EFFECTS OF TRAFFIC AND AIR POLLUTION ON RISK OF PRETERM BIRTH AND LOW BIRTH WEIGHT OUTCOMES IN MILWAUKEE COUNTY 2005-2010

by

Deborah L. Pasha James

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ABSTRACT

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The University of Wisconsin – Milwaukee, 2014
Under the supervision of Jeanne Beauchamp Hewitt

Between 2005 and 2010, infants born to non-Hispanic black mothers experienced a 3-fold elevated risk of infant mortality compared to those born to white and Hispanic mothers. Preterm birth (PTB) and low birth weight (LBW) are strong predictors of infant mortality. To our knowledge, this is the first study of Wisconsin births to evaluate the effect of *social and environmental factors* on risk of PTB and LBW. We hypothesize that the observed racial inequalities in PTB and LBW are related to traffic density and air pollution. The ***Milwaukee INFANTS Study*** used 2005-2010 electronic birth record data (N = 85,045) geocoded to the 2010 Census block level based on maternal residence. Cumulative traffic density and interpolated criteria air pollutant data were used to estimate fetal exposures. Multi-level logistic regression analysis (SAS 9.4) with a multiple imputation step to handle missing data (< 4.7%) was used to examine the effect of traffic density and air pollution on risk of PTB and LBW. We adjusted for established risk factors and a census tract level composite measure of neighborhood stress consisting of low income and lack of access to full grocery stores and transportation. In multivariable models, Milwaukee County (2005-2010) experienced a 1.9-fold increased prevalence of preterm birth (PTB) and a 2.5-fold increased prevalence of low birth weight (LBW) among infants of non-Hispanic black women, compared to infants of non-Hispanic white women. Risk of PTB and LBW differed considerably by location, as well. In unadjusted models, traffic density demonstrated a linear increase in risk across all birth outcomes ($p < 0.0001$). Second trimester exposure to $PM_{2.5}$ was associated with an increased risk of preterm birth, and additionally, across the entire pregnancy for LBW and LBW at term. In the full model, the Neighborhood Stress Index showed a 29% increased risk for PTB, a 44% increased risk for LBW, and a 51% increased risk of LBW at term. These preliminary findings warrant further research in which exposure measures more closely approximate biological uptake of toxicants from mobile and stationary sources. Program planning and policy development are discussed.

Keywords: Built Environment, Cumulative Traffic Density, Criteria Air Pollutants, Preterm Birth, Low Birth Weight, Neighborhood Stress Index, Food Deserts, Multilevel Logistic Regression, Geographical Information Systems, Milwaukee

In memory of
my grandmothers Letta M. Hills Cutler and Gladys E. Gretzner Schultz,
who emphasized the importance of healthy environments and lifestyles
and
my father Eugene E. Schultz and his friend Max Reese,
who passed from here very young
presumably due to a toxic environmental exposure

Dedicated to
my parents Judy and Al Pedersen,
my children Gabrielle J. and Nathan F. Pasha,
my dear friends and community ~ and all our children and grandchildren,
who inspired and encouraged this work

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LIST OF ABBREVIATIONS

ACTH	Adrenocorticotropic hormone
AQS	Air Quality System
ACOG	American College of Obstetrics and Gynecology
BV	Bacterial vaginosis
β-E	β-endorphin
BMI	Basal Metabolic Index
BE	Built Environment
CO	Carbon monoxide
CI	Confidence Interval
CADT	Cumulative traffic density
DOB	Date of birth
DOC	Date of conception
DWTD	Distance-weighted traffic density
EPA	Environmental Protection Agency
FSD	Statistically Fused Air and Deposition Surfaces
GAW	Gestational age at birth, in weeks
GIS	Geographic information systems
HPA axis	Hypothalamus-pituitary-adrenal
IMR	Infant mortality rate
IOM	Institute of Medicine
IRB	Institutional Review Board
IUGR	Intrauterine growth restriction
IDW	Inverse-distance weighted
LUR	Land use regression
LMP	Last menstrual period
LBW	Low birth weight
MIF	Macrophage migration inhibitory factor
NO_x	Nitrous oxides
OECD	Organization for Economic Cooperation and Development
O_3	Ozone
PM_{10}, $PM_{2.5}$	Particulate matter
PO	Post Office
PTB	Preterm birth

STDs	Sexually transmitted diseases
SGA	Small for gestational age
SIDS	Sudden Infant Death Syndrome
TIGER	Topologically Integrated Geographic Encoding and Referencing system
TDM	Transportation demand management
U.S.	United States
USDA	United States Department of Agriculture
VLBW	Very low birth weight
VOCs	Volatile organic compounds
WI	Wisconsin
WI DNR	Wisconsin Department of Natural Resources
WisDOT	Wisconsin Department of Transportation
WISH	Wisconsin Interactive Statistics on Health
WISLR	WI State Local Roads
W126	Weighted ozone
WHO	World Health Organization

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CHAPTER 1

EFFECTS OF TRAFFIC AND AIR POLLUTION ON RISK OF PRETERM BIRTH AND LOW BIRTH WEIGHT OUTCOMES IN MILWAUKEE COUNTY 2005-2010

Significance

Infant mortality and its relationship with preterm birth and low birth weight. Infant mortality, or death prior to the 365th day of age, is considered the most sensitive indicator of the overall well-being of society (Barfield et al., 2013), thereby serving as the 'canary-in-the-mine.' In 2010, the United States (U.S.) infant mortality rate (IMR) was 6.1 per 1,000 live births overall, 5.2 for the non-Hispanic white and Hispanic populations, and 11.5 for the non-Hispanic black population (Figure 1) (Matthews & MacDorman, 2013). The IMR for the U.S. and Wisconsin have steadily trended downward (Figure 2), but this is not reassuring for a number of reasons that will be discussed.

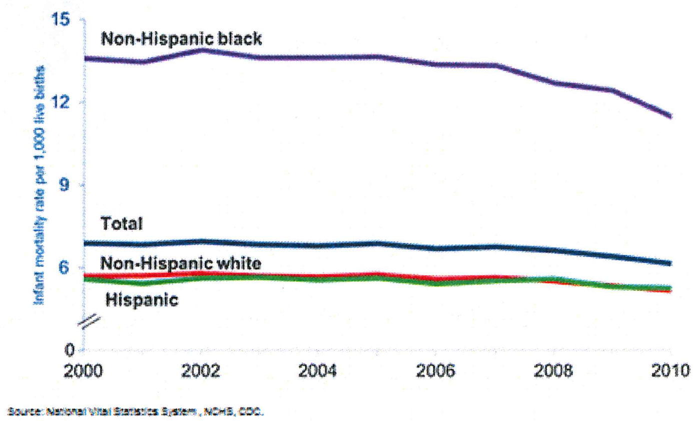
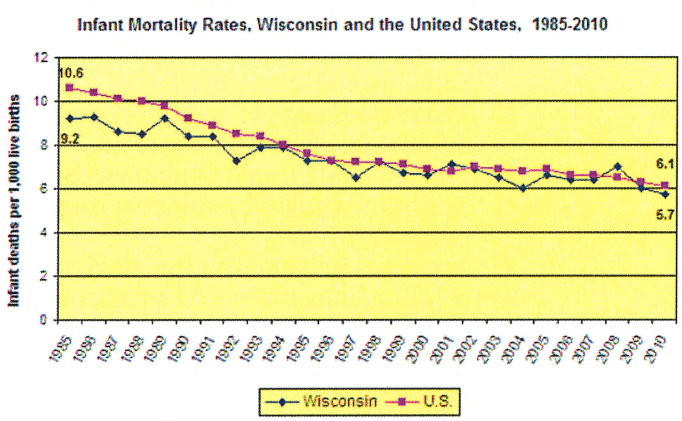


Figure 1. Infant mortality rates by race and Hispanic origin of mother: United States, 2000-2010.
Mathews & MacDorman. (2013).



Note: Rates are the number of infant deaths per 1,000 live births. Infant deaths are those that occur before 365 days of age.

Figure 2 Source: Wisconsin Interactive Statistics for Health

Based on the IMR in 2010, the U.S. ranked 32nd among the 34 nations of the Organization for Economic Cooperation and Development (OECD)

(Barfield et al., 2013). The high U.S. IMR is attributed to the elevated prevalence of preterm birth (12%) in the U.S compared to OECD countries that include developing nations.

Differential infant mortality patterns within the U.S. are striking. The IMR is higher in the southern region and several eastern states (Delaware, Maryland, Ohio) followed closely by the Midwest including Wisconsin (data not shown) (Mathews & MacDorman, 2013). The black:white ratio of IMRs is highest in Connecticut, the District of Columbia, Hawaii, New Jersey, and Wisconsin (Figure 3) (Mathews & MacDorman, 2011).

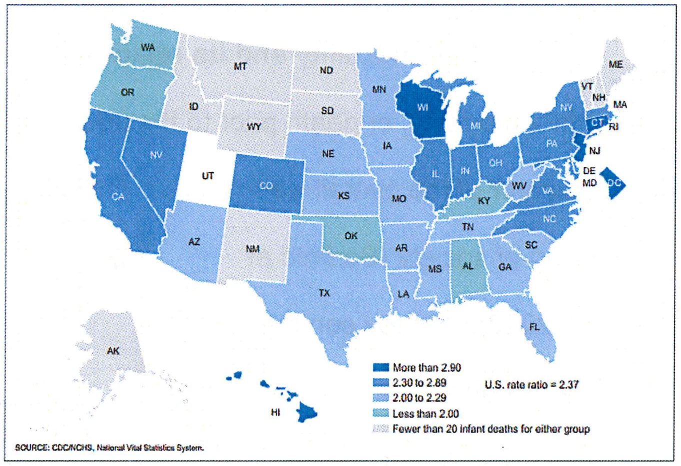


Figure 3. Black:White Infant Mortality Ratios, by State, 2005-2007.

Efforts to understand the etiology of infant mortality include surveillance of underlying causes listed on death certificates. The 10 primary causes of infant mortality—led by (1) congenital malformations, deformations, and chromosomal abnormalities (28%); (2) disorders related to short gestation and low birth weight (16.9%); and (3) Sudden Infant Death Syndrome (SIDS) (8.4%)—are shown in Table 1 (Heron, 2013). Notably, for infants of non-Hispanic black

Table 1. Leading Causes of Infant Mortality, 2010

1. Congenital malformations, deformations and chromosomal abnormalities
2. Disorders related to short gestation and low birth weight, not elsewhere classified
3. Sudden Infant Death Syndrome (SIDS)
4. Newborn affected by maternal complications of pregnancy
5. Accidents (unintentional injuries)
6. Newborn affected by complications of placenta, cord and membranes
7. Bacterial sepsis of newborn
8. Respiratory distress of newborn
9. Diseases of the circulatory system
10. Necrotizing enterocolitis of newborn

Murphy, Xu, & Kochanek, 2013.

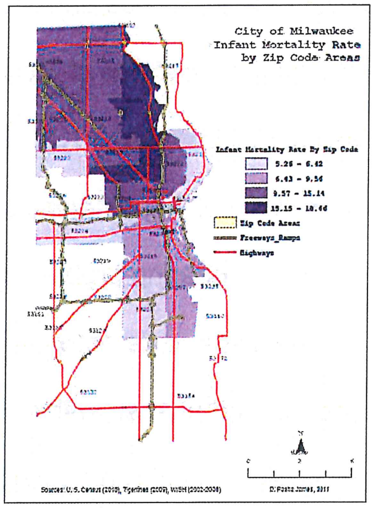


Figure 4. Infant mortality rate in City of Milwaukee by zip code areas (Wisconsin Interactive Statistics for Health [WISH] data,

women, the two leading causes are reversed: (1) disorders related to short gestation and low birth weight 22.1%) and

(2) congenital malformations, deformations, and chromosomal abnormalities (13.6%). To date, interventions have been targeted toward access to medical care, smoking cessation, and safer sleep environments—with better outcomes observed for some (Barfield et al., 2013). Nonetheless, inequities remain conspicuous (Figure 4).

Preterm birth. In the U.S., the prevalence of preterm birth (PTB) increased more than 20% between 1990 and 2006, and has since decreased by 6% between 2006 and 2010 (Martin et al., 2012). Whereas, in 2010, multiple births constituted only 3.45% of all births, they contributed disproportionately to the overall prevalence of PTB (11.99%). The prevalence of PTB among singletons in 2010 was 10.3%.

The rise in PTB in the past quarter-century has been attributed largely to increases in induced labor and cesarean deliveries in the absence of medical or obstetrical indications. Recent guidelines (American College of Obstetrics and Gynecology [ACOG], 2009) and a toolkit (Main, Oshiro, Ghagolla, Bingham, Dan-Kilduff, & Kowalewski, 2010) to curtail elective (non-medically indicated) deliveries before 39 weeks of gestation have been effective (Oshiro, Henry, Wilson, et al., 2009; Martin, Hamilton, Ventura, et al., 2012). The American College of Obstetrics and Gynecology (ACOG) recently issued new guidelines regarding cesarean deliveries (Associated Press, Feb. 19, 2014 announcement; document not publically available) with the same intent—to reduce elective deliveries before 39 weeks of gestation.

There are numerous reasons why the PTB prevalence should be drastically lowered: the clear and compelling causal link to infant mortality (Institute of Medicine [IOM], 2007; Heron, 2013; Martin, et al., 2007; Mathews & MacDorman, 2013), its causal association with acute complications (respiratory, gastrointestinal, immunological, central nervous system), and long-term sequelae including vision and hearing problems, cognitive and behavioral difficulties, social-emotional problems, and defective growth (IOM, 2007). The social and economic costs are significant, and unsustainable, as well. These include health insurance, educational (e.g., special education), and economic (predominantly, medical) costs, which add to the burden of PTB. In 2005, the societal economic burden of PTB was estimated to be in excess of *$26 billion dollars*, annually.

Low birth weight. Low birth weight (LBW) is highly correlated with PTB (Martin et al., 2012). LBW that occurs at term is considered intrauterine growth restriction (IUGR) (Matthews & MacDorman, 2013). Many studies on the effect of air pollution and/or traffic use IUGR as the outcome instead of LBW. However, vital statistics report on LBW rather than IUGR. Consequently, for this study, LBW regardless of gestational age (unless otherwise noted) is used in order to be consistent with national and state reports.

