THE TOXIC TRUTH: ENVIRONMENTAL JUSTICE AND ENVIRONMENTAL HEALTH OF MOTHERS AND CHILDREN IN MICHIGAN

By

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ABSTRACT

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The Risk-Screening Environmental Indicators (RSEI) model estimates toxicity-weighted concentrations based on human health risks from modelled exposures to Toxic Release Inventory (TRI) chemicals. Numerous studies have reported on the inequitable distribution of TRI sites and pollutant exposures among minority and low-income populations, which may be leading to poorer health outcomes and contribute to health disparities. Population groups who are most susceptible to the untoward effects of pollutants are pregnant women and infants, with minority and poorer women at greatest risk. The goal of this research is to investigate maternal and infant health outcomes associated with TRI chemical exposures in Michigan from 2008-2017 from an environmental justice perspective using an ecosyndemic theoretical approach. The objectives of this research are: 1) To outline the ecosyndemic theoretical approach as a holistic lens by which to conceptualize maternal exposures to multiple toxic chemicals. 2) To investigate the spatial and temporal patterns and clusters of RSEI toxicity-weighted concentrations and the degree to which these human health risks are more elevated in minority and low-income communities. 3) Estimate the impact(s) of maternal exposure to RSEI toxicity-weighted concentrations on adverse birth outcomes, including lethal congenital anomalies, controlling for potential maternal level confounding variables. U.S. Census data was used to measure racial composition and poverty at the census tract level. The annual RSEI toxicity-weighted concentrations across census tracts were sub-divided into exposure quartiles and these were spatially and temporally

assigned to each mother's pregnancy. The analyses were conducted using geographic information systems (GIS) and spatial epidemiological methods including cluster detection techniques. This study found that building upon the ecosyndemic framework the urban areas of Detroit and Grand Rapids were found to contain 80% of the census tracts with the highest RSEI toxicity-weighted concentrations. African Americans, Hispanics and residents living near and below poverty were most likely to live in these census tracts. These inequities persisted over time for African Americans living in Detroit and Grand Rapids and more recently for Hispanics living in Detroit, demonstrating on-going and emerging environmental injustices. Mothers exposed to the highest RSEI quartiles were at higher odds of low birth weight and preterm birth controlling for other known risk factors. The interactions between exposures to highest RSEI quartile and other behavioral and medical risks exacerbated the likelihood of these adverse birth outcomes. Finally, space-time analysis revealed several areas in Michigan with persistent clusters of lethal congenital anomalies. Clusters in Detroit and Muskegon that were in part explained by proximity to RSEI toxicity-weighted concentration values requires further investigation. Based on the study findings, recommendations include increased monitoring of TRI sites, incentivize companies to reduce their use of highly toxic chemicals and add additional environmental justice evaluations when approving new industrial facilities and targeting areas for pollution reduction, particularly census tracts in the highest RSEI quartile where mothers are at greatest risk of adverse birth outcomes. Future research should investigate possible interaction and mediating effects between chemical exposures and maternal behavioral and medical factors, further investigate the clusters of lethal birth defects in Michigan and investigate the upstream forces that contribute to environmental injustices and adverse birth outcomes in Michigan.

This dissertation is dedicated to the women and children of Michigan.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

KEY TO ABBREVIATIONS

U.S. EPA	United States Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
GIS	Geographic Information Systems
HAP	Hazardous Air Pollutant
MDHHS	Michigan Department of Health and Human Services
RSEI	Risk-Screening Environmental Indicators
TRI	Toxic Release Inventory
WHO	World Health Organization

Chapter 1. INTRODUCTION TO THE DISSERTATION STUDY

1.0. Introduction

In 1984, one of the world's worst industrial accidents occurred in Bhopal, India when the highly toxic chemical methyl isocyanate leaked from the Union Carbide Corporation's pesticide plant (Jasanoff, 1988). The disaster claimed the lives of thousands of people and permanently injured or disabled thousands of others (U.S. EPA, 2021). Investigations into the disaster revealed inadequate safety regulations, insufficient employee training and limited medical and scientific information about the chemicals due to a lack of sharing by the company. All of these factors contributed to the accident and created challenges for recovery and relief operations (Broughton, 2005; Jasanoff, 1988). Following this event, activists from around the world called for right-to-know legislation that would make information about hazardous chemicals more accessible to ensure safe operations at hazardous facilities and allow communities to develop emergency action plans in the event of an accident (Jasanoff, 1988). In response, the United States enacted the Emergency Planning and Community Right-to-Know Act (EPCRA) of 1986 (U.S. EPA, 2021). The intent of the EPCRA of 1986 was to make information available about toxic chemicals to aid communities in the protection of public health, safety and the environment from chemical hazards (U.S. EPA, 2021a). The EPCRA created the Toxics Release Inventory (TRI), a database that makes information regarding the release, off-site transfer and management of toxic chemicals available for administrative and public uses (U.S. EPA, 2021). Reporting is required for facilities in certain industrial sectors that (a) have 10 or more full-time employees and (b) manufacture more than 25,000 pounds of TRI chemicals or use over 10,000 pounds of any TRI chemical in their operations (U.S. EPA, 2020).

Previous research indicates that certain population groups including minority and low-income communities experience discriminatory citing practices of industrial facilities and waste sites and as a result, a disproportionate share of pollutant exposures (Ash, et al., 2009; Bullard, 2002; Moseley, Perramond, Hapke, & Laris, 2014). Environmental health research has shown that exposure to certain pollutants can lead to various adverse health outcomes (Landrigan, Kimmel, Correa, & Eskenazi, 2004; Padula, et al., 2018). Thus, one of the Healthy People 2030 objectives is to reduce the population's exposure to environmental pollutants (U.S. HHS, 2020). The disproportionate pollution burdens are believed to be contributing to racial and ethnic, and geographic health disparities (Bagby, Martin, Chung, & Rajapakse, 2019). The Healthy People 2030 objectives also address the social determinants of health, which refer to conditions of the environments in which people spend time that may also have an influence on health outcomes. The quality of the physical environment is one determinant of health (U.S. HHS, n.d.). Environmental factors, including air, water and soil pollution, radiation, noise, occupational risks, built environments, agricultural practices, anthropogenic changes to the climate and ecosystems, and behaviors related to one's environment, contribute to an estimated 23 percent of global deaths and 22 percent of the global disease burden. Although the environmental burden of disease is higher in developing nations, pollutant exposures also represent a major health hazard to people living in developed nations (WHO, 2016).

The extent to which exposure to environmental toxicants impact human health is not fully understood (Woodruff T. J., 2015). Researchers agree that our present understanding of human health risks from real-life chemical exposure is insufficient because it is largely based on the assessment of risks from only individual chemicals (Cory-Slechta, 2005; Woodruff T.J., 2015). Moreover, existing regulations are predominantly based on single-chemical assessments.

However, it is well understood that humans are exposed to multiple chemicals simultaneously (Cory-Slechta, 2005; Rokoff, et al., 2018; Kortenkamp & Faust, 2018). A growing body of research indicates that a lack of consideration for the combined effects from exposure to multiple chemicals and via multiple routes of exposure can lead to an underestimation of chemical risks in a population (Kortenkamp & Faust, 2018).

Some research has examined multiple chemicals, but most has focused on assessing chemicals of the same class meaning they are structurally related, often sharing the same target site and thus are typically found to have primarily additive effects (the combined effect is equal to the sum of each chemical acting independently) (Cory-Slechta, 2005; OSHA, 2016). Additionally, limited information is available regarding the combined effects of chemicals in which humans are exposed to via multiple routes (ingestion, inhalation, dermal). Thus, more studies need to consider the potential interaction effects (additive, antagonistic, synergistic) from exposure to multiple chemicals that come from different sources and multiple exposure routes to reduce risk and prevent poor health outcomes (Cory-Slechta, 2005; Kienzler, Bopp, van der Linden, Berggren, & Worth, 2016; Kortenkamp & Faust, 2018; Rokoff, et al., 2018).

Pregnant women and infants are of particular concern because they have a greater risk of experiencing health-related problems from pollutant exposures (U.S. HHS, 2020). Previous studies indicate women are often exposed to pollutants and that these environmental exposures during pregnancy may lead to adverse birth outcomes, which can have significant and lastly health effects for the infant (Anderson et al., 2003; Barker, 2006; CDC, 2019a). Biomonitoring studies indicate that people are exposed to multiple industrial chemicals throughout their lives, with initial exposures beginning before birth (Perera, et al., 2003; Institute of Medicine, 2014; Woodruff, 2015; Rokoff, et al., 2018; Wang, et al., 2018). Many of the chemicals pregnant

women are exposed to can cross the placenta, thereby exposing the developing fetus (Woodruff et al., 2011). Maternal exposures to environmental toxicants have previously been linked to several adverse birth outcomes (Landrigan, Kimmel, Correa, & Eskenazi, 2004; Ogneva-Himmelberger, Dahlberg, Kelly, & Moore Simas, 2015; Padula, et al., 2018; Stieb, Chen, Eshoul, & Judek, 2012). Therefore, there remains a need to better understanding how multiple chemical exposures influence health, as the environment could be an important area for public health intervention (Woodruff, 2015). It is important research address scientific uncertainties regarding chemical exposures among pregnant women, who are known to experience multiple chemical exposures (Woodruff, Zota, & Schwartz, 2011). Additionally, it is important to set these injustices and chemical exposures within the broader scale structures and to examine synergies between chemicals and health conditions that may be worsening the health burden within a population. One source of potential multiple chemical exposures comes from Toxics Release Inventory (TRI) facilities, the largest group of emitting facilities in the United States (U.S. EPA, 2021).

1.1. Background

The United States experienced rapid economic growth during the nineteenth and early twentieth centuries (Wright, 1990). For example, the United States' economy was smaller than both Britain's and Frances' economy in 1840 but by 1950 it was five times larger than Britain's economy and about eight times larger than France's economy (Davis, et al., 1972). The economic boom was largely due to industrial growth (Wright, 1990). The manufacturing sector was small in 1800, but by 1900 it accounted for one fourth of the national product and by 1950 it accounted for one third of the national product (Davis, et al., 1972). Together, Illinois, Indiana, Michigan, New York, Ohio, Pennsylvania, and Wisconsin were the thriving industrial areas that

produced a majority of goods purchased in North America (Cooke, 1995; High, 2003). This region became known as America's industrial heartland because it was the center of industry and manufacturing in North America (McClelland, 2013). Prominent industries in this region included steel, automotive, chemical, and paper (Feldman & Heasley, 2007).

1.1.1. American's Industrial Heartland

America's industrial heartland (Figure 1-1) was situated near two crucial resources: raw materials and water. The region was centrally located between the iron ore deposits in Minnesota and Michigan's Upper Peninsula and coal in the Appalachian Mountains (McClelland, 2013). Industries used water for the production and transportation of goods, so most industries located along prominent rivers including the Detroit and Ohio Rivers and the shores of the Great Lakes (Cooke, 1995; Feldman & Heasley, 2007; USGS, 2018).

Figure 1-1: America's Industrial Heartland.

As industries experienced rapid growth, urban areas did as well (Shaw, 2001). Together they led to widespread environmental pollution by the mid-twentieth century. Untreated wastes were often discharged directly into waterways and air pollutants were released at unregulated rates and concentrations (Feldman & Heasley, 2007). The Cuyahoga River in Ohio, for example, contained an array of industries who used the river for transportation, production and waste disposal. The river became so polluted that it caught fire at least thirteen times (Cooke, 1995; U.S. EPA, 2019). Air quality was also impacted. For example, the mill town of Donora, PA experienced a fatal air pollution disaster in 1948. The air pollutants from the town's industries mixed with fog, creating an acid smog that lingered over the city for several days, causing severe respiratory and cardiovascular problems among half of the people in the town and killing 40 residents (U.S. EPA, 2017). In addition, the Love Canal hazardous waste tragedy near Buffalo New York exposed the potential health hazards that toxic waste sites pose to humans (McElroy & Townsend, 1989). In response to the widespread pollution, states and the federal government began enacting environmental policies to help reduce air and water pollution to protect public health and the environment (U.S. EPA, 2017; U.S. EPA, 2019). Although the increased awareness of pollution and the subsequent health impacts spurred the environmental movement, it also prompted the "not in my backyard" (NIMBY) phenomenon which led to the citing of waste facilities in areas with the least political resistance, primarily minority and low-income areas. A longitudinal analysis of the 1950s - 1980s found that the discriminatory citing of these sites emerged in the 1970s (during the environmental movement) and strengthened during the 1980s (following the love canal disaster) (Saha & Mohai, 2005).

The urban landscape in the American Industrial heartland experienced dramatic changes in the last half of the twentieth century. The 1970s was a period of economic restructuring that

included a large movement of industries to the south and overseas as well as the transition from manufacturing to services (Shaw, 2001; Wilson & Wouters, 2003). These national and international economic changes impacted numerous American industries in such a way that spurred many to reduce their workforce, relocate to less expensive places or close (Wilson & Wouters, 2003). The industrial heartland was particularly devastated by the economic restructuring that took place in the last half of the twentieth century, as they were primary centers of industry. Additionally, many of the cities and towns located in this region relied on one industry or one employer (Cooke, 1995). As a result of job loss, many residents relocated away from the American Industrial heartland with a subsequent demographic shift as cities and towns experienced a declining number of residents, businesses and housing units (Dewar & Thomas, 2013; Thompson, 1999). The region experienced the greatest reduction in real incomes as well as the highest business failure rates and unemployment rates in the nation (Cooke, 1995). As a result, the region's name changed from the American Heartland to the American Rust Belt (High, 2003).

1.1.2. Emergence of the Rust Belt

The primary reasons for the emergence of Rust Belt cities included globalization, new technologies, decentralization of industries, suburbanization and various federal and state policies (Dewar & Thomas, 2013; Thompson, 1999; Sugrue, 1996). Many Rust Belt cities have lost significant portions of their population following the movement of people to other locations for work, causing many social and economic issues (Fasenfest, 2017) including racial tensions as further described below. Many cities are also described as shrinking cities, which are cities that have continued to experience population loss, economic decline and property abandonment over the past few decades (Audirac, 2018; Dewar & Thomas, 2013). As businesses and people

relocate out of a city, the tax base is reduced along with the number of available amenities, opportunities and resources (Thompson, 1999). Poverty and urban decline are two challenges shrinking cities in the Rust Belt face (Fasenfest, 2017).

Cities and towns that shrink due to economic decline often lose a disproportionate share of their young and mobile populations. These population groups have a greater ability to relocate for new job opportunities (Rieniets, 2009). Economic restructuring therefore, has resulted in unequal impacts and likely increases family poverty (Nelson, 1998; Rieniets, 2009) with primarily upper-class and middle-class whites who had the ability to move out of the inner cities and into the suburbs, which left primarily African Americans and low-income groups within the deteriorating inner city where few jobs remained (Sugrue, 1996). African American and low-income populations experienced greater burdens due to the combined effects of racial discrimination in social mobility and employment, racial residential segregation and concentrated poverty.

1.1.3. Michigan Case Study

Michigan's early economic growth came from primary and secondary industry sector activities. The primary sector prospered first with prominent activities such as lumbering and mining, followed by the secondary sector including furniture making, paper and automobile manufacturing. Michigan's population experienced rapid growth in response to economic opportunities as a result. However, during the economic restructuring in the 1970s, many manufacturing jobs were lost (Michigan Legislature, n.d.). Michigan struggled to recover economically, but over time the state was able to rebuild the economy through existing and new businesses. However, the necessity to attract investments through various means such as tax incentives in some cases drew in industries undesired elsewhere because their operations degrade

the environment and expose residents to harmful pollutants (Berglund, 2020). Legacy pollutants left behind in the water and soil from Michigan's early manufacturing and industrial activity along with new pollutant emissions from current industries have raised human health concerns (Wattigney, et al., 2019; Berglund, 2020). These pollutants have been a prominent environmental justice issue in Michigan over the years. A recent spatial analysis of environmental justice in Michigan reported an inequitable distribution of environmental goods and harms based on both race and income (Grier, Mayor, & Zeuner, 2019). Three prior studies utilized TRI data to evaluate environmental justice in Michigan. Downey (1998) investigated TRI releases in relation to income and race across Michigan. Downey (2005) evaluated TRI facilities in relation to black/white income inequality, discriminatory siting practices and residential segregation in the Detroit metropolitan area. Downey (2006) examined residential proximity to TRI facilities and the estimated human health hazard associated with their releases in relation to several demographic characteristics such as race, ethnicity and income in the Detroit Metropolitan Area. To the authors' knowledge, no studies have studied maternal exposures to modelled TRI releases in Michigan.

1.2. Study Goal

The goal of this dissertation research is to assess the likelihood of adverse birth outcomes including neonatal mortality due to lethal congenital anomalies for women living in Michigan in areas with elevated TRI emissions. This research will conceptualize and demonstrate the utility of investigating adverse birth outcomes using an ecosyndemic approach by which multiple TRI chemicals emitted into different types of media (i.e. air, water, land) are examined. A retrospective cross-sectional cohort study design (2008 to 2017) was used to examine the impacts of multiple chemical exposure on adverse birth outcomes, and spatial and temporal

patterns of lethal congenital anomalies. The research findings will be disseminated in peer-reviewed journals and at conferences and used to inform environmental injustices and public health policies and health care practice in areas with TRI sites and elevated health risks from TRI chemical exposures.

1.3. Study Objectives

1. Utilize the ecosyndemic theoretical approach as a holistic lens by which to conceptualize maternal exposures to multiple chemicals and the potential synergies with behavioral and social factors.
2. To investigate the spatial and temporal patterns and clusters of modelled human health risk from TRI releases and the degree to which these human health risks are more elevated in minority and low-income communities (environmental injustice).
3. Estimate the impact(s) of maternal exposure to modelled TRI emissions on adverse birth outcomes, including lethal congenital anomalies controlling for known risk factors and potential maternal level confounding variables.

1.4. Study Hypotheses

Study 2: Toxics Release Inventory Chemical Hazards: Racial and Ethnic Disparities in Michigan, 2008-2017.

H_0: There will be clusters of elevated human health risks from TRI chemical exposures in areas with a higher density of TRI facilities.

H_{01}: Human health risks from TRI chemical exposures will be higher in low-income communities than middle- and high-income communities and these geographic disparities may vary by the racial composition of the area.

H_{02}: The processes by which environmental injustice are defined will vary by urban area and African American and Hispanic population groups.

Study 3: Environmental Health Investigation of Toxic Release Inventory Chemicals on Maternal Health, Birth Outcomes and Neonatal Mortality in Michigan, 2008-2017.

H_{01} Mothers exposed in high levels of health risks from TRI chemical exposures will be at increased odds of adverse birth outcomes and lethal congenital anomalies.

H_{02} African American and Hispanic mothers will be at increased risk of exposure to health risks from TRI chemical exposures and these exposures will in part explain racial and ethnic disparities in adverse birth outcomes.

This dissertation study follows the three-paper dissertation format. An introduction to the dissertation is provided in Chapter 1. Following is a discussion of the theoretical framework in Chapter 2. This dissertation builds on existing theory by applying an ecosyndemic theoretical approach to conceptualize the polluted environments in which some pregnant women live and how they may share synergistic effects with their social environment. Chapter 3 presents the approach by which TRI emissions will be studied, specifically using a model developed by the EPA called Risk Screening Environmental Indicators (RSEI) toxicity-weighted concentrations (hazard assessment) and the environmental justice analysis. Chapter 4 presents the maternal exposure to RSEI toxicity weighted concentration levels and its effect on adverse birth outcomes, including cluster detection of lethal birth defects. Finally, chapter 5 summarizes the results of the former chapters and provides recommendations for future research and concluding remarks.

Chapter 2. AN ECOSYNDEMIC APPROACH FOR ENVIRONMENTAL HEALTH JUSTICE STUDIES

Abstract

The quality of the physical environment in which people obtain life-sustaining resources is to a large extent, dependent upon regulatory policies and laws that govern toxic chemical emissions. Exposure to these toxicants, individually or synergistically, during critical windows of human growth and development can alter biology leading to congenital anomalies and/or diseases and conditions that prematurely reduce life expectancy. It is well documented that minority and low-income populations experience a disproportionate share of pollutant exposures due to residencies in close proximity to industrial sites, which may be a factor contributing to population health disparities. The clustering of diseases associated with environmental changes, most notably climate-induced hazards, is referred to as an ecosyndemic. This paper extends the view of ecosyndemic theory by incorporating chemical contaminants as a frame by which to further evaluate human health risks. Further, ecosyndemic theory will be incorporated into the human ecology framework commonly used within the discipline of medical geography. Improving our understanding of the impacts of ecosyndemics on maternal and infant health will lead to the promotion of life-sustaining environmental policies and public health interventions.

2.0. Introduction

Health disparities that exist between different racial and ethnic groups may be attributed to the quality of the local environments in which people live, work and spend time (Bryant, Worjoloh, Caughey, & Washington, 2010; Commission on Social Determinants of Health, 2008; Williams, 2012). Racial and ethnic health disparities have persisted for decades and cannot be explained by individual-level risk factors alone. The Centers for Disease Control and Prevention (CDC) (2020) reports that the prevalence of diabetes for Hispanic and non-Hispanic black adults is substantially higher compared to non-Hispanic whites (Rate Ratios (RR) 1.6 and 1.4, respectively). Similar racial and ethnic disparities are observed for hypertension among Hispanics (29.0), non-Hispanic blacks (42.4) and non-Hispanic whites (27.8); obesity among Hispanic women (43.7), non-Hispanic black women (56.9) and non-Hispanic white women (39.8); and chronic kidney disease among Hispanics (2.2), non-Hispanic blacks (3.2) compared to non-Hispanic whites (1.9) (CDC, 2020). Daw (2017) utilized the National Health Interview Survey (1997-2009) to investigate the weighted mean prevalence of these four comorbidities (diabetes, hypertension, obesity and chronic kidney disease) that co-occur for Hispanics (0.22%), non-Hispanic blacks (0.33%) and non-Hispanic whites (0.16%) and found that 21% of black-white disparity in mortality hazard was explained by these four conditions. While these disparities are obvious and consistent across morbidities, comorbidities and premature mortality, the contribution(s) of the environment (physical, social and built) as causal underlying risk factors for these conditions requires further investigation (Daw, 2017).

An important hypothesis underlying the spatial unevenness of environmental risks and health disparities is referred to as environmental racism, environmental classism and/or environmental injustice (Ash, et al., 2009; Bullard, 2002; Moseley, Perramond, Hapke, & Laris,

2014; Margai, 2010; U.S. EPA, 2018). The Environmental Protection Agency (EPA) defines environmental justice as: "*the fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income, with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies. Fair treatment means no group of people should bear a disproportionate share of the negative environmental consequences resulting from industrial, governmental, and commercial operations or policies*" (U.S. EPA, 2018). The disproportionate impact of environmental hazards on people of color is referred to as environmental racism and the disproportionate impact of environmental hazards on low-socioeconomic groups is referred to as environmental classism (Bryant & Mohai, 1992; Peña-Parr, 2020). Environmental quality varies geographically. It has long been recognized that polluting industries and hazardous waste sites are more commonly located in communities comprised of low-income and minority residents (Bryant & Mohai, 1992; United Church of Christ, 1987; Lee, 2002). In addition to the location of these sites, studies have shown that low-income and non-white population groups are burdened with a higher share of toxic exposures (Cutter, 1995; Lee, 2002).

The environmental justice movement began in the United States around 1980 and was a merging of the civil rights and environmental movements (Moseley, Perramond, Hapke, & Laris, 2014). The landmark case that sparked the environmental justice movement was in 1982 involving the disposal of polychlorinated biphenyl (PCB) waste in Warren County, North Carolina. Liquid hazardous waste containing PCBs from the Ward Transformer Company had been illegally dumped along North Carolina roadways in 1978. When the state learned of the contamination, they initiated a plan to build a PCB landfill in Warren County where the contaminated soil would be taken. Warren County's population at the time was 66% African

American. The local community responded with protests; however, their efforts were unsuccessful and the PCB landfill was built in proximity to those residents (McGurty, 2007).

The subsequent landmark United Church of Christ's Commission on Racial Justice 1987 *Toxic Waste and Race* report shared findings from cross-sectional studies conducted to evaluate the locations of hazardous waste sites in relation to neighborhood demographics across the United States. The studies found associations between communities with a high composition of African American and Hispanic residents and residents of low socio-economic status and the locations of hazardous waste sites. Notably, race/ethnicity was the most significant variable associated with hazardous waste sites (United Church of Christ, 1987). In 1979 a hazardous waste landfill was sited approximately 3.5 miles from Kettleman City, California without notifying community residents, a requirement under California law (Cole, 1994). Half of the population lived below the poverty line, 95% were Hispanic, and 40% were monolingual Spanish speakers (Cole, 1994; Reimann, 2017). In the late 1980s the company sought approval to build a toxic waste incinerator at the landfill, again without notice to community residents. Once environmental organizations found out, they informed local residents. The incinerator was initially approved; however, the community took legal action and successfully had the decision overturned (Cole, 1994). Even so, community residents remain concerned about their proximity to the hazardous waste landfill as high rates of poor birth outcomes have been observed among residents (Reimann, 2017).

Racial, ethnic and income disparities have also been identified in relation to the locations of Toxic Release Inventory (TRI) facilities, which manufacture, use and/or manage certain toxic chemicals (U.S. EPA, 2021). Downey (1998) studied TRI emissions in Michigan at the state level, for urban areas and for the Detroit Metropolitan Area (DMA). At the state level, TRI

emissions were positively correlated with income and percent black, with race a better predictor of TRI emissions than income. At the urban area level, TRI emissions were negatively correlated with income but were no longer correlated percent black in the linear regression analyses. Within urban areas, income was a better predictor of TRI emissions. For the DMA, TRI emissions were negatively correlated with income, but not with percent black in the linear regression analyses. Lastly, both urban areas and the DMA were analyzed using bivariate regression analyses which found that as TRI emission increased with percent black (Downey, 1998). Pastor et al. (2004) used TRI data, census data, and Geographic Information Systems (GIS) software to evaluate the demographics of census tracts with or near TRI facilities in California. The study concluded that people of color, most notably Hispanics, were disproportionately more likely to live in a census tract with or near a TRI facility (Pastor et al., 2004). Another study (Silva, Hubbard, & Schiller, 2016) in Texas (1999-2006) found that a high number of firms reporting to the TRI database were also located in neighborhoods with a high percent of nonwhite residents. Census tracts with a higher percentage of nonwhite residents were at an increased likelihood of both already having an existing TRI reporting firm and having a new TRI reporting firm locate there, even after controlling for economic factors. Additionally, a TRI reporting firm was more likely to open in or relocate to a census tract that already had a TRI reporting firm and less likely to relocate out of that census tract later. The agglomeration of firms that released toxic chemicals within areas with high percentages of minorities exacerbated environmental justice and environmental health concerns (Silva, Hubbard, & Schiller, 2016) during this time.

Racial disparities in air quality have also been observed. A 1992 study of air quality and demographics in the United States found that African Americans and Hispanics were more likely to live in counties that violated air quality standards for three or more criteria air pollutants

(Wernett & Nieves, 1992). Another study evaluated the TRI's RSEI Scores (Ash, et al., 2009), a value based on the potential human health impacts from exposure to toxic chemicals released by the 10 most toxic TRI firms in the United States. Minority populations were found to have over half of the human health burden from these firms (Ash, et al., 2009). In addition, a 2018 study of particulate matter 2.5 micrometers or less in diameter ($PM_{2.5}$) and particulate matter 10 micrometers or less in diameter (PM_{10}) exposures calculated burden ratios, the proportional burden of each sociodemographic subgroup to the overall population burden (with > 1 indicating higher subgroup burden). For $PM_{2.5}$, the burden ratio was 1.54 for African Americans, 1.20 for Hispanics and 1.35 for people living below poverty. For PM_{10}, the burden ratio was 1.49 for African Americans, 1.23 for Hispanics and 1.35 for people living below poverty (Mikati, Benson, Luben, Sacks, & Richmond-Bryant, 2018).

Environmental factors are the primary causes of chronic diseases (Rappaport, 2012). Scientific evidence suggests that environmental exposures may increase the risk of developing several chronic diseases. For example, associations have been identified between tobacco smoke and ambient and household air pollution with asthma and Chronic Obstructive Pulmonary Disease (COPD); bisphenol A and persistent organic pollutants (POPs) with obesity; ambient air pollution, POPs, bisphenol, and phthalates with type II diabetes; tobacco smoke, ambient air pollution, POPs, and arsenic with hypertension; tobacco smoke, ambient and household air pollution, and POPs with cardiovascular disease; and ambient air pollution, POPs, arsenic, and many carcinogens with cancers (Sly, et al., 2016). Therefore, human exposure to environmental pollutants is one factor known to contribute to population-level health disparities (Bagby, Martin, Chung, & Rajapakse, 2019).

The presence of chronic diseases in pregnant women are of particular concern because they have been associated with several adverse outcomes that increase maternal, fetal and neonatal risks (Sly, et al., 2016; Yu, et al., 2017). A systemic review and meta-analysis of pregnancy in women with chronic hypertension concluded that women with this disease were at an increased relative risk (RR) of adverse outcomes, including superimposed pre-eclampsia (RR=7.7), caesarean section (RR=1.3), preterm delivery (RR=2.7), low birth weight (RR=2.7), neonatal intensive care unit (NICU) admission (RR=3.2) and perinatal death (RR=4.2) (Bramham, et al., 2014). A meta-analysis of pregnant women with pre-gestational diabetes also identified elevated odds of several adverse outcomes including preterm delivery (Odds Ratio (OR)=3.48), caesarean section (OR=3.52), NICU admission (OR=3.92) and neonatal hypoglycemia (OR=26.62) (Yu, et al., 2017). Therefore, both chronic diseases are associated with significant maternal and neonatal morbidity and mortality (Sly, et al., 2016; Yu, et al., 2017).

Medical geographers utilize the model of human ecology, which considers the interactions between humans and their environments, to study the interrelationships among people's individual-level characteristics, behaviors and culture and the social and physical environments in which they live, work and spend time to explain geographic and racial and ethnic disparities in health status. This paper builds on the model of human ecology by introducing syndemic theory, a framework by which to model common risk factors in the environment that lead to synergies or co-occurring diseases within an affected population (Mendenhall, Kohrt, Norris, Ndetei, & Prabhakaran, 2017). Comorbid diseases within a population exacerbates the overall health burden (Singer M., 1994). Syndemic studies report on the influence of upstream (social, political and economic) forces, such as inequality, marginality,

and poverty, on the evolution of disease interactions resulting in clusters within populations (Bulled & Singer, 2016). Syndemic theory has been applied to studies of infectious and non-infectious diseases and studies of health inequities (Singer, 1994; Freudenberg, Fahs, Galea, & Greenberg, 2006; Singer, 2010; Mendenhall et al., 2017; Tsai et al., 2017). Syndemic theory is also useful in identifying effective intervention strategies to address multiple diseases (Mendenhall, Kohrt, Norris, Ndetei, & Prabhakaran, 2017). While syndemic research has evolved out of the medical literature, there is a need to synthesize environmental risks that contribute to multiple diseases.

2.1. Purpose of Study

The purpose of this study is to advance the field of medical geography by incorporating ecosyndemic theory into the human ecology model. This study proposes the application of ecosyndemic theory for studies of environmental health justice in place-specific contexts. This paper focuses on the pollution landscape, a result of upstream structures, which creates conditions that lead to toxic exposures, which may lead to an array of common diseases in populations, herein referred to as an ecosyndemic. An understanding of the synergies between the structural and social setting, individual characteristics and behaviors and pollutants that lead to an increase in disease burden and environmental health injustices as a result of such structures can help to target environmental and medical interventions to alleviate the syndemic. A review of the syndemic literature is provided that leads to this paper's presentation of the ecosyndemic.

2.2. Building Blocks to Ecosyndemic Theory

2.2.1. Syndemic Theory

Wallace (1988) first introduced the concept of synergies in his evaluation of the synergistic patterns between urban decay, intravenous drug use and the diffusion of human

immunodeficiency virus (HIV) and acquired immunodeficiency disease (AIDS) in the Bronx, a borough of New York City, during the mid- to late- 1970s. As a result of economic restructuring in the early 1970s, the Bronx experienced a major economic decline as industries relocated oversees and to southern states in the country, resulting in high unemployment, which led to severe urban decay characterized by poverty and increased homelessness due to a short supply of low-income housing. This resulted in higher crime rates and increased drug use. In response to a city-wide declining economy and social and physical infrastructure, the Bronx implemented a policy called "planned shrinkage" which involved reducing budgets to fire departments, which led to fires in houses that were abandoned and further increased urban decay—a process that began with a few deteriorating structures and gradually over time it increased to large-scale abandonment (contagious urban decay). Wallace (1988) referred to this as a contagious process that continued to deteriorate the urban area. This process primarily occurred in overcrowded, poor and minority areas. Overcrowded areas were more susceptible to fire damage, which further worsened urban decay by encouraging landlord abandonment and out-migration of residents. Those experiencing forced migration were mostly poor and minority groups, who moved from the South-Central Bronx to the West and Northwest Bronx. Wallace (1988) explained how the housing destruction influenced the geography of drug use and AIDS. The areas with high concentrations of overcrowded housing units had high numbers of drug related deaths and the areas with the highest number of drug related deaths also had the highest numbers of AIDS deaths. The city's "planned shrinkage" through fire service reductions exacerbated urban decay in the South Bronx which forced the migration of populations, including intravenous drug users who were predominantly concentrated in poor communities in the South-Central Bronx, into

surrounding areas. This then activated the geographic dispersion of HIV and subsequently AIDS throughout the Bronx (Wallace R., 1988).

A follow-up paper by Wallace and Wallace (1990) used the term ‘synergies’ to describe the interactive features between planned shrinkage, contagious urban decay and social disintegration in New York City that contributed to the rise in HIV and decline in public health. Specifically, the city’s planned shrinkage worsened housing destruction and thus, overcrowding in largely poor and minority communities, which forced people to migrate to surrounding areas. When people migrated, they lost their community ties and social networks. The study found that rates of various health conditions, such as tuberculosis, salmonella, and gonorrhea were highest in areas with overcrowded housing. Drug use, homicide and suicide rates also rose. As disease burden increased, life expectancy fell. Furthermore, stressors imposed upon pregnant women increased the rates of low-birth weight resulting in infant mortality particularly among nonwhites (which spread from South Bronx to surrounding areas) increased during the process of contagious urban decay. Wallace and Wallace (1990) were innovative because they evaluated all of these health conditions and health indices together as synergies, resulting from contagious urban decay, rather than examining each condition separately. Doing so allowed for them to observe how the city’s housing destruction and the forced migration and community disintegration that followed resulted in severe impacts to public health and well-being in poor neighborhoods (Wallace and Wallace, 1990).

