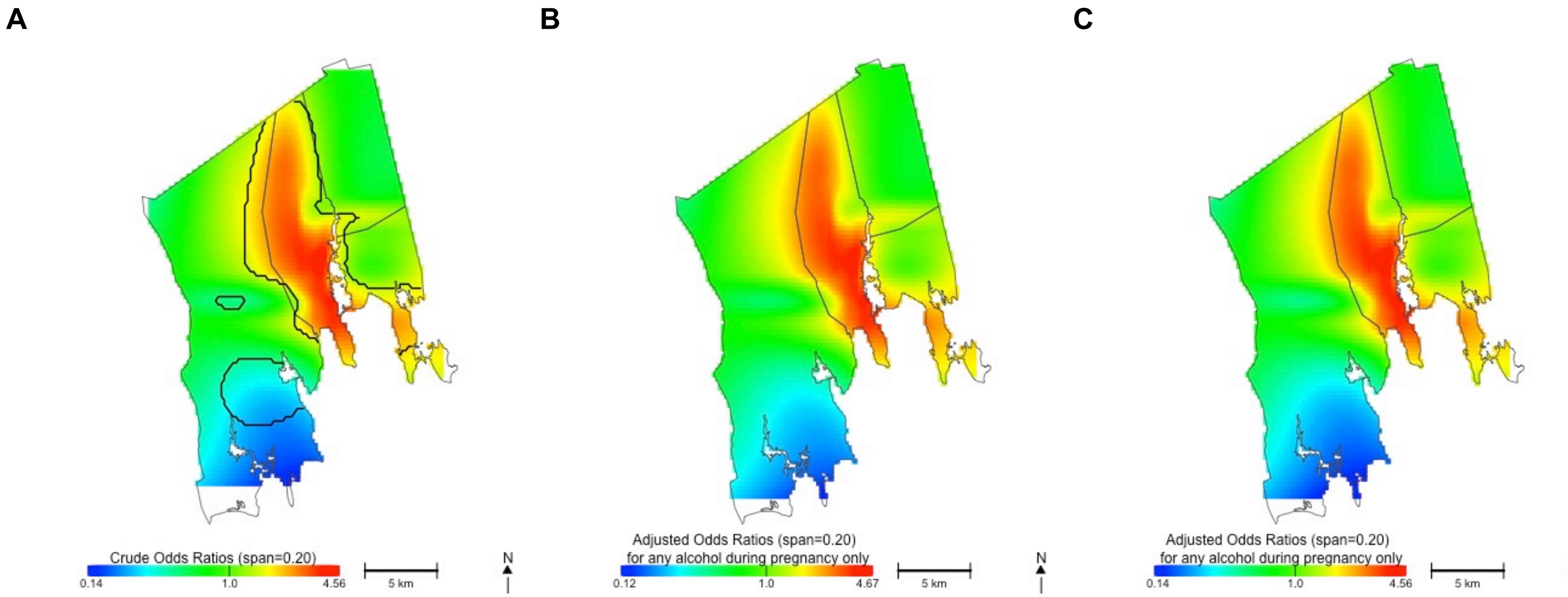


Figure A.22. Univariate adjustment for any alcohol consumption during pregnancy, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.35. (C) Adjusted, span of 0.35, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for any alcohol consumption during pregnancy.