The etiology of LBW has many of the same underlying determinants as PTB (IOM, 2007). During the period 2006-2011, Wisconsin was the only state that reported a statistically significant increase in LBW (Martin et al., 2013).

Challenges and Opportunities

While national, regional, and state-based analysis of infant mortality and birth outcomes is essential, the aggregation of data across risk groups and geographies obscures information. For example, Wisconsin's IMR has steadily improved, and is even lower than the national rate (Figure 1). At first glance, it would appear that Wisconsin infants fare better than others in the U.S., with an IMR of 5.7/1000 live births (Figure 2)

(Wisconsin Interactive Statistics for Health [WISH], 2010). At a closer look, the data show that infants in the City of Milwaukee do not have as good of a chance of survival (IMR 9.3/1000) as elsewhere, and even less so if they are black (IMR 14.3/1000) (Figure 4). However, it also becomes apparent with data on a smaller scale that infant deaths are more common in some predominantly black neighborhoods than other neighborhoods. Factors that are hypothesized to impact observed geographical and racial differences in the prevalence of PTB and LBW (see Tables 2 and 3) include high traffic volume that impacts the north and northwest areas of Milwaukee more than elsewhere in the city and air pollution that reflects traffic, local industry, and pollution from other communities.

Table 2. Prevalence of preterm birth (2010)

Race/Ethnicity	All	Black	Hispanic	White
U.S.[1]	12.0	17.1	11.8	10.8
WI[1]	10.8	17.5	10.8	10.0
Milwaukee County[2]	13.2	17.9	11.3	10.1
Milwaukee Suburbs[2]	9.5	13.1	7.6	9.4
Milwaukee City[2]	14.6	18.2	11.8	11.0

[1]Martin et al., 2012

[2]Wisconsin Interactive Statistics for Health

Table 3. Prevalence of low birth weight (2010)

Race/Ethnicity	All	Black	Hispanic	White
U.S.[1]	8.2	13.5	7.0	7.1
WI[1]	7.0	13.8	5.8	6.2
Milwaukee County[2]	9.3	14.1	6.0	6.9
Milwaukee Suburbs[2]	6.6	8.5	4.6	6.5
Milwaukee City[2]	10.3	14.3	6.1	7.3

[1]Martin et al., 2012

[2]Wisconsin Interactive Statistics for Health

Physiological Basis of the Study

The biologic bases for both **physical and social environmental stressors** on pregnancy outcomes are described briefly (Figure 5). Stress is associated with traffic volume (Ge´ne´reux, Auger, Goneau, & Daniel, 2008; Zeka, Melly, & Schwartz, 2008), noise (Bodin et al., 2009), everyday hassles such as the lack of sufficient and reliable transit (Sanchez, 1999; Sanchez, Shen, & Peng, 2004), and air pollution (Ponce, Hoggatt, Wilhelm, & Ritz, 2005; Tonne, Whyatt, Camann, Perera, & Kinney, 2004) that results from emissions generated primarily by traffic and industry. Poverty (Ewing & Kreutzer, 2006), and the inaccessibility of quality food sources (Block & Kouba, 2006; Beaulac, Kristjansson, & Cummins, 2009) serve as additional stressors.

More specifically, some toxicants such as lead, mercury, and PCBs disrupt the **endocrine system** (Hadley, 2000; Klaassen, 2008), and thereby alter signaling pathways. Exposure to **criteria air pollutants**, particularly carbon monoxide (CO),

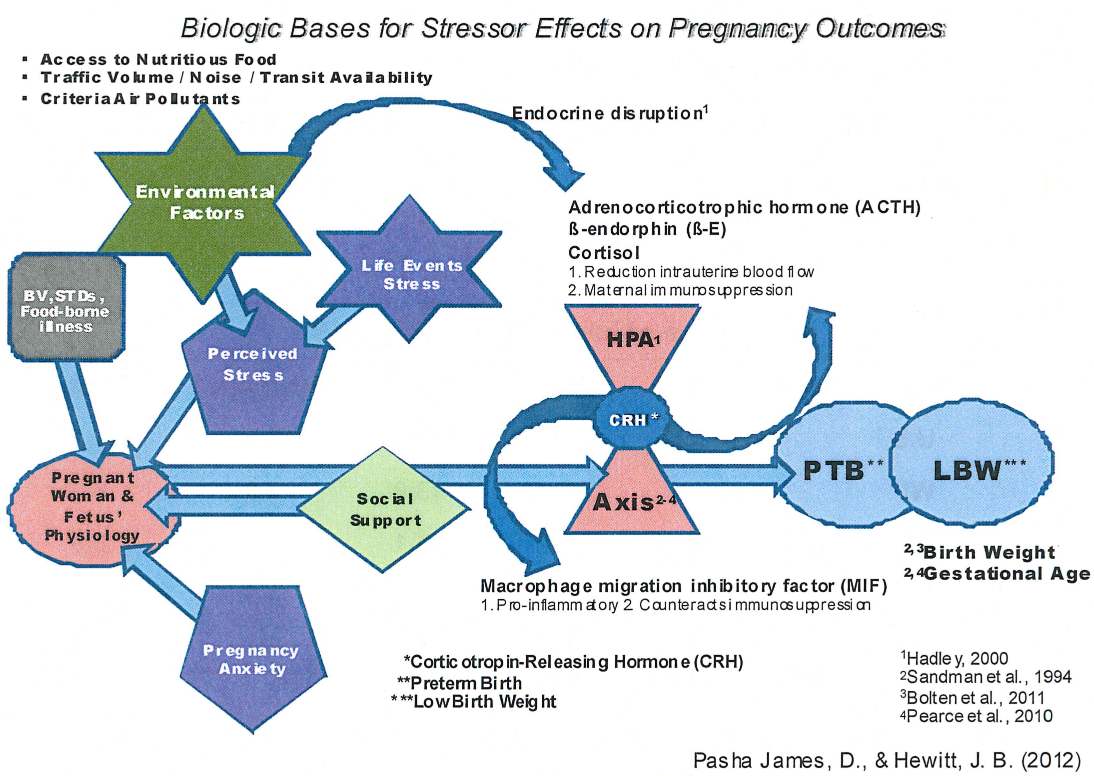


Figure 5. Biologic bases for stressor effects on pregnancy outcomes.

nitrous oxides (NO_x), particulate matter (PM_{10}, $PM_{2.5}$), and possibly, ground-level ozone (O_3) are thought to either act directly or serve as surrogate measures of the real pollutants that cause inflammation in airways and which affect signaling within the maternal endocrine system. Approximately 50% of volatile organic compounds (VOCs) and NO_x in urban areas are present due to traffic-related sources, which in the presence of sunlight create ground-level ozone (U.S. EPA, 2003). Especially in high-traffic areas, particulate matter is comprised of NO_x, VOCs, and also dust and metals (retrieved 11/25/1012 http://www.epa.gov/airquality/particlepollution/index.html) Exposure to such toxicants is disproportionately borne by persons of color and those who are economically disadvantaged (Ahern, Pickett, Selvin, & Abrams, 2003; Dole et al., 2003; Dole et al., 2004; Llop et al., 2011; Schempf, Kaufman, Messer, & Mendola, 2011).

These and other stressors such as that caused by **challenging life events** (e.g., interpersonal violence, mental health crises, premature death among family and friends) activate the hypothalamus-pituitary-adrenal (HPA) axis, and in turn, release adrenocorticotropic hormone (ACTH) and cortisol, which alter intrauterine blood flow and maternal immunity. Macrophage migration inhibitory factor (MIF) alters inflammation, as well, thereby reducing nutrients to the fetus and precipitating premature labor (Bolten et al., 2011; Hadley, 2000; Pearce et al., 2010; Sandman et al., 1994; Figure 5).

Other factors that may alter fetal growth or length of gestation include stress associated with **anxiety** about the pregnancy and/or **lack of social support** (Dole et al., 2003; Dole et al., 2004); **bacterial vaginosis** (Brotman, 2011; Klebanoff et al., 2005; Menon, Dunlop, Kramer, Fortunato, & Hogue, 2011); **sexually transmitted infections** (Brotman, 2011; Menon et al., 2011); and **food-borne illnesses** (e.g., listeriosis) (Ramaswamy et al., 2007; Tam, Erebara, & Einarson, 2010). All of these stressors can affect the pregnant woman and fetal physiology, through stimulation of corticotropin-releasing hormone (CRH) via the HPA axis.

Thus, the changes in ACTH, β-endorphin (β-E), and cortisol result in reduction of intrauterine blood flow, and are associated with hypoxia in the short term, as well as alterations in behavior and growth (Sandman et al., 1994). The increase in cortisol is also associated with LBW (Bolten et al., 2011). MIF is pro-inflammatory, which counteracts the immunosuppressive effects of corticosteroids, and has been found elevated during pregnancies that resulted in PTB (Pearce et al., 2010). The net effect of these events increases the risk of PTB (Hadley, 2000; Sandman et al., 1994; Pearce et al., 2010) and LBW (Hadley, 2000; Sandman et al., 1994; Bolten et al., 2011). Close examination of gene variants between Caucasians and African Americans has led other researchers to conclude that unmeasured genetic or environmental factors also affect these birth outcomes (Menon et al., 2011).

Purpose of the Study

Despite much publicity around infant mortality, PTB, and LBW in Milwaukee, relatively few analytical epidemiological studies have been undertaken to date to examine the potential underlying determinants of PTB and LBW. Studies using Wisconsin and City of Milwaukee birth records have analyzed factors such as parental occupation (Hewitt & Tellier, 1998), paternity (Ngui, Cortright, & Blair, 2009), prenatal care coordination (Willems Van Dijk, Anderko, & Stetzer, 2011), racial disparities (Byrd, Katcher, Peppard, Durkin, & Remington, 2007), smoking (Kvale, Glysch, Gothard, Aakko, & Remington, 2000; Jehn et al., 2001; Newburn, Remington, & Peppard, 2003), socioeconomic status (Salm Ward, Mori, Patrick, Madsen, & Cisler, 2010; Sims & Rainge, 2002) in relation to birth outcomes, as well as aberrant fetal growth patterns and infant mortality (Chen, Reich & Miranda, 2011). Thus, the purpose of this study is to examine the effect of traffic volume and air pollution on risk of PTB and LBW in Milwaukee County, with the expectation that these factors independently of other known risk factors, will explain the observed PTB and LBW prevalence that varies across the city and county.

Hypothesis #1:

Elevated traffic volume increases the risk of (a) PTB and (b) LBW outcomes independent of known risk factors.

Hypothesis #2:

Elevated air quality indicators increase the risk of (a) preterm birth (PTB) and (b) low birth weight (LBW) outcomes independent of known risk factors

Hypothesis #3:

Jointly, high traffic volume and poor air quality increase the risk of (a) PTB and (b) LBW, at a minimum, additively.

Definitions

Term	Definition
Brownfield[1]	A property, the expansion, redevelopment, or reuse of which may be complicated by the presence or potential presence of a hazardous substance, pollutant, or contaminant
Built Environment (BE)	Encompasses all buildings, spaces, and products that are created or modified by people
Infant mortality rate (IMR)[2]	The number of deaths of infants 0-364 days of age per 1,000 live births in the same year
Interpregnancy interval[3]	The interval between pregnancies, calculated as the date the last pregnancy ended and the date of the last menstrual period
Intrauterine growth restriction (IUGR)[3]	Low birth weight (< 2,500 g) at term
Low birth weight (LBW)[3,4]	Weight < 2,500 grams at birth
Natural environment	Air, land, water
Parity[3]	The number of times a woman has been pregnant more than 20 weeks
Preterm birth (PTB)[3,4,5]	< 37 weeks completed gestation
Small for gestational age[5]	< 10th percentile for gestational age
Sudden Infant Death Syndrome (SIDS)	The sudden and unexpected death of an apparently healthy infant, not explained by careful postmortem studies
Term Birth[4]	37 or more completed weeks gestation

[1]http://www.epa.gov/brownfields/basic_info.htm

[2]Barfield et al. (2013)

[3]http://www.cdc.gov/pednss/what_is/pnss_health_indicators.htm

[4]Martin et al. (2012)

[5]Institute of Medicine (2007)

CHAPTER 2

CONCEPTUAL FRAMEWORK AND REVIEW OF THE LITERATURE

In the United States (U.S.), preterm birth (PTB) increased steadily over the past 20 years or more, while low birth weight (LBW) remained a recalcitrant health problem (Menon, Dunlop, Kramer, Fortunato, & Hogue, 2011). Preterm birth and LBW are strong risk factors for infant mortality and many other adverse social, behavioral (e.g., learning disabilities), and health outcomes across the lifespan (Institute of Medicine [IOM], 2007). The disparities between non-Hispanic blacks and other racial/ethnic groups have increased during this time, but the underlying determinants remain poorly understood (Miranda, Maxson, & Edwards, 2009). Social and behavioral factors have dominated the literature. In contrast, this study is based on knowledge of social and physical environmental factors that have deteriorated in the Milwaukee area over the past several decades, especially for non-Hispanic blacks, and which may account for the observed disparities in birth outcome.

This literature review begins by describing the social and physical environments including transportation, industry, and air pollution, then summarizes risk factors for PTB and LBW, neighborhood stress, individual factors including stress, tobacco, infections, and nutrition, and family (epi)genetic factors. The paper concludes with emerging methods to assess traffic density and air pollutant exposures followed by a summary of birth outcomes associated with these exposures. Criteria used to select studies from the peer-reviewed literature included frequently cited authors from different regions of the U.S., seminal reports (e.g., from the Institute of Medicine) and research from the U.S. and other countries, as well as the quality and generalizability of research findings.

Physical and Social Environments

The conceptual model (Figure 6) frames the review of literature. The *physical environment* is comprised of the natural (air, land, and water) and built environments (e.g., homes, offices, schools, industrial and other buildings; transportation systems; parks and other recreational facilities) (Frumkin, 2010). The *social environment* includes the socioeconomic and demographic characteristics of the population, segregation and racism, and social systems including family, governmental, educational, faith, and financial systems. The conceptual model reflects those factors most likely to adversely impact gestational age and birth weight.