Building upon this concept, medical anthropologist Merrill Singer (1994) introduced the term syndemics in the mid-1990s as the situation that occurs when large scale structures lead to and reinforce the clustering of diseases and disease interactions (Singer M., 2011; Tsai, Mendenhall, Trostle, & Kawachi, 2017). Singer (1994) discussed the synergies of AIDS among

the urban poor in the United States and offered a new perspective for social scientists conducing AIDS research. Singer recognized that the terms endemic and epidemic did not sufficiently characterize the health issues among the urban poor, which are strongly influenced by large-scale social, political, and economic factors. The term syndemics was introduced in order to better describe AIDS in terms of the broader health crisis among the urban poor. For example, poverty contributes to inadequate nutrition and chronic stress, which leads to a weakened immune system, which then increases one's susceptibility to infection. In addition, broad scale socio-economic conditions increase the likelihood of substance abuse among urban poor. Substance abuse increases one's risk of HIV as well as other sexually transmitted infections through the sharing of needles, which weaken the immune system, resulting in a greater susceptibility of contracting other diseases. Singer showed how AIDS was a part of the inner-city syndemic, noting the strong interrelationships among structural conditions and health conditions and how it was leading to a greater health burden among the inner-city populations (Singer, 1994).

Freudenberg et al. (2006) revisited how New York City's 1975 political and fiscal crisis led to a syndemic among inner-city poor. In response to the fiscal crisis, the city decided to make cuts to city services, including health services and hospitals, addiction treatment resources and public safety. The city also increased taxes and transferred some responsibilities to the state government. Around this same time, federal funding for low-income housing was significantly reduced. The paper discussed how the policy decisions that were implemented in response to the economic and social issues and changes led to increased rates of tuberculosis, HIV infection and homicide in New York City (Freudenberg et al., 2006).

Mendenhall et al. (2017) spoke to how syndemic theory can be used to understand and resolve health inequities, which are more common among low-income populations such as type 2

diabetes and its comorbidity with HIV in Kenya, tuberculosis in India and depression in South Africa. There are both contextual and biological factors that influence disease burdens. Socioeconomic and political conditions can lead to an adverse health condition among the population living within that setting, and the presence of one disease can make individuals more vulnerable to another disease. For example, Mendenhall et al. (2017) found that poverty increases the risk for depression and diabetes, depression and diabetes share biological interactions, and people with diabetes are at an increased risk for tuberculosis. The authors also note the difficulties in treating syndemics as health care generally focuses on treating specific conditions, so a patient's diabetes and depression might not be considered together. The authors suggest medical care could be optimized if co-occurring diseases and their interactions were considered together and treatment for multiple diseases were integrated (Mendenhall et al., 2017).

Syndemic theory provides a biosocial framework for understanding disease and why they tend to cluster among particular populations by assessing the structural and upstream forces that induce these patterns (Singer, Bulled, Ostrach, & Mendenhall, 2017). It seeks to understand the dynamic interactions between individuals' health conditions and individuals' contextual settings, which lead to the occurrence of comorbid diseases within a population and to identify intervention strategies (Mendenhall, Kohrt, Norris, Ndetei, & Prabhakaran, 2017). A syndemic risk factor can be biological, physical, social, political, economic or environmental (Singer M., 1994; Singer, Bulled, Ostrach, & Mendenhall, 2017). The risks factors can interact with one another and share synergistic relationships, and so communities with multiple risk factors are more inclined to have a higher burden of disease (Tsai et al., 2017). Syndemic investigation

focus on those risk factors that may be worsening the independent and combined health conditions within a population (Singer M., 1994; Singer, Bulled, Ostrach, & Mendenhall, 2017).

2.2.2. Ecosyndemics

There has been a growing recognition that ecosystems, influenced by humans in ways that generate both intentional and unintentional changes, can mediate the environment and human health relationship (Singer M., 2016). Ecosyndemics, which stems from syndemics with a focus on the environment emerged to fill this gap (Singer M., 2010). An ecosyndemic is characterized by disease clustering that occurs as a result of exposure to a set of environmental conditions and can be situated within broader socioeconomic contexts (Ramirez & Lee, 2019; Singer M., 2011b). It therefore offers a framework by which to assess disease clustering and cross-level interactions (e.g. individual behaviors within the context of environmental conditions and social structures), which are of public health importance (Singer M., 2011b). Since its introduction, ecosyndemic theory has mostly been used to study climate-induced hazards and human health, including infectious diseases, respiratory illness and psychological health (Singer M., 2010; Ramirez, Lee, & Grady, 2018; Ramirez & Lee, 2019; von Glascoe & Schwartz, 2019).

Singer (2010) provided a theoretical discussion of how climate change is expected to lead to a substantial increase in syndemics. Increased global temperatures accelerate the metabolic rate of certain species, such as mosquitos, which requires the female mosquitoes to feed more frequently, thereby increasing the likelihood of vector-borne disease transmission. Increased temperatures and deterioration of the ozone layer can lead to greater ultraviolet-B radiation exposure and more frequent bouts of heat exhaustion. Heath exhaustion is a stressor among humans, which reduces individual's ability to respond to diseases and may exacerbate the effect of current chronic conditions on health, in particular diseases associated with the heart and lungs.

Additionally, ultraviolet-B radiation can cause genetic changes in microorganisms that can lead to pathogen resistance. Singer (2010) therefore, concludes that climate change will have direct, indirect, and multiple impacts on human health. Singer argues that more studies are needed to examine more specifically why syndemics emerge, the interaction pathways between different diseases and health conditions, how climate change will directly and indirectly impact human health and how public health policies and programs can address these features of syndemics including the social conditions that foster them to improve public health (Singer, 2010). Singer (2013) further argues that anthropogenic environmental changes, such as those that contribute to global warming, can lead to an ecosyndemic such as respiratory disease comorbidities and disease interactions. Additionally, respiratory health ecosyndemics was placed in a social context to discuss the roles of humans in environmental degradation, the social structures driving and minimizing resistance to environmental degradation and populations expected to be most impacted, including those experiencing social inequalities and environmental injustices as discussed later in this paper.

Ramírez, Lee & Grady (2018) applied an ecosyndemic approach to evaluate cholera and other multi-infectious disease risks in Peru during the 1997 El Niño. The study used climate, social and epidemiological data to create an ecosyndemic index. Many areas of Peru suffered from cholera and multiple infectious disease outbreaks over several weeks during the period of El Niño and urbanization and disaster impacts were found to be correlated with the ecosyndemic index. Ecosyndemic risk and social vulnerability in Guatemala during the 2014-2016 El Niῆo were explored by Ramírez & Lee (2019) using GIS. An El Niño index, health data on infectious diseases and social vulnerability data were analyzed. The study identified clusters of infectious diseases associated with El Niño. Additionally, ecosyndemic risk increased with social

vulnerability. Ramírez & Lee (2020) offered important insights into the emergence of COVID-19 in Latin America, a region already experiencing an ecosyndemic, and how COVID-19 exacerbates the existing public health burden. They suggest COVID-19 be examined within the context of ecosyndemic vulnerability to best respond to the multi-infectious diseases that exist within the region. Tallman et al. (2020) investigated two development cases studies, a highway in Peru and a hydroelectric dam in Brazil, using an ecosyndemic framework. The health and well-being of community members in both case studies were influenced through ecological, social and biological processes that modified the conditions in a way that led to disease clustering. The authors suggest that synergistic diseases, such as psychologic stress, vector-borne illnesses and sexually transmitted infections, may emerge in communities undergoing large development projects.

Von Glascoe & Schwartz (2019) discussed the respiratory syndemic occurring among immigrant children living in the San Joaquin Valley, CA. The study identified structural vulnerabilities, structural violence and ecosyndemics as creating the conditions that foster childhood asthma and other respiratory illnesses. Children in the San Joaquin Valley are exposed to multiple environmental hazards brought about through structural determinants that has created an environmental health injustice among this population, which is further exacerbated by social and structural factors such as inadequate access to health care (von Glascoe & Schwartz, 2019).

Ecosyndemic theory offers a way to examine the environmental conditions that promote disease clustering and interactions, while also considering the broader socioeconomic structures (Singer, 2011b; Ecosyndemics, 2011b). It is an effective frame for identifying the upstream factors that are inducing environmental injustices and their subsequent adverse health outcomes, which can in turn highlight areas for intervention strategies (Mendenhall et al., 2017). Combined

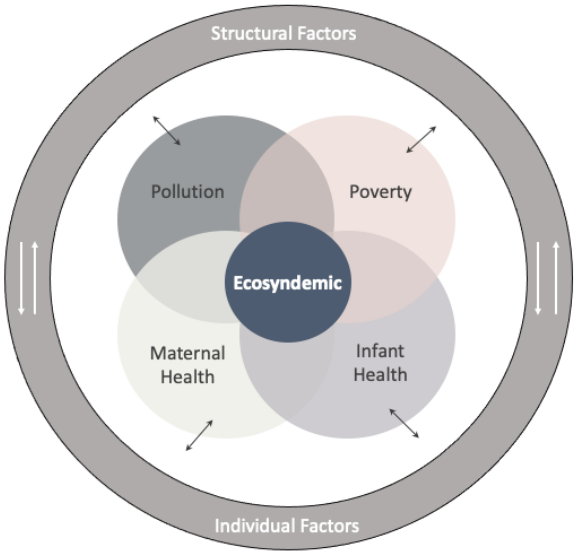
with multi-level analysis, it can help investigate how exposures to multiple pollutants, a hazard ecosyndemic, stem from social, economic and political decisions and if exposure to multiple pollutants lead to an environmental health injustice ecosyndemic. This paper builds on the ecosyndemic theory, proposing its application be expanded from climate-induced hazards to environmental pollution hazards and how exposures vary between and within population groups to develop a richer theoretical framework for examining environmental health justice. In particular, the ecosyndemic framework provides an ideal structure by which to study health and medical geography. An example framework is provided in the section that follows.

2.3. Ecosyndemic Application in Environmental Health Justice Studies

Various methods have been used to study syndemics (Shikar et al, 2021). Here a framework to incorporate health and medical geography methods with the ecosyndemic theoretical approach through studies of environmental health justice using a human ecology framework is proposed. The research should (a) begin with an investigation of the environmental setting of the place that is of concern for human health. For example, the concern may be regarding pollution from TRI facilities, which could later be studies in relation to pregnancy health. Geographic methods and tools, such as GIS, can be employed to evaluate spatial and temporal patterns of TRI facility emissions and map rates of pregnancy risk factors and adverse birth outcomes. The research should next (b) set the polluted environment within the socioeconomic context of the place by investigate the overarching socioeconomic structures that led to the placement of the TRI facilities or the movement of residents into communities in proximity to those facilities, as well as an equity assessment. In this example, the pollution landscape may result from weak environmental regulations and limited oversight and enforcement by environmental agencies, which then allows industries to emit higher levels of

pollutants at the cost of environmental degradation. The industries take advantage of weak regulations and negotiable fines and oversight to maximize efficiency and economics over social responsibility. Finally, (c) the research should evaluate the overall health burden of the place. Exposure to environmental toxicants released by polluting industries may have direct impacts on maternal health and birth outcomes or may have indirect impacts by interacting with low socioeconomic conditions (e.g. moderating or mediating the effects of pollutants) on maternal and infant health (Padula, et al., 2018). For example, maternal exposure to the pollutants may directly increase the risk of adverse birth outcomes. In addition, living in poor areas that are highly polluted (moderator) may increase women's risk of pregnancy risk factors, such as hypertension, which then acts as a mediator on birth outcomes (Grady, 2006; Grady & Ramírez, 2008). Therefore, the polluted environment, driven by broader socioeconomic structures, may create an ecosyndemic among women though increased rates of pregnancy risk factors and adverse birth outcomes. The conceptual framework of an ecosyndemic as it applies to the above example is illustrated in Figure 2-1.

Figure 2-1: Environmental Health Justice Ecosyndemic Conceptual Framework



With the ecosyndemic framework, the causes, drivers, and health consequences of the polluted landscape are identified. In this example, regulatory, political and economic structures are creating a setting that leads to a polluted landscape, which is subsequently influencing pregnancy health and leading to elevated rates of adverse birth outcomes in this area. Additionally, the social structures may be further exacerbating health consequences among low-income mothers who may experience higher levels of pollution exposures, which this paper terms *environmental health justice ecosyndemic*. Therefore, the individual mothers are nested within the biophysical environment which is further nested within the social, economic and political structures of that place. The application of health and medical geography methods can build on ecosyndemic theory by offering improved understandings of factors influencing health outcomes which can lead to improve environmental regulatory and public health policies and practices which address the most important factors causing the ecosyndemic.

2.4. Conclusion

Ecosyndemic theory provides a framework by which to examine environmental conditions that lead to disease clustering, which often result from environmental and social injustices. This study builds on the existing frame of ecosyndemics by extending it from a largely narrow focus on climate-induced environmental changes to the environmental pollution landscape and chemical exposures that may lead to the clustering of diseases and greater health burdens. The theory ties together the environmental, social and biological contexts and multi- and cross-scale dynamics between and among these that influence human health. The case study depicted also described how ecosyndemic theory can be used to examine a syndemic at multiple levels, such as the environmental hazard (multiple pollutant exposures), the social environment and the outcome(s) (multiple health conditions). Ecosyndemics should be incorporated with the human ecology model in medical geography to investigate environmental health injustices to identify and improve understandings, which may reduce inequities and improve public health. Additionally, studies of ecosyndemics are already set in the context of place, core to geographic studies. Medical geographers can implement ecosyndemic theory to assess the disease burden of populations and subpopulations and evaluate the synergies between the structures, biophysical environment and health, and between the various health conditions. Ecosyndemics, therefore, advances the existing theoretical approaches used by health and medical geographers, offering new perspectives to better understand disease burdens and identify environmental health injustices. At the same time, the distinct perspectives and tools used by geographers can further advance the field of ecosyndemics to improve the health of those most disadvantaged. For example, geospatial technologies such as remote sensing and GIS can be used to identify and map environmental hazards and diseases, detect overlapping environmental and social hazards,

evaluate spatial and temporal patterns of diseases in populations and identify disease clustering and disease risk factors.

Ecosyndemic theory presents an opportunity to build upon the theoretical approaches used by medical geographers and offers new perspectives for environment-human health research. The three steps in applying syndemic theory include: (1) examine the environmental setting of the place; (2) consider the polluted environment within the socioeconomic context by assessing the large-scale structures that led to the location of polluting industries or the movement of residents into communities with these facilities, as well as an equity assessment; and (3) assess the overall health burden of the place or related to a particular outcome (i.e. maternal health). For each step, the individual and contextual factors must be considered (Mendenhall et al., 2017). The application of syndemic theory can allow health and medical geographers to provide deeper understandings of health by examining synergies, identifying inequities and evaluating the overall health burden of a place. These are useful in identifying effective interventions to improve public health. The following chapter presents a hazard assessment of TRI sites in Michigan to identify places that contribute to potential human health risk disparities.

Chapter 3. HUMAN HEALTH RISKS FROM TOXICS RELEASE INVENTORY CHEMICAL HAZARDS: RACIAL AND ETHNIC DISPARITIES IN MICHIGAN, 2008-2017

Abstract

The Risk-Screening Environmental Indicators model estimates toxicity-weighted concentrations based on human health risks from modelled exposures to Toxic Release Inventory (TRI) chemicals. The spatial and temporal relationships between census tract level toxicity-weighted concentrations and minority and low-income residents were investigated to address environmental injustices in Michigan. This study (1) examined the TRI facilities and chemicals emitted that contributed the most to elevated toxicity-weighted concentrations in Michigan; (2) mapped annual toxicity-weighted concentrations from 2008 to 2017; and (3) documented the racial and ethnic composition and income levels of residents living in tracts with exceedingly high toxicity-weighted concentrations using a bivariate Local Moran's I. Findings indicate that 80.1% of the highest toxicity-weighted concentration tracts were in the Detroit and Grand Rapids urban areas. African Americans, Hispanics and residents living near and below poverty were most likely to live in the highest toxicity-weighted concentration tracts. Though, race and ethnicity were more important than income. The urban-level proportion of African Americans living in these tracts persisted over time in Grand Rapids and Detroit, while the urban-level proportion of Hispanics living in these tracts increased over time in Detroit demonstrating an emergence of risk. These findings suggest that the two largest urban areas in Michigan may be experiencing environmental health justice ecosyndemics among these vulnerable population groups.

3.0. Introduction

The Emergency Planning and Community Right-to-Know Act (EPCRA) of 1986 is a federal United States law that created the Toxic Release Inventory (TRI), a database that collects and reports on the release, management, and off-site transport of chemical toxicants for humans to be used administratively and for public health purposes. Reporting is mandatory for facilities in certain industrial sectors that have 10 or more full-time employees and manufacture more than 25,000 pounds of TRI chemicals or use over 10,000 pounds of any TRI chemical in their operations (U.S. EPA, 2017a). Numerous studies show that TRI sites are inequitably distributed in high minority and low-income communities, whose exposures may contribute to poorer health outcomes and racial and ethnic health disparities (Ash, et al., 2009; Bullard, 2002; Moseley et al., 2014; Pastor et al., 2004; Ringquist, 2005; Silva et al., 2016) a phenomenon referred to as environmental injustice. The pollution exposures may interact with the social environment and individual factors which may contribute to the creation of an ecosyndemic among these minority and low-income populations more commonly exposed. Environmental justice studies generally support discriminatory citing theory, meaning that TRI facilities are likely to locate in high-minority and poorer communities, rather than the move-in hypothesis, where minority or poorer people move into areas containing TRI facilities (Been and Gupta, 1997; Oakes et al., 1996; Pastor et al., 2016; Silva et al., 2016). While these and other studies have used TRI facility locations to estimate human chemical exposure (Choi et al., 2006; Legot et al., 2010; Pastor et al., 2004; Perlin et al., 1995) these studies utilize relatively simple spatial measurements. Examples of these traditional spatial measurements include the presence or absence of a TRI facility within a defined area, the measured distance between a TRI facility and a community or the use of a circular buffer around a TRI facility to capture the population within who is

potentially exposed. These approaches assume an equal output of the chemical hazard and/or an equal exposure among the people within proximity to the TRI facility (Conley, 2011). The use of area and distance measures and buffers can also lead to the Texas sharp-shooter effect and modifiable area unit problem (O'Sullivan and Unwin, 2010), thereby introducing types I and II error in individual and population exposure estimates.

The Risk-Screening Environmental Indicators (RSEI) model was created by the United States Environmental Protection Agency (U.S. EPA) to address the limitations of distance-based measures, by creating a continuous index of RSEI toxicity-weighted concentrations and RSEI Scores (U.S. EPA, 2018a; Chakraborty et al., 2011; Ogneva-Himmelberger et al., 2015). RSEI toxicity-weighted concentrations incorporate information on stack dimensions and direct and fugitive air releases, direct water releases, transfers to publicly owned treatment works, on-site land releases and transfers to offsite incineration. They also include the type(s) of chemical(s) emitted, quantity released, the chemical(s) fate and transport through the environment, population-exposure pathways, dosage(s) of exposure and estimated chemical toxicity. Chemical toxicity is based on the route of exposure and the expected chronic human health impact(s) according to the age-sex structure of the population at the census-tract level (U.S. EPA, 2018a). Higher tract-level RSEI toxicity-weighted concentrations indicate higher toxicity risk from TRI chemical exposure. There are 33 chemical categories within which there are 767 chemicals incorporated into the calculation of RSEI toxicity-weighted concentrations (U.S. EPA, 2021). RSEI Scores are calculated using the same modelling and exposure estimates as the RSEI toxicity-weighted concentrations, however, unlike the RSEI toxicity-weighted concentrations, the RSEI Scores incorporates the size of the population exposed—a population weight in its calculation.

The RSEI model has been used for studies of environmental justice (Abel et al., 2015; Ash et al., 2009; Lewis and Bennett, 2013; Shapiro, 2005). Abel et al. (2015) utilized the RSEI model in addition to socioeconomic and land use characteristics to define an environmental health risk-landscape at the census tract level in Seattle, Washington. Industrial air polluters with the greatest inhalation exposure risks were located in tracts of lower socioeconomic status, while lower inhalation exposure risks were identified in gentrified areas (Abel et al., 2015). Ash et al. (2009) utilized the Scores to identify the 10 most toxic TRI industries in the United States and found minority populations had the highest burden of chronic health risks associated with these facilities (Ash, et al., 2009). Lewis and Bennett (2013) utilized RSEI Scores and facility locations to identify areas in four New York counties, Niagara, Nassau, Kings, and Suffolk, which should be considered as environmental justice designations (Lewis and Bennett, 2013). Shapiro (2005) utilized the RSEI Scores to study racial and community level differences in chronic health risk in the United States between 1996 and 1998. This study found an overall decline in mean RSEI Scores (33.4 to 16.3) and a decline for sub-groups including Hispanics vs. non-Hispanics (-42.6%), Asians vs. non-Asians (-67.1%), and college-educated residents (-40.0%). Mean RSEI Scores increased for African Americans vs. non-African Americans (49.8%) during the two-year study time period (Shapiro, 2005).

While these four studies evaluated the RSEI Scores to document environmental injustice in their respective study locations, a different understanding of potential chronic health risks from TRI chemical exposures may be acquired by evaluating the RSEI toxicity-weighted concentrations, which do not adjust for population size and instead focus on the toxicity-risk from TRI chemical exposure. For example, an area may have a low RSEI Score but a high RSEI toxicity-weighted concentration if the population is small but exposed to either a highly toxic

chemical(s) or to a high volume of chemicals. Alternatively, an area may have a high RSEI Score but a low RSEI toxicity-weighted concentration because although the toxicity risks might be low, the population exposed is large. The relationship between the RSEI Score and RSEI toxicity-weighted concentrations may vary along a continuum with the primary driver of differences being the population size. There is a need for further research utilizing the RSEI toxicity-weighted concentrations to understand its effect on population groups within geographic areas, such as urban or rural that could not be captured by adjusting for overall population size.

Previous cross-sectional studies also focused on one time period or compared changes between two years. There is also a need to investigate RSEI toxicity-weighted concentrations over longer time periods to evaluate change and to disentangle changes in toxicity levels vs. population composition changes. Additionally, none of the studies identified the top TRI chemicals in their study areas and only two (Ash et al., 2009; Lewis and Bennett, 2013) studies identified the top TRI facilities in their study areas. There remains a need to identify the top TRI facilities and TRI chemicals in Michigan to identify which facilities and chemicals contribute the most to elevated human health risks.

3.1. Purpose of Study

This research will (1) examine the TRI facilities and chemicals emitted that contributed the most to toxicity risks from TRI chemical exposures using the RSEI Scores in Michigan from 2008 to 2017; (2) visualize the spatio-temporal patterns of annually reported RSEI toxicity-weighted concentrations at the census tract level in Michigan from 2008 to 2017; and (3) identify tracts with high RSEI toxicity-weighted concentrations and investigate the racial and ethnic composition and income levels of people living in those tracts and how they change between two census time periods: 2008-2012 and 2013-2017. Michigan is studied because its urban areas are

highly segregated by race and prior studies have shown evidence of environmental injustice (Linc Up and Detroiters Working for Environmental Justice, 2019; Moody and Grady, 2017). This study will build on these previous studies by utilizing the RSEI toxicity-weighted concentrations to study geographic trends over time and in relation to population characteristics during two time periods in Michigan.

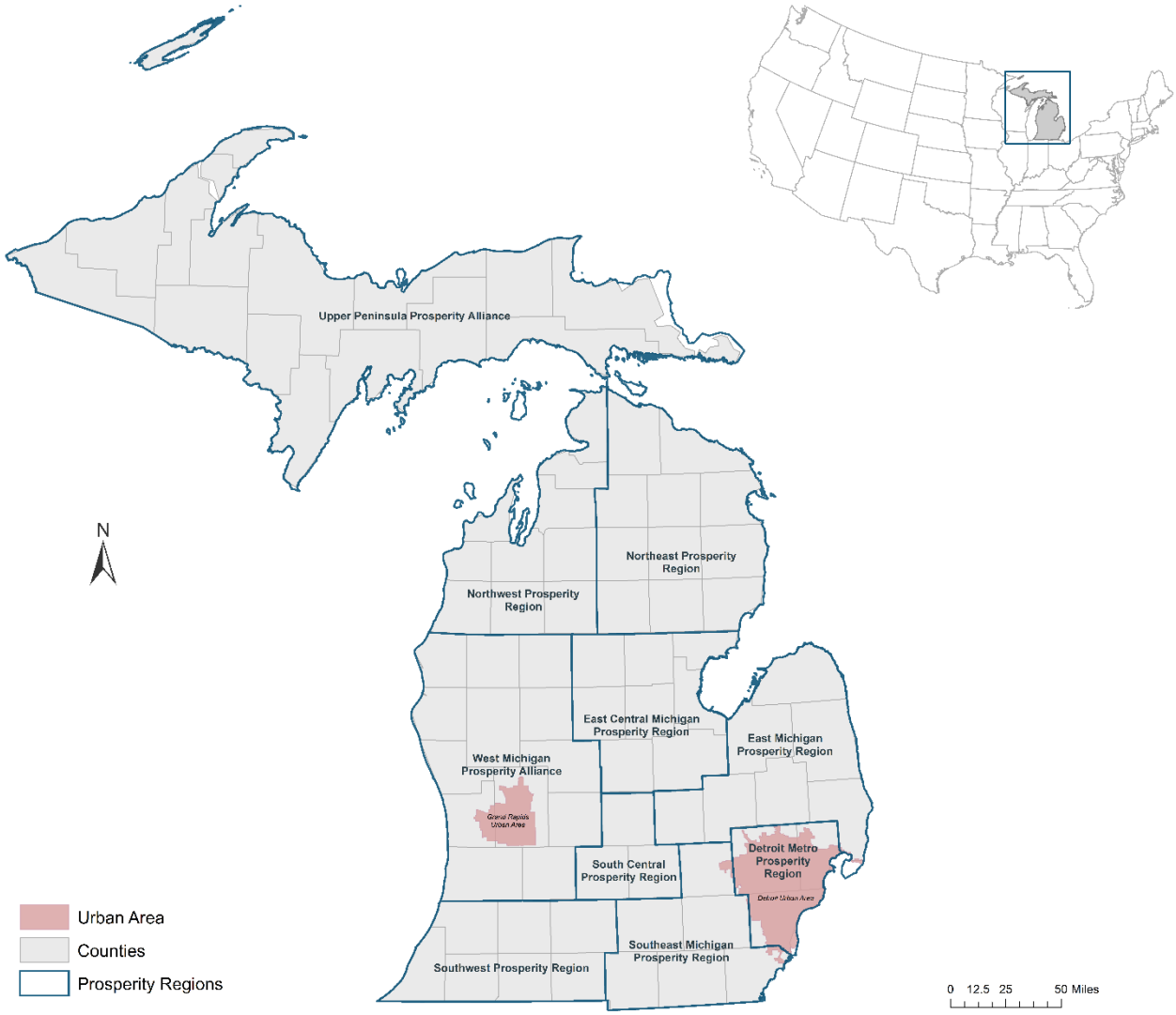
3.0.Study Area

Michigan is a Rust Belt state with 58,110 square miles of land area, 1,305 square miles of inland water, and 38,575 square miles of Great Lakes water (State of Michigan, 2019) (Figure 3-1). Michigan is commonly known as the Great Lakes State because it borders four of the five Great Lakes, which together contain one fifth of the world's supply of fresh surface water (Michigan Economic Development Corporation, 2021). The state has 83 counties on two peninsulas (Upper and Lower). Currently, the core industries in Michigan include advanced manufacturing, medical device technology, mobility and automotive manufacturing, professional and corporate services, tech, and engineering, design and development (Michigan Economic Development Coporation, 2021). To strengthen Michigan's economy, the state established the Regional Prosperity Initiative in 2013 which identified and formed ten regions based on geography and economics. The Regional Prosperity Initiative encourages local partnerships between private, public, and non-profit groups to promote the economic prosperity of the state and to improve quality of life (Michigan Economic Development Corporation, 2021).

Michigan is the 22nd largest state by area and the 10th most populous state in the United States (U.S. Census Bureau, 2020). Between 2000 and 2010 Michigan underwent a 0.55% decline in population, but then experienced a 1.04% increase in population between 2010 and 2019 (U.S. Census Bureau, 2021). Although there was modest population growth, there are some

concerning trends. The state has had fewer births with a 3.19% decline in birth rates between 2012 and 2019. The median age of those leaving the state is just under 30 years old. They also tend to be more educated (45% had a college degree). Overall, the natural increase rate fell by 43.88% between 2012 and 2019 (Wilkinson, 2020).

Figure 3-1: Michigan



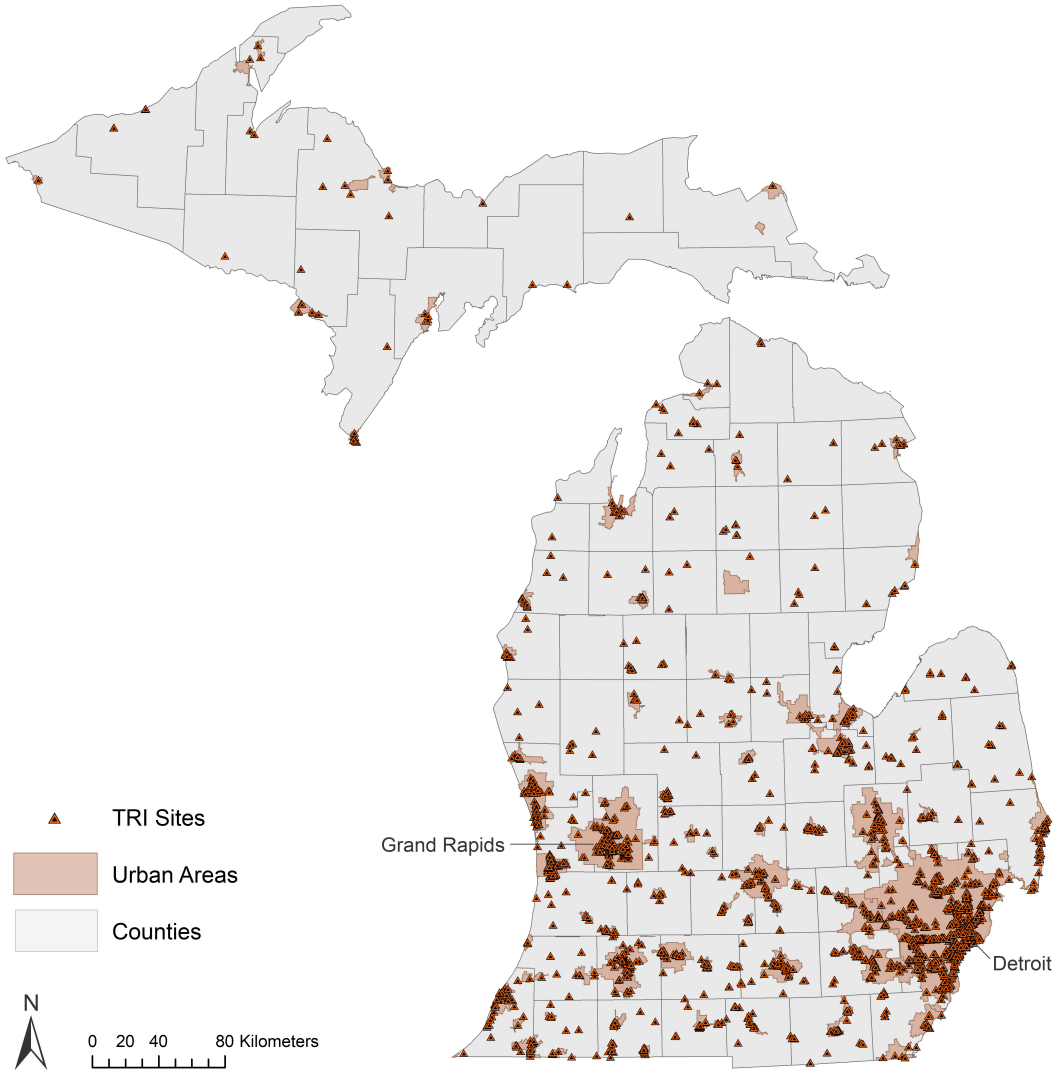
Michigan's population is 74% non-Hispanic or Latino White, 14% non-Hispanic Black or African American and 5.3% Hispanic or Latino. The poverty rate is 13% and the percent of the

population under the age of 65 years that is without health insurance is 6.9% (U.S. Census Bureau, n.d.). Approximately 82% of Michigan residents live within a metropolitan area (Mack, 2019) with Detroit and Grand Rapids the most populous cities in the state, respectively, yet their socioeconomic characteristics differ. Detroit's population declined by 6.1% between 2010 and 2019. Its median age is 34 years (U.S. Census Bureau, 2021). Fifteen percent of residents have a bachelor's degree or higher; median household income is $30,894; the poverty rate is 35%; and 9.6% of residents under the age of 65 years are without health insurance. In contrast, Grand Rapids grew by 6.9% between 2010 and 2019 (U.S. Census Bureau, n.d.). Its median age is 31 years (U.S. Census Bureau, 2021) and 36% of residents have a bachelor's degree or higher (U.S. Census Bureau, n.d.). The median household income is $50,103; 20.4% of residents live in poverty; and 9.5% of the population less 65 years old is without health insurance (U.S. Census Bureau, n.d.).

Michigan's numerous TRI facilities are dispersed throughout state (Figure 3-2). Although TRI chemicals are a concern for human health, no previous studies have investigated spatial or temporal patterns of modelled TRI chemical exposures risks in Michigan. This dissertation evaluates TRI chemicals in Michigan in relation to environmental justice and environmental health.

Michigan is in the Midwest region of the United States (EPA Region 5) and its land is surrounded by 22 percent of the world's fresh water (U.S. EPA, 2019a). There are eight large, urbanized areas (population ≥ 200,000), including Ann Arbor, Detroit, Flint, Grand Rapids, Kalamazoo, Lansing, South Bend, and Toledo (State of Michigan, 2017). Michigan had 1,048 TRI sites operating during 2008 to 2017 the study period.

Figure 3-2: TRI Sites in Michigan, 2008-2017



The total population in 2017 was 9.973 million, a 0.26% decrease from 2008. During 2008-2012, Michigan's population was approximately 13.9% African American, 76.5% White, and 4.4% Hispanic or Latino. Based on the ratio of income to poverty level, 20.8% of the population lived near and below the poverty level (U.S. Census Bureau, 2012). Between 2008-2012 and 2013-2017 there was a 2.1% decrease in African Americans, 1.3% decrease in Whites, 9.1% increase in Hispanics or Latinos, and 0.7% decrease in the population living near and

below the poverty level (U.S. Census Bureau, 2017). In summary, there were minimal changes in the composition of the population excluding a slight increase in the Hispanic population over these two time periods. There was, however, substantial geographic variation in the composition of the population as further described below.