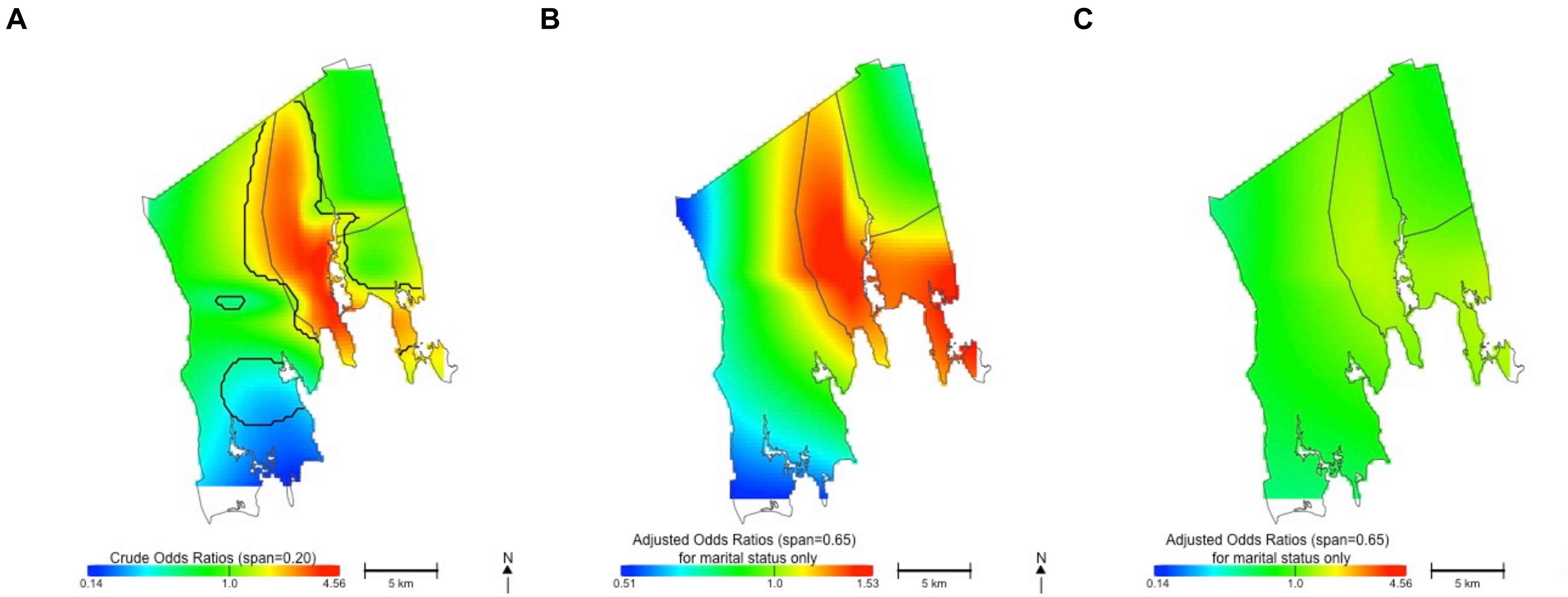


Figure A.23. Univariate adjustment for marital status, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.65. (C) Adjusted, span of 0.65, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for marital status when mapped on the adjusted scale.