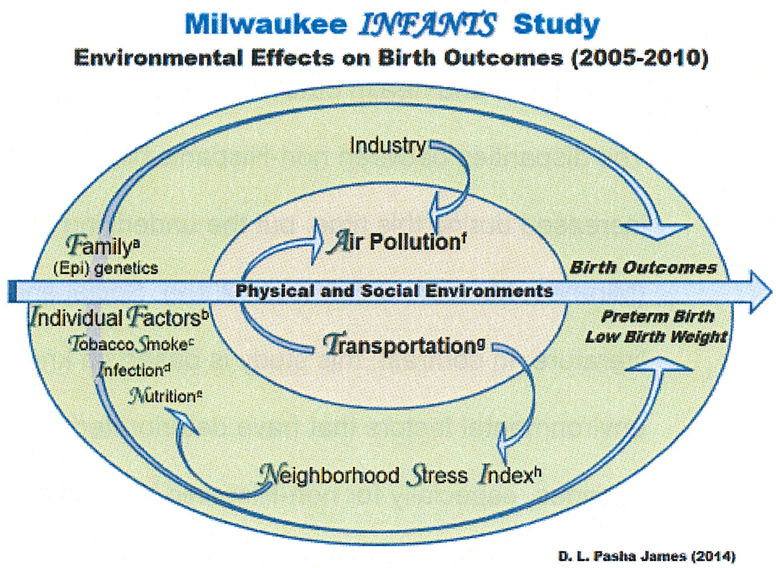


Figure 6. Conceptual model of the effect of traffic and air pollution on risk of preterm birth and low birth weight.

Transportation. Vehicular traffic is the major contributor of air pollution given local variation (Frumkin, 2010; Guidotti & Gitterman, 2007). Post World War II, urban planning emerged as a distinct discipline, while public health professionals increasingly focused on individual behavior (IOM, 2003; Kickbusch, 2003; Taylor, 1998). Significant changes in the built environment occurred at this time (American Public Health Association [APHA], 2005). For example, federal policy promoted building roadways and highways designed to move motor vehicles to distant destinations (Code of Federal Regulations [CFR], n.d.; Weiner, 2008). The Transportation Research Board report described the distribution of food over vast distances (Smith et al., 2005). Long distance transportation of food or other goods uses additional energy, thereby worsening air pollution.

Transportation-related adverse health outcomes. Several integrative reviews summarize how chronic diseases and injuries have been linked to traffic exposure (Bunn et al., 2003; Bunn et al. in Cochrane, 2008; Ewing & Kruetzer, 2006; and the World Health Organization, 2005). Research has demonstrated that traffic affects *mental health* (Leyden, 2003) and *physical activity* (Morrison, Thomson, & Petticrew, 2004); and increases the risk of *asthma and other pulmonary diseases* (Brauer et al., 2007; Brauer et al., 2002; Hunt, Abraham, Judson, & Berry, 2003; Karr et al., 2006; Morgenstern et al., 2007; Stieb, Szyszkowicz, Rowe, & Leech, 2009; Wilhelm, Qian, & Ritz, 2009; Wjst et al., 1993), *cancer* (Knox, 2006; Nie et al., 2007; Parent, Rousseau, Boffetta, Cohen, & Siemiatycki, 2006; Pearson, Wachtel, & Ebi, 2000; Sax et al., 2006; Vineis et al., 2007), *cardiovascular diseases* (Bodin et al., 2009; Hunt, Abraham, Judson, & Berry, 2003; Jerrett et al., 2009; Orru, Jõgi, Kaasik, & Forsberg, 2009; Stieb, Szyszkowicz, Rowe, & Leech, 2009); *endocrine disorders, especially diabetes and obesity* (Brook, Jerrett, Brook, Bard, & Finkelstein, 2007; Jerrett et al., 2010; *injuries* (Beck, Dellinger, & O'Neil, 2007; Ewing, Scheiber, & Zegeer, 2003; Paulozzi, 2005); and *all-cause mortality* (Laden, Neas, Dockery, & Schwartz, 2000; Samet et al., 2000).

Traffic is also a major source of noise in the community. Traffic volume is associated with noise in neighborhoods (Davies, Vlaanderen, Henderson, & Brauer, 2008), which also induces stress (Dratva et al., 2010; Wardman & Bristow, 2004) and adversely impacts quality of life (Davies et al., 2008). Furthermore, traffic-related noise disrupts sleep, induces hearing loss, and is associated with cognitive impairment in children, and hypertension and acute myocardial infarction in adults (World Health Organization [WHO], 2011).

High volume or speed of traffic make it difficult and dangerous to ride bicycles or walk in some neighborhoods. In turn, this situation limits physical activity and creates barriers in all modes of transportation to access goods and services such as groceries, employment, school, social activities, and medical appointments (Ewing & Kreutzer, 2006). Therefore, transportation and area traffic affect how people move within their neighborhood, how they interact with others, and travel throughout their community.

There are more highways through neighborhoods that are poor (Généreux, Auger, Goneau, & Daniel, 2007; Ponce, Hoggatt, Wilhelm, & Ritz, 2005), yet when wealthier people live near highways, they, too, have worse birth outcomes than their counterparts who live elsewhere. Highways encourage travel at higher speeds resulting in increased risk of injuries, deteriorating air quality, and pollution-related adverse health effects (Code of Federal Regulations [CFR], n.d.; Weiner, 2008).

Industry. Industrial pollution is emitted from both non-point (mobile) and point sources. Both contribute significantly to air pollution (Frumkin, 2010) and related health effects. In a study conducted in Italy with toll-gate workers and community controls (N = 170), uptake of air pollutants (CO, NO_x, Pb, and SO_x) were measured at eight tollgates and eight community locations (De Rosa et al., 2003). Blood samples were tested for methaemoglobin, sulphaemoglobin, carboxyhaemoglobin, lead (Pb), and zinc protoporphyrin. All but carboxyhaemoglobin were significantly elevated in the exposed workers compared to the community controls ($p < 0.0001$). Moreover, lead levels in workers were two to three times higher than the controls ($p < 0.0001$), which was associated with the use of leaded gasoline at the time of the study. Decreased sperm motility in male toll-gate workers and delayed conception in their wives were significantly (both, $p < 0.0001$) greater compared to community controls.

A study of women workers in Wisconsin (1990-1993) used occupation as recorded on the 1989 birth record form to classify them as potentially solvent-exposed during pregnancy (Hewitt & Tellier, 1998). They found small, statistically unstable elevated risks of 30% (RR = 1.3; 95% CI = 0.4 -4.7) associated with PTB and 50% associated with LBW (RR = 1.5; 95% CI = 0.4 - 4.7).

Over a period of decades, many manufacturing jobs were relocated from urban centers to the suburbs, leaving central city residents with few employment options (Williams & Collins, 1995). The result has been a loss of family-supporting, but often hazardous jobs, in urban centers that differentially exposed workers. Urban centers have been left with a plethora of brownfields—hazardous abandoned industrial sites—that continue to contaminate environments until remediated http://www.epa.gov/brownfields/basic_info.htm.

In a recent study of industrial pollution (including brownfields) in Milwaukee County, Wisconsin, Collins (2011) noted that this county ranked in the state's top 30% of areas of environmental justice concern, as designated by the EPA. Before controlling for race and poverty, all 307 census tracts in Milwaukee County, compared to Wisconsin as a whole, ranked as areas of environmental justice concern. When race and poverty were statistically controlled, the mapped data showed that industrial pollution was concentrated in 90 of the census tracts almost entirely located on Milwaukee's near north side.

Air pollution. Industrial and traffic related emissions include 6 *criteria air pollutants* (1) carbon monoxide, (2) lead, (3) nitrogen dioxide, (4) ozone [O_3], (5) particulate matter [both $PM_{2.5}$ and PM_{10}], and (6) sulfur dioxide and 187 *air toxics* (http://www.epa.gov/ttn/atw/orig189.html; see also Appendix E for the list of air toxics regulated under the Clean Air Act). Ozone is created by chemical reactions between the nitrous oxides (NO_x) and volatile organic compounds in the presence of sunlight, which especially in northern climates, usually are worse during the warmer months, although it can occur at any time of the year.

The Clean Air Act (1990) requires observance of air quality standards, known as the National Ambient Air Quality Primary standards. Primary standards are designed to protect the public's health, whereas secondary standards are intended to protect against decreased visibility and animal, crop, and building damage [Appendix E] (Environmental Protection Agency [EPA], 2012). The major anthropogenic sources of air pollution are the generation and burning of fossil fuels (e.g., to operate cars, trucks, buses, and airplanes; to heat and cool buildings and vehicles; to cook food; to manufacture and process chemicals, materials, and agricultural products) and the generation of chemical and other industrial waste. Smoking tobacco products also contributes significantly to indoor air pollution (Frumkin, 2010).

Air pollution-related adverse health outcomes. According to the EPA (http://www.epa.gov/ttn/atw/hlthef/lead.html, nd), health effects of air pollution are numerous. Carbon monoxide and lead reduce oxygen carrying capacity of the blood to organs. Lead accumulates in the body and can damage most of the major organ systems (nervous, renal, immune, reproductive, endocrine, cardiovascular) and development (EPA, nd; Weber, 1993; Rademacher, Steinpreis, & Weber, 2003; Rice, Ghorai, Zalewski, & Weber, 2011; Weber & Ghorai, 2013). Nitrogen dioxide, ozone, particulate matter, and sulfur dioxide all cause airway inflammation, and aggravate both pulmonary and cardiovascular diseases (EPA, http://www.epa.gov/region7/air/quality/health.htm, nd).

Research about air quality and mortality in 90 U.S. cities showed, on average, there was a 0.5% increase in overall mortality per 10 $\mu g/m^3$ increase in PM_{10} (Samet et al., 2000). Notably, in a national study, Milwaukee was in attainment for ozone, but ranked amongst the 20% worst counties for both appropriate monitoring and levels of $PM_{2.5}$ (Miranda, Edwards, Keating, & Paul, 2011).

Social environment. The most recent U.S. Bureau of the Census data (2010) and American Community Survey data (2008-2012) demonstrate that the City of Milwaukee has a younger population with a much larger proportion of minorities than Milwaukee County or the U.S. (Table 4). City residents are more economically challenged—twice as many of its children live below the poverty line compared to U.S. children as a whole. The median household income for City dwellers is substantially less than in the County or U.S. City of Milwaukee residents also deal with a much greater proportion of older housing stock and less access to motor vehicles for transportation than residents in the County or the U.S.

For many segments of the population, freeways divide communities and serve as barriers due to lack of adequate transportation that is reliable and affordable (i.e., automobile *vs.* public transit) (Sanchez, 1999; Sanchez, Shen, & Peng, 2004). This holds true in Milwaukee where I-94 divides the city between the predominantly non-Hispanic black community on the north side and the predominantly Latino community on the south side and where I-43 divides the more affluent east side from the most challenged neighborhoods to the west of this freeway (U.S. Census Bureau, 2010). Furthermore, highways through neighborhoods prevent people from walking or biking (active transportation) to school, work, places of worship, grocery stores, and elsewhere.

Neighborhood Stress. Various researchers have attempted to examine neighborhood level stressors such as poverty, housing, education, and employment, some in relation to birth outcomes (Elo et al., 2008; Messer et al., 2006; Messer, Vinikoor-Imler, & Laraia, 2012; Schempf, Kaufman, Messer, & Mendola, 2011). Messer and colleagues created an index that measured neighborhood attributes that distinguished areas where non-Hispanic White and non-Hispanic Black women lived.

Table 4. Comparison of socioeconomic indicators in the U.S., County of Milwaukee, and City of Milwaukee, 2010.

	U.S.	Milwaukee County	City of Milwaukee
Population (N)	308,745,538	947,735	594,833
Median age, in years	37.2	33.6	30.3
Under age 18 (%)	24.0	24.9	27.1
Male (%)	49.2	48.3	48.2
Non-Hispanic black (%)	12.6	26.8	40.0
Hispanic, any race (%)	16.3	13.3	17.3
Adults, 25 years of age and older, less than a high school education (%)	14.2	14.5	19.1
Household with own children under 18 (%)	29.8	28.0	29.6
Percent employed 16 years old or older (%)	64.7	66.9	66.0
Poverty status in past 12 months–			
Income below the poverty line (%)	20.8	31.0	41.0
In women householders, no husband present, family household (%)	46.1	54.0	58.3
Median earnings in past 12 months for population 25 years or older (2012 inflation-adjusted, dollars [$])	35,522	33,791	30,009
Vacant housing units (%)	11.4	8.2	9.9
Median household income ($)	53,046	43,599	35,823
Structure was built before 1960 (%)	30.1	62.0	70.5
No vehicle available, overall–	9	14.0	17.9
Lives in owner occupied housing (%)	3.4	4.3	6.0
Lives in renter occupied housing (%)	19.8	24.5	27.5

U.S. Bureau of the Census, 2010
American Community Survey, 2008-2012, 5-Year Estimates

The researchers constructed theoretically informed scales of physical incivilities (condition of housing and yards, commercial and public spaces, litter and graffiti), territoriality (fences, hedges, decorations, signs, and symbolic demarcations), and social spaces (presence of people, non-residential visitors, parks, porches and sidewalks), which were found to be internally consistent and informative. When the neighborhood index reflected incivilities at the census tract level, both non-Hispanic white and black women experienced low weight gain (< 15 lbs.), but no significant effect on PTB or LBW at term (Messer et al., 2012). These outcomes were not adjusted for other factors such as smoking or individual socioeconomic status.

Miranda, Messer, and Kroeger (2012) created indices of the built and social environments such as housing and crime in relation to PTB, LBW, and SGA, and found significant associations only in the crude models.