3.2. Materials and Methods

3.2.1. RSEI Toxicity-Weighted Concentration Data

This study used the RSEI model developed by the U.S. EPA's Office of Pollution Prevention and Toxics version 2.3.7. Based on the specific calculations for the toxicity weights, modeling for each type of release, and population information, the RSEI scores and RSEI toxicity-weighted concentrations are calculated as follows:

$$\text{RSEI Scores} = \text{Surrogate Dose} \times \text{Toxicity Weight} \times \text{Population}$$

$$\text{RSEI toxicity-weighted concentrations} = \text{Surrogate Dose} \times \text{Toxicity Weight}$$

The surrogate dose is the quantitative estimate of exposure potential. Surrogate dose estimates include data on pathway-specific chemical emissions, physicochemical properties and site-specific characteristics, when available, to estimate ambient concentrations in the environmental medium in which the chemical was released. The surrogate dose is then estimated by combining the ambient concentration with human exposure assumptions and the age and sex structure of the exposed population. Toxicity weights are chemical specific and exposure-route specific. As the potential for a chemical to cause adverse chronic human health effects increases, the chemical toxicity weights increase. Population refers to the size of the potentially exposed population, derived from decennial census data (U.S. EPA, 2018b).

RSEI Scores for the most toxic TRI facilities and TRI chemicals in Michigan were obtained from the EPA's Easy RSEI Dashboard (U.S. EPA, 2019b). The chemicals with the five

highest RSEI Scores were available at the county level. RSEI toxicity-weighted concentrations are not available on the Easy RSEI Dashboard, rather they are provided in the aggregated microdata shapefiles. Aggregated microdata shapefiles for all census tracts in Michigan for the TRI Core01 chemical list for years 2008 through 2017 were retrieved from the Amazon Web Services server (http://abt-rsei.s3.amazonaws.com). The locations of TRI sites with modelled releases for the years 2008-2017 were obtained by linking the TRI facility list from the EPA's Easy RSEI website (https://edap.epa.gov/public/extensions/EasyRSEI/EasyRSEI.html) with the facility data from EPA's data dictionary webpage (https://www.epa.gov/rsei/rsei-data-dictionary-facility-data) (U.S. EPA, 2019c, 2019c).

3.2.2. Population and Geographic Data

This study used the American Community Survey (ACS) census tract level 2012 and 2017 5-year estimates (U.S. Census Bureau, 2012, 2017). The census tables downloaded include Hispanic or Latino origin by race (non-Hispanic African American, non-Hispanic White and Hispanic ethnicity) and ratio of income to poverty levels of which the percentage of near and below poverty levels in the population were studied. The geographic boundary files used in this study were obtained from the state of Michigan's geographic information system (GIS) database, including the administrative boundaries of counties (n=83), adjusted urban areas (n=77) and cities (n=280) (State of Michigan, 2019). The adjusted urban areas were classified as large, urbanized areas (population $\geq$ 200,000), small urbanized areas (population 50,000 to 199,999), small urban areas (population 5,000 to 49,999) and rural areas (population < 5,000). Census tracts did not fall uniformly within the urban boundaries; therefore, population weighted centroids were calculated using the census blocks aggregated to the census tract level to identify the census tracts whose population weighted centroids fell within these urban boundaries. The

Michigan shapefiles were projected using the NAD 1983 Michigan GeoRef (Meters) coordinate system.

3.2.3. Analysis

Knowing which facilities and chemicals contributed the most to higher toxicity risk from TRI chemical exposures is important for pollution reduction management. Therefore, the top five facilities and top five emitted chemicals, including their facility locations and concentrations, were identified for this study. To visualize the RSEI toxicity-weighted concentrations over space and time in Michigan, choropleth maps were created using census tracts and a quantile classification scheme with seven classes beginning with the 2008 base year from which all subsequent years followed, 2008 to 2017 in ArcGIS v. 10.6 (ESRI, 2020).

To assess the spatial relationships between high RSEI toxicity-weighted concentration census tracts and racial, ethnic and near and below poverty groups, a bivariate spatial autocorrelation approach was used (GeoDa Software 1.14). The bivariate Local Moran's I (Anselin, 2020) captures the relationship between the value of one variable at location i, x_i (here, the RSEI toxicity-weighted concentration of a census tract) and the average of the neighboring values for another variable (here, the percent African American, or percent White or percent Hispanic to assess the relationship between risk exposures and vulnerability by race, or percent near and below poverty level to assess potential interactions with the social environment) -i.e., its spatial lag $\sum_j w_{ij} y_j$. The statistic is the product of x_i with the spatial lag of y_i $(i.e. - \sum_j w_{ij} y_j)$, with both variables standardized, such that their means are zero and variances equal to one:

$$Ii^B = cx_i \sum_j w_{ij} y_j,$$

where w_{ij} are the elements of the spatial weight matrix (a queen spatial weight matrix was applied). The Moran's I value range from -1 to +1 where -1 indicates perfect dispersion, 0

indicates a random spatial pattern and +1 indicates perfect correlation. The output included census tracts with (1) high RSEI toxicity-weighted concentrations and high percentage of the race/ethnic and poverty variable of interest (High-High) and (2) low RSEI toxicity-weighted concentrations and a high percentage of the race/ethnic and poverty variable of interest (Low-High). Scatterplots were also created to visualize these bivariate relationships. While many studies have used the Global and Local Moran's I statistics for cross-sectional univariate analysis, this study utilized the bivariate Local Moran's I to study these bivariate relationships and their changes between two time periods.

Census tracts that were in the highest 5% for RSEI toxicity-weighted concentrations were identified and the percentage of racial and ethnic groups and percent near and below poverty within those tracts were queried. The highest 5% of RSEI toxicity-weighted concentrations consisted of 138 census tracts for each year of the study period x 10 years = 1,380 tracts. Since the top 5% of census tracts for RSEI toxicity-weighted concentrations were identified for each year of the study and then compiled for the study period, there were several duplicates (i.e. census tracts that were within the highest 5% for more than one year of the study) that were removed n=1,012 (73.3%), so each of these high census tracts were only included once. The final dataset contained n=368 tracts for analysis. These census tracts were then grouped according to their respective urban areas.

Following the delineation of areas with high RSEI toxicity weighted concentrations and racial-ethnic groups and/or poverty levels the relative proportions of African Americans, Whites, Hispanic and residents living near and below poverty in high RSEI toxicity-weighted concentration tracts compared to the urban area as a whole, rate ratios were calculated by dividing the percent African American, White, Hispanic or percent near and below poverty at the

census tract level within an urban area by the percent African American, White, Hispanic and living near and below poverty of the urban area for both time periods, 2008-2012 and 2013-2017. Those census tracks with rate ratios > 1.0 indicated a disproportionately higher toxicity risk from TRI chemical exposures and vice-versa rate ratios < 1.0 indicated a disproportionally lower toxicity risk from TRI chemical exposures. These findings in the context of environmental justice are interpreted below in Results.

3.3. Results

The five industrial sectors with the highest RSEI Scores for the state of Michigan were Chemicals, Transportation Equipment, Primary Metals, Miscellaneous Manufacturing, and Fabricated Metals, respectively (U.S. EPA, 2019b). During the study period, 186 chemicals were released, managed, or transported from TRI sites in Michigan. The five chemicals with the highest RSEI Scores were as follows: Chromium and chromium compounds, Ethylene oxide, Cobalt and cobalt compounds, Nickel and nickel compounds, and Benzene Table 3-1. The 10 facilities with the highest RSEI Scores in Michigan during 2008 to 2017 are listed in

Table 3-2. Four of the ten facilities with the highest RSEI Scores in Michigan were within the Detroit urban area and three were within the Grand Rapids urban area. The chemicals with the highest RSEI Scores in the Detroit urban area were: Arsenic and arsenic compounds, Asbestos, Benzene, Chromium and chromium compounds, Cobalt and cobalt compounds, Diisocyanates, Ethylene oxide, and Nickel and nickel compounds. The chemicals with the highest RSEI Scores in the Grand Rapids urban area were: Chromium and chromium compounds, Diisocyanates, Ethylene oxide, Formaldehyde, Nickel and nickel compounds, Polycyclic aromatic compounds, and Trichloroethylene. Air releases contributed the most to high

RSEI Scores followed next by water for the state and the Detroit and Grand Rapids urban areas (U.S. EPA, 2019b).

Table 3-1. Highest Ranked Chemicals Released in Michigan by RSEI Scores, 2008-2017.

Chemical Name	RSEI Score
Chromium and chromium compounds	78,147,984
Ethylene oxide	69,895,544
Cobalt and cobalt compounds	23,260,206
Nickel and nickel compounds	7,037,140
Benzene	3,652,431
Arsenic and arsenic compounds	1,794,022
Asbestos (friable)	1,509,981
Diisocyanates	1,444,507
Acrylonitrile	1,195,540
Hydrazine	1,155,812
Others	4,603,412

Source: U.S. EPA, 2019b. The RSEI score is the result of modeled air and water emissions and off-site transfers of TRI chemicals; It evaluates the surrogate dose, toxicity weight, and the population.

Table 3-2. Ten Highest Ranked Facilities in Michigan by RSEI Scores, 2008-2017.

Facility	City	County	Urban Area	RSEI Score
Medplast Medical Inc. Medplast Sterilization	Grand Rapids	Kent	Grand Rapids	32,838,532
Taminco Higher Amines Inc.	Riverview	Wayne	Detroit	21,865,613
Benteler Automotive Hagen Facility	Grand Rapids	Kent	Grand Rapids	20,367,181
Basf Corp	Wyandotte	Wayne	Detroit	16,023,413
Le Jones Co. LLC	Menominee	Menominee	Menominee	13,426,293
Cannon-Muskegon	Muskegon	Muskegon	Muskegon	9,609,141
Bosch Emissions Systems US	Kentwood	Kent	Grand Rapids	7,575,774
Oerlikon Metco (US) Troy	Troy	Oakland	Detroit	7,307,117
SMS Group Warren Workshop	Warren	Macomb	Detroit	6,571,425
Michigan Seamless Tube LLC	South Lyon	Oakland	South Lyon-Howell	3,499,547

Source: U.S. EPA, 2019b. The RSEI score is the result of modeled air and water emissions and off-site transfers of TRI chemicals; It evaluates the surrogate dose, toxicity weight, and the population.

The census tract level RSEI toxicity-weighted concentrations in Michigan ranged from 0 to > 3,400,000 (Table 3-3). The highest mean RSEI toxicity-weighted concentration was in 2008 (13,406.79) and the lowest mean was in 2010 (5,228.82). The highest median RSEI toxicity-

weighted concentration was in 2012 (3,886.09) and the lowest median was in 2014 (1,589.35). The highest maximum RSEI toxicity-weighted concentration was in 2008 (3,420,940) (U.S. EPA, 2017b). While the maximum RSEI toxicity-weighted concentration declined over the time period there were substantial changes between 2009-2011 and an increase between 2016 and 2017.

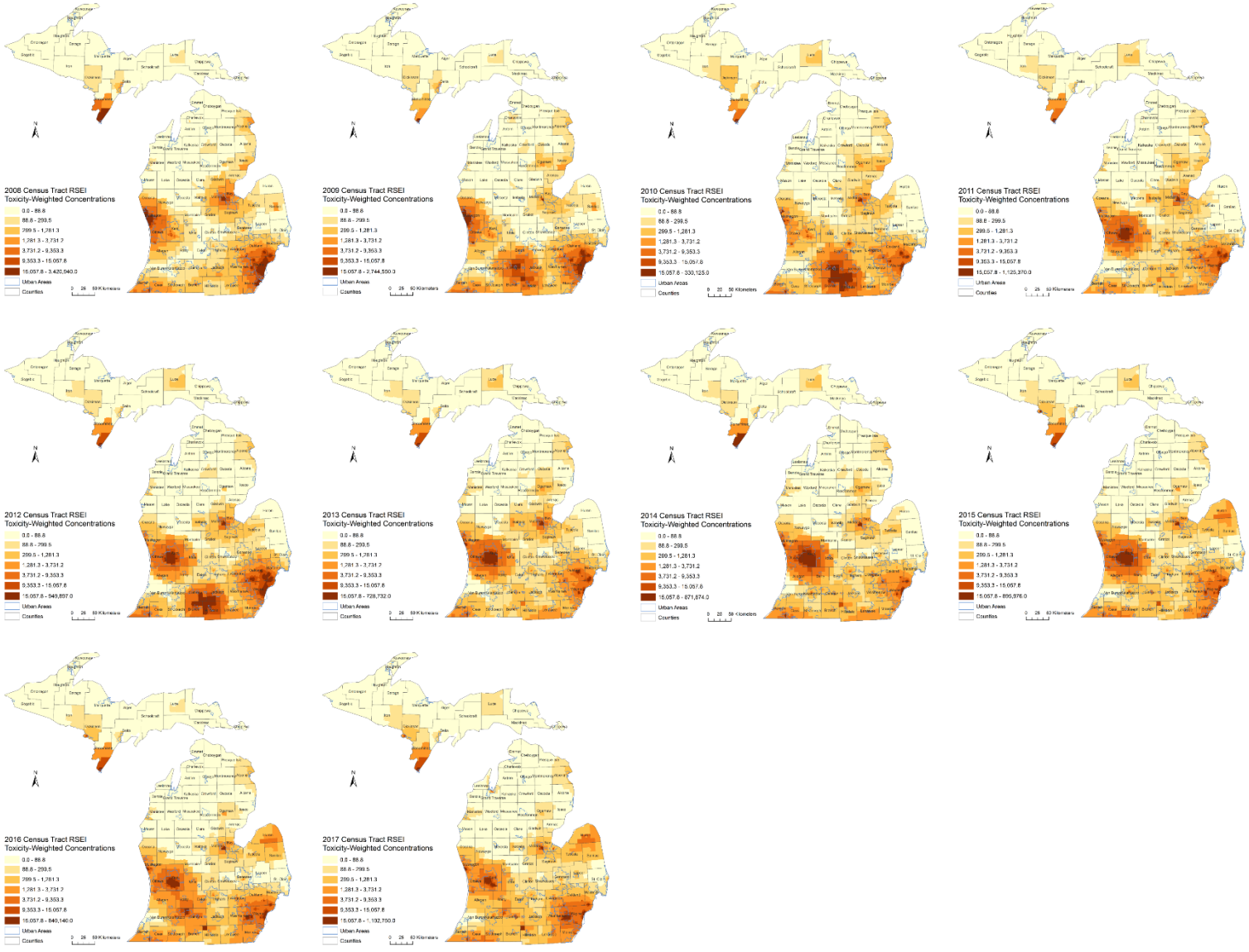
Table 3-3. RSEI Toxicity-Weighted Concentrations Across Census Tracts, by Year in Michigan, 2008-2017.

Year	Mean	Median	Maximum[a]	(%) Subsequent Year Annual Change in Mean
2008	13,406.79	1,916.80	3,420,940	--
2009	11,523.73	2,301.89	2,744,550	-14.05
2010	5,228.82	2,298.51	330,125	-54.63
2011	8,068.03	2,298.61	1,125,370	54.30
2012	11,513.27	3,886.09	949,897	42.70
2013	7,492.71	2,288.06	728,732	-34.92
2014	7,438.78	1,589.35	871,874	-0.72
2015	7,844.55	2,315.09	895,976	5.45
2016	7,124.89	2,553.37	840,140	-9.17
2017	6,590.05	2,103.73	1,192,750	-7.51

Source: U.S. EPA, 2017b.
Note: The RSEI toxicity-weighted concentration is the result of modeled air and water emissions and off-site transfers of TRI chemicals; It evaluates the surrogate dose and toxicity weight.
[a]All minimum concentrations = 0.

Figure 3-3 show the spatio-temporal changes in RSEI toxicity-weighted concentrations in Michigan from 2008 to 2017. The urban areas of Detroit, Muskegon, Marinette-Menominee, Midland, and South Bend consistently contained the highest RSEI toxicity-weighted concentrations during the study period, and the urban area of Grand Rapids contained high RSEI toxicity-weighted concentrations since 2011.

Figure 3-3. RSEI Toxicity-Weighted Concentrations by Census Tract, Michigan 2008-2017.



Census tracts in the highest 5% for RSEI toxicity-weighted concentrations across the study period were predominantly (96.6%) located in urban areas (n=1,333) (Figure 3-4). More specifically, 87.4% (n=1,206) in large, urbanized areas, 8.8% (n=121) in small, urbanized areas, 0.4% (n=6) in small urban areas, 2.7% (n=37) overlapped both small urban and rural areas, and 0.7% (n=10) in rural areas (State of Michigan, 2017). The Detroit, Grand Rapids, Marinette-Menominee, and South Bend urban areas all contained one or more census tracts in the highest 5% for RSEI toxicity-weighted concentrations during all ten years of the study period. The Midland urban area contained one or more census tracts in the highest 5% for RSEI toxicity-weighted concentrations nine of the ten study years and the Muskegon urban area contained one or more census tracts in the highest 5% for RSEI toxicity-weighted concentrations eight of the ten study years (Table 3-4).

Figure 3-4: Michigan Census Tracts in the Highest 5% for RSEI Toxicity-Weighted Concentrations, 2008-2017

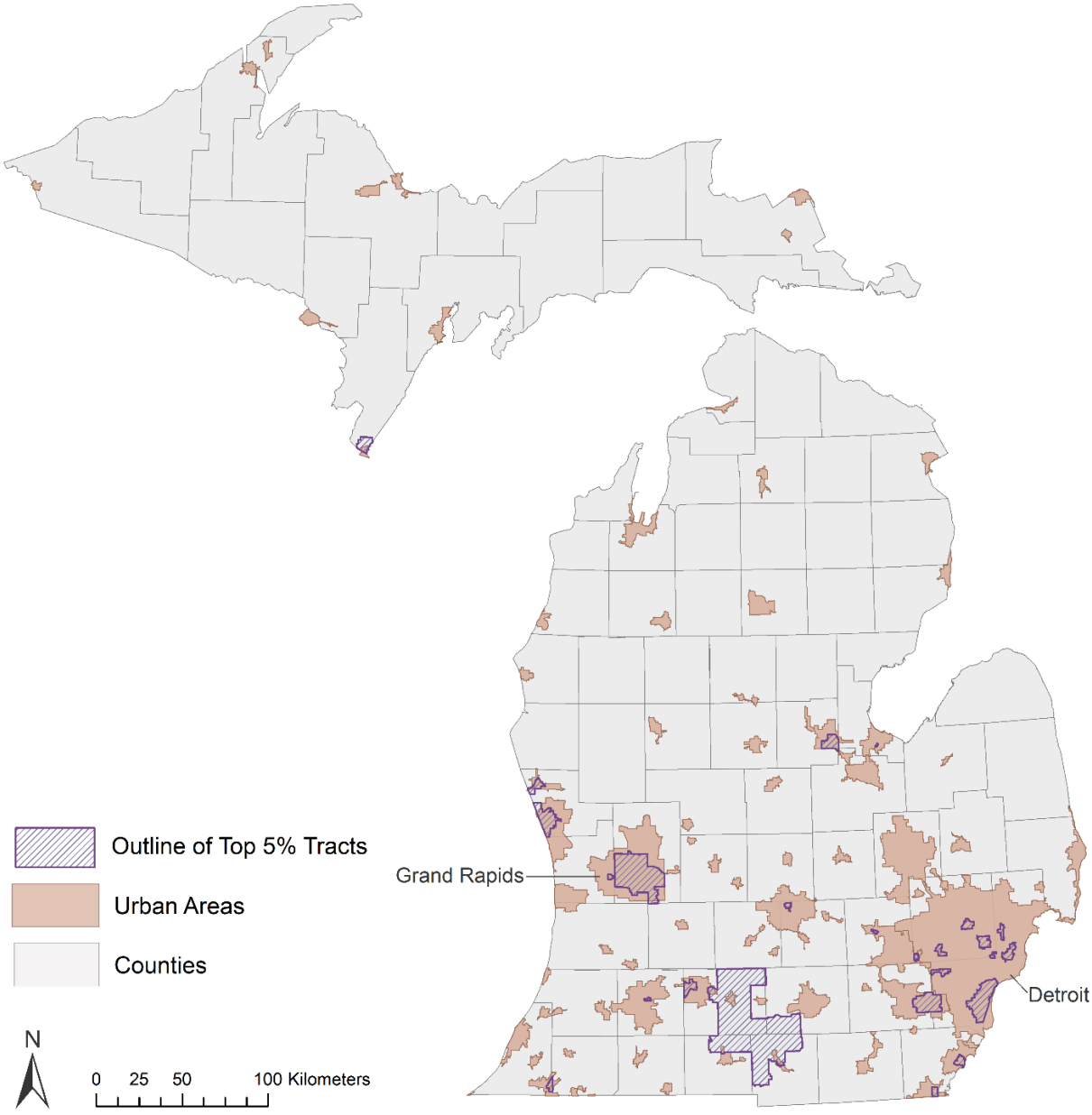


Table 3-4. Summary of Urban Areas with Census Tracts in the Highest 5% of RSEI Toxicity-Weighted Concentrations in a year, 2008-2017.

Urban Area	Urban Area Classification+	No. years one or more census tracts in the top 5%	No. different census tracts in the top 5%	Cumulative[a] No. census tracts in the top 5%	% total (cumulative)
Detroit	Large Urbanized	10	165	590	42.75
Grand Rapids	Large Urbanized	10	98	529	38.33
Muskegon	Small Urbanized	8	21	64	4.64
Ann Arbor	Large Urbanized	4	34	51	3.70
Midland	Small Urbanized	9	7	41	2.97
Marinette-Menominee[b]	Rural & Small Urban	10	3	29	2.10
South Bend	Large Urbanized	10	3	22	1.59
Lansing	Large Urbanized	2	6	10	0.72
Non-Urban	Rural	3	7	10	0.72
Marshall	Small Urban	2	4	6	0.43
South Lyon-Howell	Small Urbanized	4	3	6	0.43
Battle Creek	Small Urbanized	2	5	5	0.36
Hillsdale[b]	Rural & Small Urban	2	4	4	0.29
Monroe	Small Urbanized	1	3	4	0.29
Kalamazoo	Large Urbanized	3	1	3	0.22
Whitehall[b]	Rural & Small Urban	3	1	3	0.22
Bay City	Small Urbanized	1	1	1	0.07
Coldwater[b]	Rural & Small Urban	1	1	1	0.07
Toledo	Large Urbanized	1	1	1	0.07

Sources: U.S. EPA, 2017b; State of Michigan, 2019.
Note: The RSEI toxicity-weighted concentration is the result of modeled air and water emissions and off-site transfers of TRI chemicals; It evaluates the surrogate dose and toxicity weight. +Urban Area Classifications are described as: "1 Rural Area; 2 Small Urban Area (5,000 to 49,999); 3 Small Urbanized Area (Population 50,000 to 199,999); 4 Large Urbanized Area (Population 200,000 or More)" (State of Michigan, 2017).
[a]The cumulative number includes census tracts that were in the highest 5% of Toxicity-weighted concentrations in more than one year, therefore representing the total number of census tracts in the urban area for the duration of the study period.
[a]Contains one or more census tracts that falls within two classification, partly urban and partly rural.

Nine urban areas had one or more census tract in the highest 5% for RSEI toxicity-weighted concentrations during the study period. Between the two time periods, 2008-2012 and 2013-2017, four urban areas experienced an increase (Ann Arbor, Battle Creek, Grand Rapids, and Marinette-Menominee), four urban areas experienced a decrease (South Lyon-Howell, Muskegon, Detroit, and Midland) and South Bend experienced no change in the number of census tracts in the highest 5% of RSEI toxicity-weighted concentrations. The Detroit (42.8%) and Grand Rapids (38.3%) urban areas contained 81.1% of the highest 5% census tracts for RSEI

toxicity-weighted concentrations. The Detroit and Grand Rapids urban areas contained higher densities of TRI sites as well as the most census tracts in the highest 5% for RSEI toxicity-weighted concentrations than the other urban areas in the state. In general, the census tracts in the highest 5% for RSEI toxicity-weighted concentrations located in the Detroit urban area contained a higher density of TRI sites with few exceptions, such as along I-96 between the cities of Plymouth and Detroit, in and around Wayne and in the northeastern area of Detroit with TRI sites mostly concentrated along major roads. Taminco Higher Amines Inc is south of Detroit City in Riverview, Basf Corp is south of Detroit City in Wyandotte, Oerlikon MEtco (US) Troy is northwest of Detroit City in Troy and SMS Group Warren Workshop is north of Detroit City in Warren (data not shown). In the Grand Rapids urban area, the census tracts in the highest 5% for RSEI toxicity-weighted concentrations had a higher density of TRI sites compared to the rest of the Grand Rapids urban area. The TRI sites were concentrated along major roadways and the Grand River, primarily located within industrial complexes. Medplast is in the City of Grand Rapids, Bentelor Automotive Hagan Facility is south of the City of Grand Rapids in Wyoming, and Bosch Emissions Systems US is southeast of the City of Grand Rapid in Kentwood (data not shown).

3.3.1. High RSEI and Population Characteristics

The bivariate Local Moran's I values ranged between -0.214 and 0.375 in the Detroit urban area and between -0.279 and 0.267 in the Grand Rapids urban area (Figures 3-11 to 3-18). For both urban areas, RSEI toxicity-weighted concentrations and percent White consistently showed a negative spatial autocorrelation, while RSEI toxicity-weighted concentrations and percent African American, percent Hispanic and percent living near and below poverty consistently showed a positive spatial autocorrelation. In the Detroit urban area, the correlation

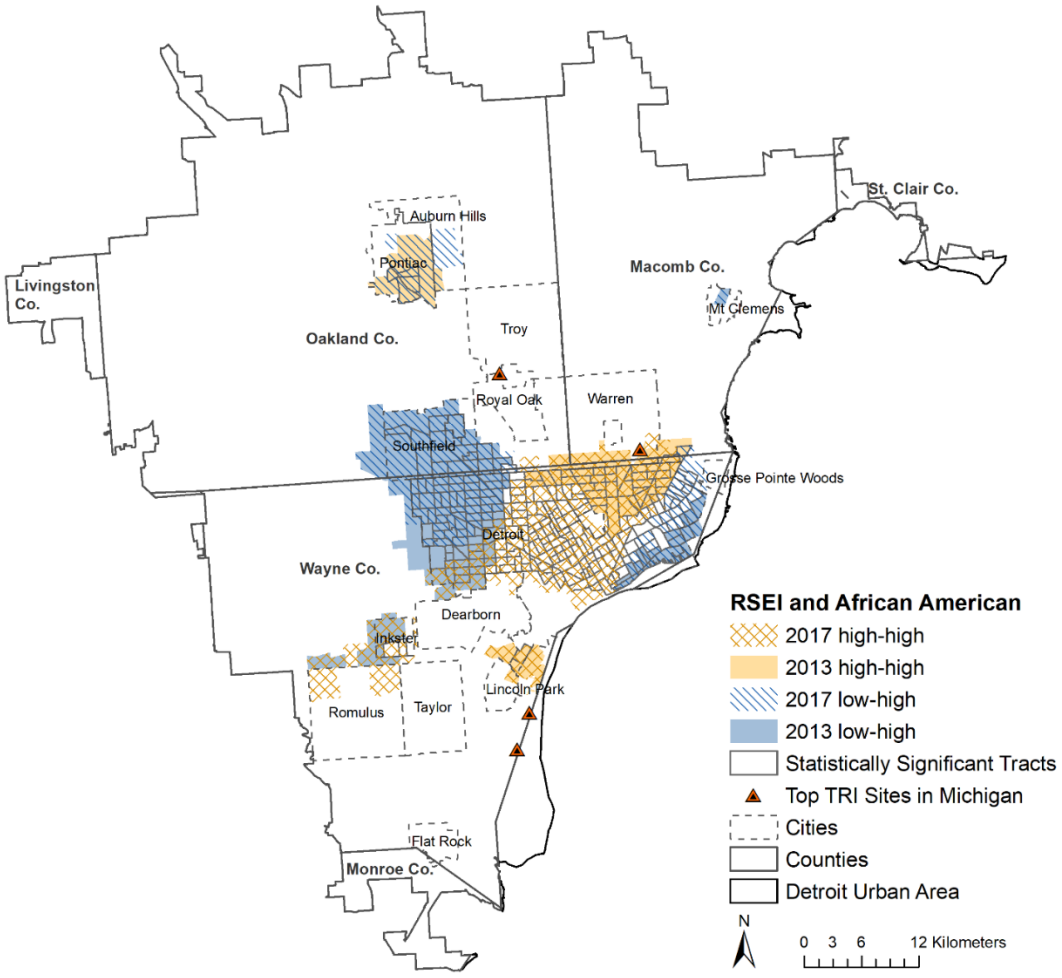
between the highest RSEI toxicity-weighted concentrations and each of the demographic variables (percent White, African American, Hispanic and living near and below poverty) was higher in 2017 than in 2013, with a mix of increasing and decreasing trends between these years. The tracts with the highest RSEI toxicity-weighted concentrations also experienced a high percentage of Hispanics in the Detroit urban area during 2013-2017. In the Grand Rapids urban area, the correlation between high RSEI and African Americans, White and Hispanics were higher in 2013 than in 2017; however, the correlation between RSEI and White and RSEI and Hispanic decreased each year.

In Detroit, there were some noticeable changes between 2013 and 2017. There were more census tracts with High-High spatial autocorrelation in 2017 than in 2013 for percent African American, Hispanic and near and below poverty, indicating increasing inequality over this period. The city of Pontiac experienced a notable shift between 2013 and 2017 containing High-High census tracts for African Americans, Hispanics and near and below poverty in 2013, but it shifted to Low-High census tracts for African Americans, Hispanics and near and below poverty in 2017. There was some overlap between areas with a high percentage of African Americans, Hispanics and near and below poverty. There was very little overlap between areas with a high percentage of Whites, Hispanics and near and below poverty, but no overlap for Whites and African Americans.

High RSEI toxicity-weighted concentrations and a high percentage of African Americans persisted between 2013-2017 in northeast and southwest Detroit, with expansion of high RSEI toxicity-weighted concentrations and a high percentage of African Americans into Detroit in 2017. This expansion of high RSEI toxicity-weighted concentrations and a high percentage of African Americans also occurred in Romulus. There were low RSEI toxicity-weighted

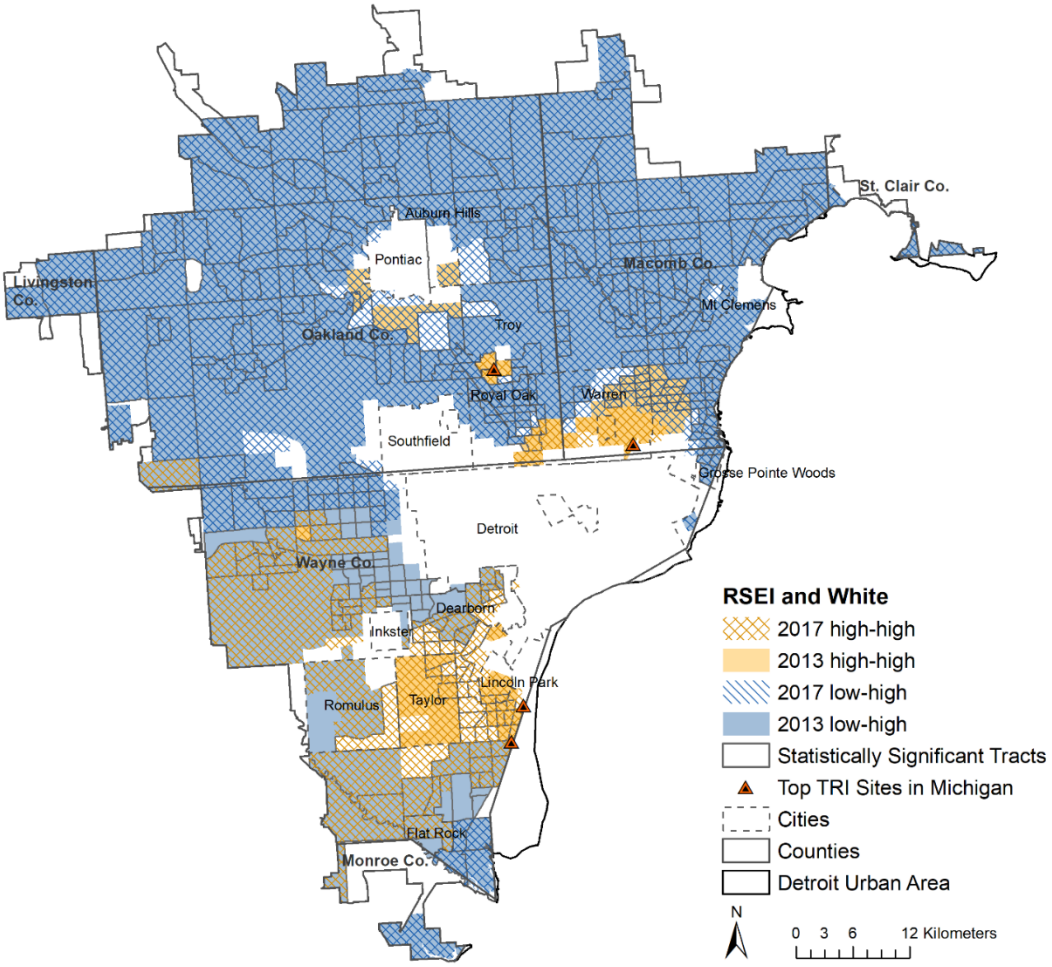
concentrations and a high percentage of African Americans in northwest Detroit, Southfield and southwest Detroit bordering Gross Pointe. Pontiac historically had High-High spatial autocorrelation and over time lower RSEI toxicity-weighted concentrations. Additionally, high RSEI toxicity-weighted concentrations and a high percentage of African Americans extended into Auburn Hills over time. The findings suggest that while many African Americans are migrating away from areas with high RSEI toxicity-weighted concentrations in Detroit and Pontiac, the area with high RSEI toxicity-weighted concentrations and a high percentage of African Americans is also expanding within Detroit and Romulus. The relationship between high RSEI toxicity-weighted concentrations and a high percentage of African Americans is still largely within urban areas (Figure 3-5).

Figure 3-5. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent African American, Detroit Urban Area, 2013-2017.