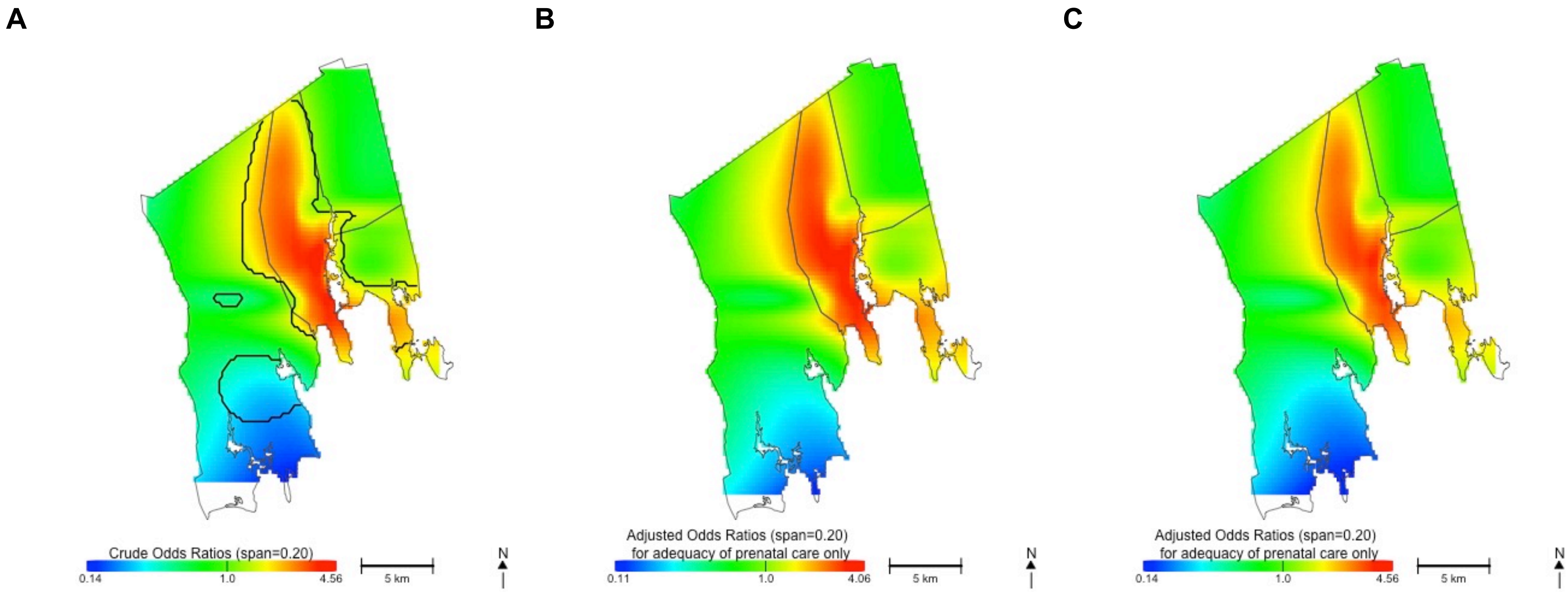


Figure A.24. Univariate adjustment for adequacy of prenatal care, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.20. (C) Adjusted, span of 0.20, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for adequacy of prenatal care when mapped on both the crude and the adjusted scales.