Food insecurity and food deserts. Poverty and lack of access to transportation and affordable quality food sources are neighborhood level factors that affect individuals. For example, Block and Kouba (2006) noted that non-Hispanic black neighborhoods had many grocery stores, but few supermarkets, and the price of food was comparable, but the quality was worse in the predominantly non-Hispanic black area. Farley et al. (2006) examined neighborhood stressors in Louisiana, as well, in association with gestational age and birth weight-for-gestational-age. Despite methodological rigor, they saw no significant relationship between these birth outcomes and density of alcohol and tobacco outlets, fast-food restaurants, and grocery supermarkets. In another study, Cook et al. (2004) found that, after adjusting for poverty, people who had experienced food insecurity as children had poorer health outcomes (1.90, 95% CI = 1.66, 2.18) and a greater number of hospitalizations (1.31, 95% CI = 1.16, 1.48) over a lifetime compared to those who had not suffered food insecurity as children.

Racism. Descriptions of racism at the community level have been described by Massey and Denton (1988, 1989) and more recently by Lee et al., 2008). In these national studies, Milwaukee was ranked amongst the most segregated cities in the U.S., across all significant types of segregation. Miranda and colleagues found that PTB and LBW were more likely in racially isolated neighborhoods (Anthopolos, James, Gelfand, & Miranda, 2011). In a cross-sectional study of U.S. metropolitan areas, Kramer and Hogue (2008) observed that black women were almost three times more likely to give birth to very preterm infants with 2.5 times more variation across cities ($p < 0.0001$). In another study of segregation and prematurity in U.S. metropolitan areas, Kramer, Cooper, Drews-Botsch, Waller, & Hogue (2010) attributed 28% of the geographic variation in very preterm birth disparities to isolation segregation. The underlying causes are not clearly understood at present.

Individual Factors. Individual psychosocial or physiological factors may influence the physiological stress responses that impact gestation and development (Chapter 1, Figure 5). These factors are: low educational attainment, unmarried status, race/ethnicity (non-Hispanic black), no prenatal care, very short or very long pregnancy interval, diabetes, hypertension, cigarette smoking, infection, and weight gain that is insufficient or excessive. The Institute of Medicine (2007) report on causes of preterm birth clearly articulates the risks associated with all of the above factors. Martin et al. (2012) examined the traditionally recognized factors that include mother less than 15 years old, poor nutrition, late or no prenatal care, and socioeconomic status.

Race/ethnicity. Differences between birth outcomes in non-Hispanic white and non-Hispanic black populations are well known (Ahern, Pickett, Selvin, & Abrams, 2003; Dole et al., 2004). However, race does not fully explain the risk of adverse birth outcomes given that Asian, Native American, and Hispanic infants fare much better than non-Hispanic black infants (Martin et al., 2012; Pearl, Braveman, & Abrams, 2001), despite similar socioeconomic disadvantages. Research has not conclusively demonstrated that prenatal care prevents PTB (Alexander & Kotelchuck, 2001; Lu &

Halfon, 2003). Even when non-Hispanic blacks have received prenatal care, their risk of PTB is nearly double (OR = 1.8) that of non-Hispanic white women) (Vintzileos, Ananth, Smulian, Scorza, & Knuppel, 2002).

Stressors. Dole et al. (2003, 2004) performed studies in a prospective cohort, to examine stressors and supports and their effects on PTB. Increased risks of PTB were found with pregnancy-related anxiety (RR = 2.1, 95% CI = 1.5 - 3.0), and life events to which the respondent assigned a negative impact weight (RR = 1.8, 95% CI = 1.2 -2.7). Perceptions of racial discrimination (RR = 1.4, 95% CI = 1.0 - 2.0) and unsafe neighborhood (RR = 1.2, 95% CI 0.9 – 1.7) were weakly associated with PTB. Levels of social support or depression were not associated with differences in birth outcomes. In a second study (2004) they found that, compared to women living with their partner, non-Hispanic White women were at higher risk of PTB if not living with a partner (RR=1.8, 95% CI = 1.2 - 2.7) than African American women (RR = 1.2, 95% CI = 0.8 - 1.8). No associations were found in relation to BV or smoking in either study.

The known interrelationships between stress, inflammation, and PTB have been reviewed extensively elsewhere (Hogue, Hoffman, & Hatch, 2001; Wadhwa, Culhane, Rauh, & Barve, 2001). In addition to these numerous possible effects on the developing fetus, related genetic differences and the differential responses to stress have been raised (Hogue, & Bremner, 2005). Researchers in New Orleans studied the birth outcomes from a prospective cohort who had previously participated in cardiovascular reactivity measurement as a measure of response to stress (Harville, Gunderson, Matthews, Lewis, & Carnethon, 2010). Overall, there was little association with birth outcomes, compared to non-reactive women of the same race; reactive non-Hispanic White women had slightly more risk of PTB (RR = 1.39, 95% CI = 1.03 – 1.88) and reactive non-Hispanic black women had no increased risk of PTB (RR = 1.00, 95% CI = 0.83 – 1.20).

Tobacco smoke. Smoking more than 9 cigarettes per day has been shown to be significantly associated with increased prevalence of PTB (Ahern, Pickett, Selvin, & Abrams, 2003; Jaddoe et al., 2008) and LBW (Jaddoe et al., 2008). Small to moderate levels of risk (1.2-1.5) are associated with smoking 10-20 cigarettes per day (½ to 1 pack per day), which increases to 1.5 to 2.0 for women who smoke one or more packs per day (IOM, 2007).

The prevalence of self-reported smoking during pregnancy from birth records in North Carolina was 11% (Gray, Edwards, & Miranda, 2010; Vinikoor-Imler, Gray, Edwards, & Miranda, 2012). In the prospective cohort study, also conducted in North Carolina, the smoking prevalence was 17.6% (Maxson, Edwards, Ingram, & Miranda, 2012). In Wisconsin, the prevalence of maternal smoking (2009-2010) was 14.9% statewide, 12.5% in Milwaukee County, and 13.0% in the City of Milwaukee (Voskuil, Palmersheim, Glysch, & Jones, 2010).

Cigarette smoking is one of the most prevalent, yet preventable determinants of negative pregnancy outcomes including abruptio placenta, decreased birth weight, and infant mortality (Cnattingius, 2004). The risk of smoking during pregnancy ranges between 1.2-1.6 for PTB and 1.5-2.9 for SGA with a dose-response evident for both. The timing of exposure to cigarette smoke during pregnancy determines some or all of the risk (IOM, 2007; Cnattingius, 2004). Quitting smoking before or early in pregnancy mitigates the risk.

Infections. Sexually transmitted diseases (STDs) such as chlamydia are correlated with PTB (Martius et al., 1988). The mechanisms between STDs and PTB, as well as non-STD bacterial vaginosis (BV) with PTB are not clear, although a combination of social factors and biological mechanisms have been implicated (Verstraelen et al., 2007; Wadhwa et al., 2001). Preterm delivery has been found to be more frequent in women with BV than without ($p < 0.001$) (Klebanoff et al., 2005). Other researchers have not confirmed this relationship on a consistent basis (Dole et al., 2003; 2004). By comparison to women who report low levels of stress, women who are moderately or highly stressed are more than twice as likely to develop BV (Culhane et al., 2001).

Other types of infection also are associated with increased risk of PTB or other adverse pregnancy outcomes. Infection with *Listeria monocytogenes* and *Salmonella enterica* during pregnancy can be fatal to the fetus (Tam, Erebara, & Einarson, 2010). Among fetuses that survive, intrauterine infection with these organisms may result in PTB or neonatal sepsis.

There are divergent opinions on whether periodontal disease is associated with PTB. To establish whether periodontal disease and treatment are factors in PTB, a randomized controlled trial was conducted with 786, mostly non-Hispanic black, pregnant women in Philadelphia, PA (Srinivas & Parry, 2012). The researchers did not find an association between the periodontal disease and PTB.

Associations have been found between infections and preterm birth, and thus to low birth weight (Menon, Dunlop, Kramer, Fortunato, & Hogue, 2011). In a review of the current scientific body of knowledge in this area, they described that concentration of cytokines (i.e. inflammatory response) in amniotic fluid varied by race. They speculated about the underlying mechanisms as possibly being due to genetic or epigenetic effects, or interactions with race/ethnicity.

Nutrition. Guidelines for weight gain during pregnancy are based on pre-pregnancy weight and height (BMI = weight in kg / height in m^2) (IOM, 2009) (Appendix C). However, pre-pregnancy weight and height are not uniformly available from health records and are only available on electronic birth records that use the 2003 standard version. Hendler et al. (2005) noted that BMI is one of the best markers of nutritional status. In their cohort at 10 medical centers, a lower rate of spontaneous PTB was present in obese women. When pre-pregnancy weight and BMI are not available, weight gain during pregnancy can be used as a proxy of nutrition during pregnancy (Abrams, Altman, & Pickett, 2000; IOM, 2009). In addition, the Institute of Medicine committee (2009) advised that special attention should be given to women who are low-income and racial/ethnic minority, as they are at increased risk of being overweight or obese at the time of conception. Furthermore, they may have diets lower in nutritional value, and have less access to places to be physically active (IOM, 2009).

As part of a prospective cohort study, Miranda and colleagues surveyed 615 pregnant women in North Carolina, to measure vitamin D. They obtained maternal blood samples and conducted an electronic medical record review. After controlling for cotinine and heavy metals, as well as maternal age, race, education, insurance, parity, and infant sex, they found that maternal genotypes for the vitamin D receptor influenced birth weight differentially by race (Swamy, Garrett, Miranda, & Ashley-Koch, 2011).

Family (epi)genetics. Individuals respond differently to chemical agents in the environment, which may modify their risk for diseases. In addition, chemical exposures may alter protein expression that not only affects the exposed individual, but also can be transmitted across generations without further exposure (Nebert & Carvan, 1997). Endocrine disrupting (EDs) chemicals in the environment masquerade as natural hormones, and by doing so, alter the natural function of the endocrine system. The effect of EDs may be to alter neurological behavior, reproductive or immune function, or to increase the risk of cancer (Guidotti & Gitterman, 2007).

In Chicago, researchers studied differences in birth outcomes by race and maternal place of birth (David & Collins, 1997; Collins, David, Rankin, & Desireddi, 2009; Love, David, Rankin, & Collins, 2010). The David and Collins team examined the 'weathering' hypothesis, which refers to accelerated aging of the mother due to her exposures to adverse social and physical environments. They consistently found that mothers born in Africa had better birth outcomes than U.S.-born non-Hispanic black mothers, and more similar to U.S.-born non-Hispanic white mothers. Of interest, when infants were born in more affluent neighborhoods, the risk of LBW persisted if their maternal grandmother had lived in a poor neighborhood (Collins et al., 2009).

In a similar study conducted in New York City, a protective effect was observed among infants born to South American black and U.S. born non-Hispanic white mothers (Howard, Marshall, Kaufman, & Savitz, 2006). In parental race combinations, the protective effect persisted for black mothers, but not for white mothers.

The current body of literature on risk factors for PTB and LBW minimally address the potential influence of the built environment. In the past decade or so, a growing body of literature has presented the potential effects of traffic and air pollution on these outcomes. These exposures have been measured using various methods, which are described below.

Key Methods Used to Study Traffic and Air Pollution in Relation to Birth Outcomes

Wilhelm and Ritz and their collaborators have performed numerous studies since the late 1990s to evaluate the effects of air pollution on birth outcomes in southern California (Ritz & Yu, 1999; Ritz, Yu, Chapa, & Fruin, 2000). They studied the effects of traffic and related pollutants on birth outcomes using birth records, hospital record cohorts, as well as some *de novo* surveys to augment existing records. They controlled for most potential confounders (maternal age, education, race, economics, previous birth history, medical problems, prenatal care, infant sex, seasonality) other than tobacco smoking, which was not available except for studies that used survey methods (Ghosh, Wilhelm, Dunkel-Schetter, Lombardi & Ritz, 2010; Ritz, Wilhelm, Hoggatt & Ghosh, 2007). They frequently reported on preterm PTB and LBW at term, also called intrauterine growth restriction (IUGR).

Traffic. Wilhelm and Ritz (2003) measured traffic by summarizing all major traffic within 750 feet of the maternal residential address during pregnancy. In two notable international studies, one conducted in Vancouver, British Columbia, Canada (Brauer et al., 2008) and the other in North Rotterdam, the Netherlands (van den Hooven et al., 2009), combinations of distance to nearest major road and the DWTD method were used to estimate effects of traffic exposure on birth outcomes. These studies were able to control for most confounding variables and used well accepted methods to measure exposure to traffic air pollutants. Brauer et al. (2008) estimated residential exposure to traffic by proximity to nearest major roads and highways (residence within 50 m; ADT was unspecified) and simultaneously controlled for the effect of criteria air pollutants. Van den Hooven et al. (2009) additionally controlled for length of road segments (within 500 m and a 150 m radius for the buffer zone) and change in residence during pregnancy. Notably, major roads were classified as those with more than 10,000 vehicles per day.

Miranda, Edwards, Chang, and Auten (2013) evaluated the effects of traffic on birth outcomes in North Carolina using road classification data to estimate traffic volume. The metric was maternal residence less than 250 m, between 250 m and 500 m, and greater than 500 m of a major roadway. Excluding records with congenital anomalies and missing variables, they analyzed 74% of available birth records at the census tract level and controlled for maternal race, age, education, nativity, marital status, tobacco use, season of birth, parity, infant sex, urbanization, and income.

A grid method refines summaries of traffic and air pollutant exposures and accounts for road-length segments. In a study that analyzed singleton births (1996-2002) in Eastern Massachusetts, Zeka, Melly, and Schwartz (2008) controlled for mother's age, education, race, cigarette use, Kotelchuck Index (a measure of adequacy of prenatal care), medical conditions, prior pregnancy history, gestational age, infant gender, and year of birth. They could not geocode 4.9% of the addresses. Average daily traffic count (ADT) was used to calculate the cumulative traffic density (CADT) by 100-meter grid squares. They also statistically controlled for the percent of land in each tract used for recreation and conservation.