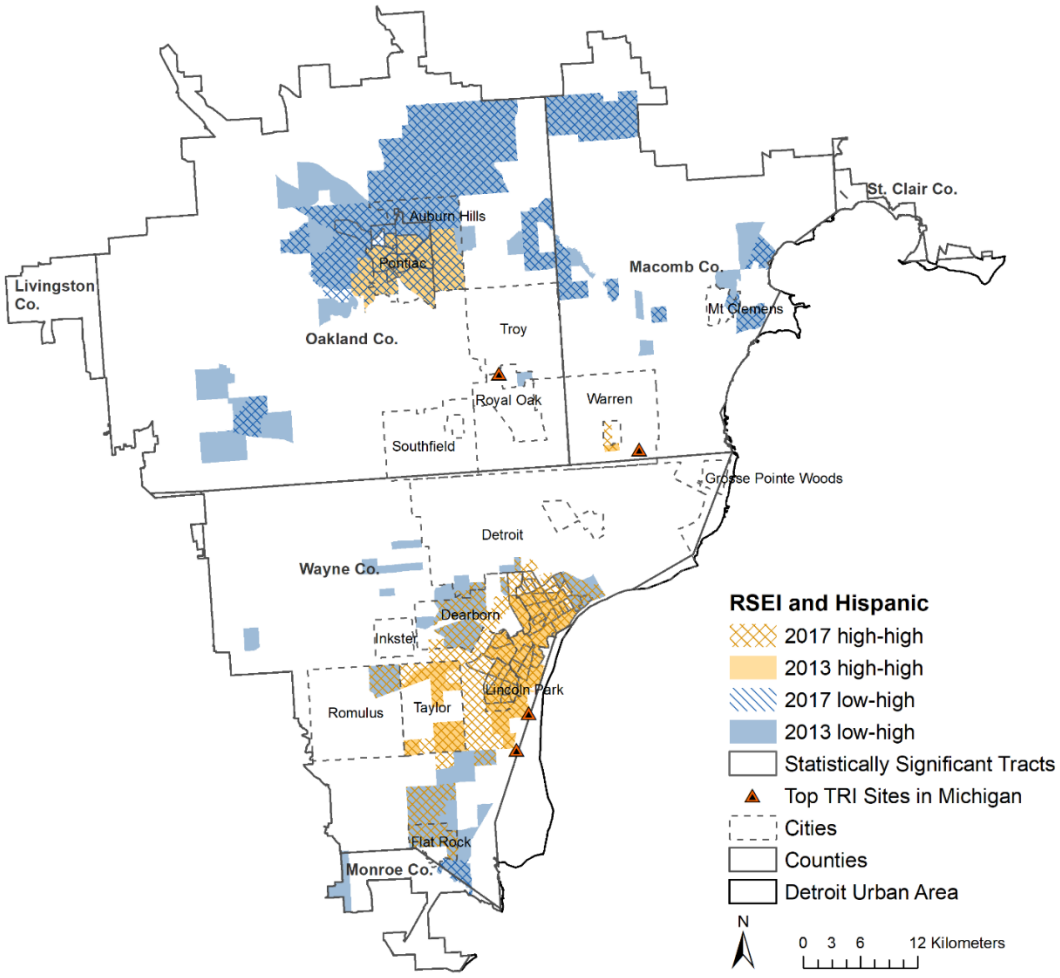
There was persistent high RSEI toxicity-weighted concentrations and a high percentage of Whites in Warren and Royal Oak suburbs north of Detroit as well as in the Taylor and Lincoln Park suburbs southwest of Detroit. Over time there was an emergence of High-High spatial autocorrelation in Dearborn, Romulus, Canton and Westland. There was persistent low RSEI toxicity-weighted concentrations and a high percentage of Whites in Oakland and Macomb counties. Cities and townships with no spatial autocorrelation identified included Detroit, Southfield and Pontiac demonstrating the extreme racial and ethnic segregation in the Detroit Urban Area (Figure 3-6).

Figure 3-6. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent White, Detroit Urban Area, 2013-2017.



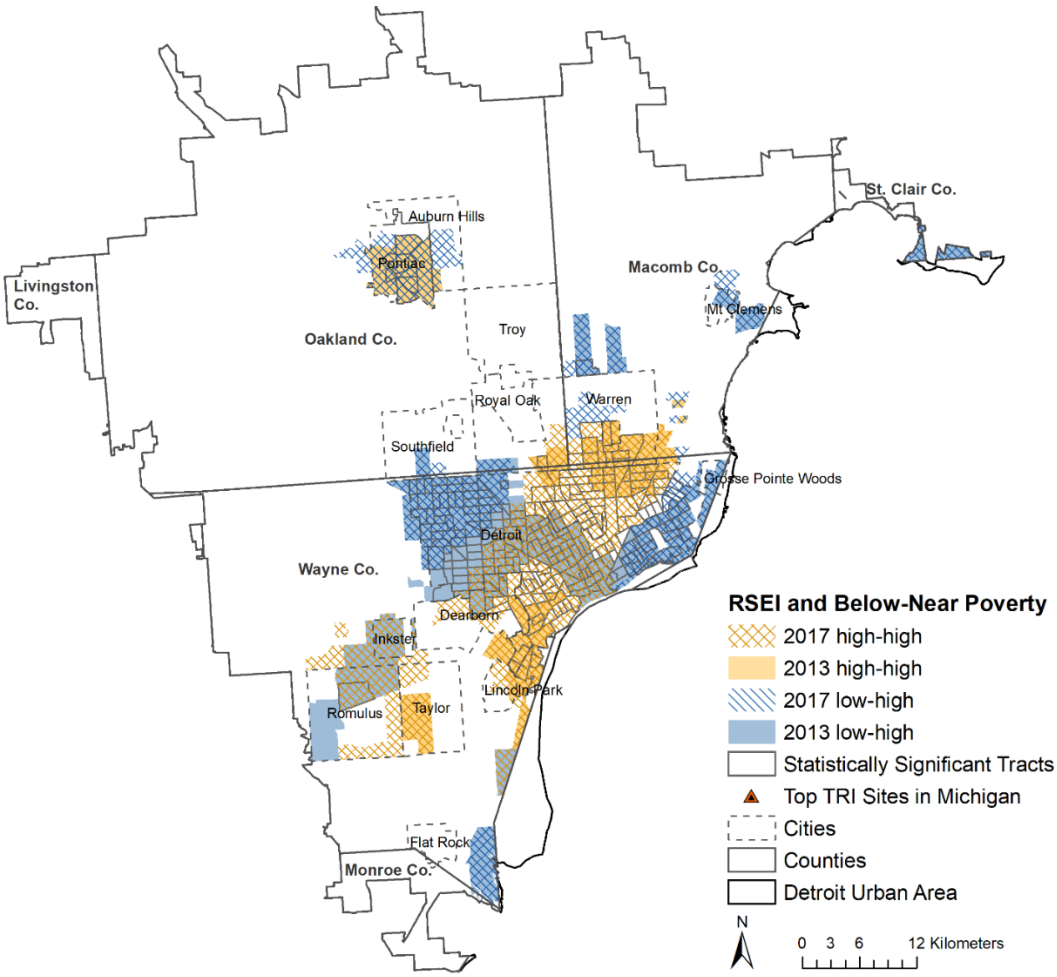
In the southeast portion of the Detroit Urban Area, high RSEI toxicity-weighted concentrations and a high percentage of Hispanics was identified, with movement toward southeast Detroit, Dearborn, Romulus and Flat Rock over time. Historically, there was also High-High spatial autocorrelation in Pontiac, but over time we observed reductions in RSE toxicity-weighted concentrations in the city. Low RSEI toxicity-weighted concentrations and a high percentage of Hispanics dominate the area to the west and north of Pontiac (Figure 3-7).

Figure 3-7. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent Hispanic, Detroit Urban Area, 2013-2017.



High RSEI toxicity-weighted concentrations and a higher percentage of residents below or near poverty were located along the border of the cities of Detroit and Warren and north-central Detroit, and south of Detroit in River Rogue, Lincoln Park and Taylor. The western and eastern edges of Detroit and Gross Pointe experienced persistent low RSEI toxicity-weighted concentrations and a low percentage of residents living near and below poverty. Southern Detroit, northern Dearborn and parts of Inkster and Romulus historically contained Low-High spatial autocorrelations that shifted to High-High over time, whereas in Pontiac a shift from High-High to Low-High spatial autocorrelation was observed (Figure 3-8).

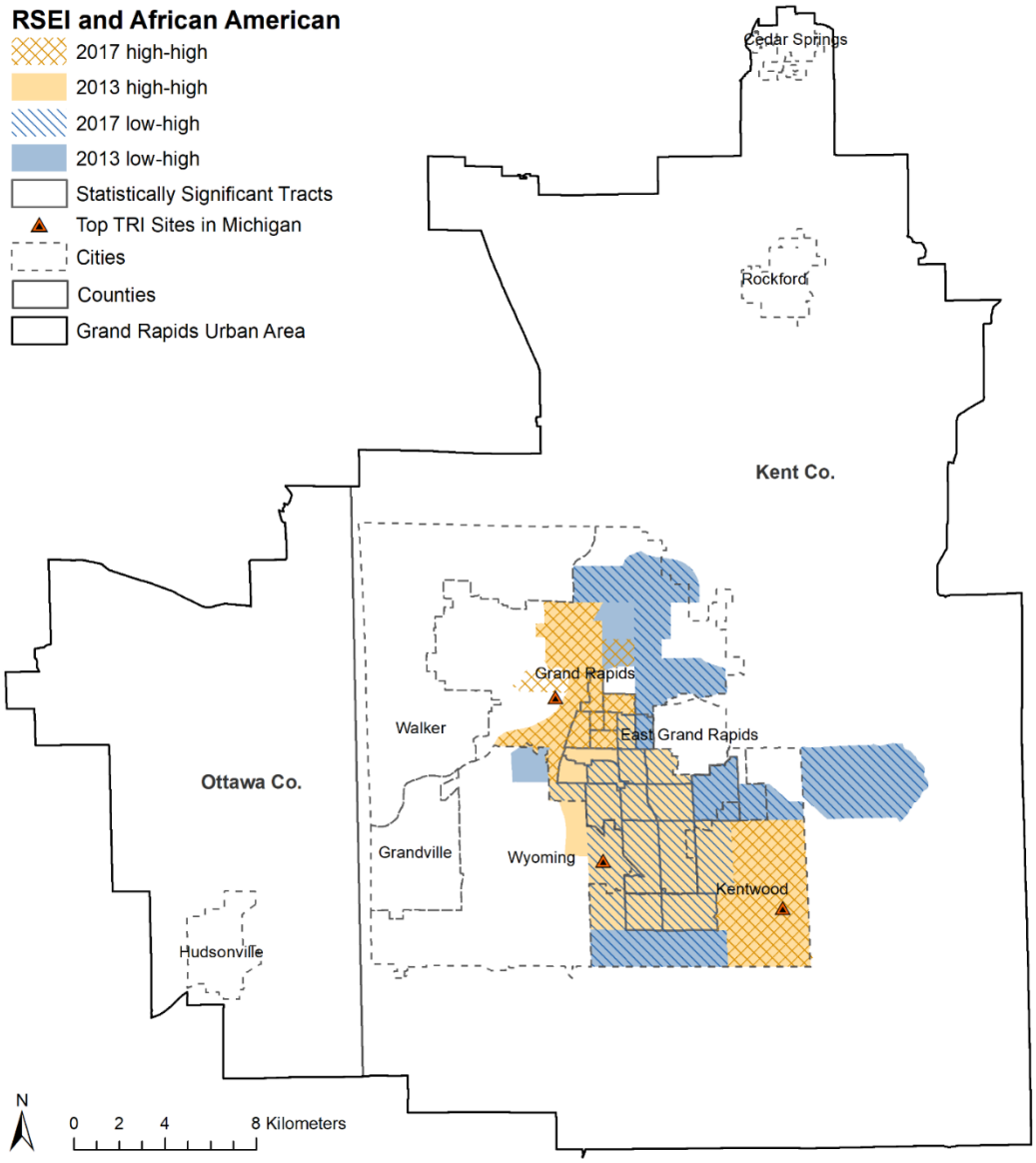
Figure 3-8. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent Near and Below Poverty, Detroit Urban Area, 2013-2017.



In Grand Rapids, the spatial pattern of census tracts with High-High and Low-High spatial autocorrelation were similar during 2013-2015. This spatial pattern changed in 2016 and remained similar in 2017. There were fewer census tracts with high RSEI toxicity-weighted concentrations and a high percentage of African American, Hispanic and residents near and below poverty in 2017 than in 2013; however, there was one more tract with high RSEI toxicity-weighted concentrations and a high percentage of Whites in 2017, up from 2013. This is different than the pattern observed in Detroit.

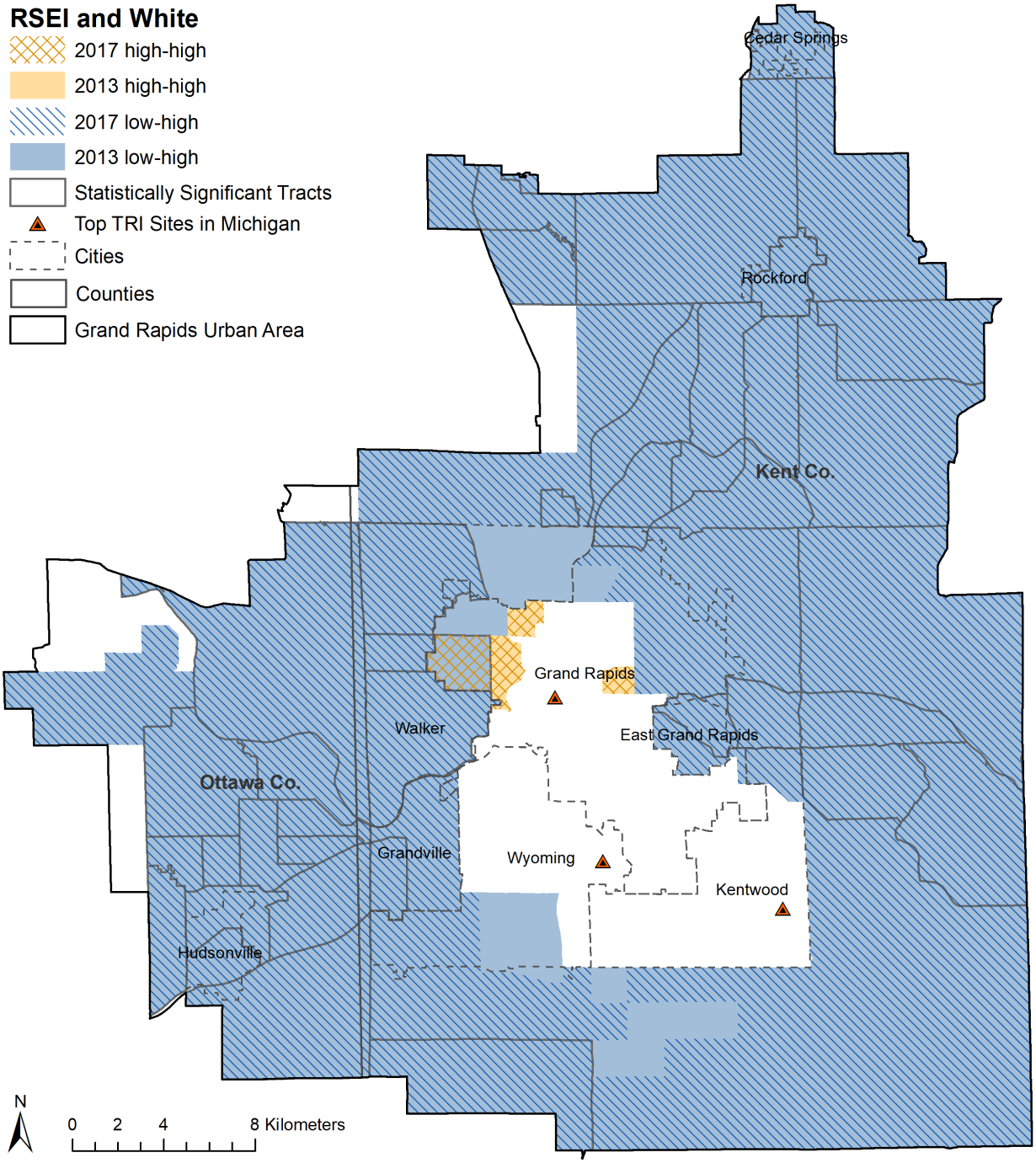
There was a notable shift in the southern part of Grand Rapids and the northeastern part of Wyoming between 2013 and 2017. This area had high RSEI toxicity-weighted concentrations and a higher percentage of African Americans, Hispanics and residents near and below poverty in 2013, but then had low RSEI toxicity-weighted concentrations for these same variables in 2017. Persistently high RSEI toxicity-weighted concentrations and a high percentage of African Americans were observed in east Grand Rapids and Kentwood. South Grand Rapids and the suburbs just to the south of the city experienced a shift to low RSEI toxicity-weighted concentrations and a high percentage of African Americans in 2017 (Figure 3-9).

Figure 3-9. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent African American, Grand Rapids Urban Area, 2013-2017.



There were very few census tracts with a high percentage of Whites and high RSEI toxicity-weighted concentrations. The areas surrounding the City of Grand Rapids where whites largely live experienced low RSEI toxicity-weighted concentrations, with a few small pockets of persistent high RSEI toxicity-weighted concentrations and a high percentage of Whites in northeast and northwest Grand Rapids (Figure 3-10).

Figure 3-10. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent White, Grand Rapids Urban Area, 2013-2017.



High RSEI toxicity-weighted concentrations and a high percentage of Hispanics persisted in the east-central area of Grand Rapids. There were a few tracts in Wyoming and Kentwood as well, but a reduction (low RSEI toxicity-weighted concentrations) was observed in these areas (Figure 3-11). High RSEI toxicity-weighted concentrations and a high percentage of residents living below or near poverty were predominantly located in the City of Grand Rapids, but there were also a few tracts in east Wyoming and one tract in Kentwood, however, over time these High-High tracts were only located in Grand Rapids. Areas with low RSEI toxicity-weighted concentrations and a high percentage of residents living below or near poverty were fairly dispersed across the urban area but were persistently located in Ottawa County and the cities of Walker, Grand Rapids, Wyoming and Kentwood (Figure 3-12).

Figure 3-11. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent Hispanic, Grand Rapids Urban Area, 2013-2017.

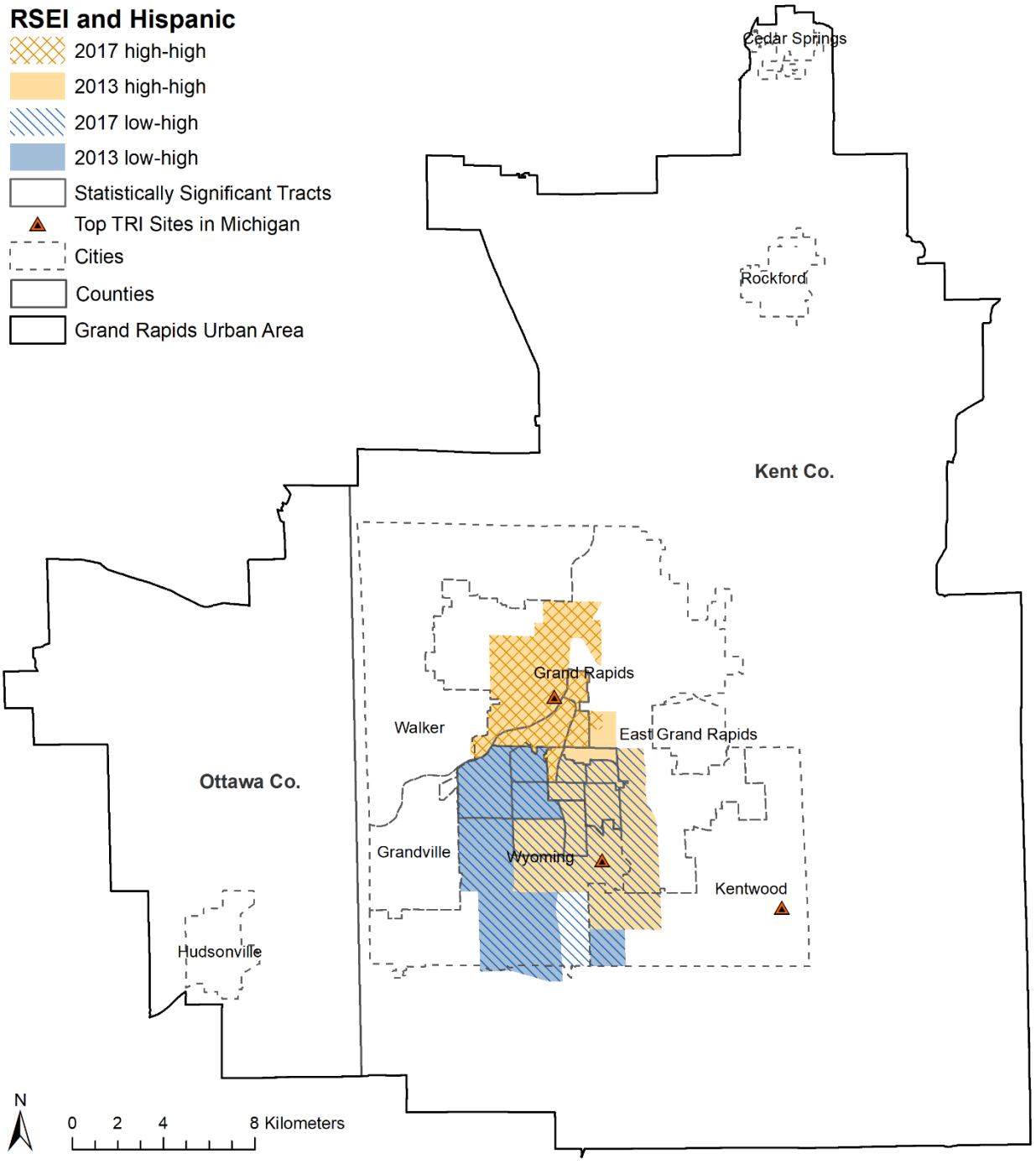
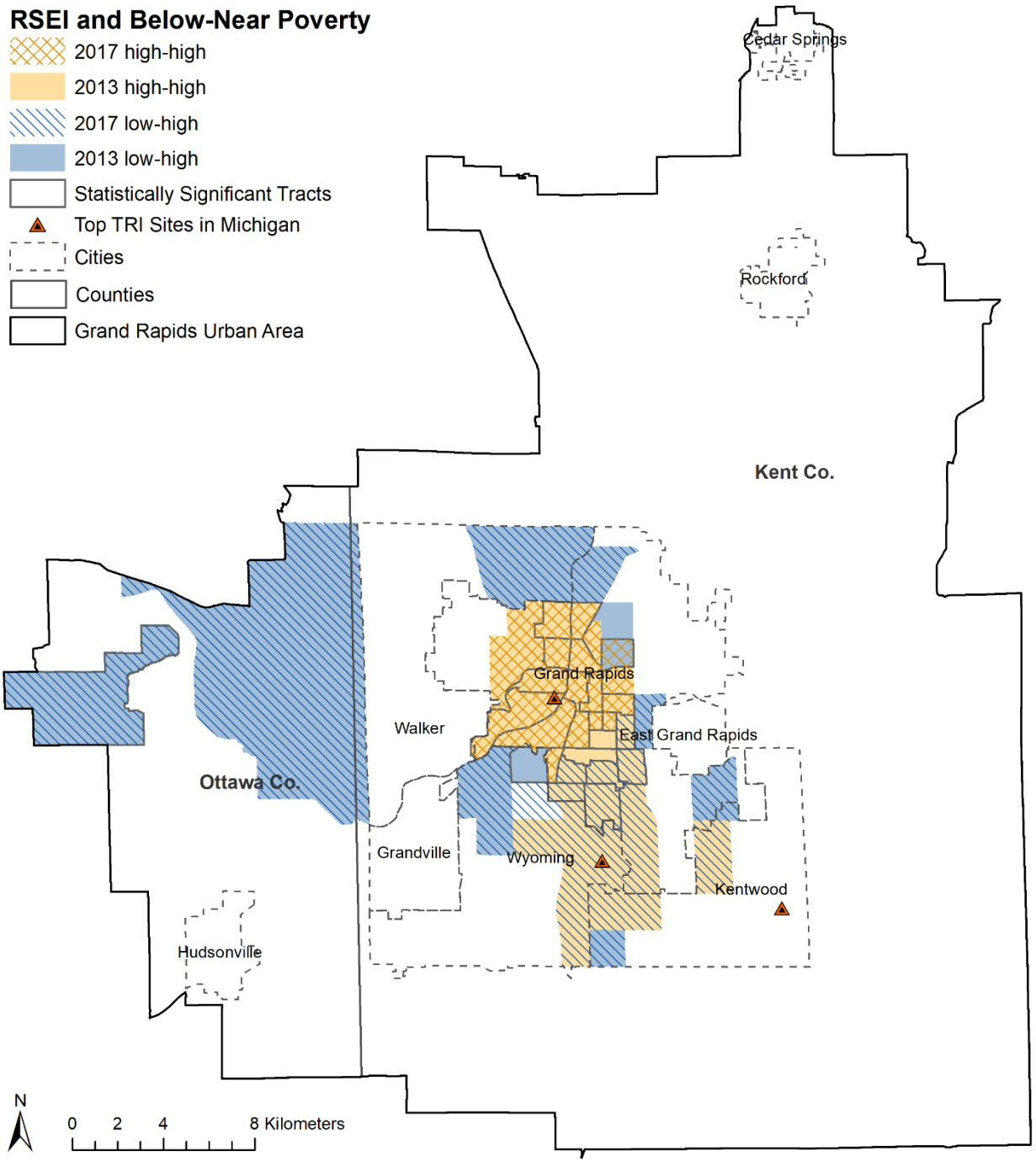


Figure 3-12. Bivariate Moran's I: RSEI Toxicity-Weighted Concentrations and Percent Near and Below Poverty, Grand Rapids Urban Area, 2013-2017.



3.3.2. Rate Ratios for the Two Time Periods

The urban areas of Detroit, Grand Rapids, Muskegon, Menominee-Marinette, Midland and South Bend had consistently high RSEI toxicity-weighted concentrations. Rate ratios for populations living in census tracts in the highest 5% for RSEI toxicity-weighted concentrations during the study period varied (Table 3-5). During the 2008-2012 period, African Americans living in Monroe experienced the highest risk (Rate Ratio (RR)=3.38) followed by Ann Arbor (RR=2.9) and Muskegon (RR=2.1). Hispanics living in Lansing also experienced an increased risk (RR=2.84) followed by Detroit (RR=2.49). During the 2013-2017 period, the risk for African Americans living in Monroe fell out of the top 5% with declines also seen in Ann Arbor (RR=1.96) and Muskegon (RR=0.96). Hispanics living in Lansing also fell outside of the top 5% tracts however, those living in Detroit drastically increased Detroit (RR=4.26). In 2013-2017 people living in the top 5% RSEI toxicity-weighted concentration tracts were also more likely to be poor; except in a greater percentage of non-poor living in high RSEI toxicity-weighted concentration tracts were observed in Kalamazoo and Muskegon.

Table 3-5. Percentage of Racial/Ethnic and Population Living Near and Below Poverty in Highest 5% Tracts for RSEI Toxicity-Weighted Concentrations Divided by Percentage of Racial/Ethnic and Population Living Near and Below Poverty by Urban Location by Time Period.

Time Period	Location	African American	White	Hispanic	Near and Below Poverty
		Rate Ratio	Rate Ratio	Rate Ratio	Rate Ratio
2008-2012	Ann Arbor	2.87	0.79	0.79	1.29
	Battle Creek	0.13	1.26	0.66	0.49
	Coldwater	0.00	1.09	0.08	0.82
	Detroit	0.50	1.16	2.49	0.98
	Grand Rapids	1.81	0.84	1.62	1.39
	Hillsdale	1.47	1.00	1.11	1.19
	Lansing	1.77	0.77	2.84	1.55
	Marinette-Menominee	1.28	1.02	1.28	1.13
	Marshall	1.01	1.01	1.01	1.00
	Midland	0.65	0.99	1.19	1.51
	Monroe	3.38	0.88	1.75	1.68
	Muskegon	2.10	0.81	1.06	1.37
	South Bend	1.46	0.97	1.44	1.31
	South Lyon-Howell	1.05	0.99	1.68	1.70
	Whitehall	0.74	1.04	0.91	0.75
2013-2017	Ann Arbor	1.96	0.88	1.29	1.26
	Battle Creek	1.24	0.91	0.95	1.28
	Bay City	1.67	0.96	1.69	1.49
	Detroit	0.83	0.89	4.26	1.42
	Grand Rapids	1.48	0.91	1.36	1.20
	Kalamazoo	1.43	1.00	1.01	0.74
	Marinette-Menominee	1.29	1.01	1.14	1.19
	Midland	0.97	0.99	1.48	1.32
	Muskegon	0.92	1.06	1.03	0.85
	South Bend	1.44	1.00	0.35	1.51
	South Lyon-Howell	1.31	0.97	1.41	1.25
	Toledo	0.08	1.01	0.26	1.76

Sources: U.S. EPA, 2017b; U.S. Census Bureau, 2012, 2017. The RSEI toxicity-weighted concentration is the result of modeled air and water emissions and off-site transfers of TRI chemicals; It evaluates the surrogate dose and toxicity weight.

3.4. Discussion

The findings from this study offer new perspectives on the spatial and temporal burdens of RSEI scores and toxicity-weighted concentrations in Michigan. There was temporal variation in the mean, median and maximum RSEI toxicity-weighted concentrations during the study period. The results indicate that the highest toxicity risk from TRI chemical exposures were found in large and small urbanized areas, small urban areas, and rural areas. The study identified the urban areas of Detroit and Grand Rapids as potential areas of concern for environmental regulatory and public health agencies regarding exposure to TRI chemicals, as just over 80% of the census tracts in the highest 5% for toxicity risk from TRI chemical exposures were in these two urban areas across all years of the study period. Together these two urban areas contain a majority of the state's population, jobs, and economic productivity (Public Sector Consultants and Metropolitan Policy Program at Brookings, 2016).

Urban areas contained a higher density of TRI sites than rural areas in Michigan. This is consistent with the geographic distribution nationwide (Perlin et al., 1995; Wilson, et al., 2012). The highest density of TRI sites was located within the Detroit urban area, followed next by the Grand Rapid urban area. The Detroit and Grand Rapids urban areas contained higher densities of both TRI sites and the greatest number of census tracts in the highest 5% for RSEI toxicity-weighted concentrations. There were a few exceptions, but overall, areas with higher densities of TRI sites contained census tracts in the highest 5% for RSEI toxicity-weighted concentrations in the Detroit urban area. In the Grand Rapids urban area, census tracts in the highest 5% for RSEI toxicity-weighted concentrations were in areas with a higher density of TRI sites. Although this was the general pattern observed across Michigan, there were also areas that had TRI sites and no tracts in the highest 5%, or that had tracts in the highest 5% and no TRI sites, reinforcing the

effectiveness of using modelled emission data rather than just presence or absence of a facility and/or distance-based measures.

This study found positive spatial autocorrelation (clusters) between high RSEI toxicity-weighted concentrations and percent African American, percent Hispanic and percent living near and below the poverty level. In general, African Americans living in tracts with high RSEI toxicity-weighted concentrations persisted over time. This finding supports the trend in lead emissions observed by Moody and Grady (2017), which reported the relocation of lead emitting facilities out of Black segregated neighborhoods in Pontiac and nearby areas and into neighborhoods with higher levels of Black segregation in and around southern Detroit, Dearborn, River Rough, and Ecorse. In Detroit, poor and minority communities appear to be experiencing an increasing share of elevated toxicity risk from TRI chemical exposures. Hispanic populations experienced the greatest increase over time with high RSEI toxicity-weighted concentrations as evidence of emerging trends over time. These findings demonstrate the persistent and emerging dynamics of environmental justice in Detroit. Additionally, the race/ethnicity variables had higher spatially correlation than the income variable. This is an important finding, though it is not the first study to report such a result (United Church of Christ, 1987).

In the Grand Rapids urban area, a noticeable shift in spatial autocorrelation was observed in southern Grand Rapids and northeastern Wyoming. The Neighborhood Environmental Action Report (Linc Up and Detroiters Working for Environmental Justice, 2019) previously described environmental injustices in the southeastern neighborhoods of Grand Rapids, which was one of the areas this study found to have high RSEI toxicity-weighted concentrations and a high percentage of African American and Hispanic populations. The findings suggest that the Grand Rapids urban area became more, not entirely, equitable over time in terms of the share of RSEI

toxicity-weighted concentrations. This differs from Detroit where the environmental burden among the different population groups seems to have become more inequitable. This trend may in part be explained by changing population composition characteristics and urban structure. The City of Grand Rapids and the surrounding area has been one of the fastest growing regions in Michigan for the past several years. The Grand Rapids urban area experienced significant population growth between the 2012 and 2017 5-year ACS censuses compared to the only slight population growth in the Detroit urban area during this same period (Open Data Network, 2018).

The key strengths of the study include: first, the use of the RSEI model, which (1) takes into account source-specific information regarding the chemical(s) release, evaluating the stack height, gas exit velocity, and the fate and transport of the chemical(s) by using site- and time-specific atmospheric and groundwater models; (2) examines the annual amount of each chemical released per year and weights them by their toxicity; (3) the route and level of human exposure is considered; (4) offers an efficient and flexible way to evaluate environmental risks; (5) the model has been peer-reviewed and its' methodology is transparent (U.S. EPA, 2018b). Second, choosing to investigate the RSEI toxicity-weighted concentrations rather than the RSEI Scores since they do not include a population weight by which to further study population composition in relation to urban and rural differences. Third, the study used two methods to evaluate environmental justice, including bivariate Local Moran's I and rate ratios of RSEI toxicity-weighted concentrations and the racial, ethnic, and poverty characteristics of census tracts and urban areas. This approach provided valuable insight into the share of toxicity risk from TRI chemical exposure within each urban area.

This study is not without limitations. First, environmental justice areas were identified, but future research should investigate the TRI facilities and TRI chemicals emitted in these areas.

Second, Hispanics are a growing population in Michigan and were found to be living in census tracts with high RSEI toxicity-weighted concentrations. Therefore, the move-in hypothesis should be further explored for this population. The RSEI model also has limitations, including: first, TRI emissions are self-reported by the industries, so it is possible they are not accurate. De Marchi and Hamilton (2006) argue that facilities often under-report their emissions to the U.S. EPA to either minimize costs associated with measuring emissions and/or to wrongfully insinuate the facility has reduced their emission. Therefore, if facilities are regularly under-reporting their chemical releases, the RSEI values are likely based on conservative estimates. Second, many industrial plants do not have to report their emissions of toxic chemicals because they fall under the minimum reporting threshold (Currie et al., 2015; U.S. EPA, 2018b). Third, it does not include information on mobile sources or Superfund (hazardous waste) sites, so not all sources of environmental risk are included. Fourth, sometimes the chemical group is reported rather than data on the specific type of chemical. In most instances, the model will assume the most toxic form of the chemical was released (U.S. EPA, 2017a). Finally, it assumes populations are continuous exposed throughout the year (Chakraborty et al., 2011; U.S. EPA, 2018b).

3.5. Conclusion

These findings extend ecosyndemic theory by demonstrating that an ecosyndemic can also occur at the environmental hazard level with multiple chronic pollution exposures, rather than just the health outcome level. This study suggests that a pollution ecosyndemic is present in Michigan's Detroit and Grand Rapids urban areas. The TRI chemicals may have synergistic or interaction effects with one another along with the social environment as observed in the poverty relationships, as well as individual factors.