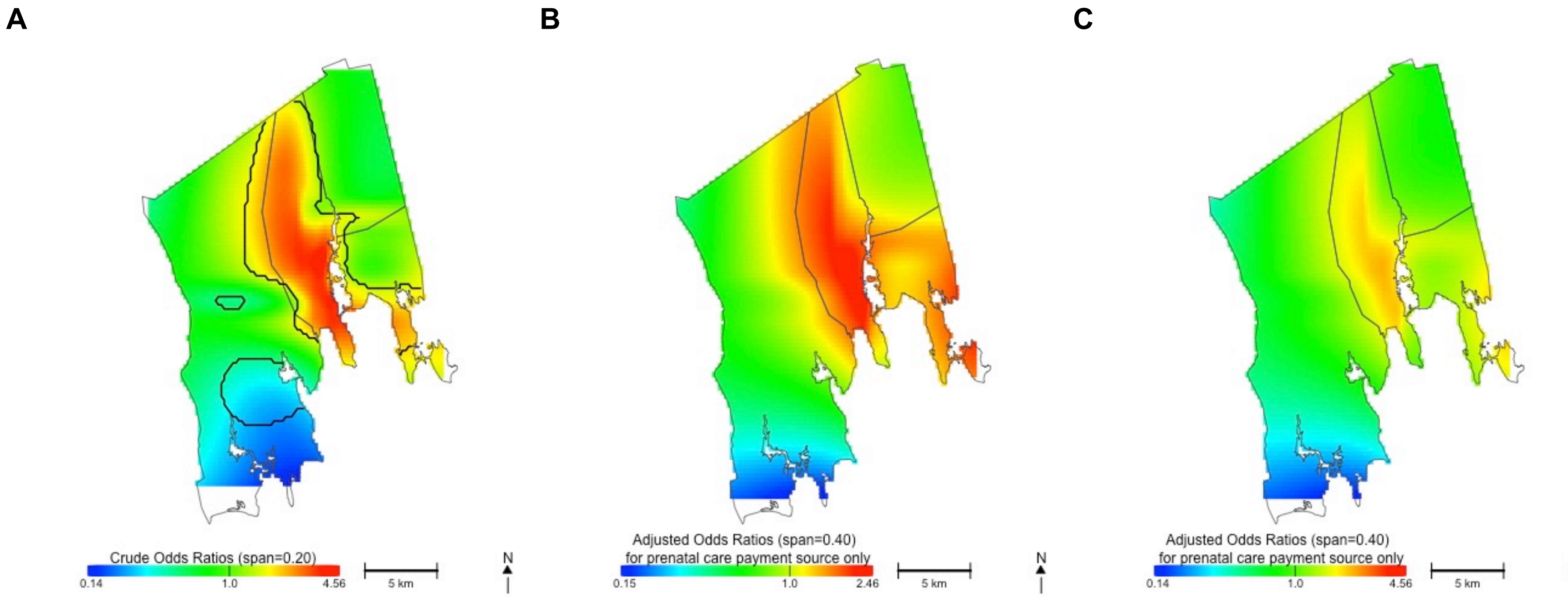


Figure A.25. Univariate adjustment for prenatal care source of payment, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.40. (C) Adjusted, span of 0.40, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for prenatal care source of payment when mapped on the raw scale.

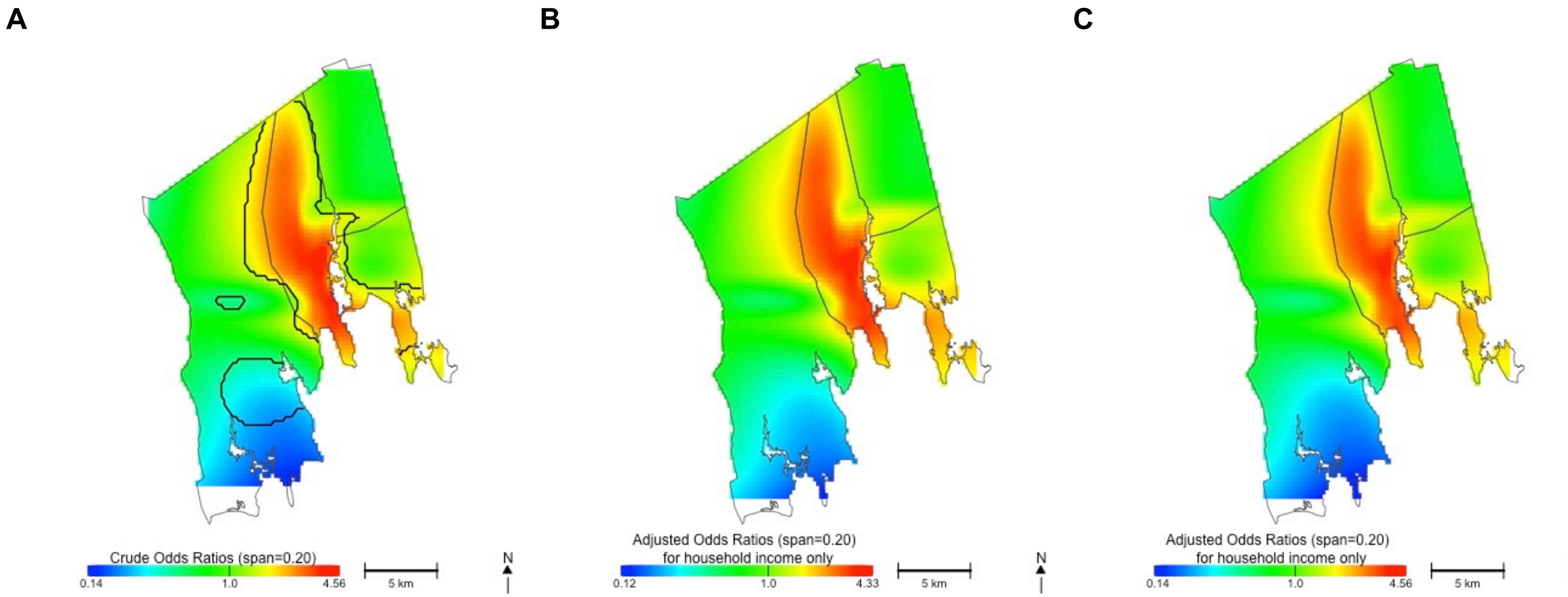


Figure A.26. Univariate adjustment for household income, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.20. (C) Adjusted, span of 0.20, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for block group median household income on both the crude and adjusted scales.