Air pollution. Wilhelm and Ritz (2003) measured distance of the mother's known address during pregnancy to criteria air pollutant monitors to estimate air pollution (CO, NO, PM, O_3). In some cases, they reported average annual background pollutants (Ponce, Hoggatt, Wilhelm, & Ritz, 2005; Wilhelm & Ritz, 2003; Wu et al., 2009), or otherwise sampled from zip codes or addresses within five miles of stations (Wilhelm & Ritz, 2005; Wu, Wilhelm, Chung, & Ritz; 2011; Wilhelm et al., 2011; Wilhelm et al., 2012).

Researchers in North Carolina linked 2002-2004 birth records on singletons using addresses with air pollutants from monitoring stations at the county level, and in the same study, a separate method used only births that occurred in buffers (20, 10, and 5 km) (Gray, Edwards, & Miranda, 2010). They controlled for major confounders including smoking during pregnancy. In another study of the effects of $PM_{2.5}$ on singleton births (2004-2008), Chang, Reich, and Miranda (2011) developed metrics using ambient concentrations measured by the Air Quality System (AQS) and predictions from the Statistically Fused Air and Deposition Surfaces (FSD) data base . After excluding records with congenital anomalies, 83% of birth records with maternal residential addresses were geocoded and linked to air pollutants in 12-km square grid cells. In addition to the usual confounders, they controlled for seasonality at conception.

Brauer et al. (2008) used land use regression (LUR) and inverse-distance weighted (IDW) procedures to evaluate the effects of criteria air pollutants, while controlling for traffic density. Van den Hooven et al., (2009) used various methods to assess average air pollution exposure including calculations within 10 km of an air monitoring station and IDW to three closest monitors within 50 km.

Kloog, Melly, Ridgway, Coull, and Schwarz. (2012) used a 10 x 10 km grid to measure satellite data for $PM_{2.5}$ air pollution exposures. They, along with Brauer et al. (2008) and Wilhelm and Ritz (2003), simultaneously reported findings for air pollution and traffic exposures.

An ozone metric called W126 uses a weighting procedure, which was developed to emphasize the effects of peak ozone levels on crops (Ellingsen et al., 2008; Lefohn, 1997). There is recent interest to apply this method to study the effects of ozone on human health. To our knowledge, W126 has not been used previously in studies on birth outcomes.

Findings from Key Studies of Traffic and Air Pollution in Relation to Birth Outcomes

In their multivariable, adjusted model that examined traffic and included background concentrations of criteria air pollutants (excluding multiple births and caesarean sections) and many potential confounders, Wilhelm and Ritz (2003) observed a narrow range of very modest elevated risks (aOR 1.01-1.14) of PTB among infants that weighed less than 2,500 g (PTB/LBW). Only the 4th quintile distance-weighted traffic density (DWTD) was significantly elevated (aOR 1.14, 95% CI = 1.01-1.28). The exception was observed when the 3rd trimester occurred during the Fall/Winter, which resulted in a 24% increased risk of PTB/LBW at the highest quintile of DWTD exposure (aOR 1.24, 95% = 1.04-1.47).

More recently, Wilhelm et al. (2011, 2012) reported on speciated constituents of air pollution. Using land use regression (LUR) models, they found that various chemicals in addition to the criteria air pollutants were associated with a 6-30% risk of PTB per interquartile range (Wilhelm et al., 2011). However, for LBW at term, the adjusted odds ratios ranged between 3-8%, and only 2 of 11 pollutants (NO and NO_2) reached statistical significance (Wilhelm et al., 2012).

Noting that North Carolina is an attainment state by EPA standards, Gray et al. (2010), nonetheless, found reductions in birth weight of 5.3 g (95% CI = 3.3-7.4) for PM_{10} and 4.6 g (95% CI = 2.3-6.8) for $PM_{2.5}$ for each interquartile increase in PM when measured throughout the pregnancy. In another study, Miranda and colleagues (2013) analyzed 74% of available birth records at the census tract level. In the multivariable adjusted model (maternal race, age, education, nativity, marital status, tobacco use, season of birth, parity, infant sex, urbanization, and income), PTB and LBW were significantly increased ($p < .05$) 3% to 5% for those who resided less than 250 m compared with women who resided further from a major roadway.

In a study of 70,249 singleton births (1999-2002) adjusted for maternal age, education, ethnicity, income, parity, smoking, birth month, birth year, and infant sex, Brauer and colleagues (2008) found an increased risk of SGA (birth weight < 10^{th} percentile for sex and gestational age in weeks) within 50 m of highways (aOR = 1.26, 95% CI = 1.07–1.49). Elevated criteria air pollutants were inconsistently and weakly associated with PTB and LBW at term.

Among pregnant women in North Rotterdam (from the Generation R Study, a prospective cohort study in the Netherlands),15.5% reported smoking during pregnancy and 36.5% continued using alcohol (van den Hooven et al., 2009). After controlling for maternal age, ethnicity, education, BMI, parity, smoking, alcohol consumption, seasonality, and criteria air pollutants, few risk estimates reached statistical significance. The risk of PTB increased significantly in the 2^{nd} DWTD quartile (aOR = 1.37, 95% CI = 1.02- 1.84), and birth weight was reduced significantly within 100-150 m of major roads (regression coefficient -41g, 95% CI = -69g to -12g). Van den Hooven et al., (2009) noted that residential mobility did not have a detectable effect on exposure estimates.

Traffic density was estimated within 100 m grid squares by Zeka et al. (2008). They did not find an effect on PTB (aOR = 1.00, 95% CI = 0.98 - 1.01) or SGA (aOR =

1.02, 95% CI = 1.00 - 1.03). In a subsequent study, Kloog et al. (2012) focused on air pollutants and traffic. For each 10 μg/m^3 increase of $PM_{2.5}$ exposure during the entire pregnancy period, they detected a small increased risk of PTB, OR = 1.06 (95% CI = 1.01–1.13). There were no significant associations with specific trimesters. Neither $PM_{2.5}$ nor normalized cumulative traffic density had an effect on risk of PTB. Birth weight, however, was negatively associated with exposure to $PM_{2.5}$ (-1.38g, CI = -2.11g-0.65g).

Summary

This paper reviewed emerging methods to study traffic density and air pollution in relation to birth outcomes. We described existing evidence that has been done by leading researchers in the U.S. and abroad. We also examined traditional risk factors in relation to PTB and LBW.

CHAPTER 3
EFFECTS OF TRAFFIC AND AIR POLLUTION ON RISK OF PRETERM BIRTH IN MILWAUKEE COUNTY, 2005-2010

In 2010, the infant mortality rate (IMR) in the U.S. at 6.1 per 1000 live births (Matthews & MacDorman, 2013) ranked 32nd among the 34 nations of the Organization for Economic Cooperation and Development (OECD) (Barfield et al., 2013). The high U.S. IMR is attributed to the elevated prevalence of preterm birth (PTB) (12%) in the U.S compared to OECD countries that include developing nations. In the U.S., preterm birth is the leading cause of infant mortality in children of non-Hispanic black mothers and the second leading cause for all children regardless of maternal race and ethnicity (Heron, 2013). In 2010, infants of non-Hispanic black mothers were twice as likely to die before their first birthday (11.5/1000 live births) as infants of non-Hispanic white or Hispanic mothers (5.2 for both) (Matthews & MacDorman, 2013).

The risk of infant mortality also differs geographically. The IMR is higher in the southern region of the U.S. and several eastern states (Delaware, Maryland, Ohio) followed closely by the Midwest including Wisconsin (Mathews & MacDorman, 2013). The black:white ratio of IMRs is highest in Connecticut, the District of Columbia, Hawaii, New Jersey, and Wisconsin (Mathews, & MacDorman, 2011).

Preterm birth prevalence increased more than 20% between 1990 and 2006, and has since decreased by 6% between 2006 and 2010 (Martin et al., 2012). The rise in PTB in the past quarter-century has been attributed largely to increases in induced labor and cesarean deliveries in the absence of medical or obstetrical indications. To curtail elective (non-medically indicated) deliveries before 39 weeks of gestation, guidelines (American College of Obstetrics and Gynecology [ACOG], 2009) and a toolkit (Main et al., 2010) recently were issued (Oshiro, Henry, Wilson, Branch, & Varner, 2009; Martin et al., 2012). The ACOG has announced new guidelines regarding cesarean deliveries (Associated Press, February 19, 2014 announcement; document not publically available) with the same intent—to reduce elective deliveries before 39 weeks of gestation.

As reviewed by the Institute of Medicine, other factors associated with an increased risk of PTB include both maternal age less than 16 and 35 or older; non-Hispanic black race; low educational attainment and socioeconomic status; unmarried status; low social support; use of tobacco, alcohol, and/or illicit drugs; chronic or catastrophic stress; personal racism; poor nutrition; inadequate or excessive weight gain; short stature; lack of physical activity; employment that involves prolonged standing, heavy work, or working shifts or nights; parity; intendedness of pregnancy; infections; multiple gestations; late or no prenatal care; history of PTB; congenital anomalies; preeclampsia; and male infants (IOM, 2007).

Factors that also have been implicated in precipitating PTB include exposures to certain toxicants (e.g., lead) and neighborhoods that are segregated (i.e., stress-inducing) (IOM, 2007). Using industrial emission data from the Environmental Protection Agency (EPA), Collins (2011) showed that, adjusted for race and poverty, the preponderance of environmental justice issues was on Milwaukee's near north side. Neighborhood factors and toxicants have not been well studied, but are plausibly associated with increased risk of PTB and deserve greater attention. The prevalence of PTB differs by race/ethnicity and within smaller geographical areas as previously summarized (Chapter 1, Table 2), where clear differences emerge between the City of Milwaukee and suburban Milwaukee County.

It is imperative that the underlying determinants of PTB be identified and addressed urgently due to its causal link to acute complications, long-term sequelae, and infant mortality, as well as social and economic costs—estimated to be $26 billion in the U.S. annually (IOM, 2007). The purpose of this study was to examine the effect of traffic and air pollution on preterm birth in Milwaukee County while adjusting for known PTB risk factors, as well as an index of neighborhood stress.

Methods

Study design, data sources, and protection of human subjects. An historical cohort study was created using available electronic data from Wisconsin birth records (2005-2010) linked to exposure data from the Wisconsin Department of Transportation (average daily traffic counts, 2004-2010), Wisconsin Department of Natural Resources (criteria and hazardous air pollutants, 2004-2010), and neighborhood stress indicators from the U.S. Department of Agriculture (2006-2010). The research and use of birth data were approved by the Wisconsin Division of Public Health. The study was approved as minimal risk by the Institutional Review Board for the Protection of Human Subjects at the University of Wisconsin-Milwaukee (Appendix A).

Population. Milwaukee County consists of the City of Milwaukee, and during the study period, 12 suburban jurisdictions. According to the U.S. Bureau of the Census, in 2010, the City of Milwaukee population was 594,833 and the suburban population was 352,902. Wisconsin used the 1989 Birth Certificate for reporting birth data through 2010. Therefore, the years of this study were selected to use the same birth registration form and to provide more than sufficient power (data not shown; Martin et al., 2012).

Electronic birth records and geocoding of maternal residential addresses. Electronic birth records were obtained through the Wisconsin Division of Public Health, Vital Records Office through a memorandum of understanding. All singleton births registered with the state that occurred between January 1, 2005 and December, 31, 2010 in Milwaukee County were eligible for the study. Data on the county and minor civil division of the mother's residence were used to determine residence eligibility.

Vital Statistics provided the dataset of 89,481 birth records that included births outside of the county. There were 89,158 births in Milwaukee County, of which 1,201

(1.4%) had no codeable maternal address. The remaining dataset consisted of 87,957 birth records, of which 2,912 (3.3%) were multiple births; 6 were missing gestational age; and 1 other birth erroneously had been coded to the census block-group level. The final set of singleton birth records available for analyses was 85,038.

The maternal mailing address at the time of delivery as available on the birth record was used to generate geocodes. The Vital Statistics Office provided geocoded birth records coded to the block level for these analyses. The records were geocoded using the Centrus Desktop product by Information Technology. The software returned codes indicating the source and quality of its geocode assignments (personal communication, L. Ninneman, WI Vital Records, September 26, 2013). Street network data derived from the U.S. Census Bureau TIGER (Topologically Integrated Geographic Encoding and Referencing system) dataset was used to assign latitude and longitude coordinates. Assignment of exposures to traffic and criteria air pollutants were based on the centroid of the census block. There were 9,744 blocks with at least one birth. More than 3,000 blocks had no births.

Traffic and air pollution exposures. Methods used to calculate cumulative traffic density and interpolate criteria air pollutants are described below.

Cumulative traffic density. The spatial dataset of roads and highways for Milwaukee County was obtained from the Wisconsin Department of Transportation's WISLR (WI State Local Roads) database (WisDOT, 2009). This dataset included average daily traffic (ADT) as the attribute AVG_DLY_TRFC. Wisconsin Department of Transportation provided traffic count points for major roadways in Milwaukee County for the study years (WisDOT TRADAS, 2004-2010; personal communications, R.A. McDonald & J. Tyson, 2012). TRADAS data include ADT as the attribute RDWY_AADT. Using ArcGIS 10.1 (ESRI, Redlands, CA) software, TRADAS points and WISLR roadways data were spatially joined by J. Witebsky, a geographical information system (GIS) specialist. She then used joined TRADAS points to interpolate traffic counts for segments without counts between major roadways. For roadways with no spatially joined TRADAS points, she used the 2009 AVG_DLY_TRFC value to estimate ADT. If both attributes were lacking (some minor streets), she gave ADT an arbitrary value of 150. Freeway segments in WISLR were digitized into single freeway lines and values of RDWY_AADT averaged over the length of the lines were used to estimate ADT.

The research team used methods described by Zeka, Melly, and Schwartz (2008) and Kloog, Melly, Ridgway, Coull, and Schwartz (2012) to summarize traffic using the formula:

$$CADT = \Sigma\ (ADT * \text{road segment length})$$

A grid over the entire county of 200 x 200 meter cells was used to calculate cumulative traffic density (CADT) from ADT in units of vehicle counts-meters. (This value was transformed for reporting purposes to counts-kilometers [Zeka et al., 2008]). Because the state geocoded birth data to 2010 census blocks, Witebsky assigned an average of the CADT for the four grid points nearest the 2010 TIGER/line centroid point (INTPTLAT, INTPTLON) for each census block.