Overall, population groups experiencing a disproportionate share of elevated toxicity risk from TRI chemical exposures are African Americans, Hispanics and populations living near and below poverty in urban areas of Michigan. Notably, the spatial autocorrelation between census tract level demographics and RSEI toxicity-weighted concentrations was higher for race than for income. African Americans living in the Grand Rapids urban area and Detroit experienced persistent environmental injustice, while Hispanics living in the Detroit urban area experienced emerging environmental injustice, both trends important for the study of environmental justice. These vulnerable population groups are likely less able to change their conditions due to limited political influence and financial and mobility challenges. Moseley (2014) identifies economic, sociopolitical, and racial factors as general reasons for the distribution of environmental hazards and environmental benefits. Therefore, the structural setting in has predisposition minority and low-income populations to experience inequitable pollutant exposures which may have synergistic and interacting effects that further harm human health, further exacerbating environmental and health equity concerns.

The TRI facilities and the TRI chemicals released, managed, or transferred from these facilities should be investigated in the areas where environmental injustices were identified. In particular, the companies contributing the most to human health risk from TRI chemical exposures, Medplast Medical Inc. Medplast Sterilization, Taminco Higher Amines Inc., Benteler Automotive Hagen Facility, Basf Corp, Le Jones Co. LLC, Cannon-Muskegon, Bosch Emissions Systems US, Oerlikon Metco (US) Troy, SMS Group Warren Workshop and Michigan Seamless Tube LLC., respectively, should be monitored closely and incentivized to reduce their release of toxic chemicals into the environment. Future research in Michigan should investigate the results from this study in relation to other U.S. EPA environmental indicators and environmental justice

indexes; and compare the discriminatory citing hypothesis with the move-in hypothesis for Hispanic populations who were identified as experiencing disproportionate burdens from toxicity risk from TRI chemical exposures. Future environmental justice research should also use the RSEI model to study exposure risks among populations in other states.

Chapter 4. ENVIRONMENTAL HEALTH INVESTIGATION OF TOXIC RELEASE INVENTORY CHEMICALS ON MATERNAL HEALTH, BIRTH OUTCOMES AND NEONATAL MORTALITY IN MICHIGAN, 2008-2017

Abstract

Pregnant women in the United States are at risk of multiple chemical exposures, many of which have been linked to adverse health outcomes among women and their babies. This study examined maternal exposure to modelled Toxic Release Inventory (TRI) chemicals on adverse birth outcomes, including lethal congenital anomalies, in Michigan. During the 2008-2017 study period, Michigan TRI facilities released a combined 186 different toxic chemicals into the air, waterways and on land. The Risk-Screening Environmental Indicators (RSEI) model, which includes the type of chemical release, quantity and toxicity of the chemical, fate and transport through the environment, the route of exposure and dose of exposure to produce health risk-related values, and geospatial technologies were used to define maternal exposure at place of residence. Logistic regression models were implemented to estimate the odds of low birth weight and preterm birth among mothers with varying exposures, while controlling for potential confounding variables. Space-time scan statistics were used to examine the spatial and temporal distribution of lethal congenital anomalies in Michigan. The study found a statistically significant association between higher RSEI exposure quartiles and an increased odds of low birth weight and preterm birth. Several important interactions with the RSEI exposure quartiles were identified, including smoking, age, gestational hypertension and premature rupture of the membranes, which exacerbated the RSEI effects on birth outcomes. The results of the space-time analysis identified statistically significant clusters of lethal congenital anomalies in the urban areas of Detroit, Ann Arbor, Lansing and Holland, and in the area encompassing Gladwin,

Arenac and Bay Counties. Further analysis indicated that maternal exposure to elevated RSEI toxicity-weighted concentrations may in part be a contributing factor to these clusters. The findings from this research inform environmental regulatory and public health policies and health care practice in areas with elevated RSEI levels from TRI sites.

4.0. Introduction

Research indicates that people are exposed to multiple industrial chemicals throughout their lives, with initial exposures beginning before birth (Institute of Medicine;, 2014; Woodruff, 2015). Exposure to certain chemicals can increase an individual's risk of an adverse health outcome and depends on the (a) type of chemical, (b) dose of exposure, (c) duration of exposure, (d) frequency of exposure, (e) stage of the life course at time of exposure, and (f) underlying health status (ATSDR, n.d.). Extrinsic factors (i.e. environmental exposures) may interact with intrinsic factors (i.e. biological factors) to negatively impact health (American College of Obstetricians and Gynecologists [ACOG], 2013).

Several studies (National Cancer Institute, 2010; Sutton, Perron, Giudice, & Woodruff, 2011; Woodruff, Zota, & Schwartz, 2011) indicate that both preconception and prenatal exposure can have a significant adverse impact on one's reproductive and developmental health throughout their life. Impacts include adverse birth outcomes, birth defects, childhood and adult cancers, reproductive functions, and cognitive, neurological and reproductive development (ACOG, 2013). Improving birth outcomes is an important research focus because they can have significant and lastly effects. Adverse birth outcomes increase infants' risk of both short-term and long-term morbidity and mortality (Anderson et al., 2003; Barker, 2006; CDC, 2019a). For example, birth defects, low birth weight, and premature birth are the leading causes of infant mortality in the United States (CDC, 2019b). Adverse birth outcomes have also been linked to various health and developmental problems (Anderson, Doyle, FRACP, & Victorian Infant Collaborative Study Group, 2003; Barker, 2006). In addition, early-life exposures may make individuals more vulnerable to future insults by reducing their ability to respond (Bellinger, Matthews-Bellinger, & Kordas, 2016; Cory-Slechta, 2005). It is understood that these outcomes

can result from environmental exposures (Padula, et al., 2018; Porpora, et al., 2019; Ritz, et al., 2002; Stieb, Chen, Eshoul, & Judek, 2012).

4.1. Background

4.1.1. Environmental Health Assessment of Birth Outcomes

Women in the United States are likely exposed to multiple chemicals during pregnancy (Wang, et al., 2018; Woodruff et al., 2011). A biomonitoring study by Wang et al. (2018) evaluated environmental organic acids among a diverse group of pregnant women (n=75) in San Francisco. The databased included 696 environmental organic acids. Maternal serum at the time of delivery was collected and analyzed. An average of 56 environmental organic acids were detected in maternal serum samples (Wang, et al., 2018). Additionally, a study by Woodruff et al. (2011) which used blood, serum, and urine samples among a representative sample of women across the United States drawn from the National Health and Nutrition Examination Study (NHANES) 2003-2004 detected multiple industrial chemicals among 99-100 percent of the pregnant women (n=238). A total of 43 chemical analytes in various chemical classes were detected. Some of the chemicals identified are banned substances such as bisphenol A (BPA), dichlorodiphenyltrichloroethane (DDT), polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs). Some chemicals persist in bodies for long periods of time. Chemicals that are banned may be removed from certain products but are allowed in other products. Many chemicals are known to cross the placenta and have been linked to adverse reproductive and developmental outcomes (Woodruff et al., 2011). In addition, other studies (described in more detail below) examining maternal exposure to chemicals and their birth outcomes have detected multiple chemicals in nearly all the study participants (Perera, et al., 2003; Rokoff, et al., 2018).

Various toxicants can be transferred from the mother to her fetus via the placenta (Landrigan et al., 2004). Embryos and fetuses are more sensitive and more vulnerable to environmental toxicants because they have different exposure pathways and physiologies than adults (Landrigan et al., 2004; Perera et al., 2003; TENDR, 2016). Fetuses are undergoing rapid growth and development with many organs and systems in various stages of development. Disruption can lead to improper development and increase the risk of acquiring a chronic disease later in life due to this alteration and because they have more years of life for a disease to develop than adults (Landrigan et al., 2004). Additionally, prenatal exposures may result in near-term risks such as miscarriages, stillbirths, low birth weight, birth defects and other health deficits (ATSDR, 2014).

Previous studies have linked prenatal exposures to environmental agents to a number of adverse health outcomes, such as spontaneous abortion, low birth weight (infant born < 2,500 grams), preterm birth (infant born < 37 weeks gestation), intellectual disabilities, mental retardation and behavioral disorders (Landrigan, Kimmel, Correa, & Eskenazi, 2004; Ogneva-Himmelberger, Dahlberg, Kelly, & Moore Simas, 2015; Padula, et al., 2018; Stieb, Chen, Eshoul, & Judek, 2012). These adverse outcomes are especially likely if there is a lack of high-quality health care to address the exposure(s). Although some scientific evidence exists, most studies have focused on criteria air pollutants rather than toxic chemicals emitted from industrial facilities. One source of toxic chemicals are Toxic Release Inventory (TRI) sites, which have been less studied. The TRI was created under the Emergency Planning and Community Right-to-Know Act (EPCRA) of 1986. Certain industries are required to report to the EPA if they have 10 or more full-time employees and manufacture more than 25,000 pounds of TRI chemicals or use over 10,000 pounds of any TRI chemical in their operations (EPA

[Environmental Protection Agency], 2017a). The TRI collects data from these facilities on the release, management and off-site transport of toxic chemicals. Reporting is mandatory for facilities in certain industrial sectors that have 10 or more full-time employees and manufacture more than 25,000 pounds of TRI chemicals or use over 10,000 pounds of any TRI chemical in their operations (EPA, 2017). Maternal and neonatal health investigations of estimated prenatal exposures to TRI chemicals and maternal proximity to TRI facilities are discussed next.

An investigation of fugitive and stack air releases of developmental toxins and nondevelopment toxins from TRI facilities in relation to infant health at the county level in the United States found that an additional one thousand pounds per square mile of all toxins would reduce gestation by 0.115 weeks and birth weight by 1.47 grams and increase infant mortality by 1.06. The effects were stronger when evaluating air releases of developmental toxins only, as one thousand pounds per square mile of developmental toxins would reduce gestation by 0.0247 weeks and 2.86 grams and increase infant mortality by 2.49. These seemingly modest effects are quite sizeable when considered in terms of probability. Maternal age, race, ethnicity, education, smoking, alcohol, infant sex and year and county fixed effects were controlled for in the study (Currie & Schmieder, 2009).

Maternal residential proximity to TRI facilities on conotruncal heart defects among their children in Texas was evaluated using a case-control study design. The study calculated odds ratios using logistic regression, while controlling for maternal age, race/ethnicity, education and maternal and paternal occupational exposures. Only a small association was identified between women living within 1 mile of a TRI facility and conotruncal heart defects (aOR= 1.10, 95% CI = 0.91, 1.33) (Langlois, et al., 2009).

Agarwal, Banternghansa, & Bui (2010) analyzed TRI releases on infant and fetal mortality rates at the county level in the U.S. The study controlled for two criteria air pollutants, particulate matter 10 micrometers or less in diameter (PM_{10}) and ozone, as well as maternal age, race of the parents, education, marital status, smoking, alcohol and the level of prenatal care. When aggregated TRI releases were analyzed, no significant association was found. When TRI releases were analyzed by environmental medium, air releases had a statistically significant effect on infant mortality rates (0.0214 and 0.0213 without PM_{10} and ozone, respectively). Of these air releases, carcinogenic chemicals had the greatest adverse effect on infant mortality (Agarwal, Banternghansa, & Bui, 2010).

Maternal residential proximity to the top 10 TRI polluters in Memphis, TN was evaluated in relation to cases of low birth weight and preterm birth. Maternal residence (n=369) was classified as ≤5 miles, 6-10 miles, >10 miles of the TRI sites. Logistic regression was used controlling for maternal age, education, marital status, employment, substance use (alcohol, drugs tobacco) and sexually transmitted diseases. Women living within 5 miles of two of the TRI sites were more likely to have a preterm birth (OR= 4.018, 95% CI 1.103, 14.643; OR= 2.667, 95% CI 1.036, 6.862). No statistical association was observed between maternal proximity to TRI sites and low birth weight (Braud, Nouer, & Lamar, 2011).

The spatiotemporal association between maternal residential proximity to select TRI facilities, 19 coke and steel production facilities, and their releases on birth outcomes was analyzed in Alabama. Covariates controlled for included maternal age, race, education, method of payment, parity and birth year. A small association was found between residential proximity (≤ 5.0 km) to the industrial facilities and preterm birth (OR= 1.05, 95% CI 1.01, 1.09). Additionally, high levels of VOC emissions were associated with low birth weight (OR= 1.17,

95% CI 1.06, 1.29) and the emission of metals were associated with preterm birth (OR= 1.07, 95% CI 1.01, 1.14) (Porter, Kent, Su, Beck, & Gohlke, 2014).

A case-control study estimated maternal residential exposure to chemicals released from TRI facilities in Texas using an emissions-weighted proximity model. The logistic regression analysis controlled for maternal age, race/ethnicity, education, infant sex, gestational weeks, birth year and the public health service region of maternal residence. Exposed pregnant women had a statistically higher risk when compared to unexposed pregnant women of having a low birth weight infant (aOR= 1.02-1.60). Further analysis was done on the ten TRI chemicals with the highest aORs, including: acetamide (aOR= 1.60, 95% CI 1.09, 2.34), p-phenylenediamine (aOR= 1.32, 95% CI 1.07,1.63), 2,2-dichloro-1,1,1- trifluoroethane (aOR= 1.21, 95% CI 1.10, 1.34), 1,2- phenylenediamine (aOR= 1.20, 95% CI 1.02, 1.41), resmethrin (aOR= 1.14, 95% CI 1.01, 1.30), toluene-2,6-diisocyanate (aOR= 1.14, 95% CI 1.02, 1.28), tributyltin methacrylate (aOR= 1.14, 95% CI 1.05, 1.23), propetamphos (aOR= 1.11, 95% CI 1.01, 1.23), 1,1,1-trichloroethane (aOR= 1.10, 95% CI 1.05, 1.15) and creosote (aOR= 1.09, 95% CI 1.02, 1.16) (Gong, Lin, & Zhan, 2018).

A study by Padula et al. (2018) used the California Communities Environmental Health Screening Tool, which evaluates 19 pollution and population indicators, including releases from TRI facilities to estimate pollution burden scores for census tracts to investigate associations between maternal environmental exposures and preterm birth in Fresno County, CA. The following variables were adjusted for in the logistic regression analysis: maternal age, race/ethnicity, education and form of payment. The results showed small, stable associations between maternal pollution burden scores and preterm birth (OR 1st quintile = 1.38, 95% CI

0.79, 2.40; OR 2nd quintile = 1.78, 95% CI 1.09, 2.88; OR 3rd quintile = 1.98, 95% CI 1.23, 3.19; OR 4th quintile = 1.98, 95% CI 1.23, 3.19) (Padula, et al., 2018).

Studies evaluating maternal exposures to TRI releases on birth outcomes have primarily relied on distance-based measures, which can lead to inaccurate exposure estimates due to the modifiable area unit problem (Conley J. F., 2011; O'Sullivan & Unwin, 2010). To address this limitation, this study uses the EPA's Risk-Screening Environmental Indicators (RSEI) model which models the release, management and transfer of 767 chemicals and 33 chemical categories (EPA, 2019b). One of the modelled outputs are RSEI toxicity-weighted concentrations. These values are based on stack and fugitive air releases, direct water releases, transfers to publicly owned treatment works and transfers to offsite incineration, considering multiple variables including: the type of emission, quantity of the chemical release, fate and transport through the environment, chemical toxicity, exposure pathways and dose of exposure. Exposure is estimated using the decennial census to geographically model the age-sex composition of the population and the toxicity chemicals is based on the route of exposure and the expected chronic human health impacts (EPA, 2018b). Higher RSEI toxicity-weighted concentrations indicated greater human health risks from TRI chemical exposures. The RSEI model has been used most commonly for environmental justice research, but it also has some limited use for studies of environmental health. Following is a review of studies that have used the RSEI model to evaluate health outcomes.

Lucier et al. (2011) assessed school performance using proximity measures to TRI facilities and the RSEI toxicity-weighted concentrations as the primary exposures, controlling for school-level variables, including percentage of children receiving free school lunch, percentage of minority students, percentage of teachers with emergency credentials, attendance rates,

student-teacher ratios, and percentage of students with disabilities. Seven proximity measures were used, including whether or not a TRI facility was located within one mile of each school, the number of facilities within one, two and three miles of each school, distance from the centroid of the three facilities contributing the highest volume of toxic emissions to each school, distance from the centroid of the five nearby facilities with the highest RSEI toxicity scores to each school, and the RSEI toxicity-weighted concentrations. School performance was measured using annual standardized test results from the Louisiana Department of Education. The study created an elasticity model by which to reduce the heteroskedasticity and non-normality and the influence of the outliers, and multivariate regression models were estimated to study these relationships. The authors found that school performance scores decreased for schools located closest to TRI facilities, particularly those emitting chemicals identified as neurotoxins that are known to affect cognitive development. School performance scores also decreased, for schools located in areas with the highest RSEI toxicity-weighted concentrations.

Moore and Hotchkiss (2016) used the RSEI model to evaluate the association between proximity to Hazardous Air Pollutants (HAPs) emitted from TRI facilities and respiratory diseases in hospitalized children aged 0 to 17 years at the Zip Code level in Tennessee, controlling for Zip Code level socioeconomic status. The study examined the spatial patterns of HAP emissions and observed Zip Codes with low total emissions but a high toxicity of emissions as well as Zip Codes with high total emissions but a low toxicity of emissions. The study also used generalized linear regression models to estimate these relationships with respiratory diseases. The study found statistically significant associations between HAP emissions and the incidence of respiratory disease among children in Tennessee (2.71% increase, 99% CI for any respiratory disease in Zip Codes with at least one TRI facility compared to Zip Codes with no

TRI facilities). Furthermore, one standard deviation increase in RSEI toxicity-weighted emissions had a greater marginal effect than one standard deviation increase in total emissions on any respiratory disease (total emissions: 0.183, NSR; toxicity-weighted emission: 0.243, NSR), chronic bronchitis (total emissions: 0.0120, 95% CI; toxicity-weighted emission: 0.0175, 99% CI) and asthma (total emission: -0.00309, NSR; toxicity-weighted emission: 0.0809, 95% CI). However, the positive association observed between total emissions and acute bronchitis and bronchiolitis (0.0992; 95% CI) was removed after considering the toxicity of the emissions (-0.0198; NSR). These findings indicate the importance of considering the toxicity of chemicals emitted and not just the quantity of chemicals emitted (Moore & Hotchkiss, 2016).

Ogneva-Himmelberger et al. (2015) investigated maternal exposure to hazardous air pollutants (HAPs) as measured by the RSEI model to estimate its impact on gestational age for mothers exposed in Worcester, MA. Singleton, live births (n=7,136) were stratified by race/ethnicity (non-Hispanic Black, non-Hispanic White, and Hispanic) and gestational age (weeks). Preterm birth (< 37 weeks of gestation) was the primary outcome, including very preterm (< 32 weeks) and extremely preterm (< 28 weeks). The RSEI scores at the census tract level were smoothed using a kernel density function in ArcGIS (v. 10.1). The births were spatially joined to the RSEI density output using the mother's residential location at the time of the infant's birth. The study created kernel density maps for each mother's race, performed cluster analysis, and ran Monte-Carlo simulations to assess the statistical significance of the clusters. The study ran a Welch's t-test and an ANOVA. The study found that when categorized by level of prematurity, preterm births were significantly associated with the RSEI hazard when considering all races together (F-statistic = 7.632, p value < 0.05), and for non-Hispanic white mothers (F-statistic = 4.207, p value < 0.05) and Hispanic mothers (F-statistic = 7.033, p value <

0.05) when evaluated separately (Ogneva-Himmelberger et al., 2015). Although the study evaluated birth outcomes, the study did not mention controlling for certain maternal characteristics which could lead to confounding. Also, the study used the RSEI hazard which does not include fate and transport modeling.

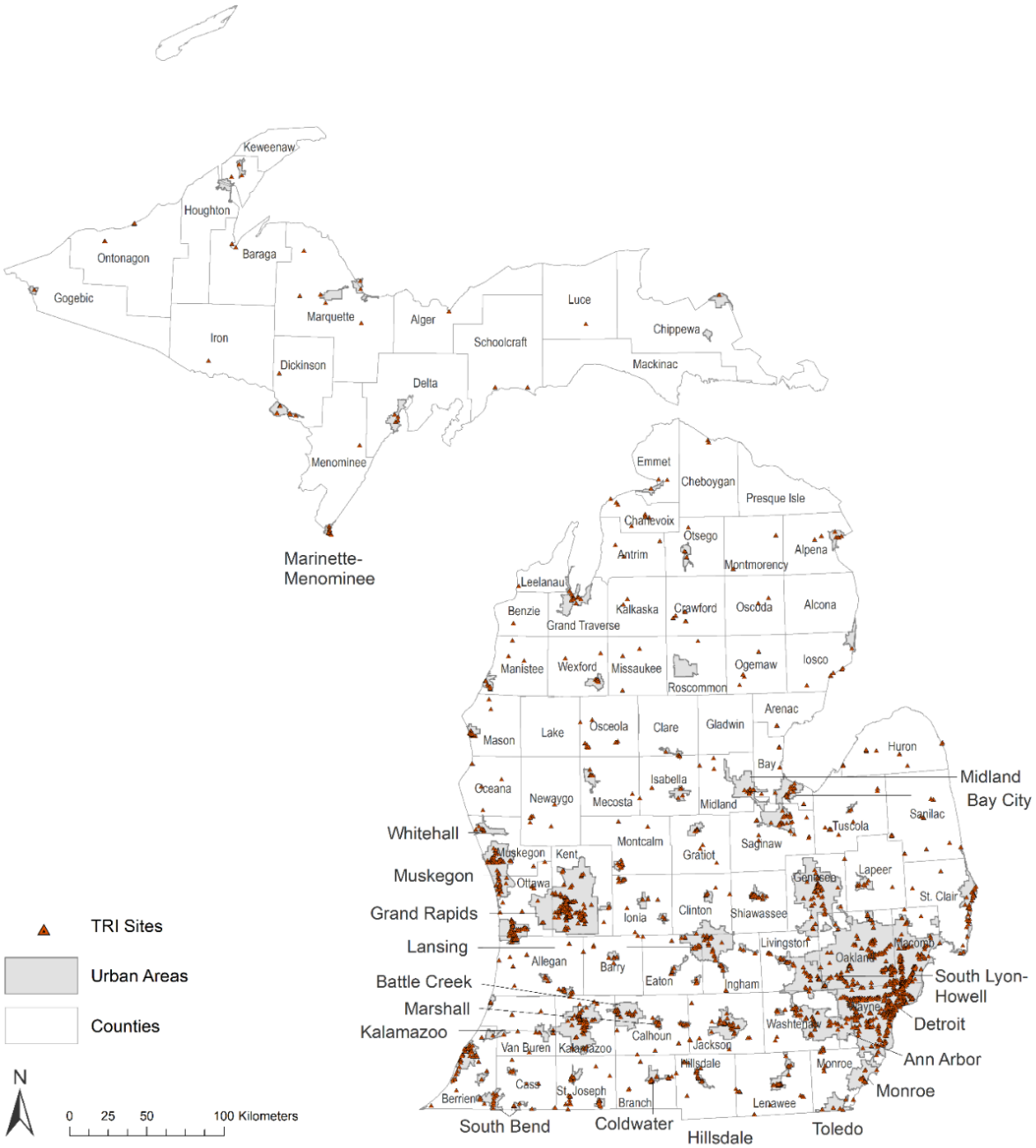
Maternal exposures to toxic chemicals in their neighborhoods may influence birth outcomes, such as low birth weight, preterm birth, fetal growth and birth defects. There remains a gap in our understanding of TRI chemical exposures on birth outcomes. Therefore, this study used the RSEI model to evaluate census tract level RSEI toxicity-weighted concentrations on adverse birth outcomes. This was the first study to my knowledge to use the RSEI model to evaluate a health outcome in Michigan. Additionally, this study was the first to use the RSEI toxicity-weighted concentrations to evaluate maternal exposures and adverse birth outcomes. Although the RSEI scores have been used in prior studies to evaluate various health outcomes, this study chose not to include a population weight in its calculation because mothers only are studied and therefore, used the RSEI toxicity-weighted concentrations.

4.2. Study Area

Michigan is a state located in the Midwestern region of United States (State of Michigan, 2019). Michigan is the 10th most populous state with an estimated 9.99 million residents in 2019 (U.S. Census Bureau, 2020). The population density is 176.7 people per square mile (Duffin, 2020). The three major industries in Michigan include manufacturing, tourism and agriculture (State of Michigan, 2019). Michigan had 1,048 TRI sites in operation between 2008 to 2017 (Figure 4-1). A nation-wide assessment of modelled TRI releases and their potential chronic human health risks ranked Michigan 10th out of 57 U.S. states and territories (EPA, EasyRSEI,

2019). Michigan has elevated rates of low birth weight and preterm births and neonatal mortality when compared to the national average (CDC, 2018; United Health Foundation, 2020).

Figure 4-1: Toxic Release Inventory Sites in Michigan, 2008-2017



4.3. Study Objectives

The objective of this study is to estimate the effect of maternal exposure to RSEI toxicity-weighted concentrations on the likelihood of adverse birth outcomes, including neonatal mortality from lethal congenital anomalies for women living in Michigan, 2008-2017. Direct and indirect relationships between RSEI toxicity-weighted concentrations and adverse birth outcomes or lethal congenital anomalies will be studied, controlling for potential confounding variables. The two hypotheses of the study are:

H_{01} Mothers exposed in high RSEI exposure quartiles will be at increased odds of adverse birth outcomes (low birth weight and preterm birth) and lethal congenital anomalies.

H_{02} African American and Hispanic mothers will be at increased risk of exposure to RSEI toxicity-weighted concentrations, and these exposures will in part explain racial and ethnic disparities in adverse birth outcomes.

4.4. Study Design

This study utilized a retrospective cross-sectional cohort study design (2008 to 2017) to investigate the impacts(s) of RSEI-Toxicity weighted concentrations on maternal health, adverse birth outcomes and congenital anomaly related infant mortality in Michigan. A description of the data and methods that will be used in this study follows.

4.5. Data

4.5.1. TRI Chemical Data

The U.S. EPA's Office of Pollution Prevention and Toxics developed the RSEI model. The model uses precise modeling for each type of chemical release, specific calculations for the chemical toxicity weights and population characteristics to calculate RSEI toxicity-weighted

concentrations for census tracts across the United States. The calculations for RSEI toxicity-weighted concentrations are summarized below.

RSEI toxicity-weighted concentrations = Surrogate Dose × Toxicity Weight

Where surrogate dose is the estimate of human exposure potential which includes data on pathway-specific chemical emissions, physicochemical properties and site-specific characteristics, when available. These data are used to estimate the ambient chemical concentration in the environmental medium in which it was released. The surrogate does is then calculated by combining the ambient chemical concentration with human exposure assumptions for each chemical and the age and sex structure of the exposed population. Population refers to the size of the potentially exposed population, based on the 2010 decennial census. The toxicity weights are specific to each chemical and exposure-route. The chemical toxicity weight increases as the potential for that chemical to cause an adverse chronic human health effect increases. (U.S. EPA, 2018b).

Aggregated microdata shapefiles containing the census tract level RSEI toxicity-weighted concentrations for the years 2008-2017 for Michigan were downloaded from the Amazon Web Services server (http://abt-rsei.s3.amazonaws.com). The TRI Core01 chemical list files were used. The geographic locations of TRI sites in operation during 2008-2017 with modelled releases were obtained from the EPA (U.S. EPA, 2019d, 2019c).

4.5.2. Geographic Data

This study used geographic boundary files retrieved from Michigan's Geographic Information System (GIS) database, including counties (n=83), adjusted urban areas (n=77) and cities (n=280) (State of Michigan, 2019). The census tract was the primary unit of analysis (n=2,791). The NAD 1983 Michigan GeoRef (Meters) coordinate system was used.

4.5.3. Birth and Linked Infant Death Data

The Michigan Department of Health and Human Services Vital Statistics infant birth and linked infant mortality records were used for this study. These individual records contain information on mothers and infants as further described below. Only live, singleton births among mothers who conceived from January 2008 to April 2016 and delivered between September 2008 and December 2017 in Michigan were included in this study.

The types of adverse birth outcomes assessed included low birth weight (newborns weighing < 2,500 grams) and preterm birth (infants born < 37 weeks of gestation) (Merck Sharp & Dohme Corp., 2019; WHO, 2006). Exclusion criteria consisted of births that occurred outside of Michigan (n=12,921), records with a missing address (n=23), births given by non-Michigan residents (n=631), non-singleton births (n=41,773) and births that occurred between January 1 and June 2, 2008 (n=48,937) for which there was no exposure to assign. The mother's address at the time of her infant's birth was used as the place of her TRI chemical exposure risk as further described below.

Potential confounding variables in the RSEI toxicity-weighted concentrations and adverse birth outcome relationship included: mother's age in years as a dichotomous variable (> 34=1, 25-34 years=0), educational attainment (high school diploma or GED=1, some college or college degree=0), pre-pregnancy body mass index (BMI) as a dichotomous variable (<18.5 (underweight)=1, 18.5-24.9 (normal)=0), quality of prenatal care (inadequate=1, adequate or intermediate=0), smoked tobacco during pregnancy (yes=1), alcohol consumption during pregnancy (yes=1), maternal medical conditions including chronic hypertension (yes=1), gestational hypertension (yes=1), chronic diabetes (yes=1), vaginal bleeding (yes=1), premature rupture of the membranes (yes=1), uterine rupture (yes=1) and pregnancy complications short

labor (yes=1), marital status (married=0, all others=1), and residence (urban=1, non-urban=0). Infant characteristics that were controlled for include infant's sex (female=1, male=0) and birth defects (yes=1). The lethal birth defects studied from the linked infant death file included cause of death.

4.6. Methods

4.6.1. Geocoding

Maternal addresses were geocoded using the SAS software® (v. 9.4) street geocode procedure (https://support.sas.com/rnd/datavisualization/mapsonline/html/geocode.html). The street lookup data is the TIGER release ver. 15. The street files were obtained for the United States but queried for Michigan during the geocoding process. With this program, the mother's addresses were geocoded to the appropriate address or defaulted to city or Zip Code centroids. Following the SAS software street geocoding procedure, the records that were unmatched or matched only to the Zip Code or city were then geocoded in GIS. Of the total birth records (n=1,134,485), 97.2% (n=1,102,706) geocoded to the street, 2.75% (n=31,185) geocoded to the Zip Code, 0.0004% geocoded to the city (n=5) and 0.05% (n=589) were not geocoded. The unmatched records were removed. The geocoded birth records were spatially joined to the census tract in which the mother resided at the time of her infant's birth (n=1,133,896).

4.6.2. Exposure Assessment

To assign maternal exposures, the census tract RSEI toxicity-weighted concentrations were spatially joined to the individual birth records. Women who were pregnant during two calendar years were weighted according to their number of weeks' gestation during each of those calendar years to assign them with an appropriate exposure. For example, mothers whose three trimesters of pregnancy fell within one calendar year were assigned one RSEI exposure value.

Mothers whose pregnancy spanned two calendar years were assigned the RSEI toxicity-weighted concentration of each of those years, weighted according to the number of weeks gestation during each of the calendar years, and assigned one RSEI exposure value based on this calculation. The RSEI exposure variable for all women was then recoded into exposure quartiles and each mother was grouped into their respective exposure quartile (1, 2, 3 or 4) for the year that she gave birth (Table 4-1). During the 2008-2017 period, 186 TRI chemicals were released in Michigan (EPA, EasyRSEI, 2019). Some of the chemicals are known developmental toxins, neurological toxins, developmental neurotoxins and teratogenic toxins (ATSDR, 2019).

Table 4-1: RSEI Toxicity-Weighted Concentration Quartiles Assigned as Maternal Exposure, Michigan, 2008-2017.

Quartile	Range	Percentile
1	0 - 183.006	25
2	183.007 - 1,426.249	50
3	1,426.250 - 5,972.424	75
4	5,972.425 - 252,571.00	100

4.6.3. Sample Size and Power Calculations

The birth dataset used for this study included n=1,041,749 births over the 10-year period. Mothers were stratified by race and ethnicity, Non-Hispanic White (n=718,344), Non-Hispanic Black (n=197,478) and Hispanic (n=72,944). Figure 4-2a shows that for a Power=0.80 to 0.95 to detect and odds ratio (OR=1.01) the sample size required would range from 377,509 to 625,005 which is an adequate sample size for Non-Hispanic White and Hispanic mothers. Figure 4-2b shows that for a Power=0.80 to 0.95 to detect and odds ratio (OR=1.03) the sample size required would range from 42,790 to 70,839 which is an adequate sample size for Non-Hispanic African

American mothers. As demonstrated, there is a sufficient sample size to detect small changes in the odds of adverse birth outcomes for the three groups of mothers in this study.