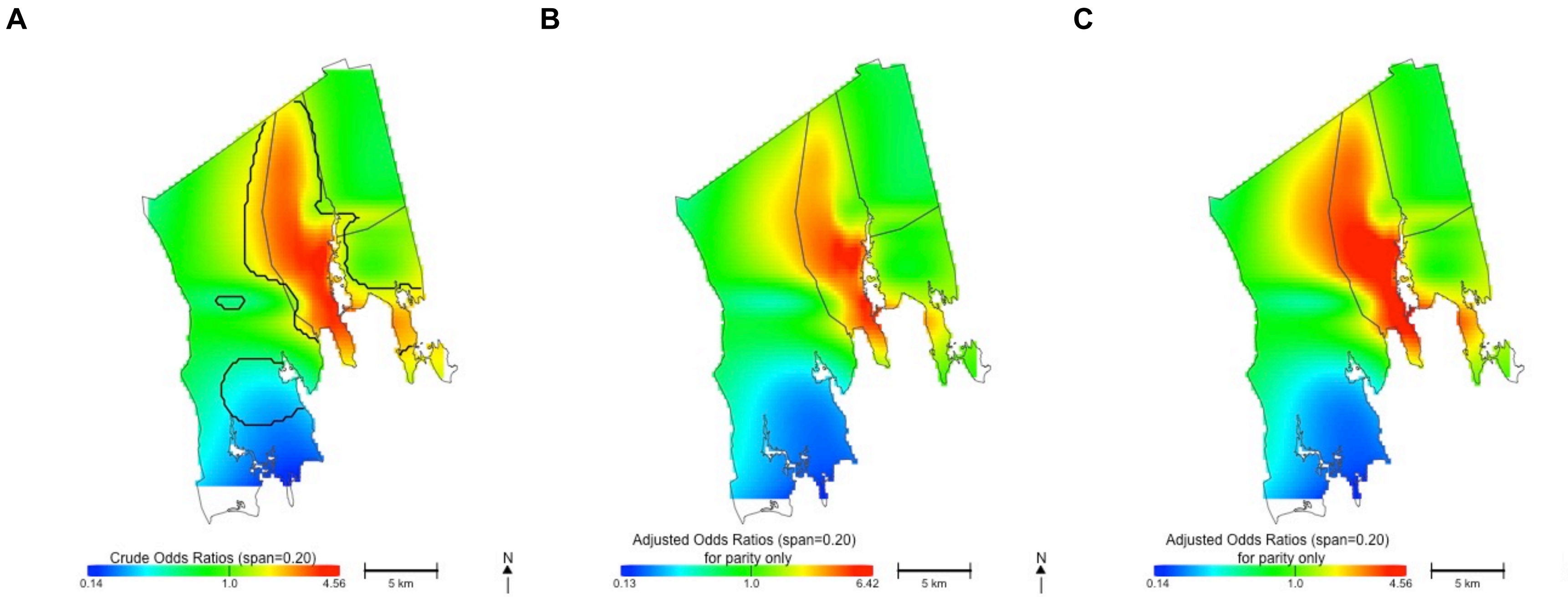