There were 760 births distributed amongst 72 census blocks that did not connect with the grid used for estimating traffic density. This occurred for one of two reasons, either the block was within a large area with no roads near the center of the block (e.g. city/county park or rural area of the county, many of which were seen on the map to be in the southern part of the county), or less frequently, there was a gap because the state road dataset does not include roads within subdivisions. As a result, we assigned a value of ‘0’ traffic exposure to these 760 births. Across the county traffic density was skewed, resulting in some neighborhoods’ experience of significantly more traffic (Appendix D).

Traffic load values were scaled to kilometers (divided by 1000). The mean of the cumulative average daily traffic (CADT) was 1,986. The traffic data (Tl_qntl) varied between years, thus the values assigned to each pregnancy reflected the estimated date of conception.

Criteria air pollutant data. The criteria and hazardous air pollutants (HAPS) data for 2004-2010 for Milwaukee and surrounding counties were obtained from the Wisconsin Department of Natural Resources (WI DNR) in pipe delimited format in a zipped file. The information included Environmental Protection Agency (EPA) tables defining parameter codes, units, and methods (http://www.epa.gov/ttn/airs/airsaqs/manuals/codedescs.htm) (Appendix E). A separate file containing site locations was provided (Appendix F). Each monitor id is composed of the state code, county code, site id, parameter code and parameter occurrence code (POC). The POC is used to distinguished between monitors at sites where the same parameter is measured using the same method by more than one monitor. (Personal communication, G.D. Hetherington, Air Monitoring Data Manager, WI DNR, 12/13/2012).

Four criteria air pollutants are monitored at stations in Southeast WI. These are NO_X, CO, $PM_{2.5}$, and O_3. However, due to data limitations, 2 air quality measures, which are $PM_{2.5}$ and O_3, were used for this study because they were consistently available across the study years. The weighting method for O_3 was suggested by the Wisconsin Department of Natural Resources (DNR) (personal communication, J. Meyer, 4/05/2013). W126 is an exponential transformation of O_3 values that emphasize the higher values (http://www.epa.gov/ttn/analysis/w126.htm). The method was developed to capture the effect of O_3 on vegetation. Potential value in studying the impact of O_3 using this method is under consideration for studying human health. In our study, analyses were performed using the O_3 untransformed and weighted (Appendix G). We report the weighted analyses.

Particulate matter 2.5 ($PM_{2.5}$). For $PM_{2.5}$, there is the possibility of spatial variation within the county (although graphs of the station averages through time did not reveal much variability). Therefore, $PM_{2.5}$ loads were estimated (interpolated) for each census block and each day, and these were summed to trimesters. The $PM_{2.5}$ values were assigned to blocks by distance-weighted interpolation from the monitoring sites (Appendix F). The majority of the variation was temporal rather than spatial.

When averaged to the month, $PM_{2.5}$ numbers from the stations in Milwaukee County typically moved together in lockstep. As a result, any method of spatial interpolation for the trimesters combined similar values.

The Milwaukee County stations for which $PM_{2.5}$ measurements were tracked are presented (Appendix F). No Milwaukee County areas are closer to any stations outside the county. At all stations, $PM_{2.5}$ values are recorded in micrograms per cubic meter ($\mu g/m^3$) in 24 hours. The sampling frequency varies from daily, to every 3rd, 6th or occasionally, 12th day.

The steps used to calculate the $PM_{2.5}$ load for a trimester for each infant are:

1. Distances (d) from each station to each 2010 Census block centroid were calculated.
2. For sampling frequency less than once a day at a station, the most recent sample value was used for the missing days, so data was complete for each station during the period it is active.
3. A distance-weighted average of the available station values was calculated for each block and each day. The square of the distance was used to emphasize the closest station in the average:

$$PM_{2.5\ block} = (\sum PM25 * 1/d^2)/(\sum 1/d^2)$$

4. These weighted daily average values were summed for the three trimesters for each infant.
5. For trimesters at the end of 2010 which are “short”, the trimester sum was inflated to the full number of days.

Ozone. Since ozone is a “regional” pollutant, variations in sample values among stations in the same region (e.g., Milwaukee County) at the same time should be attributed to microclimate differences at the stations rather than a pattern within the county (J. Kahl, personal communication, 3/29/2013). As a result, the research team ruled out use of interpolation methods for O_3. Ozone is typically monitored during the summer months. Only the DNR site monitors during the winter. Samples are taken hourly. Ozone values are typically low during the night and increase during the daylight hours as sunlight interacts with chemicals in the atmosphere, peaking in late afternoon.

The method used to calculate ozone load for trimesters for each infant was:

1. Ozone sample values were converted to parts-per-million (PPM). The W126 calculations discussed below are based on PPM values, so it was decided to be consistent in this regard.
2. Daylight (8 a.m. to 8 p.m.) ozone values were summed for each day at each station where data were available. If there were missing hourly values, the sum was inflated to represent 12 hours.
3. These daily sums were averaged over all the available sites for each day. Any missing daily average was replaced with the average for the previous day. This only occurred during winter if the single available DNR site was un-operational.

The W126 ozone score is a weighting which emphasizes high-ozone values compared to lower values. The W126 score takes the hourly PPM ozone value (O_3) at each station and applies this formula:

$$W126 = O_3 * \frac{1}{1+4403*\exp(-126*O3)}$$

W126 trimester values were calculated through the steps above by starting with the weighted hourly values.

The graphs show the county average daily sums for the study period, for ozone and W126 (Appendix G). The W126 values emphasize the ozone peaks.

In summary, $PM_{2.5}$ loads depended on dates and locations, since there was a small amount of variation over the county. However, the variation was mostly temporal not spatial. The ozone load data depended solely on the *dates* in the trimester, not on location, since we assumed ozone was uniform across the county on a given day.

Potential confounding variables. Relevant independent variables were used to control for confounding when available on the electronic birth record. In addition, a Neighborhood Stress Index derived from a USDA dataset was used to control for census-tract level indicators of socioeconomic stress.

Trimester calculation. The computation for trimesters one, two, and three for each birth involved summing the available data. These were called "loads." We computed air pollution "load" values for each infant during the first, second, and third trimesters of the pregnancy. Date of birth (DOB) was only known to the year and month due to a confidentiality requirement of the Vital Records Office. We calculated trimesters assuming all births occurred on the first of the month. This was done to make sure (to the extent possible) that the first trimester was calculated with the inclusion of the date of conception (DOC).

The other component of trimester calculation is gestational age. There were two estimates of gestational age at birth, in weeks (GAW). First was the variable GAGEWKS (calculated from last menstrual period [LMP and DOB if LMP available, or clinical estimate gestational age otherwise]. The second was GESTEST (clinical estimate from health care provider estimate). The method recommended by Wisconsin Vital Records Office was GAGEWKS, which we used for this study. There is considerable controversy about estimating gestational age; however, at this time, use of the LMP is the predominant method (Martin et al., 2012). We used this variable to optimize consistency both with available data and the calculation generally accepted in the literature.

Date of conception (DOC) was calculated as DOB – 7*GAW. The first trimester was 13 weeks (91 days) starting at DOC. The next 13 weeks (91 days) were the second trimester. The third trimester was defined as 7 weeks (63 days). This shortened third trimester (33 weeks total gestation) is consistent with the overall goal of understanding air pollution's contribution to PTB, rather than impacts of air pollution on characteristics of infants born full term. At the same time, it also obviates the dilemma of term infants having greater exposures than preterm infants, contrary to expected risk (Hewitt, 1997).

For the purpose of computing air pollution load, we estimated the ozone and $PM_{2.5}$ for each day and summed them for each trimester for each infant. Mathematically, there is no difference in using a sum *vs.* an average in regression modeling, except that the 3rd trimester (3 sum), being based on fewer days, will appear to have a different mean value.

There were eight premature births in December 2010, which was the last month of the study and the last month of the air quality data, where the start of the 3rd trimester is in December 2010. For these eight, the 3rd trimester air quality loads could not be computed. These were considered missing and were handled along with the other missing values in the multiple imputation step.

For the birth outcome modeling, it was decided to use the 1st trimester, 2nd trimester, and total load for $PM_{2.5}$ and the W126-weighted O_3. For logistic modeling, the trimester for each pollutant was standardized to zero mean and standard deviation of one. This does not change significance but helps scale the confidence limits for the odds ratios to make them more interpretable. The total (three-trimester load) was defined as the sum of the standardized loads for the three trimesters. The interpretation of the OR was the change in odds of PTB for a 1-standard deviation change in the air quality measure.

Data Analysis

Missing data. Less than 5% (4.7%) of the birth record cases had one or more missing values; most had only one missing value. Overall, missing data were more common in unmarried, black mothers who gave birth to preterm or low birth weight infants. Missing data by race were: 6.2% of non-Hispanic blacks, 4.8% of Hispanics, and 3.1% of non-Hispanic whites. Data were missing for 7.4% of PTB. Data on fathers was not provided on the electronic birth records unless the mother and father were married. This resulted in substantial missing data (55.1% for fathers' education, 25.9% for fathers' age).

Descriptive and bivariate analyses. We used SAS version 9.4 to calculate percentages, medians, means, and χ^2 to describe the population and compare characteristics (data not shown). Cross tabulations (2x2 and 2x*N*) were done to compute Mantel-Haenszel Odds Ratios and 95% Confidence Intervals (CIs). We created maps using ArcGIS 10.1 (ESRI, Redlands, CA) software where statistical findings suggested spatial patterns.

Multi-level risk factor analyses. Multiple imputation was performed using SAS Proc MI. Each imputation uses a complete set of the data, with the missing values filled in by regression of the variables with missing values against those without missing values, and adding a random component (error term) to capture the variability in the data. The random component makes each imputation slightly different. The research analysis is then performed on each imputation and the results statistically averaged over the imputations (SAS Proc MIANALYZE). As often recommended (Sternes et al., 2009), 20 imputations were used here.

Neighborhood Stress Index (LILATracts_Vehicle) was measured at the tract level, while other variables from the birth record were measured at the individual level using maternal resident addresses at the census block level. Therefore, multilevel logistic regression was performed from the multiply-imputed data using SAS Proc GLIMMIX. This yielded 4 models for PTB. The year of infant births was included as a predictive variable. We employed a test for trend for traffic density.

Results

Descriptive statistics. Mothers in the City of Milwaukee were younger, less well educated, and more likely to be non-Hispanic black or Hispanic than suburban mothers (data not shown). Parity was slightly higher amongst City mothers, and they were 50% more likely to have had a previous PTB. They were considerably less likely to begin prenatal care in the 1st or 2nd trimester as compared to suburban mothers. The mean number of prenatal visits were slightly less amongst City mothers, and they were less likely to have had adequate care as measured by the Kotelchuck Index. Mothers in the City were almost twice as likely to have STDs reported on the birth record. However adverse health conditions such as diabetes and abruptio placenta were similar throughout the county. Weight gain differences by race were minimal. City mothers were 3 times more likely to have certified nurse midwives attend the birth than suburban mothers, and slightly less likely to have cesarean delivery or induction. Plurality (twins and higher order) and male births were nearly identical. Smoking during pregnancy was reported by 12% of City and 9.8% of suburban mothers. City mothers were much more likely to have PTB (both early and late), and were more likely to have very low and low birth weight infants (< 1500 g and < 2500 g, respectively).

Data for City fathers was missing in more than 30% of cases, as compared with 13% in the suburbs (data not shown); the City data was comparable with that nationwide for non-marital births during the same period (Martin et al., 2012). City fathers were more likely to be non-Hispanic black, Hispanic, or other race, with suburban fathers 4 times more likely to be non-Hispanic white. In the City, 80% of fathers had completed high school or more education, as compared with 95% of suburban fathers.

There was a change in traffic over time. The average percentage of change, for those blocks with decreasing traffic, was 10% (data not shown). The average for those increasing was 11%. Overall, the distribution of traffic data values throughout the county was very skewed.

The percentage of stressed census tracts in the City of Milwaukee was 34.1%, whereas it was 11.5% in the suburbs. In the crude model, we observed a 30% increased risk of PTB associated with the Neighborhood Stress Index (low income, no vehicle, greater than ½ mile to a full grocery store. In the final model, we eliminated adjustments for a number of potential confounders (maternal age risk, unmarried status, low educational attainment, and race) due to collinearity with the Index. Controlling for short pregnancy interval, no prenatal visits, smoking, STDs, and weight gain risk, and air pollution and traffic, there remained a 30% increased risk of PTB associated with neighborhood stress.

GIS mapping. Annually, on average during the study period, the birth rates (births by total population per tract) were similarly highest on the near north and south sides and the northwest side of the City (Appendix I; Birth Rate over the study period, annualized).

The maps describing traffic density and birth outcomes provide a visual display of the areas where the highest traffic density occurred in association with prevalence of PTB (Appendix J). Higher prevalence of PTB during the study period occurred on the near north side of the City, which corresponded to higher quintiles of cumulative traffic density, as well as more highways through neighborhoods. Since the effects of air pollution on birth outcomes were more temporal than spatial, we do not present maps of these results.

We examined the relationship between neighborhoods (census tracts) where households were: (a) low income compared to the metropolitan area, (b) greater than 100 households reported no access to a vehicle, and (c) the distance to full grocery stores was greater than ½ mile with those who did not meet these criteria. A high prevalence of PTB was concentrated in the census tracts in the near north and northwest parts of the city (Appendix J).

Multilevel logistic regression. Weighted ozone levels had no effect on the risk of PTB (Table 5). Elevated $PM_{2.5}$ levels were statistically significant in Trimester 1 in the unadjusted model and in Trimester 2 in model 2, which adjusted for maternal age, unmarried status, race, low education, short pregnancy interval, no prenatal visits, smoking, STDs, weight gain risk, and neighborhood stress. However, for traffic, there was a statistically significant increased risk observed in all quintiles in the unadjusted model. The test for trend between increasing traffic load and PTB in the unadjusted model was statistically significant ($\chi^2 = 65.91$, $p < 0.0001$). The observed increased risk of PTB attributed to traffic Quintile 4 remained significant in all multilevel models (Table 5). In the multilevel model that examined O_3 and traffic simultaneously, traffic Quintile 4 was significant in terms of the risk for PTB. O_3 was associated with elevated risk of PTB when exposure occurred during the 1st trimester (Table 5).