Figure 4-2a: Sample Size and Power Calculation

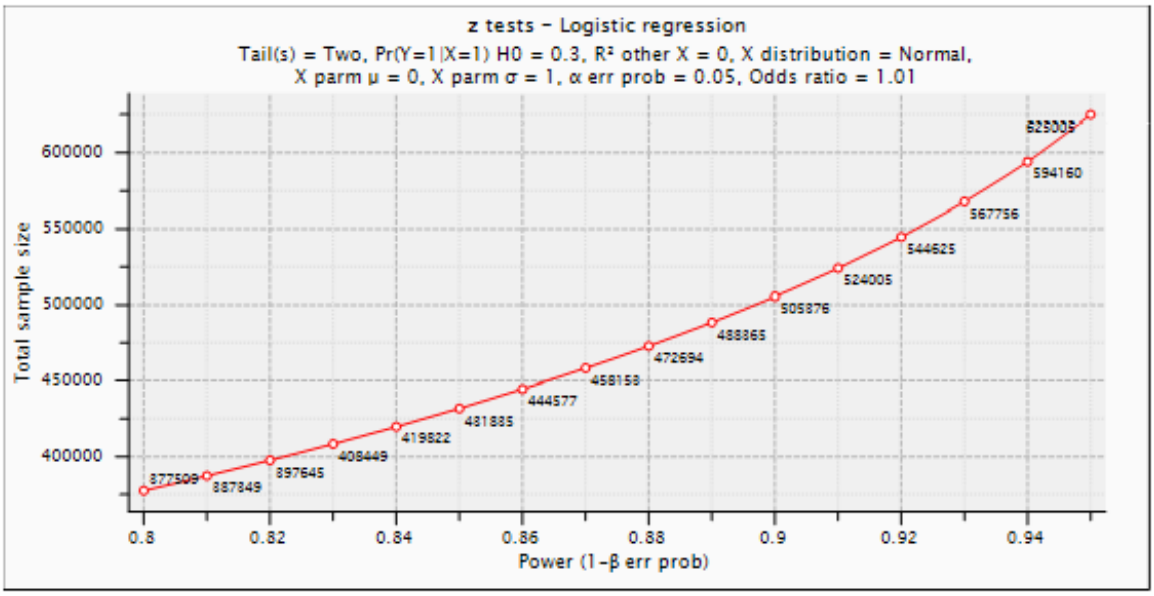
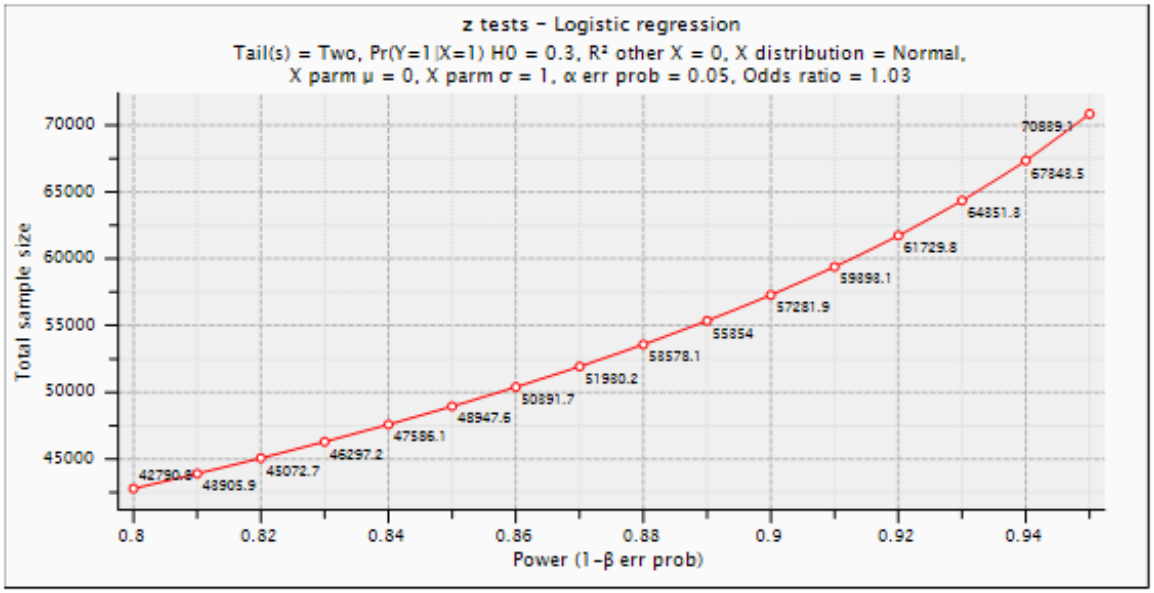


Figure 4-3b: Sample Size and Power Calculation



4.6.4. Descriptive Analysis

Descriptive statistics were generated to assess the quality and structure of the birth and linked infant mortality records and maternal RSEI toxicity-weighted concentration exposure. Histograms, frequencies and univariate and bivariate analyses were conducted to assess the degree of correlation between variables. The birth data was also examined with the RESI modeled data to assess these bivariate relationships.

4.6.5. Analytical Analysis

Regression Models of Adverse Birth Outcomes

Logistic regression models were estimated to determine the likelihood of low birth weight and preterm births among women exposed to varying levels of RSEI toxicity-weighted concentrations, while controlling for known risk factors. The covariates were selected based on known risk factors for each adverse birth outcome, while gauging the fit of the model. Additionally, the independent variable were tested for multicollinearity using both correlation coefficients and Variance Inflation Factor (VIF) values. These regression models were estimated using PROC Logistic in SAS software v 9.4 (SAS Institute Inc., 2016). Four models were constructed for each outcome, an overall model for all women and the three race/ethnicity-stratified models.

For a binary response, Y, the birth outcome can take on two possible values (e.g., low birth weight=0, otherwise, low birth weight=1). If x is an explanatory variable and $\pi = \Pr(Y = 1|x)$ is the probability to be modeled. The linear logistic model has the form:

$$logit(\pi) \equiv \log\left(\frac{\pi}{1-\pi}\right) = \alpha + \beta_1(RSEIQ4v1) + \beta_2(MAge) + \beta_3 \ldots\ldots\ldots \beta_s + \mu_i$$

Where α is the intercept low birth weight and β are slope coefficients. The error term μ_i is assumed to be normally distributed with a mean=0.

$$In(ODDS) = In\left(\frac{Y}{1-Y}\right) = a + bX$$

Where Y is the predicted probability of the outcome (i.e., low birth weight or preterm birth) and 1-Y is the predicted probability of the other outcome (i.e., not low birth weight or not preterm birth). The output provided model fit statistics, including Akaike Information Criterion [AIC], R^2 and Chi-Square test statistic, as well as odds ratios (OR), 95% Confidence Intervals and associated p-values (SAS Institute, 2021).

Cluster Analyses of Infant Deaths

Space-time scan statistics available in SaTScan software package v 9.7 (Kulldorff, 2009) were used to analyze the geographic and temporal distribution of infant mortality attributable to birth defects in Michigan between 2008-2018 to establish if there were clusters of lethal birth defects and if those clusters could in part be explained by the RSEI toxicity-weighted concentrations of the census tract in which the infant was born (assuming maternal exposure in that tract). Clusters are reported when the observed number of infant deaths exceeds the expected number of infant deaths. Bernoulli and discrete Poisson models (Kulldorff, 1997) were used for space-time analyses of lethal birth defects. The Bernoulli model uses a case-control design. For this study, the cases were infant deaths attributable to lethal birth defects and the controls were infant deaths due to other causes. The probability of each infant outcome was assumed to be independent. For the Poisson model, the number of cases is assumed to be Poisson distributed. The method tests the null hypothesis which expects that the number of cases (i.e., lethal birth defects) is proportional to population size of the location (i.e., births in census tracts) (Kulldorff, 1997; Kulldorff, 2021). For this study, the Poisson analysis included unadjusted and adjusted models. The adjusted model included the maximum RSEI toxicity-weighted concentration of the census tract as a covariate. Both the Bernoulli model and Poisson model calculate the relative

risk (RR) and the log-likelihood ratio from the number of observed and expected infant deaths for each location and size of the scanning window, and the statistical significance of the clusters are derived from Monte-Carlo (999) hypothesis testing (Kulldorff, 1997; Kulldorff, 2021).

For both the Bernoulli and Poisson models, the infant mortality rate associated with birth defects for Michigan (25.7 per 1,000) was used to set the maximum cluster size (MDHHS, 2021). The time periods of one and five years were used as the temporal parameters. Other cluster size parameters were explored, including 2k, 5k, 8k, and 10k circles. However, it was decided that using the infant mortality rate among infants with a birth defect in Michigan was conceptually more meaningful than using distance measures from census tract centroids. Even with the distance-based parameters, the clusters appeared in similar locations as with the rate-based parameters, indicating persistence in these areas. To map the clusters of lethal defects for geographic visualization the clusters and their associated relative risks obtained from the output of the Bernoulli and Poisson models were input into ArcGIS v. 10.6 (ESRI, 2020) for visualization. "SaTScan™ is a trademark of Martin Kulldorff. The SaTScan™ software was developed under the joint auspices of (i) Martin Kulldorff, (ii) the National Cancer Institute, and (iii) Farzad Mostashari of the New York City Department of Health and Mental Hygiene" (Kulldorff, 2009).

4.7. Results

4.7.1. Descriptive Results

The birth outcomes of interest in this study show the overall rate of low birth weight in Michigan was 6.5 per 100 live births and preterm birth was 9.9 per 100 live births (Table 4-2). Non-Hispanic Black women had the highest rates of low birth weight and preterm birth, followed next by preterm birth among Hispanic women. The lowest rates of low birth weight and

preterm birth are observed among non-Hispanic white women. Of the infant deaths for which there was a matching birth record, 6.2 per 100 were attributable to a birth defect. Non-Hispanic white women had the highest rates of lethal birth defects, followed by non-Hispanic black women.

Table 4-2: Low Birth Weight, Preterm Birth and Lethal Birth Defect Rates[1] Overall and Stratified by Race and Ethnicity, Michigan, 2008-2017.

Race or Ethnicity	Outcome	Number	Rate[1]
All Women	Low Birth Weight	68,094	6.5
(n=1,041,749)	Preterm Birth	102,921	9.9
	Lethal Birth Defect	1,374	6.2
Non-Hispanic White	Low Birth Weight	36,807	5.1
(n=718,344)	Preterm Birth	60,048	8.4
	Lethal Birth Defect	861	62.7
Non-Hispanic Black	Low Birth Weight	23,319	11.8
(n=197,478)	Preterm Birth	30,501	15.5
	Lethal Birth Defect	329	23.9
Hispanic	Low Birth Weight	4,234	5.8
(n=72,944)	Preterm Birth	7,537	10.4
	Lethal Birth Defect	121	8.8

[1]Rate per 100 live births

The characteristics of mothers in this study are provided in Table 4-3. Just over half of the mothers (55%) were between the ages of 25-34 years old, one-third were less than 25 years old, and the smallest percentage of mothers were over the age of 34 years. Most of the mothers were non-Hispanic white, followed next by non-Hispanic black and finally Hispanic. Nearly 60% of mothers either had some college experience or completed a college degree and 25.7% had a least a high school diploma or GED. Married mothers comprised almost 60% of all mothers in the study. Adequate or intermediate prenatal care was received by a vast majority of the mothers. Almost 17% of mothers smoked during their pregnancy and less than 1% consumed alcohol during their pregnancy. Slightly over 40% of mothers had a normal BMI, while about

25% were obese and less than 5% were underweight. Most (61.3%) of the mothers lived in an urban area rather than a rural area.

Table 4-3: Descriptive Characteristics of Mothers in Michigan, 2008-2017.

Variables		Number	Percent
Age	< 25 years old	327,716	31.5
	25-34 years old	578,197	55.5
	> 34 years old	135,815	13.0
Race and Ethnicity	Non-Hispanic White	718,344	69.0
	Non-Hispanic Black	197,478	19.0
	Hispanic	72,944	7.0
Educational Attainment	High School or GED	268,088	25.7
	College (some or completed)	623,879	59.9
Marital Status	Currently Married	597,895	57.4
	All Others	443,612	42.6
Prenatal Care	Adequate	708,515	68.0
	Intermediate	229,042	22.0
	Inadequate	90,879	8.7
Smoked During Pregnancy	Yes	174,715	16.8
	No	862,115	82.8
Alcohol During Pregnancy	Yes	6,121	0.6
	No	1,029,359	98.8
Weight	Underweight (BMI < 18.5)	35,160	3.4
	Normal (BMI 18.4-24.9)	438,134	42.1
	Obese (BMI >29.9)	265,758	25.5
Urban-Rural Residence	Urban	638,829	61.3
	Non-Urban	402,915	38.7

The maternal medical conditions of interest in this study show the rate of infections during pregnancy was the highest among mothers in Michigan (16.9 per 100). The rate of gestational hypertension (5.1 per 100) followed by pregnancy complications short labor was 4.8 per 100 and next by premature rupture of the membranes with a rate of 4.2 per 100. Other important maternal medical conditions included chronic hypertension (1.4 per 100), vaginal bleeding (1.2 per 100), chronic diabetes (0.8 per 100) and uterine rupture (0.1 per 100). Refer to

Table 4-4. There are defined pathways by which each of these medical conditions may contribute to low birth weight or preterm birth.

Table 4-4: Maternal Medical Conditions of Interest, Michigan, 2008-2017.

Variables	Number	Rate[1]
Chronic Hypertension	14,104	1.4
Gestational Hypertension	53,476	5.1
Chronic Diabetes	7,896	0.8
Vaginal Bleeding	12729	1.2
Premature Rupture of the Membranes	44,023	4.2
Uterine Rupture	1,071	0.1
Pregnancy Complications Short Labor	49,529	4.8
Infection(s)	176,480	16.9

[1]Per 100 women.

When mothers are stratified by race and ethnicity, the percentage of those 35 years and older were similar among all mothers (Table 4-5). Non-Hispanic white women tended to have higher levels of education, with one-quarter having a high school diploma or GED as their highest level of education compared to just under 50% of non-Hispanic black mothers and Hispanic mothers with a high school diploma or GED as their highest level of education demonstrating large racial and ethnic disparities in education. Most (80.7%) non-Hispanic black women were unmarried, half (53.5%) of Hispanic women were unmarried, and one-third of non-Hispanic white mothers were unmarried. Prenatal care varied, with nearly 7% of non-Hispanic white mothers receiving inadequate prenatal care, compared to 15% and 11% of non-Hispanic black and Hispanic mothers, respectively. Rates of smoking during pregnancy were highest among non-Hispanic white (18.5%) women followed closely by non-Hispanic black women (15.5%) and only 3.9% of Hispanic women smoked. Rates of alcohol consumption was similar among all mothers (< 1.0%). Of the women who were underweight, 9% were non-Hispanic black mothers and around 6% were non-Hispanic white and Hispanic mothers. Nearly all (92.8%) non-

Hispanic black mothers, 69.6% of Hispanic mothers and half (50.8%) of non-Hispanic white mothers' residence was in an urban area as compared to a rural area.

Non-Hispanic white women had the highest rates of gestational hypertension (5.5%) vaginal bleeding (1.3%) premature rupture of membranes (4.3%), pregnancy complications due to short labor (5.0%) and infections (65.4%) compared to non-Hispanic black and Hispanic women although these differences did not appear to be statistically different. These medical conditions may be underreported among African American and Hispanic women though since they had higher rates of inadequate and intermediate prenatal care. Non-Hispanic black women had the highest rates of chronic hypertension (2.3%) and uterine rupture (0.4%) with an equal percentage of non-Hispanic black and Hispanic women reporting diabetes (1.0%). These racial and ethnic differences in maternal medical conditions and their contribution to low birth weight and premature birth are further studied below.

Table 4-5: Descriptive Statistics of Mothers by Race and Ethnicity for Important Risk Factors for Adverse Birth Outcomes, Michigan 2008-2017.

Variable	Race or Ethnicity	Number	Percent
Age	Non-Hispanic White	97,489	18.5%
(older maternal age >35 years)	Non-Hispanic Black	18,895	19.0%
	Hispanic	9,223	20.9%
Educational Attainment	Non-Hispanic White	167,256	25.9%
(high school or GED only – no college)	Non-Hispanic Black	69,955	45.7%
	Hispanic	21,471	46.4%
Marital Status	Non-Hispanic White	235,708	32.8%
(unmarried)	Non-Hispanic Black	159,220	80.7%
	Hispanic	39,055	53.5%
Prenatal Care	Non-Hispanic White	49,134	6.9%
(inadequate)	Non-Hispanic Black	28,828	15.1%
	Hispanic	7,976	11.1%
Smoked during Pregnancy	Non-Hispanic White	132,743	18.5%
(yes)	Non-Hispanic Black	30,378	15.5%
	Hispanic	2,854	3.9%
Alcohol consumption	Non-Hispanic White	4,274	0.6%
(yes)	Non-Hispanic Black	1,309	0.7%
	Hispanic	354	0.5%
Weight	Non-Hispanic White	23,661	6.9%
(underweight)	Non-Hispanic Black	6,227	9.0%
	Hispanic	1,861	6.4%
Urban-Rural Residence	Non-Hispanic White	364,896	50.8%
(urban area)	Non-Hispanic Black	183,193	92.8%
	Hispanic	50,760	69.6%
Chronic Hypertension	Non-Hispanic White	8,621	1.2%
(yes)	Non-Hispanic Black	4,450	2.3%
	Hispanic	622	0.9%
Gestational Hypertension	Non-Hispanic White	39,444	5.5%
(yes)	Non-Hispanic Black	9,215	4.7%
	Hispanic	2,854	3.9%
Chronic Diabetes	Non-Hispanic White	4,670	0.7%
(yes)	Non-Hispanic Black	2,021	1.0%
	Hispanic	714	1.0%
Vaginal Bleeding	Non-Hispanic White	9,465	1.3%
(yes)	Non-Hispanic Black	1,643	0.8%
	Hispanic	809	1.1%
Premature Rupture of the Membranes	Non-Hispanic White	30,545	4.3%
(yes)	Non-Hispanic Black	8,122	4.2%
	Hispanic	2,860	3.9%

Table 4-5 (cont'd)

Uterine Rupture (yes)	Non-Hispanic White	248	0.03%
	Non-Hispanic Black	718	0.4%
	Hispanic	67	0.1%
Pregnancy Complications Short Labor (yes)	Non-Hispanic White	35,718	5.0%
	Non-Hispanic Black	7,698	4.0%
	Hispanic	3,069	4.2%
Infection(s) (yes)	Non-Hispanic White	115,089	65.4%
	Non-Hispanic Black	43,290	24.6%
	Hispanic	10,454	5.9%

The percentage of male and female infants born in Michigan was evenly split as shown in Table 4-6. A little over half of the infants were male (51.2%). The percentage of infant deaths by sex was slightly higher among male infants (52.0%) than female infants.

Table 4-6: Number and Percentage of Infants Born and Died by Sex, Michigan 2008-2017.

Infant Sex	Infant Births		Infant Deaths	
	Number	Percent	Number	Percent
Male	533,862	51.2	712	52.0
Female	507,863	48.8	656	48.0

4.7.2. Logistic Regression Results for Low Birth Weight

The results from the logistic regression model for mothers overall are shown in Table 4-7. When RSEI exposure quartiles 2-4 were compared with the reference category exposure quartile 1, mothers exposed in quartiles 3 and 4 were at significantly increased odds of having a low birth weight infant. For mothers exposed in quartile 2 the odds of low birth weight was borderline (OR=1.024, 95% CI 0.998-1.051). However, for mothers exposed to quartiles 3 and 4 the odds of low birth weight was significant for quartile 3 (OR=1.125, 95% CI 1.096-1.154) and quartile 4 (OR=1.270, 95% CI 1.238-1.300) controlling for potential confounding and known risk factors for low birth weight as presented in the table. These findings show that with

increasing RSEI exposure, mothers are at increasing odds of having a low birth weight infant. The most important risk factor for low birth weight was inadequate prenatal care (OR=3.258, 95% CI 3.171-3.347) followed by chronic diabetes (OR=1.729, 95% CI 1.597-1.871), a high school educational attainment (OR=1.680, 95% CI 1.634-1.728), unmarried (OR=1.653, 95% CI 1.621-1.686), gestational hypertension (OR=1.426, 95% CI 1.297-1.568), alcohol consumption (OR=1.409, 95% CI 1.377-1.442) and smoked during pregnancy (OR=1.197, 95% CI 1.174-1.221). These findings show that receiving health care during pregnancy to monitor behaviors and treat medical conditions is very important.

Table 4-7: Logistic Regression Models for Low Birth Weight All Women, Michigan, 2008-2017.

Final Logistic Regression Model Results				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	<.0001	1.024	0.998	1.051
Exposure quartile 3 vs 1	0.0048	1.125	1.096	1.154
Exposure quartile 4 vs 1	<.0001	1.270	1.238	1.302
Prenatal care 1 vs 0	<.0001	3.258	3.171	3.347
Educational attainment 1 vs 0	<.0001	1.680	1.634	1.728
Smoked 1 vs 0	<.0001	1.197	1.174	1.221
Alcohol consumption 1 vs 0	<.0001	1.409	1.377	1.442
Gestational hypertension 1 vs 0	<.0001	1.426	1.297	1.568
Chronic diabetes 1 vs 0	<.0001	1.729	1.597	1.871
Marital status 1 vs 0	<.0001	1.653	1.621	1.686

N=873,347. R-Square = 0.0163 and adjusted R-Square = 0.0449.

Importantly, when the race variable (black vs all other races) was added into the logistic regression models, the effects of the RSEI exposure (quartiles 1-4) on low birth weight was no longer significant, and so it appears that mother's race and RSEI toxicity-weighted concentrations are correlated. In response to this finding, the logistic regression models were

stratified by mother's race and ethnicity (non-Hispanic white, non-Hispanic black and Hispanic mothers).

Non-Hispanic White Mothers: Low Birth Weight

The results of the logistic regression model for low birth weight births among non-Hispanic white women are shown in Table 4-8). When exposure quartiles 2-4 were compared to the reference category quartile 1, only quartile 4 was statistically significant. Non-Hispanic white mothers exposed to quartile 4 experienced an increased odds of giving birth to a low birth weight infant (OR=1.092, 95% CI 1.048-1.138). Since non-Hispanic white mothers had the highest rate of smoking and smoking is a strong risk factor for low birth weight, it was hypothesized that a synergistic effect of RSEI exposure*smoking might also exist to result in low birth weight. The interaction effect of exposure*smoking during pregnancy was also compared to the reference category of quartile 1 (women who did not smoke during pregnancy) and mothers exposed in quartiles 1, 2, and 4 were at a statistically significant higher odds of having a low birth weight infant with a rise in the odds of low birth weight for women exposed to quartile 4 OR=1.609 (95% CI 1.507-1.718). Other risk factors included gestational hypertension (OR=3.37, 95% CI 3.257-3.487), chronic hypertension (OR=3.070 95% CI 2.861-3.294), inadequate prenatal care was another important risk factor (OR=1.754 95% CI 1.686-1.825) followed by alcohol consumption during pregnancy (OR=1.519 95% CI 1.351-1.709), mothers with chronic diabetes (OR=1.426 95% CI 1.275-1.595), unmarried mothers (OR=1.354 95% CI 1.318-1.390), female infants compared to male infants (OR=1.202 95% CI 1.174-1.230), and mothers with a high school diploma or GED compared to mothers with a college degree or some college experience (OR=1.197 95% CI 1.165-1.229).

Table 4-8: Logistic Regression Models for Low Birth Weight, Non-Hispanic White Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.3051	0.998	0.967	1.029
Exposure quartile 3 vs 1	0.0101	0.98	0.949	1.013
Exposure quartile 4 vs 1	<.0001	1.055	1.019	1.092
Prenatal care 1 vs 0	<.0001	1.754	1.685	1.824
Educational attainment 1 vs 0	<.0001	1.197	1.165	1.229
Smoked 1 vs 0	<.0001	1.676	1.628	1.725
Alcohol consumption 1 vs 0	<.0001	1.519	1.35	1.709
Chronic hypertension 1 vs 0	<.0001	3.067	2.858	3.291
Gestational hypertension 1 vs 0	<.0001	3.367	3.254	3.483
Chronic diabetes 1 vs 0	<.0001	1.425	1.274	1.593
Marital status 1 vs 0	<.0001	1.351	1.316	1.388
Infant sex 1 vs 0	<.0001	1.202	1.174	1.23
Final Logistic Regression Model Results				
Exposure quartile 2 vs 1	0.5558	1.028	0.991	1.066
Exposure quartile 3 vs 1	0.2665	1.021	0.983	1.06
Exposure quartile 4 vs 1	<.0001	1.092	1.048	1.138
Exposure quartile*Smoked 1 vs 0	<.0001	1.807	1.725	1.894
Exposure quartile*Smoked 2 vs 0	<.0001	1.647	1.564	1.735
Exposure quartile*Smoked 3 vs 0	0.1473	1.553	1.459	1.654
Exposure quartile*Smoked 4 vs 0	0.0078	1.609	1.507	1.718
Prenatal care 1 vs 0	<.0001	1.754	1.686	1.825
Educational attainment 1 vs 0	<.0001	1.197	1.165	1.229
Alcohol consumption 1 vs 0	<.0001	1.519	1.351	1.709
Chronic hypertension 1 vs 0	<.0001	3.07	2.861	3.294
Gestational hypertension 1 vs 0	<.0001	3.37	3.257	3.487
Chronic diabetes 1 vs 0	<.0001	1.426	1.275	1.594
Marital status 1 vs 0	<.0001	1.354	1.318	1.39
Infant sex 1 vs 0	<.0001	1.202	1.174	1.23

N=635,805, R-Square=0.0141 and adjusted R-Square=0.0445.

Non-Hispanic Black Mothers: Low Birth Weight

Two logistic regression models were estimated for low birth weight births among non-Hispanic black women. The results of both models are shown in Table 4-9. In model 1, when compared to the reference exposure quartile 1, only exposure quartile 4 was statistically significant. For non-Hispanic black mothers exposed in quartile 4 the odds of low birth weight was significant (OR=1.122, 95% CI 1.031-1.220) controlling for potential confounding and known risk factors listed in the table. The most important risk factor for low birth weight among non-Hispanic black women in model 1 was gestational hypertension (OR=3.883, 95% CI 3.570-4.223) followed by chronic hypertension (OR=2.85, 95% CI 2.555-3.178), smoking (OR=1.546, 95% CI 1.443-1.656), maternal infections (OR=1.417, 95% CI 1.330-1.509), inadequate prenatal care (OR=1.348, 95% CI 1.248-1.456), unmarried (OR=1.329, 95% CI 1.253-1.410), alcohol consumption (OR=1.314, 95% 0.982-1.758), older maternal age (OR=1.251, 95% CI 1.175-1.333), female infants (OR=1.229, 95% CI 1.166-1.295), chronic diabetes (OR=1.216, 95% CI 1.018-1.454) and an educational attainment of a high school education compared to some college or a college degree (OR=1.130, 95% CI 1.069-1.194).

Since non-Hispanic black mothers are at increased risk of medical conditions with increasing age, it was hypothesized that a synergistic effect of RSEI exposure*increasing age might also exist to result in low birth weight. When the exposure quartiles were modeled as an interaction term with non-Hispanic black women of older age (>34 years) the interaction effect was statistically significant for quartile 3 (OR=1.141, 95% CI 1.030-1.264) and quartile 4 (OR=1.376, 95% CI 1.261-1.502) when compared to the reference category of 0 (25-34 years). Thus, longer exposure to living in neighborhoods with higher RSEI scores appears to increase the odds of low birth weight for non-Hispanic black women. The most important risk factor for

low birth weight in this model was gestational hypertension (OR=3.888, 95% CI 3.574-4.229) followed by chronic hypertension (OR=2.837, 95% 2.544-3.164), smoking (OR=1.532, 95% CI 1.430-1.641), maternal infections (OR=1.420, 95% CI 1.333-1.513), inadequate prenatal care (OR=1.350, 95% CI 1.250-1.458), unmarried (OR=1.326, 95% CI 1.250-1.406), alcohol consumption (OR=1.304, 95% CI 0.974-1.745), female infants (OR-1.229, 95% CI 1.167-1.295), chronic diabetes (OR=1.215, 95% CI 1.016-1.452) and mothers whose highest level of education was a high school diploma or GED compared to mothers with a college degree or some college experience (OR=1.129, 95% CI 1.068-1.193). Thus, while the interactions of quartiles 3 and 4 with older maternal age increased the odds of low birth weight for non-Hispanic black women the risk factors for low birth weight remained relatively similar.

Table 4-9: Logistic Regression Models for Low Birth Weight, Non-Hispanic Black Women, Michigan, 2008-2017.

Final Logistic Regression Model 1 Results				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.3758	1.097	0.993	1.213
Exposure quartile 3 vs 1	0.856	1.066	0.975	1.165
Exposure quartile 4 vs 1	0.0239	1.122	1.031	1.220
Prenatal care 1 vs 0	<.0001	1.348	1.248	1.456
Older maternal age 1 vs 0	<.0001	1.251	1.175	1.333
Educational attainment 1 vs 0	<.0001	1.130	1.069	1.194
Smoked 1 vs 0	<.0001	1.546	1.443	1.656
Alcohol consumption 1 vs 0	0.0663	1.314	0.982	1.758
Chronic hypertension 1 vs 0	<.0001	2.850	2.555	3.178
Gestational hypertension 1 vs 0	<.0001	3.883	3.570	4.223
Chronic diabetes 1 vs 0	0.0313	1.216	1.018	1.454
Maternal infection(s) 1 vs 0	<.0001	1.417	1.330	1.509
Marital status 1 vs 0	<.0001	1.329	1.253	1.410
Infant sex 1 vs 0	<.0001	1.229	1.166	1.295
Final Logistic Regression Model 2 Results				
Exposure quartile*Older maternal age 1	0.3373	1.266	1.065	1.504
Exposure quartile*Older maternal age 2	0.7473	1.157	0.994	1.347
Exposure quartile*Older maternal age 3	0.4584	1.141	1.030	1.264
Exposure quartile*Older maternal age 4	0.0003	1.376	1.261	1.502
Prenatal care 1 vs 0	<.0001	1.350	1.250	1.458
Educational attainment 1 vs 0	<.0001	1.129	1.068	1.193
Smoked 1 vs 0	<.0001	1.532	1.430	1.641
Alcohol consumption 1 vs 0	0.0741	1.304	0.974	1.745
Chronic hypertension 1 vs 0	<.0001	2.837	2.544	3.164
Gestational hypertension 1 vs 0	<.0001	3.888	3.574	4.229
Chronic diabetes 1 vs 0	0.0324	1.215	1.016	1.452
Maternal infection(s) 1 vs 0	<.0001	1.420	1.333	1.513
Marital status 1 vs 0	<.0001	1.326	1.250	1.406
Infant sex 1 vs 0	<.0001	1.229	1.167	1.295

Model 1: N=53,394, R-Square=0.0289 and adjusted R-Square=0.0578.
Model 2: N=60,023, R-Square=0.0290 and adjusted R-Square=0.0579.

Hispanic Women: Low Birth Weight

The results of the logistic regression low birth weight model for Hispanic mothers are shown in Figure 4-10. When exposure quartiles 2-4 were compared to the reference group quartile 1, none were statistically significant, demonstrating that exposure to RSEI levels were not a significant risk factor for low birth weight for Hispanic women. Since Hispanic mothers have a high odds of gestational hypertension, it was hypothesized that a synergistic effect of RSEI exposure*gestational hypertension might also exist to result in low birth weight. However, the interaction term exposure*gestational hypertension when comparing quartiles 1-4 with the reference category 0 (no gestational hypertension), quartiles 1, 3, and 4 were statistically significant. Women with gestational hypertension in exposure quartiles 3 and 4 had an increasing odds of having a low birth weight infant (OR=4.968, 95% CI 3.575-6.903 and OR=5.018, 95% CI 3.773-6.674, respectively). Chronic hypertension was also an important risk factor for low birth weight (OR=3.592 95% CI 2.675-4.822), followed by smoking during pregnancy (OR=1.747, 95% CI 1.505-2.2027), inadequate prenatal care (OR=1.47, 95% CI 1.246-1.735), older maternal age (OR=1.272, 95% CI 1.122-1.441), having a high school diploma of GED compared to some college or a college degree (OR=1.201, 95% 1.077-1.338) and being unmarried (OR=1.192, 95% CI 1.066-1.333) were risk factor for low birth weight among Hispanic mothers. Interestingly, Hispanic women's risk factors for low birth weight did not include other maternal medical conditions -e.g., diabetes and infections more commonly observed in non-Hispanic white and black women.

Table 4-10: Logistic Regression Models for Low Birth Weight, Hispanic Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.2149	0.872	0.749	1.015
Exposure quartile 3 vs 1	0.0866	0.848	0.722	0.995
Exposure quartile 4 vs 1	0.1287	0.986	0.855	1.137
Maternal age 1 vs 0	0.0002	1.272	1.123	1.442
Prenatal care 1 vs 0	<.0001	1.466	1.242	1.73
Educational attainment 1 vs 0	0.0009	1.202	1.078	1.339
Smoked 1 vs 0	<.0001	1.745	1.503	2.025
Chronic hypertension 1 vs 0	<.0001	3.588	2.672	4.817
Gestational hypertension 1 vs 0	<.0001	4.806	4.127	5.598
Marital status 1 vs 0	0.0019	1.193	1.067	1.335
Final Logistic Regression Model Results				
Exposure quartile 2 vs 1	0.5634	0.915	0.776	1.078
Exposure quartile 3 vs 1	0.0939	0.86	0.722	1.023
Exposure quartile 4 vs 1	0.1898	1	0.858	1.166
Exposure quartile*Gestational hypertension 1 vs 0	0.001	5.461	4.045	7.372
Exposure quartile*Gestational hypertension 2 vs 0	0.4096	3.933	2.889	5.354
Exposure quartile*Gestational hypertension 3 vs 0	0.0163	4.968	3.575	6.903
Exposure quartile*Gestational hypertension 4 vs 0	0.0056	5.018	3.773	6.674
Maternal age 1 vs 0	0.0002	1.272	1.122	1.441
Prenatal care 1 vs 0	<.0001	1.47	1.246	1.735
Educational attainment 1 vs 0	0.001	1.201	1.077	1.338
Smoked 1 vs 0	<.0001	1.747	1.505	2.027
Chronic hypertension 1 vs 0	<.0001	3.592	2.675	4.822
Marital status 1 vs 0	0.0021	1.192	1.066	1.333

N=27,681, R-Square=0.0174 and adjusted R-Square=0.0515.

4.7.3. Logistic Regression Results for Preterm Birth

All Women: Preterm Birth

The logistic regression model results for preterm birth among all women are shown in Table 4-11. When compared to the reference category exposure quartile 1, exposure quartiles 2

and 4 were at significantly increased odds of having a preterm birth. Exposure quartile 2 had a slightly protective effect on mothers (OR=0.955, 95% CI 0.917-0.994), while mothers in exposure quartile 4 was at increased odds (OR=1.137, 95% CI 1.092-1.185) controlling for potential confounding and known risk factors as listed in the table. Since premature rupture of the membranes is an important risk factor of preterm birth, the interaction term exposure*premature rupture of the membranes was further evaluated. Quartiles 1-4 were compared to the reference category 0 (no premature rupture of the membranes). For mothers exposed to quartiles 1-4 who experienced premature rupture of the membranes the odds of preterm birth was significant with quartile 1 (OR=4.159, 95% CI 3.779-4.577), quartile 2 (OR=4.077, 95% CI 3.749-4.433), quartile 3 (OR=3.670 95% CI 3.401-3.961) and quartile 4 (OR=4.829, 95% CI 4.426-5.268) controlling for known risk factors as listed in the table. These findings show at quartiles 3 and 4 a synergistic effect between elevated RSEI toxicity-weighted concentration exposures and premature rupture of membranes, here important causes of preterm birth. Gestational hypertension was the next most important risk factor (OR=3.481, 95% CI 2.997-4.043) followed by vaginal bleeding (OR=2.999, 95% CI 2.781-3.234), underweight mothers (OR=2.743 95% CI 2.596-2.897), uterine rupture (OR=2.398, 95% CI 1.648-3.489), smoking during pregnancy (OR=1.795, 95% CI 1.735-1.857), inadequate prenatal care (OR=1.574, 95% CI 1.504-1.648), chronic diabetes (OR=1.291, 95% CI 1.228-1.357) and lastly pregnancy complications short labor (OR=1.154, 95% CI 1.095-1.216). Like the logistic regression models for low birth weight, the exposure quartiles were not significant when the race variable (black vs all other races) was included in the model and so separate models for each racial and ethnic group of interest were also constructed.