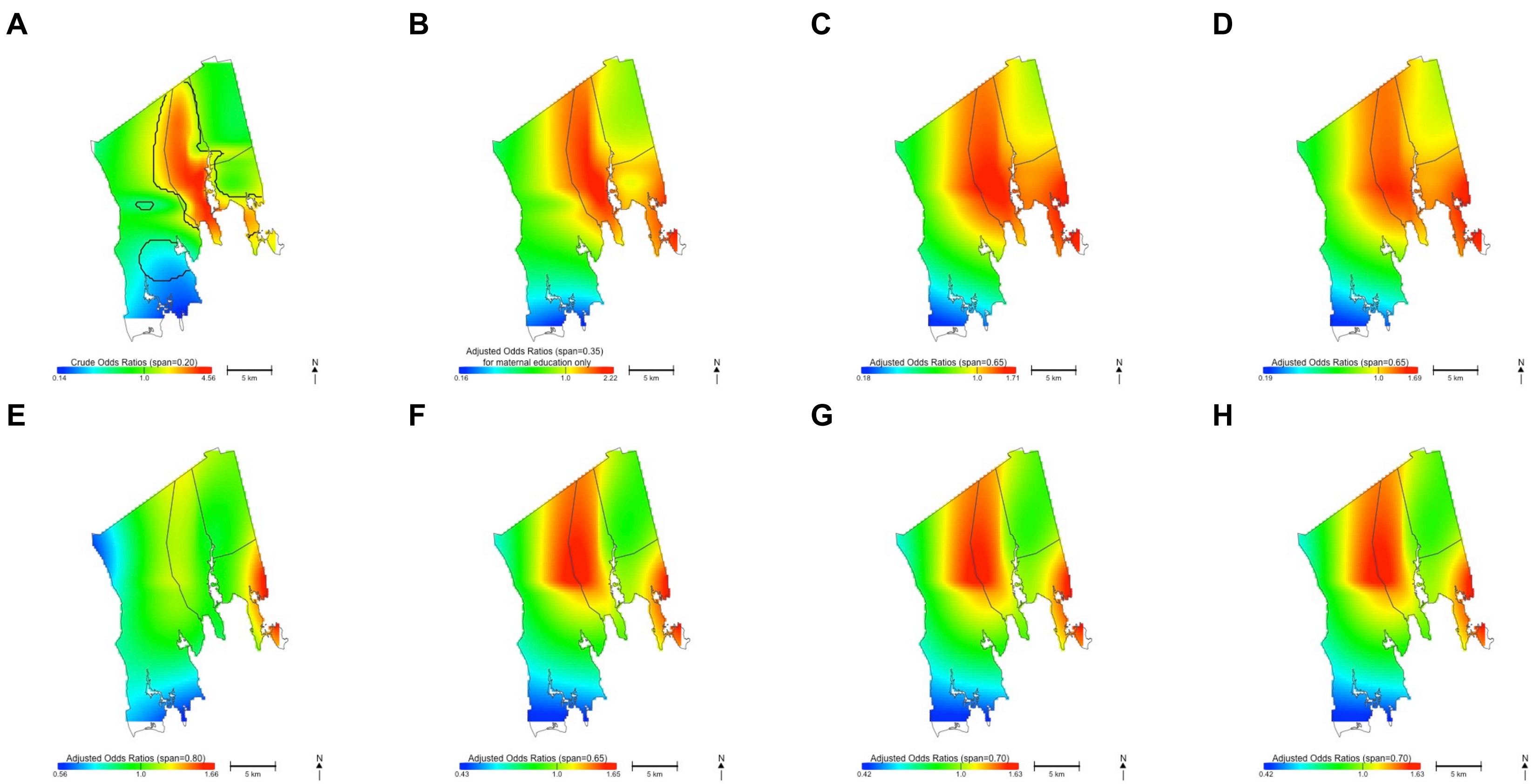