Table 5. Multilevel logistic regression, Preterm Birth, Milwaukee County (2005-2010)

	Unadjusted Model[5]		Full Model 1[6]		Final Model 2[7]		Final Model 3[8]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Neighborhood Stress	1.313	1.255 - 1.373	1.025	0.974 - 1.078	1.029	0.978 - 1.083	1.290	1.183 - 1.407
$PM_{2.5}$[1] Trimester 1	1.041	1.020 - 1.064	0.969	0.935 - 1.004	0.974	0.940 - 1.008	0.972	0.939 - 1.007
$PM_{2.5}$ Trimester 2	0.986	0.966 - 1.007	1.040	1.002 - 1.078	1.039	1.003 - 1.077	1.036	1.000 - 1.074
$PM_{2.5}$ All Trimesters	1.008	0.996 - 1.020	0.994	0.968 - 1.020	0.989	0.964 - 1.016	0.988	0.963 - 1.014
Ozone[2] Trimester 1	0.977	0.957 - 0.998	1.022	0.992 - 1.053	1.010	0.981 - 1.040	1.011	0.982 - 1.041
Ozone Trimester 2	0.988	0.969 - 1.009	1.003	0.957 - 1.051	0.992	0.947 - 1.038	0.993	0.949 - 1.039
Ozone All Trimesters	0.992	0.979 - 1.006	1.005	0.971 - 1.040	1.012	0.978 - 1.046	1.012	0.979 - 1.047
Traffic[3,4] Quintile 2	1.129	1.054 - 1.209	1.036	0.964 - 1.113	1.031	0.961 - 1.106	1.037	0.963 - 1.116
Traffic Quintile 3	1.201	1.121 - 1.285	1.030	0.959 - 1.107	1.033	0.963 - 1.108	1.056	0.979 - 1.139
Traffic Quintile 4	1.236	1.240 - 1.418	1.093	1.019 - 1.173	1.102	1.028 - 1.181	1.127	1.046 - 1.214
Traffic Quintile 5	1.261	1.179 - 1.350	1.016	0.946 - 1.091	1.021	0.952 - 1.096	1.060	0.982 - 1.144

[1]Particulate matter ($PM_{2.5}$)
[2]Weighted ozone (W126)
[3]Cumulative average traffic
[4]Test for trend $p < 0.0001$
[5]Unadjusted model (crude Odds Ratios)
[6]*Full model* adjusted for maternal age, unmarried, race, low education, pregnancy interval, no prenatal visits, diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child, smoking, sexually transmitted diseases, weight gain risk, neighborhood stress, PM2.5, ozone, traffic density, birth year.
[7]*Final model 2 adjusted for variables in the full model excluding:* diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child.
[8]*Final model 3 adjusted for variables in full model 2 excluding:* maternal age, unmarried, race, low education.

Discussion

Traffic and air pollution findings. In this study of PTB in Milwaukee County, we applied the grid method developed by Schwartz and colleagues (Kloog et al., 2012; Zeka et al., 2008) to assign traffic exposures to birth outcomes. In the unadjusted analyses, we observed a small (13% to 26%), statistically significant linear increase in the risk of PTB. The effect of traffic density remained significant across the multilevel models only in the fourth quintile of traffic density. Despite very modest results in the regression modeling, the maps illustrate a higher concentration of traffic density and highways through neighborhoods on the City of Milwaukee's near north side where PTB outcomes were concentrated. At the same time, we did not observe an effect of O_3 on risk of PTB and the findings were inconsistent for $PM_{2.5}$.

These findings are similar to those of other researchers who have been studying the effect of traffic- and air pollution related exposures on pre-term birth (Brauer et al., 2008; Gray, Edwards, & Miranda, 2010; Kloog et al., 2012; van den Hooven et al., 2009; Wilhelm & Ritz, 2003; Wilhelm et al., 2012; Zeka et al., 2008). The impact of a small elevation in risk attributable to a common exposure can have a substantial effect on the population as a whole (Freis & Sellers, 2004). Additionally, there is some, albeit inconsistent evidence, that also links traffic density and air pollution to adverse effects such as impaired glucose tolerance (i.e., pre-diabetes) (Fleisch et al., 2014) and fatal cardiac events (Madrigano et al., 2013).

The effect of traffic and air pollution on the risk of PTB in this study is suggestive of a very small effect that increases with greater exposure. However, the effect was obscured by other factors that have larger impacts (e.g., crude odds ratios in this study: lack of any prenatal care [3.3], previous PTB [2.86], hypertension [2.29], non-Hispanic black race [1.84]], unmarried status [1.80], diabetes [1.52], smoking [1.49], neighborhood stress [1.31]). We speculate that other environmental factors, which are associated with traffic and air pollution, such as noise, may account for the weak and inconsistent effect demonstrated in this study. Future studies should examine these factors more precisely. In the meantime, transportation and air pollution policies are needed, nonetheless, to address the impact these factors have *on the entire population* producing many adverse health effects that are costly, debilitating, mostly chronic, and often fatal. Notably, these exposures in Milwaukee (and elsewhere) are disproportionately borne by economically disadvantaged groups and racial/ethnic minorities (Collins, 2011).

We were able to control for cigarette smoking. When smoking was added to the model, our findings remained comparable to those of Wilhelm and Ritz (e.g., 2003; 2012). Reliability of reported tobacco smoking has been questioned (Klebanoff, Levine, Clemens, DerSimonion, & Wilkins, 1998; Maxson, Edwards, Ingram, & Miranda, 2012). Nonetheless, the prevalence of self-reported smoking during pregnancy in this study was comparable to others who used birth record data such as Gray, Edwards, and Miranda (2010) with 11%, and Maxson et al. (2012) with 17.6%, in a prospective cohort study. Similarly, the prevalence of smoking based on survey data in Wisconsin (2009-2010) was 14.9% statewide, 12.5% in Milwaukee County, and 13.0% in the City of Milwaukee (Voskuil, Palmersheim, Glysch, & Jones, 2010). The unadjusted effect of smoking on risk of PTB in this study was 1.49; 95% CI = 1.40-1.58). This is consistent with the 20%-50% increased risk for smoking 10-20 cigarettes per day and 50% to doubling of risk among women who smoke a pack a day or more (IOM, 2007; Cnattingius, 1993).

Methodological issues. Electronic birth records are invaluable data sources for surveillance and research purposes. The 1989 version of the U.S. standard birth record, from which the data in this study were derived, has a number of limitations including the lack of information on maternal and paternal occupations, socioeconomic status (other than education), the full spectrum of STDs, pre-pregnancy height and weight, and the use of WIC and prenatal care coordination services. The 2003 standard birth record addresses these issues with the exception of parental occupations and use of prenatal care coordination (National Center for Health Statistics, 2000).

Missing data. Due to incomplete or invalid maternal residence, 1.4% of the data in Milwaukee County could not be geocoded. In an early study done in southern California, 22% of the dataset was not geocodeable (Wilhelm & Ritz, 2003). In eastern Massachusetts, 4.9% of data were missing maternal residence data (Zeka et al., 2008). Other researchers have reported differences in missing or invalid address by urban (7.7%) and rural (35.8%) locations (Miranda et al., 2013). The small proportion of birth records in this study with missing or invalid addresses would suggest that the degree of bias would be very small or inconsequential.

There were 4.7% of missing values on birth records that were replaced by multiple imputation. We used multiple imputation methods to avoid bias that can be introduced by excluding subjects (Sterne et al., 2009).

Strengths and limitations. Several strengths of this study pertain to the methods used. For the traffic analyses, we replicated methods of Schwartz and colleagues (Kloog et al., 2012; Zeka et al., 2008), which used a discrete grid pattern that accommodated the street network in Milwaukee County. This method was more precise for the geography and available data (traffic and birth records) because it summarized all area traffic within the four closest grid squares to the block centroid of the mothers' addresses. Another strength of this study was the novel use of a weighted metric for O_3. This method placed emphasis on the higher levels of O_3 by trimester and displayed markedly reduced variance.

Traffic and air pollutant data in the third trimester were truncated at 63 days. This procedure controlled for greater exposures that term infants may experience due to longer gestation as compared to that of preterm infants (Hewitt, 1997). In a case-control study, Wilhelm and Ritz (2011) used a similar approach that matched gestational exposure windows.

This study applied an index of neighborhood stress from an existing U.S.D.A. database, which to the best of our knowledge, has not been used before in health outcomes research. Miranda, Messer, and Kroeger (2012) tested 7 indices of built environment features of neighborhoods such as housing damage, crime, and incivilities. They found small statistically significant effects on risk of PTB only in the unadjusted models.

Random misclassification. The major limitation of this study concerns imprecision in measuring exposure and outcome data. There is inherent imprecision in measuring exposures for both traffic and criteria air pollutants. Imprecision occurred in estimating the date of conception, and the related, calculation of trimesters due to having only the month and year of birth in addition to issues in recalling the last menstrual period (LMP) (Mathews & MacDorman, 2013; VandenHooven et al., 2012). These errors are expected to bias the odds ratios towards the null.

According to the EPA (http://www.epa.gov/airquality/greenbk), as of 2013, the greater Milwaukee area was listed as a non-attainment area for $PM_{2.5}$ and for 1-hour O_3. When regulatory standards under the Clean Air Act have been met for three years, there is no requirement to continue monitoring these regulated pollutants. As a result, there is discontinuity in data for surveillance and research purposes. Furthermore, it is based on an erroneous assumption that once attainment has been achieved and sustained for 3 years, the area will maintain this status indefinitely. However, this assumption can neither be supported nor refuted without ongoing surveillance data.

Recommendations and Conclusion

Policy. The Precautionary Principle recommends policies and action based on available evidence (Grandjean, 2004). Based on this study and other evidence, policies must be developed to reduce traffic and air pollution. This can be done by facilitating transport to work, school, shopping, and other destinations through the use of public transit and other multimodal transportation such as walking and bicycling (Ewing & Kruetzer, 2006). Incentivized use of public transit and carpooling would have the effect of diverting traffic away from neighborhoods where people live. Public transportation funds should be used to support the enhancement and cost effectiveness of using public transit. Additionally, equitable maintenance of roads in all neighborhoods is needed to reduce noise, stress, and the need for vehicle repairs. In addition, quality, affordable food needs to be available in all neighborhoods year round. This can be accomplished by developing an array of strategies to supplement grocery stores such as farmers markets, food cooperatives, mobile food venues, and local agriculture.

There is a need for ongoing surveillance of criteria air pollutants. A minimum number of pollutants ought to be measured regardless of attainment status. The optimal number of monitoring sites should be used especially in locations that have demonstrated significant problems (e.g., Los Angeles area). Data that measure environmental and social factors, as well as human health, must be made available for community health assessment and research.

Research. Robust multidisciplinary research is an effective strategy to examine underlying determinants (include both physical and social environments) for their potential impact on birth outcomes and infant mortality. There is an urgent need to better understand the effect of the environment on human health, especially the very youngest. This requires human and technological resources to extract information from available data to inform decision-making. The Institute of Medicine (2007) recommends further research on the role of neighborhood conditions including environmental toxicants to understand the causes of preterm birth.

CHAPTER 4

EFFECTS OF TRAFFIC AND AIR POLLUTION ON RISK OF LOW BIRTH WEIGHT IN MILWAUKEE COUNTY, 2005-2010

Infants born low birth weight (LBW) are 24 times more likely to die in their first year of life as infants who weigh 2500 g or more at birth (Mathews & MacDorman, 2013). Using the World Health Organization (WHO) weight-for-age growth percentiles based on United States (U.S.) norms, an infant who weighs 2500 g is at the 5th percentile for girls and 2nd percentile for boys (http://www.cdc.gov/growthcharts/who_charts.htm#The_Growth_Charts). The risk of death for infants who are very low birth weight (VLBW), less than 1500 g, is more than 100 times that of infants who weigh at least 2500 g at birth. The IMR is a critical leading indicator of any nation's general health and socioeconomic well-being (MacDorman & Mathews, 2008).

According to Barfield et al. (2013), in 2010, the U.S. ranked 32nd amongst 34 member nations of the Organization for Economic Cooperation and Development (OECD). The U.S. 2010 IMR at 6.1 per 1,000 live births was three times worse than that of other industrialized countries that have the lowest IMR, i.e. Iceland, Finland, and Japan. Premature birth is the leading cause (MacDorman & Mathews, 2013). They estimate that if the U.S. IMR by gestational age followed Sweden's pattern of infant mortality (sustained low IMR), almost 8,000 infant lives would be saved each year in the U.S.

. Because LBW is strongly correlated with PTB and also has such a strong impact on the risk of infant mortality (Martin et al., 2012), factors that underlie LBW (and PTB) must be better understood in order to intervene effectively. In 2010, in the U.S., infants of non-Hispanic black mothers were twice as likely to die before their first birthday (11.5/1000) compared to infants of non-Hispanic white or Hispanic mothers (5.2/1000 for both) (Matthews & MacDorman, 2013). The U.S. IMR differs regionally, as well. The South, several eastern states (Delaware, Maryland, Ohio), and the Midwest including Wisconsin (Mathews & MacDorman, 2013) have higher IMRs than elsewhere. The black:white ratio was highest in Connecticut, the District of Columbia, Hawaii, New Jersey, and Wisconsin (Mathews, & MacDorman, 2011) with no obvious commonality. The majority (69.7%) of non-Hispanic blacks in Wisconsin reside in Milwaukee County (Census Bureau, 2010). The prevalence of LBW differs by race/ethnicity and within Milwaukee County (Wisconsin Interactive Statistics on Health [WISH]). Infants born to non-Hispanic white mothers who live in the City experienced a slightly increased risk of LBW, as well.