Table 4-11: Logistic Regression Models for Preterm, All Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	<.0001	0.953	0.917	0.99
Exposure quartile 3 vs 1	0.0359	1.001	0.964	1.039
Exposure quartile 4 vs 1	<.0001	1.154	1.111	1.2
Prenatal care 1 vs 0	<.0001	1.575	1.505	1.649
Smoked 1 vs 0	<.0001	1.795	1.735	1.857
Underweight 1 vs 0	<.0001	1.291	1.228	1.357
Gestational hypertension 1 vs 0	<.0001	2.746	2.599	2.901
Chronic diabetes 1 vs 0	<.0001	3.48	2.996	4.042
Vaginal bleeding 1 vs 0	<.0001	2.999	2.781	3.234
Uterine rupture 1 vs 0	<.0001	2.384	1.638	3.469
Complications in pregnancy short labor 1 vs 0	<.0001	1.153	1.094	1.215
Premature rupture of the membranes 1 vs 0	<.0001	4.117	3.946	4.295
Final Logistic Regression Model Results				
Exposure quartile 2 vs 1	<.0001	0.955	0.917	0.994
Exposure quartile 3 vs 1	0.4329	1.015	0.976	1.056
Exposure quartile 4 vs 1	<.0001	1.137	1.092	1.185
Exposure quartile*Premature rupture of the membranes 1 vs 0	<.0001	4.159	3.779	4.577
Exposure quartile*Premature rupture of the membranes 2 vs 0	<.0001	4.077	3.749	4.433
Exposure quartile*Premature rupture of the membranes 3 vs 0	<.0001	3.67	3.401	3.961
Exposure quartile*Premature rupture of the membranes 4 vs 0	<.0001	4.829	4.426	5.268
Prenatal care 1 vs 0	<.0001	1.574	1.504	1.648
Smoked 1 vs 0	<.0001	1.795	1.735	1.857
Underweight 1 vs 0	<.0001	2.743	2.596	2.897
Gestational hypertension 1 vs 0	<.0001	3.481	2.997	4.043
Chronic diabetes 1 vs 0	<.0001	1.291	1.228	1.357
Vaginal bleeding 1 vs 0	<.0001	2.999	2.781	3.234
Uterine rupture 1 vs 0	<.0001	2.398	1.648	3.489
Complications in pregnancy short labor 1 vs 0	<.0001	1.154	1.095	1.216

N=305,825, R-Square=0.0238 and adjusted R-Square=0.0544.

Table 4-12 provides the results of the logistic regression model for non-Hispanic white mothers. Independently, smoking (OR=1.405, 95% CI 1.357-1.454) premature rupture of the

membranes (OR=4.350, 95% CI 4.177-4.531) were important risk factors for preterm birth among non-Hispanic white mothers. Consequently, the interactions exposure*smoked during pregnancy and exposure*premature rupture of the membranes quartiles were compared to the reference category 0 (no smoking during pregnancy and no premature rupture of the membranes, respectively). The odds ratio of preterm birth was significantly higher among non-Hispanic white mothers in the interaction exposure*smoked during pregnancy quartile 1 (OR=1.398, 95% CI 1.324-1.476), interaction quartile 2 (OR=1.392, 95% CI 1.312-1.477), interaction quartile 3 (OR=1.437, 95% CI 1.340-1.541) and interaction quartile 4 (OR=1.426, 95% CI 1.325-1.536) when controlling for all other covariates presented in the table. Smoking during pregnancy was consistently significant and positive by itself. For mothers in exposure*premature rupture of the membranes the odds of preterm birth was significant with quartile 1 (OR=4.485, 95% CI 4.142-4.857), with quartile 2 (OR=4.265, 95% CI 3.966-4.586), with quartile 3 (OR=3.939, 95% CI 3.658-4.242) and with quartile 4 (OR=5.034, 95% CI 4.593-5.517) when controlling for potential confounders and known risk factors listed in the table. Without the interaction terms, the exposure quartiles by themselves were either not significant or only exposure quartile 3 was significant, but negative. In addition, several other factors were significantly associated with preterm birth among non-Hispanic white women. Uterine rupture was the second most important risk factor (OR=4.194, 95% CI 2.793-6.299) followed by chronic diabetes (OR=3.267, 95% CI 2.966-3.598), vaginal bleeding (OR=3.233, 95% CI 3.009-3.474), gestational hypertension (OR=2.499, 95% CI 2.398-2.603), inadequate prenatal care (OR=1.395, 95% CI 1.382-1.466), older maternal age (OR=1.308, 95% CI 1.269-1.348), maternal infections (OR=1.271, 95% CI 1.231-1.313), complications in pregnancy short labor (OR=1.242, 95% CI 1.176-1.312) and a

high school education or GED compared to some college or a college degree (OR=1.239, 95% CI 1.202-1.278).

Table 4-12: Logistic Regression Models for Preterm Birth, Non-Hispanic White Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.9712	0.98	0.948	1.013
Exposure quartile 3 vs 1	0.0035	0.95	0.918	0.983
Exposure quartile 4 vs 1	0.3277	0.992	0.955	1.03
Prenatal care 1 vs 0	<.0001	1.397	1.33	1.468
Educational Attainment 1 vs 0	<.0001	1.237	1.199	1.275
Maternal Age 1 vs 0	<.0001	1.31	1.271	1.349
Smoked 1 vs 0	<.0001	1.405	1.357	1.454
Gestational hypertension 1 vs 0	<.0001	2.5	2.399	2.604
Chronic diabetes 1 vs 0	<.0001	3.263	2.963	3.593
Vaginal Bleeding 1 vs 0	<.0001	3.232	3.008	3.473
Uterine Rupture	<.0001	4.172	2.778	6.267
Complications in pregnancy short labor 1 vs 0	<.0001	1.242	1.176	1.312
Premature rupture of the membranes 1 vs 0	<.0001	4.35	4.177	4.531
Maternal Infection(s) 1 vs 0	<.0001	1.27	1.23	1.312
Final Logistic Regression Model Results				
Exposure quartile*Smoked 1 vs 0	0.0166	1.398	1.324	1.476
Exposure quartile*Smoked 2 vs 0	0.0374	1.392	1.312	1.477
Exposure quartile*Smoked 3 vs 0	0.004	1.437	1.34	1.541
Exposure quartile*Smoked 4 vs 0	0.0124	1.426	1.325	1.536
Exposure quartile*Premature rupture of the membranes 1 vs 0	<.0001	4.485	4.142	4.857
Exposure quartile*Premature rupture of the membranes 2 vs 0	<.0001	4.265	3.966	4.586
Exposure quartile*Premature rupture of the membranes 3 vs 0	<.0001	3.939	3.658	4.242
Exposure quartile*Premature rupture of the membranes 4 vs 0	<.0001	5.034	4.593	5.517
Prenatal care 1 vs 0	<.0001	1.395	1.328	1.466
Educational Attainment 1 vs 0	<.0001	1.239	1.202	1.278
Maternal Age 1 vs 0	<.0001	1.308	1.269	1.348
Gestational hypertension 1 vs 0	<.0001	2.499	2.398	2.603
Chronic diabetes 1 vs 0	<.0001	3.267	2.966	3.598
Vaginal Bleeding 1 vs 0	<.0001	3.233	3.009	3.474
Uterine Rupture 1 vs 0	<.0001	4.194	2.793	6.299
Complications in pregnancy short labor 1 vs 0	<.0001	1.242	1.176	1.312
Maternal Infection(s) 1 vs 0	<.0001	1.271	1.231	1.313

N=377,319, R-Square=0.0221 and adjusted R-Square=0.0537.

Non-Hispanic Black Women: Preterm Birth

The results of the logistic regression model for preterm births among non-Hispanic black women are shown in Table 4-13. Quartile 4 exposure was significant for preterm birth (OR=1.188, 95% CI 1.023-1.378). Gestational hypertension and premature rupture of the membranes were important risk factors for non-Hispanic black women, so the interactions exposure*gestational hypertension and exposure*premature rupture of the membranes were included. Quartiles 1-4 were compared to the reference category quartile 0 (no gestational hypertension and no premature rupture of the membranes, respectively). An increased odds of preterm birth was observed among non-Hispanic black women in exposure*gestational hypertension quartile 3 (OR=3.688, 95% CI 2.747-4.951) and quartile 4 (OR=4.960, 95% CI 3.810-6.456) while controlling for potential confounding and known risk factors of preterm birth as listed in the table. For non-Hispanic black mothers in the exposure*premature rupture of the membranes quartiles, only those in quartile 4 had a significantly increased odds of preterm birth (OR=4.960, 95% CI 3.810-6.456) controlling for other known covariates. Other important risk factors of preterm birth among non-Hispanic black mothers were identified, including chronic diabetes (OR=3.440, 95% CI 2.043-5.792), chronic hypertension (OR=3.384, 95% CI 2.444-4.686), vaginal bleeding (OR=2.470, 95% CI 1.744-3.498), being underweight (OR=1.486, 95% CI 1.248-1.727), inadequate prenatal care (OR=1.408, 95% CI 1.225-1.619), older maternal age (OR=1.303, 95% CI 1.158-1.467), urban compared to rural residence (OR=1.298, 95% CI 1.086-1.556), being unmarried (OR=1.286, 95% CI 1.160-1.427), smoking during pregnancy (OR=1.260, 95% CI 1.116-1.423), having obtained a high school education compared to some college or a college degree (OR=1.233, 95% CI 1.118-1.359) and maternal infections (OR=1.211, 95% CI 1.084-1.352).

Table 4-13: Logistic Regression Models for Preterm Birth, Non-Hispanic Black Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.7297	1.072	0.901	1.276
Exposure quartile 3 vs 1	0.6317	1.112	0.951	1.301
Exposure quartile 4 vs 1	0.0207	1.188	1.023	1.378
Prenatal care 1 vs 0	<.0001	1.405	1.222	1.615
Educational attainment 1 vs 0	<.0001	1.233	1.118	1.359
Maternal age 1 vs 0	<.0001	1.293	1.148	1.455
Underweight 1 vs 0	<.0001	1.467	1.247	1.726
Marital status 1 vs 0	<.0001	1.29	1.162	1.431
Smoked 1 vs 0	0.0001	1.272	1.126	1.437
Chronic hypertension 1 vs 0	<.0001	3.412	2.463	4.726
Gestational hypertension 1 vs 0	<.0001	3.704	3.063	4.48
Chronic diabetes 1 vs 0	<.0001	3.496	2.077	5.884
Vaginal bleeding 1 vs 0	<.0001	2.515	1.777	3.56
Premature rupture of the membranes 1 vs 0	<.0001	4.107	3.454	4.883
Maternal infection(s) 1 vs 0	0.0009	1.206	1.079	1.347
Urban-Rural Residence 1 vs 0	0.0139	1.256	1.047	1.506
Final Logistic Regression Model Results				
Exposure quartile*Gestational hypertension 1 vs 0	0.927	2.766	1.569	4.875
Exposure quartile*Gestational hypertension 2 vs 0	0.314	3.375	2.024	5.629
Exposure quartile*Gestational hypertension 3 vs 0	0.033	3.688	2.747	4.951
Exposure quartile*Gestational hypertension 4 vs 0	0.003	4.208	3.092	5.727
Exposure quartile*Premature rupture of the membranes 1 vs 0	0.109	4.108	2.635	6.405
Exposure quartile*Premature rupture of the membranes 2 vs 0	0.2	3.836	2.5	5.886
Exposure quartile*Premature rupture of the membranes 3 vs 0	0.604	3.265	2.382	4.476
Exposure quartile*Premature rupture of the membranes 4 vs 0	0	4.96	3.81	6.456
Prenatal care 1 vs 0	<.0001	1.408	1.225	1.619
Educational attainment 1 vs 0	<.0001	1.233	1.118	1.359
Maternal age 1 vs 0	<.0001	1.303	1.158	1.467
Underweight 1 vs 0	<.0001	1.468	1.248	1.727
Marital status 1 vs 0	<.0001	1.286	1.16	1.427
Smoked 1 vs 0	0	1.26	1.116	1.423
Chronic hypertension 1 vs 0	<.0001	3.384	2.444	4.686
Chronic diabetes 1 vs 0	<.0001	3.44	2.043	5.792

Table 4-13 (cont'd)

Vaginal bleeding 1 vs 0	<.0001	2.47	1.744	3.498
Maternal infection(s) 1 vs 0	0.001	1.211	1.084	1.352
Urban-Rural Residence 1 vs 0	0.004	1.298	1.086	1.551

N=16,010, R-Square=0.0406 and adjusted R-Square=0.0724.

Hispanic Women: Preterm Birth

The results of the logistic regression model for Hispanic women are provided in Figure 4-14. Notably, Hispanic mothers living in neighborhoods with increasing RESEI toxicity-weighted concentration exposures were not at significant odds of having a preterm birth. The most important risk factor for preterm birth for Hispanic women was premature rupture of membranes (OR=4.403, 95% CI 3.85-5.034). In comparison with the reference group of exposure*premature rupture of the membranes quartile 0 (no premature rupture of the membranes), quartiles 1 and 4 were statistically significant, while quartiles 2 and 3 were not. Mothers in exposure quartile 1 and 4 who experienced premature rupture of the membranes had an increased odds of having a premature delivery (OR=4.730, 95% CI 3.530-6.338 and OR=6.073, 95% CI 4.872-7.570, respectively). Maternal medical conditions were important risk factors for preterm birth among Hispanic mothers, including gestational hypertension (OR=3.057, 95% CI 2.659-3.513), chronic hypertension (OR=2.558, 95% CI 1.963-3.333), vaginal bleeding (OR=2.431, 95% CI 1.866-3.166), chronic diabetes (OR=2.143, 95% CI 1.634-2.81) and pregnancy complications short labor (OR=1.423, 95% CI 1.205-1.682). In addition, older maternal age (OR=1.298, 95% CI 1.179-1.428), an educational attainment of a high school diploma or GED rather than some college or a college degree (OR=1.29, 95% CI 1.131-1.336), smoked during pregnancy (OR=1.161, 95% CI 1.019-1.322), inadequate prenatal care (OR=1.156, 95% CI 1.007-1.327) and being unmarried (OR=1.138, 95% CI 1.044-1.241) were also important risk factors.

Table 4-14: Logistic Regression Models for Preterm Birth, Hispanic Women, Michigan, 2008-2017.

Model Results without the Interaction Term				
Variable	p-value	Odds Ratio	95% Wald Confidence Limits	
Exposure quartile 2 vs 1	0.7508	0.988	0.88	1.111
Exposure quartile 3 vs 1	0.1059	0.92	0.813	1.04
Exposure quartile 4 vs 1	0.4127	1.004	0.898	1.123
Prenatal care 1 vs 0	0.0278	1.167	1.017	1.34
Educational attainment 1 vs 0	<.0001	1.233	1.134	1.34
Maternal age 1 vs 0	<.0001	1.3	1.182	1.431
Smoked 1 vs 0	0.0314	1.154	1.013	1.315
Marital status 1 vs 0	0.0033	1.138	1.044	1.241
Chronic hypertension 1 vs 0	<.0001	2.542	1.95	3.313
Gestational hypertension 1 vs 0	<.0001	3.053	2.656	3.51
Chronic diabetes 1 vs 0	<.0001	2.144	1.635	2.811
Vaginal bleeding 1 vs 0	<.0001	2.416	1.855	3.148
Complications in pregnancy short labor 1 vs 0	<.0001	1.423	1.204	1.681
Premature rupture of the membranes 1 vs 0	<.0001	4.403	3.85	5.034
Final Logistic Regression Model Results				
Exposure quartile*Premature rupture of the membranes 1 vs 0	0.0018	4.73	3.53	6.338
Exposure quartile*Premature rupture of the membranes 2 vs 0	0.158	3.744	2.891	4.848
Exposure quartile*Premature rupture of the membranes 3 vs 0	0.7367	3.056	2.292	4.074
Exposure quartile*Premature rupture of the membranes 4 vs 0	<.0001	6.073	4.872	7.57
Prenatal care 1 vs 0	0.0396	1.156	1.007	1.327
Educational attainment 1 vs 0	<.0001	1.229	1.131	1.336
Maternal age 1 vs 0	<.0001	1.298	1.179	1.428
Smoked 1 vs 0	0.0245	1.161	1.019	1.322
Marital status 1 vs 0	0.0032	1.138	1.044	1.241
Chronic hypertension 1 vs 0	<.0001	2.558	1.963	3.333
Gestational hypertension 1 vs 0	<.0001	3.057	2.659	3.513
Chronic diabetes 1 vs 0	<.0001	2.143	1.634	2.81
Vaginal bleeding 1 vs 0	<.0001	2.431	1.866	3.166
Complications in pregnancy short labor 1 vs 0	<.0001	1.423	1.205	1.682

N=29,020, R-Square=0.0283 and adjusted R-Square=0.0603.

4.7.4. Space-Time Scan Statistics Results

There were 1,374 reported lethal birth defects and 1,041,749 births for which there was a matching record from the cleaned and geocoded infant birth dataset of live, singleton births among mothers who lived in Michigan. The number of infant deaths attributable to a birth defect ranged between 104 to 172 per year. Looking at lethal birth defects by race and ethnicity, 63.1% were among non-Hispanic white women, 24.1% were among non-Hispanic black women and 8.8% were among Hispanic women. Male infants accounted for 52%, while female infants accounted for 48% of the lethal birth defects. Of the lethal birth defects, 52.8% were among women living in large urbanized areas, 8.6% were among living in small urbanized areas, 0.6% were among women living in small urban areas and 38% were among women living in rural areas.

Bernoulli Models

Using a Bernoulli model with the time aggregation set at a minimum of five years, 36 clusters of lethal congenital anomalies (herein referred to as infant deaths) were identified (refer to Figure 4-4 and Table 4-15). Five of these clusters were statistically significant. The significant clusters were in south Detroit, southwest Detroit and north Dearborn, south Ann Arbor urban area and north Milan, Dearborn, and north Holland urban area, respectively by significance level. In south Detroit, the observed number of infant deaths was 18 and the expected number was 0.46 (Relative Risk (RR)=39.9). In southwest Detroit and north Dearborn, the observed number of infant deaths was 15 while the expected number was 1.40 (RR=10.8). In south Ann Arbor urban area and north Milan cluster, the observed number of infant deaths was 8 and the expected number was 0.56 (RR=14.4). In Dearborn, the observed number of infant deaths was 11 and the expected number was 1.51 (RR=7.4). In the north Holland urban area, the expected number of

infant deaths was 12 while the observed number was 1.95 (RR=6.2). The maximum RSEI toxicity-weighted concentrations of these census tracts during the years of these significant clusters were identified ranging between 5,481.71 and 26,551.90 with these elevated values high for both the earlier 5-year time period (2008-2013) and later 5-year time period (2014-2018); and the highest RSEI toxicity-weighted concentrations were within significant clusters in Detroit suggestive of persistent high exposures for women in Detroit. Other nonsignificant clusters where the observed number of infant deaths were greater than expected, but the difference between the observed and expected were not significantly different, were in the urban areas of Detroit and Ann Arbor as well as Flint, Saginaw, Lansing, Battle Creek, Kalamazoo, Grand Rapids, Holland and Muskegon, and in the non-urban areas located south of Lansing, in north Lenawee County, north of Midland in Gratiot, and east of Muskegon and northwest of Grand Rapids. The three non-significant clusters of infant deaths with the highest RSEI toxicity weighted concentrations were in Grand Rapids (clusters 6, 30) and Lansing (cluster 25).

Figure 4-4: SaTScan Bernoulli Model, 5-year Clusters, Michigan, 2008-2018.

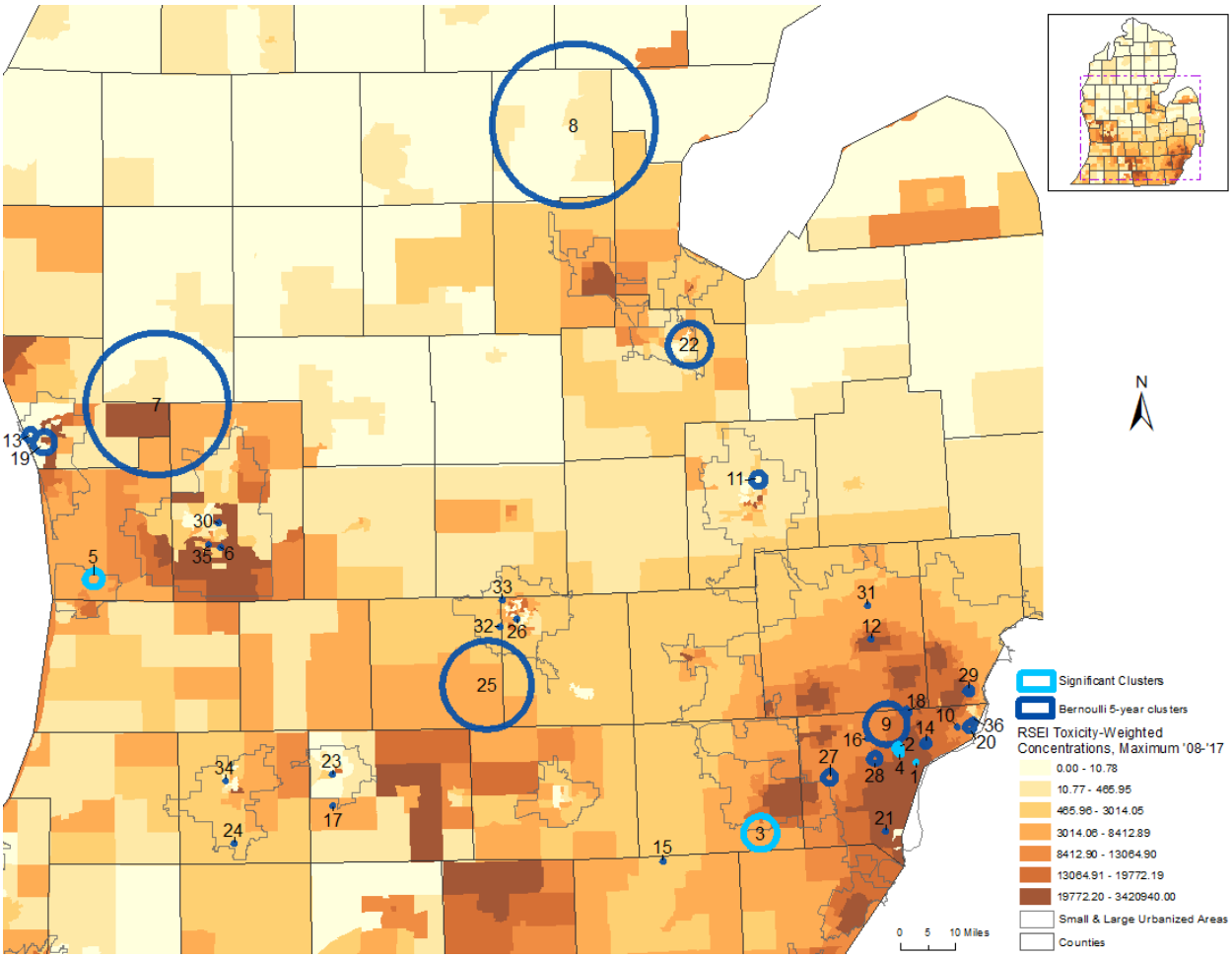


Table 4-15: SaTScan Bernoulli Model Clusters of Lethal Birth Defects, 5-year Maximum, Michigan, 2008-2018.

Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2014 - 2018	39.9	49.2	<0.001	24522.30
2	2008 - 2013	10.8	22.1	<0.001	20298.00
3	2014 - 2018	14.4	13.9	0.002	7674.08
4	2008 - 2013	7.4	12.5	0.009	26551.90
5	2008 - 2013	6.2	11.8	0.013	5481.71
6	2014 - 2018	19.2	10.1	0.103	94598.10
7	2008 - 2013	3.6	10.1	0.107	67.53
8	2008 - 2013	5.5	9.7	0.141	13.65
9	2008 - 2013	2.1	9.4	0.182	12702.60
10	2014 - 2018	26.7	9.4	0.201	6042.45
11	2008 - 2013	7.1	7.7	0.638	3.28
12	2008 - 2013	11.1	7.5	0.704	75547.40
13	2008 - 2013	8.1	7.3	0.782	2.23
14	2008 - 2013	10.1	7.1	0.847	18009.60
15	2008 - 2013	14.4	7.0	0.872	346.57
16	2008 - 2013	14.4	7.0	0.872	11062.60
17	2014 - 2018	14.2	6.9	0.879	4052.84
18	2008 - 2013	6.2	6.9	0.896	14513.70
19	2014 - 2018	4.7	6.8	0.903	10989.30
20	2014 - 2018	6.1	6.8	0.903	5040.08
21	2008 - 2013	13.6	6.8	0.914	30614.50
22	2014 - 2018	3.1	6.8	0.915	5602.06
23	2008 - 2013	9.3	6.7	0.937	1587.36
24	2008 - 2013	13.2	6.6	0.939	113.75
25	2008 - 2013	3.7	6.4	0.967	4254.33
26	2014 - 2018	12.2	6.3	0.971	12.91
27	2014 - 2018	7.9	6.0	0.990	10232.50
28	2008 - 2013	5.2	5.9	0.995	16413.20
29	2008 - 2013	10.3	5.7	0.998	15295.90
30	2014 - 2018	10.2	5.7	0.998	42464.00
31	2008 - 2013	9.9	5.6	0.998	3991.79
32	2014 - 2018	9.4	5.4	0.999	489.53
33	2008 - 2013	9.3	5.4	0.999	4344.16
34	2014 - 2018	9.2	5.3	0.999	4.81
35	2008 - 2013	6.7	5.3	0.999	7528.22
36	2014 - 2018	8.4	5.0	0.999	4678.86

Using a Bernoulli model with the time aggregation set at a minimum of one year, importantly 48 clusters were identified, of which fourteen were significant (refer to Figure 4-5 and Table 4-16). The significant clusters were located in south Detroit, southwest Detroit, north Holland urban area, Dearborn, northwest Detroit, west Lansing urban area and just west of the urban area, south Ann Arbor urban area and just south of the urban area, north Lenawee County, east Detroit, northwest of Grand Rapids and east of Muskegon, northwest Detroit, Woodhaven, just west of Detroit, within the Detroit urban area, and northwest Detroit, listed in order of significance level. In south Detroit, the observed number of infant deaths was 18 while the expected number was 0.25 (RR=73.6). In southwest Detroit, the observed number of infant deaths was 13 and the expected number was 0.51 (RR=25.7). In the north Holland urban area, the number of observed infant deaths was 10 and the number of expected cases was 0.34 (RR=29.6). In Dearborn, the number of observed infant deaths was 9 and the number expected was 0.25 (RR=35.8). In northwest Detroit, the number of observed infant deaths was 10 and the expected number was 0.63 (RR=16.1). In west Lansing just west of the capital area, the number of observed infant deaths was 11 while the number expected was 1.0 (RR=11.1). In the south Ann Arbor urban area and just south of the urban area, the number of observed infant deaths was 8 and the number expected was 0.42 (RR=19.1). In north Lenawee County, the number of observed infant deaths was 4 and the number expected was 0.03 (RR=123.3). In east Detroit, the number of observed infant deaths was 4 and the number of expected was 0.04 (RR=109.0). In the area northwest of Grand Rapids and east of Muskegon, the number of observed infant deaths was 9 while the number expected was 0.67 (RR=13.2). In northwest Detroit, the number of observed infant deaths was 8 and the number expected was 0.53 (RR=15.3). In Woodhaven, the number of observed infant deaths was 4 while the number expected was 0.05 (RR=85.9). In the area just

west of Detroit City, the number of observed infant deaths was 4 and the number of expected cases was 0.05 (RR=74.6). In northwest Detroit, the number of observed infant deaths was 10 and the number of expected was 1.08 (RR=9.4). The maximum RSEI toxicity-weighted concentrations of these census tracts during the year(s) the significant clusters were detected ranged between 57.52 and 19,937.10 with clusters observed across the time periods, and slightly higher concentration after 2012.

Other nonsignificant clusters were observed in the urban areas of Detroit, Ann Arbor, Flint, Saginaw, Midland, Lansing, Battle Creek, Kalamazoo, Grand Rapids, Holland and Muskegon, and in the non-urban areas located southwest of Lansing, in north Lenawee County, north of Midland in Gratiot, and east of Muskegon and northwest of Grand Rapids.

Figure 4-5: SaTScan Bernoulli Model, 1-year Clusters, Michigan, 2008-2017.

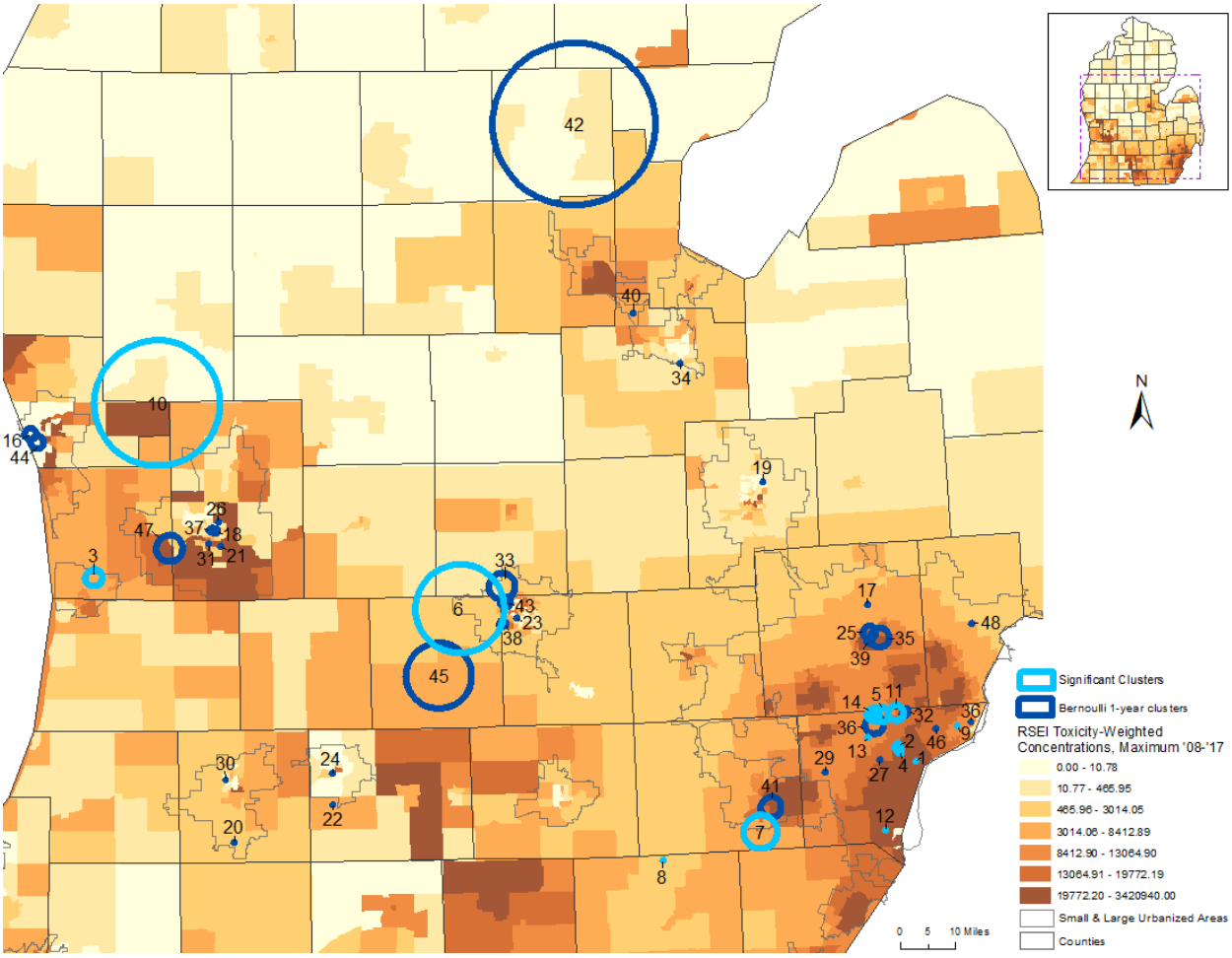


Table 4-16: SaTScan Bernoulli Model Clusters of Lethal Birth Defects, 1-year Maximum, Michigan, 2008-2018.

Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2014 - 2015	73.6	60.4	< 0.001	19937.10
2	2011 - 2012	25.7	29.9	< 0.001	13950.70
3	2009	29.6	24.4	< 0.001	4579.15
4	2011	35.8	23.6	< 0.001	9862.20
5	2012	16.1	18.5	< 0.001	10878.50
6	2013	11.1	16.5	0.003	154.53
7	2014 - 2016	19.1	16.1	0.005	4741.76
8	2008	123.3	15.6	0.010	346.57
9	2016	109.0	15.1	0.014	6042.45
10	2011	13.2	14.9	0.018	57.52
11	2012	15.3	14.4	0.022	12808.60
12	2012	85.9	14.1	0.027	9664.38
13	2009	74.6	13.5	0.046	10242.00
14	2012 - 2014	9.4	13.5	0.047	9883.40
15	2011 - 2013	16.5	13.1	0.061	13179.50
16	2010	34.8	13.0	0.066	2.17
17	2012	65.9	13.0	0.067	3991.79
18	2008	34.1	12.9	0.078	398.08
19	2010	63.0	12.8	0.084	1.01
20	2013	63.0	12.8	0.084	100.62
21	2016	56.7	12.4	0.131	33843.50
22	2017	53.5	12.1	0.159	1179.28
23	2014	52.5	12.1	0.174	2.72
24	2013	51.5	12.0	0.183	6.64
25	2010 - 2014	6.2	11.8	0.212	30049.70
26	2015	45.7	11.5	0.273	38544.20
27	2010	45.0	11.4	0.290	5590.89
28	2015	43.6	11.3	0.320	5187.44
29	2016	43.0	11.2	0.333	7914.84
30	2015	40.5	11.0	0.392	4.66
31	2010	40.5	11.0	0.392	7528.22
32	2012	40.5	11.0	0.392	13714.90
33	2013 - 2015	11.7	10.9	0.436	303.61
34	2015	33.0	10.2	0.636	5.54
35	2010	13.1	9.9	0.715	3696.32
36	2012 - 2015	5.1	9.9	0.729	10654.10
37	2008	28.3	9.6	0.812	5.09

Table 4-16 (cont'd)

38	2016	27.5	9.5	0.840	522.59
39	2010	26.7	9.4	0.867	3446.51
40	2010	26.2	9.3	0.885	1331.57
41	2016	25.3	9.1	0.915	123706.00
42	2009 - 2013	5.6	9.0	0.932	13.65
43	2013 - 2015	10.7	8.8	0.958	401.64
44	2010	21.6	8.5	0.987	3.72
45	2013	13.1	8.3	0.992	198.73
46	2015	19.5	8.1	0.996	7631.74
47	2008	12.7	8.1	0.996	2003.00
48	2013	19.3	8.1	0.996	1753.37

Poisson Models

The unadjusted Poisson model that took into account the underlying number of births in the modeling parameters, set to a minimum time aggregation of five years identified eleven clusters, with one significant cluster (refer to Figure 4-6 and Table 4-17). The significant cluster was located north of Midland in Gladwin, Arenac and Bay Counties. The number of observed infant deaths was 11 and the number of expected cases was 1.71 (RR=6.5). Interestingly this cluster did not contain a high level of RSEI toxicity-weighted concentration (13.65). This significant cluster of infant deaths was observed during the earlier 5-year time period (2008-2013). Other nonsignificant clusters were observed in the Detroit urban area, north Muskegon urban area including the area outside of the urban area to the west and northwest, south-central Michigan including nearly all the Battle Creek urban area and part of the urban areas of Jackson and Lansing, and the east-central region including all the Bay City urban area, most of the Saginaw urban area, and just the eastern edge of the Midland urban area. Alike the Bernoulli models, non-significant clusters of infant deaths were observed across both 5-year time periods—the earlier (2008-2013) and later (2014-2018).