Figure A.27. Univariate adjustment for parity, 2002-2008. Odds ratios (ORs) are relative to the area of the study towns. (A) Crude, optimal span of 0.20 (global p<0.001). (B) Adjusted, span of 0.20. (C) Adjusted, span of 0.20, mapped on crude odds scale. The black contour lines indicate areas of significantly increased (red) and decreased (blue) risk of teen birth at the 0.05 level. An area of increased ORs remains after adjustment for parity on both the crude and adjusted scales.


A
Crude Odds Ratios (span=0.20)
0.14
1.0
4.56
5 km
N
B
Adjusted Odds Ratios (span=0.35)
for maternal education only
0.16
1.0
2.22
5 km
N
C
Adjusted Odds Ratios (span=0.65)
0.18
1.0
1.71
5 km
N
D
Adjusted Odds Ratios (span=0.65)
0.19
1.0
1.69
5 km
N
E
Adjusted Odds Ratios (span=0.80)
0.56
1.0
1.66
5 km
N
F
Adjusted Odds Ratios (span=0.65)
0.43
1.0
1.65
5 km
N
G
Adjusted Odds Ratios (span=0.70)
0.42
1.0
1.63
5 km
N
H
Adjusted Odds Ratios (span=0.70)
0.42
1.0
1.63
5 km
N

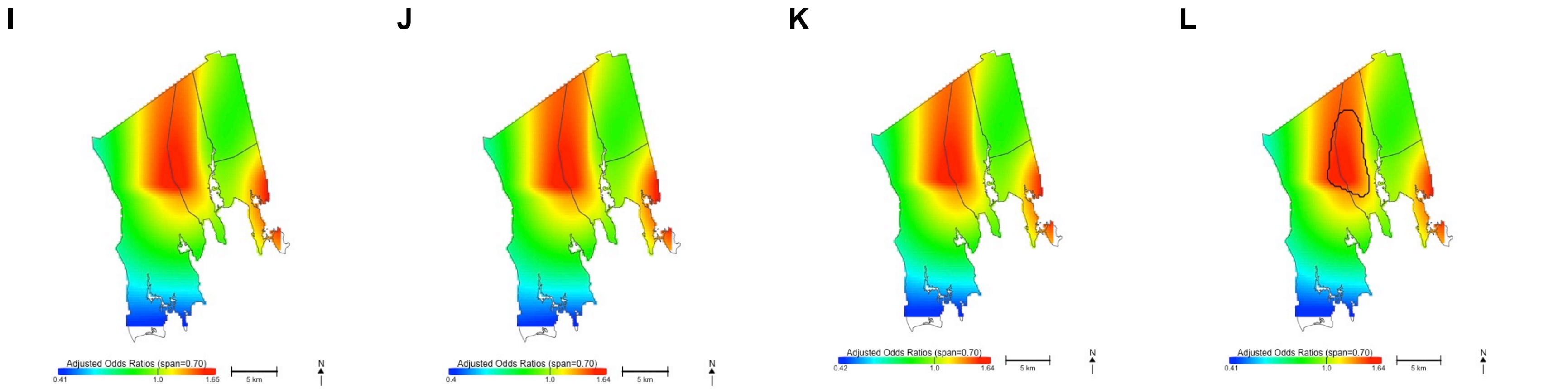


Figure A.28. Stepwise covariate adjustment, 2002-2008. Odds ratios (ORs) are relative to the surface area. (A) Crude, span of 0.20. (B) Adjusted, for maternal education only. (C) Adjusted, paternal education added. (D) Adjusted, maternal race added. (E) Adjusted, marital status added. (F) Adjusted, parity added. (G) Adjusted, prenatal care payment source added. (H) Adjusted, alcohol consumption during pregnancy added. (I) Adjusted, adequacy of prenatal care added. (J) Adjusted, household income added. (K) Adjusted, maternal ancestry added. (L) Fully adjusted, smoking during pregnancy added. A statistically significant area of increased ORs, accentuated by the black contour line, remained after stepwise adjustment for selected covariates ($p<0.001$).

APPENDIX B: SUPPLEMENTAL MATERIAL FROM CHAPTER 3

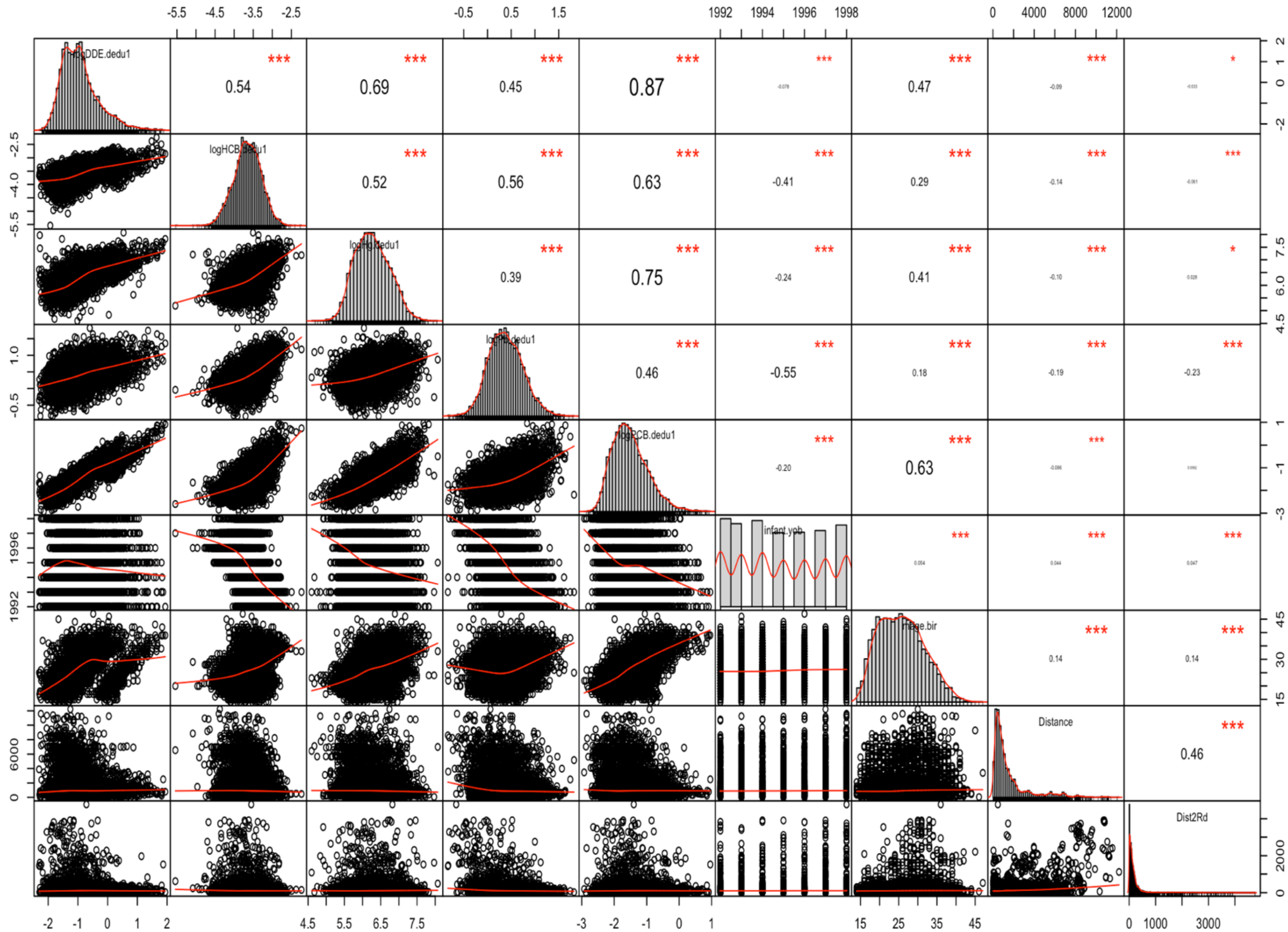


Figure B.1. Correlation chart for predicted exposures and continuous covariates for the Massachusetts Birth Record Cohort, 1993-1998. Exposure and continuous covariate distributions and associations are presented for log cord serum DDE, log cord serum HCB, log maternal hair Hg, log cord blood Pb, log cord serum PCB, infant year of birth, maternal age at birth, residential distance to the New Bedford Harbor, and residential distance to a major roadway.