Adjusting for the RSEI toxicity-weighted concentrations resulted in one, non-significant cluster. This one cluster was larger and located a bit north of the significant cluster in the unadjusted model with a decrease in RR=6.4 to RR=4.4 after adjustment. This decrease in RR after adjusting for RESI exposures suggests that maternal RSEI exposures may in part explain this cluster but because the level of RESI toxicity-weighted concentration was quite low this hypothesis vs. the movement farther north into rural areas will require further investigation.

Figure 4-6: SaTScan Poisson Model, 5-year Clusters, Michigan, 2008-2017.

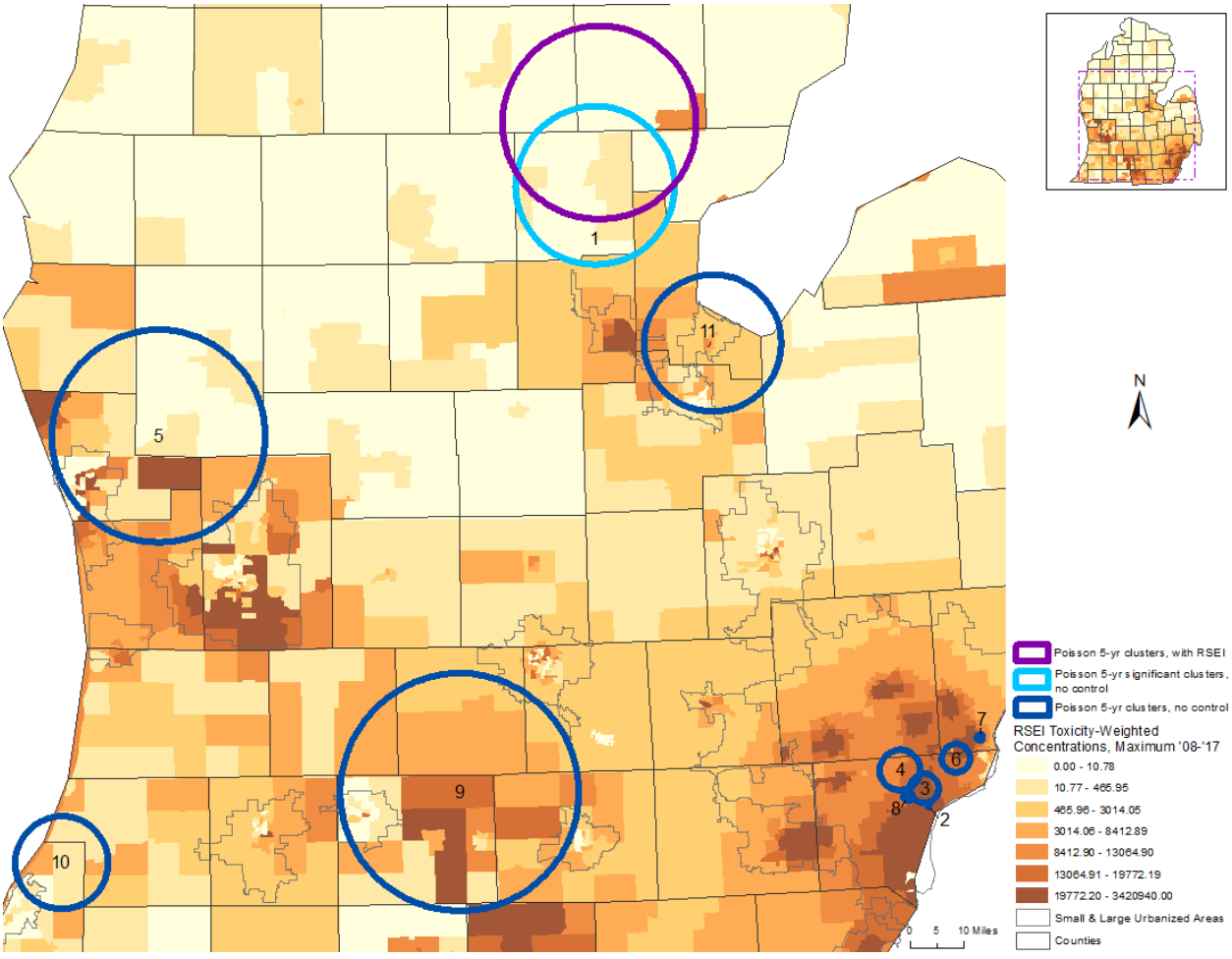


Table 4-17: SaTScan Poisson Model Clusters of Lethal Birth Defects, 5-year Maximum, Michigan, 2008-2018.

Unadjusted Model					
Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2008 - 2013	6.5	11.2	0.026	13.65
2	2014 - 2018	13.0	9.8	0.128	24522.30
3	2008 - 2013	2.2	8.8	0.288	25483.50
4	2008 - 2013	2.1	8.5	0.365	12702.60
5	2008 - 2013	2.1	8.5	0.369	0
6	2008 - 2013	2.3	6.6	0.933	19772.20
7	2008 - 2013	12.2	6.3	0.97	15295.90
8	2008 - 2013	4.7	6.0	0.989	21141.40
9	2008 - 2013	1.9	5.9	0.992	14415.50
10	2008 - 2013	3.5	5.8	0.992	237.41
11	2008 - 2013	2.0	5.7	0.996	1673.01
Adjusted Model					
Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2008 - 2013	4.4	7.7	0.424	0

The unadjusted Poisson model set to a minimum one-year time aggregation identified thirteen clusters (Figure 4-7 and Table 4-18). Only one cluster was significant, which was in south Detroit. The number of observed cases was 6 while the number of expected cases was 0.20 (RR=30.6). The maximum RSEI toxicity-weighted concentration during the years the significant cluster was detected (2014-2015) was 19,937.10. Other nonsignificant clusters were observed in the Detroit urban areas, north of Midland in Gladwin, Arenac and Bay Counties, east-central Michigan including the eastern parts of the urban areas of Bay City and Saginaw, Muskegon urban area, the area consisting of the western part of the Lansing urban area and the area just west of the urban area, in the western portion of the Grand Rapids urban area, and in the area east of Muskegon and north-west of Grand Rapids. When adjusting for the RSEI toxicity-

weighted concentrations, only one cluster emerged, and it was not significant. This cluster identified with was smaller and located in southwest Muskegon and north Norton Shores where there was no significant cluster in the unadjusted model.

Figure 4-7: SaTScan Poisson Model, 1-year Clusters, Michigan 2008-2017

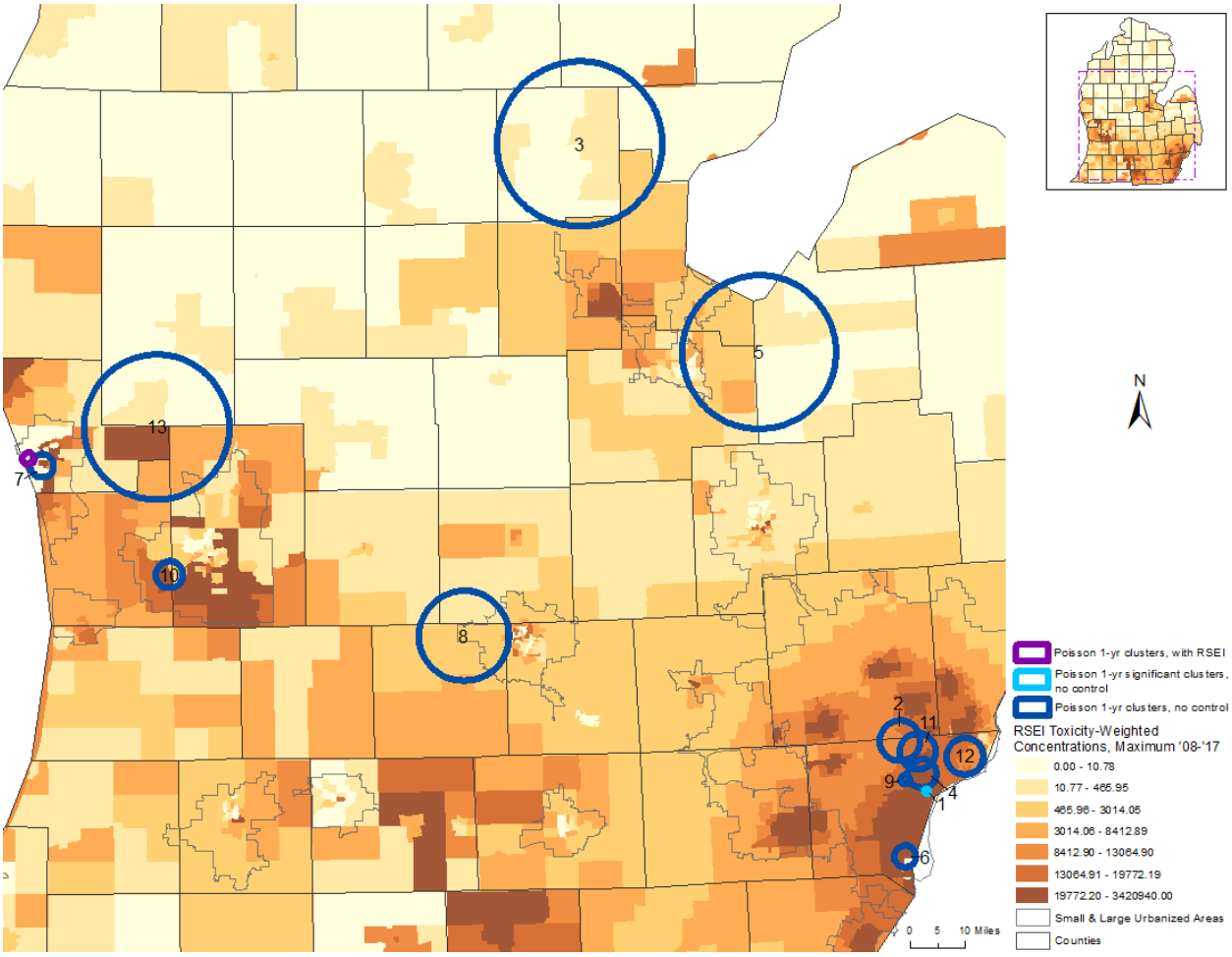


Table 4-18: SaTScan Poisson Model Clusters of Lethal Birth Defects, 1-year Maximum, Michigan 2008-2018.

Unadjusted Model					
Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2014 - 2015	30.6	14.7	0.021	19937.10
2	2012 - 2015	2.6	11.1	0.353	11548.40
3	2009 - 2013	6.7	10.5	0.566	13.65
4	2012 - 2015	2.7	9.8	0.763	20467.30
5	2008 - 2010	3.6	9.5	0.835	3.27
6	2012 - 2016	6.1	8.8	0.964	12107.00
7	2013 - 2017	4.9	8.7	0.973	10989.30
8	2013	8.3	8.7	0.979	154.53
9	2011 - 2012	9.9	8.4	0.995	14442.00
10	2008	13.4	8.4	0.995	2003.00
11	2012 - 2015	2.5	8.2	0.997	13870.40
12	2015 - 2017	2.7	8.0	0.999	6984.36
13	2009 - 2012	3.9	8.0	0.999	67.53
Adjusted Model					
Cluster	Year(s)	Relative Risk	Log-Likelihood Ratio	p-value	Maximum RSEI Toxicity-Weighted Concentration
1	2008 - 2010	18.8	8.0	1.00	2.23

4.8. Discussion

Logistic Regression

Higher RSEI exposure quartiles were significantly associated with an increased odds of low birth weight births in the analysis of all women, non-Hispanic white women and non-Hispanic black women. Among non-Hispanic white women, the interaction term exposure quartile*smoked during pregnancy was more important than just the exposure quartiles by themselves. Similarly, the interaction term exposure quartile*older maternal age was more important than just the exposure quartiles by themselves for non-Hispanic black women. In the model for Hispanic women, the exposure quartiles were not significant by themselves, however

the interaction of the exposure quartiles and gestational hypertension were statistically significant and was the most important risk factor for having a low birth weight infant. These findings demonstrate that maternal exposure to increasing RSEI toxicity-weighted concentrations had independent and interactive effects such that synergies were observed between increasing RSEI exposure and smoking, older age and gestational hypertension. In addition, inadequate prenatal care had a notably high OR in the analysis of low birth weight among all women and both chronic and gestational hypertension contained high ORs in each of the low birth weight models, suggesting a consequence of women not receiving regular health care during pregnancy for the treatment of these conditions. Finally, women who were unmarried were at higher odds of low birth weight for all mothers demonstrating the potential need for additional family (social) support. Diabetes and alcohol usage were significant risk factors for low birth weight for non-Hispanic white and black women, while older age and lower educational levels were significant risk factors for low birth weight for non-Hispanic black and Hispanic women. These findings provide targeted areas for intervention to improve maternal health and reduce low birth weight for new mothers in Michigan.

RSEI exposure quartile 4 was significantly associated with an increased odds of preterm birth in the analysis of all women and premature rupture of membranes was the most important risk factor. However, the interaction effect of the exposure quartiles with premature rupture of the membranes among all women was associated with notably large odds ratios demonstrating a synergistic effect. For the race-stratified models, the exposure quartiles were significantly associated with a higher odds of preterm birth when combined with other risk factors as an interaction term. In the analysis of non-Hispanic white women, the interaction terms exposure quartiles 3 and 4*smoked during pregnancy and exposure quartile 4*premature rupture of the

membranes yielded high odds ratios. The interaction effects were greater than their individual effects on preterm birth. The analysis of non-Hispanic black women revealed that the interaction of exposure quartile 4*gestational hypertension and exposure quartile 4*premature rupture of the membranes was greater than their individual odds with preterm birth. Similarly, the exposure quartile 4*premature rupture of the membranes interaction term in the analysis of Hispanic women had higher Odds ratios than these variables individually. These findings across all women in general, and stratified by race and ethnicity in particular show that the highest quartile of RSEI toxicity-weighted concentration exposures exacerbates the effects of these maternal medical conditions on preterm birth. This suggests that addressing these maternal medical conditions without interventions that also protect women from toxicant chemical exposures may minimize improvements in these health outcomes and ultimately limit a reduction in preterm birth. Other maternal medical conditions that were significant for preterm birth across all mothers were gestational hypertension, chronic diabetes and vaginal bleeding. Of these, the odds associated with gestational hypertension were highest among non-Hispanic black and Hispanic women; the odds associated with chronic diabetes were highest among non-Hispanic black followed by non-Hispanic white and Hispanic women; and the odds associated with vaginal bleeding were highest among non-Hispanic white followed by non-Hispanic black and Hispanic women demonstrating the importance of addressing maternal medical conditions to reduce the incidence of preterm birth in Michigan.

Non-Hispanic black mothers of older maternal age exposed in the highest quartile had an elevated risk of having a low birth weight baby compared to mothers of all ages, indicative of an ecosyndemic. The socio-economic structures along with the pollution environment may be wearing down these women, degrading their overall health and ability to respond to additional

insults and stressors, thereby influencing birth outcomes. This study also identified several important interaction effects between extrinsic and intrinsic factors, including between the RSEI exposure quartile 4 and maternal behavioral and medical conditions on low birth weight and preterm birth, also common with the presence of an ecosyndemic, which together have a greater adverse impact on birth outcomes than they do by themselves.

The odds ratios for the RSEI exposure quartiles in this study were consistent with previous environmental health studies. One of these prior studies evaluated maternal residential proximity to industrial facilities, including TRI facilities, and their releases on low birth weight and preterm birth outcomes (Porter et al., 2014) and another study assessed pregnant women's estimated TRI chemical exposure on low birth weight (Gong et al., 2018). While the odds ratios for the exposure quartiles were small, the interactive effects of the exposure with maternal behavioral characteristics (i.e., smoking) and medical conditions (i.e., gestational hypertension and premature rupture of the membranes) were large supporting these previous studies and also advancing this line of research to include synergistic effects of TRI emissions (here elevated RSEI toxicity-weighted concentration exposures and adverse birth outcomes).

A previous study by Kezios et al. (2017) reported that maternal smoking and maternal exposure to PCB byproducts were found to increase the risk of low birth weight infants. These exposures together caused greater harm than individually (Kezios et al., 2017). Valavanidis at al. (2009) found that the negative effects of maternal exposure to air pollution on infant health were considerably larger among smokers than nonsmokers. The finding from this study compliments these two prior studies by showing an increased odds of adverse birth outcomes among the combined interaction of women living in the highest exposure quartile who smoked during pregnancy than the odds of adverse birth outcomes for these exposures independently. For non-

Hispanic white women who lived in the highest RSEI quartile 4 and smoked during pregnancy and were at increased odds of low birth weight and preterm birth with a slightly stronger effect on low birth weight demonstrating the importance of continuing education about the harmful effects of smoking during pregnancy.

Premature rupture of the membranes has been linked to environmental exposures in previous studies. Maternal exposure to air pollutants is the most well document, with associations identified between $PM_{2.5}$, CO, SO_2 and O_3 exposure and premature rupture of the membranes (Pereira et al., 2015; Han et al., 2020; Wallace et al., 2016). In addition, a few studies reported that higher maternal lead levels increase the risk of premature rupture of the membranes (Falcón, Viñas, & Luna, 2003; Huang et al., 2018). The findings from these previous studies indicate the importance of improving maternal awareness of premature rupture of membranes to prevent the onset and improve its management if it is diagnosed. Education alone however, may not fully address the problem of premature rupture of membranes and future interventions should also address the neighborhoods of women experiencing high RSEI toxicity-weighted concentration exposures.

Hypertensive disorders of pregnancy contribute to maternal and neonatal morbidity and mortality (Kahn & Trasande, 2018). Previous studies have identified an increased risk of gestational hypertension among pregnant women exposed to air pollutants, including particulate matter, NO_x, SO_2, PAH and VOCs (Vinikoor-Imler et al., 2011; Zhu et al., 2017). The biological mechanisms thought to be underlying these associations are oxidative stress, epigenetic changes, endocrine disruption and abnormal placental vascularization (Kahn & Trasande, 2018). Although these studies suggest maternal exposure to air pollution may increase their risk of gestational

hypertension, there is a lack of research examining the mediating effects of gestational hypertension in the environmental exposure(s) and adverse birth outcomes relationships.

Finally, inadequate prenatal care and lower educational levels were significant risk factors for low birth weight and preterm birth for all women in Michigan. Ensuring high quality education and access to preconceptual and prenatal health care will be ongoing important initiatives to improve maternal health and pregnancy outcomes in Michigan.

Cluster Detection of Lethal Birth Defects

Spatial scan statistics using SaTScan software has previously been used to study the spatial distribution of birth defects in Texas (Cech et al., 2008) and North Carolina (Root et al., 2009). This was the first study to the author's knowledge to investigate the spatial and temporal patterns of lethal birth defects in Michigan. Comparing the output of two different space-time scan statistics, a Bernoulli model and Poisson model, and two different time aggregations, this study showed that the clusters and elevated relative risk of lethal birth defects were identified in similar areas across Michigan. This comparison indicated areas with persistent clusters, affirming the need for closer consideration by public health departments.

There was consistency in cluster locations between the two Bernoulli models. The significant clusters were identified in the urban areas of Detroit, Ann Arbor, Lansing and Holland using both one-year and five-year time aggregations. Many of the census tracts in these areas had high RSEI toxicity-weighted concentrations. An unadjusted and adjusted Poisson model was run for each of the same time aggregations. The Poisson models indicated a significant cluster in the Gladwin, Arenac and Bay County area with the five-year time aggregation and a significant cluster in south Detroit with the one-year time aggregation. The adjusted model included the RSEI toxicity-weighted concentration covariate, which removed all

but one cluster which was not significant in either model. This finding suggests that the RSEI toxicity-weighted concentrations may help explain some of the urban and also rural clusters of lethal defects across Michigan between 2008-2018. The strengths and limitations of the study are outlined below.

Strengths

A key strength of the study was the use of a the RSEI toxicity-weighted concentrations at the census tract level, which offered an improved estimate of maternal exposure to TRI emitted chemicals than previous studies. The RSEI model considers not only the quantity of the chemicals released, but also the quantity, their fate and transport through the environment, the route of exposure and dose of exposure. Second, the geocoding match rate of birth records was 99% which is well over the minimum acceptable geocoding success rate (Cromley & McLafferty, 2002) so births lost to unmatched geocoding was not a major source of geographic bias in the state. Third, this study used a robust infant birth and linked infant dataset which included many individual-level variables, which allowed for a more comprehensive risk analysis able to detect small changes in effects of RSEI toxicity-weighted concentration exposures and other individual-level risk factors for low birth weight and preterm birth. Fourth, this study's cluster detection method performed a sensitivity analysis by using two different models and two different time aggregations to evaluate the spatial and temporal distribution of lethal defects in Michigan.

Limitations

Although this study had individual-level birth records, it did not have individual-level toxicant data. Rather, an estimated pollution exposure level among pregnant women was derived from the RSEI toxicity-weighted model. This area-level (census tract) measure, however, was

modeled at the individual-level assuming all women living within a census tract in a given year were assumed to have the same exposure. Second, the RSEI model produces annual output so this study was unable to evaluate critical windows of exposure during trimesters of pregnancy or seasonal changes. While exposure bias may exist because of the two reasons above, this is the first study that has utilized a composite measure of multiple toxicants known to be risk factors for adverse birth outcomes and infant defects justifying the need to study the RESI toxicity-weighted concentration data in relation to pregnancy outcomes. Third, women may have moved during their pregnancy or spent substantial amounts of times outside of their census tracts, which this study will not account for which may have also resulted in exposure bias. Fourth, the interaction terms modeled represent synergistic effects which conceptually was meaningful from an ecosyndemic perspective. Future research, however, should also model the mediating effects of maternal medical conditions in the RSEI toxicity-weighted concentration and adverse birth outcomes relationships. Lastly, the Bernoulli model does not allow for the adjustment for covariates which may be important risk factors of lethal defects. The space-time Poisson model on the other hand did allow for the adjustment of the RSEI toxicity-weighted concentrations. While this study detected where lethal birth defects are significantly elevated in Michigan and which of the clusters were in part explained by the RSEI toxicity-weighted concentration level, future research may model other covariates including interactions/synergies that may further explain underlying causes of birth defects that lead to infant mortality.

4.9. Conclusions

This study found small, yet significant increased odds of low birth weight in the logistic regression models that included all mothers, non-Hispanic white mothers and non-Hispanic black mothers exposed in higher RSEI exposure quartiles. Additionally, this study highlights the

importance of the interaction effects between RSEI exposure quartiles and several variables including maternal smoking during pregnancy among non-Hispanic white mothers, older maternal age among non-Hispanic black mothers and gestational hypertension among Hispanic mothers. The findings indicate the importance for pregnant women to receive health care during pregnancy, the prevention and control of gestational and chronic hypertension and a reduction in smoking during pregnancy.

This study found small, yet a significantly higher odds of preterm birth in the logistic regression models for all mothers and non-Hispanic black mothers exposed in higher RSEI exposure quartiles. The results suggest the importance of maternal smoking cessation and the prevention and control of gestational hypertension, chronic diabetes, premature rupture of the membranes, vaginal bleeding and uterine rupture. This study also identified important interaction effects with the RSEI exposure quartiles including maternal smoking during pregnancy, premature rupture of the membranes and gestational hypertension.

The space-time analysis identified persistent clusters of lethal birth defects during the study period. Areas with significant clustering of lethal birth defects included the urban areas of Detroit, Ann Arbor, Lansing, Holland and Muskegon, North Lenawee County and in the Gladwin, Arenac and Bay County area. In particularly, significant clustering was detected in south Detroit in all but one of the models, identifying it as an important area for further consideration.

This research advances the field of environmental health through the examination of multiple toxic chemical exposures using a sophisticated human health risk screening model. Both have been limited in previous literature. The findings from this study provide additional insight on maternal exposure to TRI chemicals and adverse birth outcomes. The findings should be used

to inform environmental regulatory and public health policies and programs, particularly focusing on communities with high human health risks from modelled TRI chemical exposures, to improve birth outcomes among women living in these communities. Communities will also likely experience other types of health benefits also known to be influenced by environmental pollutants. In addition, this research builds upon our existing knowledge of health impacts associated with humans' exposure to multiple chemicals for health care providers. The findings and recommendations hold the potential to have extensive benefits considering the numerous short-term and lifelong impacts that can be prevented with healthy birth outcomes.

Future research should also incorporate other environmental hazards, such as ambient air pollutants, drinking water quality and hazardous waste sites, that may be contributing to adverse birth outcomes including lethal birth defects. Padula et al. (2018) noted that environmental exposures may contribute to or exacerbate pregnancy risk factors, such as hypertension. Future research should also assess the potential mediating effects of maternal medical conditions (chronic and gestational hypertension, chronic diabetes, premature rupture of the membranes and vaginal bleeding) in the RESI toxicity-weighted concentration and adverse birth outcome relationship. While changes in behavior that improve maternal health will always be important, this study highlighted the need to emphasize the need for reductions in toxic pollutant exposures on the environmental side and improvements in access to preconceptual and prenatal care on the prevention and treatment side. While maternal medical conditions may be treated by high quality health care, the continued presence of environmental exposures will perpetuate the problem. To improve maternal health in Michigan and reduce the incidence of low birth weight and preterm birth for all women this direction of research and practice should be encouraged.

Finally, to reduce racial and ethnic disparities in maternal health and low birth weight and preterm birth it will be even more important to address environmental toxic exposures because of the apparent clustering of non-Hispanic black women in high RSEI toxicity-weighted concentration neighborhoods—areas that generally also have a lack of available and accessible health care resources.

Chapter 5. DISCUSSION

This dissertation study offers a way to conceptualize and evaluate toxic chemical exposures in relation to environmental justice and environmental health using an environmental health justice ecosyndemic theoretical framework. Ecosyndemic theory suggests that the environmental conditions in which people spend time are influenced by and intersect with contextual and individual factors in ways that can lead to disease clustering within a population or a geographic area. This paper reveals that an ecosyndemic can occur at multiple levels. First, at the environmental level with multiple pollutant exposures at high levels in largely high minority and low-income populations; and second at the heath outcome level with multiple adverse health conditions, such maternal morbidity and poor birth outcomes. By incorporating ecosyndemic theory with the human ecology model, medical geographers can offer deeper understandings of environmental justice, environmental health and health equity.

This dissertation study also analyzed TRI chemical concentrations to investigate environmental justice in Michigan. The EPA's RSEI model was used to map the potential of human exposure to TRI toxic chemicals and socio-demographic characteristics of the population to evaluate the potential of human health risk across Michigan over time. H_0 was generally supported, but there were a few exceptions. Much of the elevated human health risks from TRI chemical exposures were in areas with a higher density of TRI facilities, but there were also some areas with low health risk and a high density of TRI facilities and vice versa a few areas with high health risks and a low density of TRI facilities. The study concluded that census tracts with the highest RSEI toxicity-weighted concentrations were in the urban areas of Detroit and Grand Rapids. Population groups experiencing an elevated share of health risks from exposure to TRI chemicals were African American and Hispanic residents and people living near and below

the poverty level. Non-Hispanic African Americans living in the Grand Rapids and Detroit urban areas faced a persistent burden, whereas Hispanics living in the Detroit urban area experienced an emerging burden. Consequently, it is probable an ecosyndemic is occurring in the two largest urban areas of Michigan. Therefore, H_{01} and H_{02} were supported by the study findings. The multiple toxic chemicals in which residents, particularly minorities, are exposed may have synergistic and interacting effects at the societal and individual levels, accentuation environmental and health equity concerns. This study also further informs the debate of the discriminatory citing hypothesis with the move-in hypothesis for non-Hispanic black and Hispanic populations who were identified as experiencing disproportionate burdens from toxicity risk from TRI chemical exposures.

This dissertation study also included a retrospective, cross-sectional cohort study of mothers and their infants in Michigan (n=1,041,749) to evaluate TRI chemical exposure risks on maternal health, adverse birth outcomes and lethal defects attributable to congenital anomalies. Maternal addresses were geocoded and spatially joined with the RSEI toxicity-weighted concentrations to assign the exposure value. SAS 9.4 was used to run logistic regression analyses of low birth weight and preterm birth and SaTScan 9.7 was used to run space-time analyses of lethal birth defects.

This study found that maternal exposure to increasing levels of RSEI toxicity-weighted concentrations whether non-Hispanic white or non-Hispanic black increased the odds of having a low birth weight or premature infant. Importantly, this finding was not observed for Hispanic women. However, the synergies by which RSEI levels impacted low birth weight specifically appeared to vary by each population group, with smoking having a greater RSEI synergistic effect for non-Hispanic white women, increasing age having a greater RSEI synergistic effect for

non-Hispanic black women and gestational diabetes having a greater RSEI synergistic effect for Hispanic women after controlling for potential confounding and known risk factors for low birth weight. Therefore, the study findings generally support H_{01} and H_{02}.

The study also found a statistically significant increased odds of preterm birth among all mothers and in the race-ethnicity stratified model for non-Hispanic black mothers exposed in higher RSEI quartiles. The synergies by which RSEI levels impacted preterm birth overwhelmingly supported gestational hypertension and premature rupture of membranes particularly in RSEI quartile 4 across all groups of women. While gestational hypertension and premature rupture of membranes are important independent risk factors for preterm birth, their synergistic effects in the presence of exposure to high RSEI levels is an extremely important area for future research. Future research should further study these RSEI and behavioral, demographic and medical synergies to reduce the incidence of low birth weight and preterm birth in Michigan and to inform other states across the country where RSEI data are also available.

The spatial scan statistics results identified areas in Michigan with persistent clusters of infant mortality attributable to a birth defects. The areas with persistent statistically significant clusters included the urban areas of Detroit, Ann Arbor, Lansing and Holland and the Gladwin, Arenac and Bay County area. Notably, when using the Poisson space-time model, adjusting for the RSEI exposure quartiles removed all but one of the clusters, which was not significant, indicating that the exposure may be explaining in part, some of the clusters of lethal birth defects across Michigan during 2008-2018. Further analyses that control for maternal level risk factors in addition to the RSEI exposure is warranted.

The study findings indicate women are exposed to multiple extrinsic and intrinsic stressors during their pregnancy, including environmental, medical and behavioral, which have

both individual and interaction effects that may influence birth outcomes. Contributing factors are related to both individual and large-scale factors which lead to toxic chemical exposures among pregnant women, influence women's behavioral characteristics and effect women's access to health care. The synergies between these factors increase the overall health burden among pregnant women and thereby influence birth outcomes, as explained by ecosyndemic theory. In the model for non-Hispanic black mothers for example, an increased odds of low birth weight was observed for older women, but not for younger women. This is possibly indicative of an ecosyndemic in which the large-scale structures and pollutant exposures may be degrading their overall health and reducing their ability to respond to insults over time, which may be the reason for higher odds of low birth weight among older but not younger non-Hispanic black mothers.

These synergies in themselves however do not fully explain the racial and ethnic disparities in adverse birth outcomes in Michigan. However, when studies go beyond the epidemiology of population groups to include the geography of where populations live, work and play and are exposed it becomes clearer that non-Hispanic black and Hispanic women (and many non-Hispanic white women too, but not as many) reside in neighborhoods with elevated RSEI toxicity-weighted concentration levels and importantly, these levels will also vary within cities. Thus, while racial and ethnic disparities in adverse birth outcomes are not apparent within elevated RSEI neighborhoods because high RSEI exposures affects whoever is exposed; racial and ethnic disparities in adverse birth outcomes are observable across local areas with higher incidences in neighborhoods in RSEI quartile 4. Racial and ethnic disparities are therefore, largely linked to geography with higher levels of pollution and less available and accessible health care services, an underlying preface of environmental injustice.

Chapter 6. RECOMMENDATIONS

A few different solutions can be implemented to reduce the impact of TRI chemicals on environmental disparities and health impacts in Michigan. *First*, the EPA and Michigan Department of Environment, Great Lakes & Energy should implement and improve the onsite use, management and disposal of TRI chemicals and increase the monitoring of TRI sites to ensure they are complying with the EPCRA to reduce toxic chemicals entering the environment resulting in potential exposures among the public, particularly in the top 5% census tracts. This strategy will ensure strict oversight of the industries to ensure accurate reporting and compliance with regulations in terms of toxic chemical emissions. Additionally, it would help to reduce air and water releases of toxic chemicals and better manage and control the fate of toxic chemicals in the environment through improved emissions and filtering mechanisms, thereby reducing the public's exposure to these toxic chemicals.

Second, the EPA and Michigan Department of Environment, Great Lakes & Energy should consider offering incentives for companies who reduce their use of highly toxic chemicals. Additionally, an improved set of considerations, including an environmental justice analysis, should be added to the review process of newly proposed TRI sites. The use of bivariate correlations between places with high RSEI toxicity-weighted concentrations and high poverty and high minority can be useful in the review process as well as in targeting areas for pollution reduction.

Third, this was the first study to use the RSEI model in Michigan and the first study to use the RSEI toxicity-weighted concentrations to evaluate a health outcome, which has provided evidence that the RSEI model and methods are reliable and can be applied to research questions in other areas in the United States. Future research should use the RSEI model to study the share

of exposure risks and human health outcomes among populations in other states. Further conceptualization of research questions that evaluate the benefits and limitations of the RSEI score vs. toxicity-weighted concentrations is also warranted.

Fourth, maternal health programs should focus on increasing the level of medical care mothers receive during pregnancy, improve preconception and pregnancy health through a reduction in the onset and control of hypertension and diabetes and reduce the number of women who smoke during pregnancy through maternal education and smoking cessation programs. In addition, future research should investigate interaction effects and possible mediating effects between environmental exposures and maternal behavioral and medical characteristics.

Fifth, future research conducting cluster analyses to investigate maternal exposure to RSEI toxicity-weighted concentrations on birth defects should consider the inclusion of additional covariates to control for known risk factors of lethal birth defects and how these risk factors may be similar or vary across clusters detected in Michigan. Additionally, study findings should encourage public health departments to further investigate the areas where the persistent clusters of lethal birth defects were identified in this study.

Sixth, future research should also seek to investigate the upstream forces that are leading to a pollution environment in which racial and ethnic minorities are experiencing an increased health burden and that lead to adverse birth outcomes, including interaction effects among maternal characteristics that also impact birth outcomes, to better understand this ecosyndemic and offer recommendations to improve the overall health of all Michigan residents.

These environmental and health solutions are targeted interventions to reduce environmental injustices and racial disparities in adverse birth outcomes, while improving the overall health of mothers and infants in Michigan.

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