Together, LBW and preterm birth (PTB, < 37 completed weeks of gestation), are recognized as the second of five leading causes of infant mortality (Martin et al., 2012). Congenital malformations rank first, overall, then LBW/PTB, followed by sudden infant death syndrome (SIDS), newborns affected by maternal conditions of pregnancy, and unintentional injuries (Murphy, Xu, & Kochanek, 2013). However, for infants of non-Hispanic black women, LBW/PTB, is the leading cause of infant mortality. Low birth weight (LBW) is highly correlated with PTB, in part, because it is defined irrespective of gestational age (IOM, 2007; Martin et al., 2012). LBW at term (i.e., ≥ 37 weeks completed gestation), also called intrauterine growth restriction (IUGR; Matthews & MacDorman, 2013), is commonly used as the outcome of interest in epidemiological studies due to its independence from PTB. However, national and international vital statistics emphasize LBW regardless of gestational age (Martin et al., 2012; WHO/UNICEF, 2004).

The prevalence of LBW increased more than 20% between 1990 and 2006, then decreased by 3% between 2006 and 2010 (Martin et al., 2012). The initial upward trend reflects the increase in cesarean deliveries and medically induced labor that was evident in the 1990s and early 21st century. Recent small declines in LBW prevalence reflect attempts to curtail these interventions when not medically indicated (American College of Obstetrics and Gynecology, 2009; Main, et al., 2010). However, during the period 2006-2011, Wisconsin was the only state that reported a statistically significant increase in LBW (Martin et al., 2013), for which there is no existing explanation.

The City of Milwaukee differs from the County and U.S. on a number of social factors including the proportion of adults with less than a high school education (19.2% vs. 14.5% and 14.3%, respectively); the proportion of persons living below the poverty level (28.3% vs. 20.9% and 14.9%), and the median annual household income ($35,823 vs. $43,599 and $53,046) that may influence inequities in LBW prevalence across these geographies (U.S. Census Bureau, 2010). Milwaukee has been ranked as one of the most segregated cities in the U.S. (Lee et al., 2008; Massey & Denton, 1988, 1989) and it has been found that LBW is more likely to occur in racially isolated neighborhoods (Anthopolos, James, Gelfand, & Miranda, 2011). Neighborhoods where minority populations live are more likely to suffer from environmental inequities (Collins, 2011; Miranda, Edwards, Keating, & Paul, 2011; Schempf, Kaufman, Messer, & Mendola, 2011). Research has demonstrated that Milwaukee County experienced a disproportionate concentration of industrial emissions (as reported to the Environmental Protection Agency [EPA]) on the near north side of the City where most non-Hispanic blacks live (Collins, 2011).

The etiology of LBW across populations has many of the same underlying determinants as PTB (IOM, 2007). Obstetric interventions, maternal demographics, and medical conditions are implicated as causes of both LBW and PTB (Martin et al., 2012). As reviewed by the Institute of Medicine (2007), risk factors for LBW include maternal age less than 16 and 35 or older; non-Hispanic black race; low educational attainment and socioeconomic status; unmarried status; low social support; use of tobacco, alcohol, and/or illicit drugs; chronic or catastrophic stress; personal racism; poor nutrition; unintended pregnancy; short inter-pregnancy interval; multiple gestations; congenital anomalies; employment that involves prolonged standing, heavy work, or working shifts or nights; lead poisoning, noise pollution, and crime; and neighborhood conditions including segregation (IOM, 2007).

There also is increasing evidence that traffic and air pollution may affect the risk of low birth weight (predominantly as 'at term'). Most of the studies from the U.S. have been done in southern California (e.g., Ritz & Yu, 1999; Wilhelm & Ritz, 2003; Wilhelm et al., 2012), New York City (e.g., Jung et al., 2014; Tonne, Whyatt, Camann, Perera, & Kinney, 2004), North Carolina (e.g., Anthopolos, James, Gelfand, & Miranda, 2011; Gray, Edwards, & Miranda, 2010; Gray, Gelfand, & Miranda, 2011), and Boston/Eastern Massechusetts (Kloog, Melly, Ridgway, Coull, & Schwartz, 2012; Zeka, Melly, & Schwartz, 2008). When evident, the effect of traffic (and less frequently, air pollution) on risk of LBW in these studies has been small (ORs < 50%), and often, inconsistent, although recent evidence suggests that policies which address traffic generated air pollution can decrease risk of adverse birth outcomes (Jung et al., 2014).

Social and economic costs for LBW are difficult to fully quantify. In 2001, based on a probability sample (~20%) of U.S. hospitals, an estimated 4.6 million infant hospitalizations occurred (Russell et al., 2007). Six percent of these hospitalizations were due to LBW or PTB, yet they incurred 47% of the total hospitalization costs in the U.S. Low birth weight comprised 66% of the diagnoses that required hospitalizations. Mean cost per hospitalization for either LBW or PTB as the diagnosis was $15,100, more than 25 times the cost of uncomplicated deliveries, which averaged $600. Direct costs due to hospitalization of LBW infants are only the 'tip of the iceberg' due to lifetime social, educational, and health problems. Long-term consequences of LBW include developmental problems (IOM, 2007), increased risk of hypertension, ischemic heart disease, stroke, and type 2 diabetes, and increased mortality due to cardiac disease (Class, Ricker, Lichtenstein, & D'Onofrio, 2014). Low IMRs and LBW prevalence elsewhere (Barfield et al., 2013; MacDorman & Mathews, 2009) demonstrate that these are preventable adverse birth outcomes, but the social, economic, and physical environments in U.S. areas are much more heterogeneous than Europe, for example. Thus, Milwaukee County provides an opportunity to examine social and environmental factors that may be determinants of the high prevalence of LBW, overall, and the inequities between non-Hispanic black and non-Hispanic white infants, in particular. Thus, the aim of this study was to assess the effect of traffic and air pollution on the risk of LBW and LBW at term in Milwaukee County controlling for potential risk factors including neighborhood stress.

Methods

Study design, data sources, and protection of human subjects. An historical cohort study was created using electronic data from Wisconsin birth records (2005-2010) linked to exposure data from the Wisconsin Department of Transportation (average daily traffic counts, 2004-2010), Wisconsin Department of Natural Resources (criteria and hazardous air pollutants, 2004-2010), and neighborhood stress indicators from the U.S. Department of Agriculture (2006-2010). Approval for the study was obtained from the Wisconsin Division of Public Health and the Institutional Review Board (IRB) for the Protection of Human Subjects at the University of Wisconsin-Milwaukee. The IRB deemed this study to be minimal risk (Appendix A).

Population. Singletons born between January 1, 2005 and December 31, 2010 were eligible for the study if the mother resided in Milwaukee County (pop. 947,735; U.S. Census Bureau, 2010) at the time of birth and maternal residence was available for geocoding.

Electronic birth records and geocoding of maternal residential addresses. Electronic birth records were obtained through the Wisconsin Division of Public Health, Vital Records Office through a memorandum of understanding. The Wisconsin Office of Vital Statistics provided the dataset of 89,481 birth records; 1,201 (1.4%) had no codeable maternal address; 87,957 birth records remained. After excluding 2,912 (3.3%) records of multiple births, 6 with gestational age missing, and one record geocoded to the census block-group level, there were 85,038 singleton birth records available for analyses. There were 9,744 census blocks with at least 1 birth; more than 3,000 blocks had no births.

Traffic and air pollution exposures. Methods used to calculate cumulative traffic density and interpolate criteria air pollutants are summarized here.

Cumulative traffic density. The spatial dataset of Milwaukee County roads and highways with average daily traffic (ADT) was obtained from the Wisconsin Department of Transportation (WisDOT, 2009). ArcGIS 10.1 (ESRI, Redlands, CA) software was used to spatially join TRADAS points and WISLR roadways data by the research team's geographical information system (GIS) specialist. For roadways with no spatially joined TRADAS points, the 2009 AVG_DLY_TRFC value was used to estimate ADT. If both TRADAS points and WISLR roadway data were lacking (some minor streets), ADT was assigned a value of 150. The methods described in Zeka et al. (2008) and Kloog et al. (2012) were applied to the traffic data using the formula:

$$CADT = \Sigma \text{ (ADT*road segment length)}$$

A grid over the entire county of 200 x 200 meter cells was used to calculate cumulative traffic density (CADT) from ADT in units of vehicle counts-meters, and subsequently transformed to counts-kilometers [Zeka et al., 2008]). Because the state geocoded birth data to 2010 census blocks, the GIS specialist assigned an average of the CADT for the four grid points nearest the 2010 TIGER/line centroid point for each census block. Less than 1% of births (n = 760) did not connect with the grid; these births were assigned a value of '0' for traffic exposure. The traffic data varied between years, thus the values assigned to each pregnancy reflected the estimated date of conception.

Criteria air pollutant data. The criteria and hazardous air pollutants (HAPS) data for 2004-2010 for Milwaukee and surrounding counties were obtained from the Wisconsin Department of Natural Resources (WI DNR). They also provided Environmental Protection Agency (EPA) tables defining parameter codes, sample durations, units, methods, and sampling (Appendix E) (http://www.epa.gov/ttn/airs/airsaqs/manuals/codedescs.htm) and air monitoring site locations (Appendix F). Four criteria air pollutants (NO_X, CO, $PM_{2.5}$, and O_3) are monitored at stations in Southeast WI; however, only $PM_{2.5}$ and O_3 were consistently available across the study years. The weighting method for O_3 was suggested by the DNR (personal communication, J. Meyer, 4/05/2013). The W126 method is an exponential transformation of O_3 values that emphasize the higher values (http://www.epa.gov/ttn/analysis/w126.htm). We performed analyses using the O_3 untransformed and weighted. We report the weighted analyses (Appendix G).

Particulate matter 2.5 ($PM_{2.5}$). For $PM_{2.5}$, the majority of the variation was temporal rather than spatial. Therefore, $PM_{2.5}$ loads were estimated (interpolated) for each census block and each day, then summed to trimesters. $PM_{2.5}$ values were assigned to census blocks by distance-weighted interpolation from the monitoring sites. The square of the distance was used to emphasize the closest station in the average using the formula:

$$PM_{2.5\ block} = (\sum PM25 * 1/d^2)/(\sum 1/d^2)$$

For trimesters at the end of 2010 which are "short", the trimester sum was inflated to the full number of days.

Ozone. Since ozone is a "regional" pollutant, variations in sample values among stations in the same region (e.g., Milwaukee County) at the same time should be attributed to microclimate differences at the stations rather than a pattern within the county (J. Kahl, personal communication, 3/29/2013). As a result, the research team ruled out use of interpolation methods for O_3. Ozone in this area is monitored (Appendix F) during the summer months, except for one site (DNR), which monitors O_3 during the winter. Samples were taken every hour, 8 a.m. to 8 p.m., when O_3 values, measured in parts per million (ppm), are typically elevated, peaking in late afternoon. For missing hourly values, the sum was inflated to represent 12 hours. Daily sums were averaged over all the available sites for each day. Any missing daily average was replaced with the average for the previous day, which only occurred during winter if the DNR site was un-operational. The W126 ozone score is a weighting that emphasizes high-ozone values.

The W126 score takes the hourly ppm ozone value (O_3) at each station and applies the formula:

$$W126 = O_3 * \frac{1}{1+4403*\exp(-126*O3)}$$

Potential confounding variables. Relevant independent variables were used to control for confounding when available on the electronic birth record. In addition, a Neighborhood Stress Index derived from a USDA dataset (http://www.ers.usda.gov/data-products/food-access-research-atlas.aspx) was used to control for census-tract level indicators of socioeconomic stress, namely, low income, no access to a vehicle, and distance greater than ½ mile to a full grocery store.

Trimester calculation. The computation for trimesters one, two, and three for each birth involved summing the available data, called "loads." We computed air pollution "load" values for each infant during the 1st, 2nd, and 3rd trimesters of the pregnancy. Date of birth was only known to the year and month due to a confidentiality requirement of the Vital Records Office. We calculated trimesters assuming all births occurred on the first of the month to ensure to the extent possible that the 1st trimester was calculated with the inclusion of the date of conception (DOC). Gestational age was based on the last menstrual period, when available, or clinical estimate of gestational age expressed in weeks (GAW), otherwise, to be consistent with the predominant method used (Martin et al., 2012).

Date of conception (DOC) was calculated as DOB – 7*GAW. The 1st and 2nd trimesters were based on 13 weeks (91 days) each. The third trimester was defined as 7 weeks (63 days). The total gestation was truncated at 33 weeks, consistent with the goal of understanding air pollution's contribution to LBW independent of gestational age.

We estimated the $PM_{2.5}$ and O_3 for each day and summed them for each trimester for each infant. For the LBW multilevel logistic regression modeling, we used the 1st trimester, 2nd trimester, and total load for $PM_{2.5}$ and the W126-weighted O_3; the trimester for each pollutant was standardized to zero mean and standard deviation of one. The odds ratio (OR) is interpreted as the change in odds of LBW for a 1-standard deviation change in the air quality measure.

Data Analysis

Missing data. Less than 5% (4.7%) of the birth record cases had one or more missing values; most had only one missing value. Overall, missing data were more common in unmarried, black mothers who gave birth to preterm or low birth weight infants. Missing data by race were: 6.2% of non-Hispanic blacks, 4.8% of Hispanics, and 3.1% of non-Hispanic whites. Data were missing for 7.4% of PTB. Data on fathers was not provided on the electronic birth records unless the mother and father were married, which resulted in substantial missing data.

Descriptive and bivariate analyses. We used SAS version 9.4 to calculate percentages, medians, means, and χ^2 to describe the population and compare characteristics. Mantel-Haenszel Odds Ratios and 95% Confidence Intervals (CIs) were computed. Maps were created using ArcGIS 10.1 (ESRI, Redlands, CA) software where statistical findings suggested spatial patterns.

Multi-level risk factor analyses. Multiple imputation was performed using SAS Proc MI. Each imputation uses a complete set of the data, with the missing values filled in by regression of the variables with missing values against those without missing values, and adding a random component (error term) to capture the variability in the data. The random component makes each imputation slightly different. The research analysis was performed on each imputation and the results statistically averaged over the imputations (SAS Proc MIANALYZE). Twenty imputations were used (Sternes et al., 2009).

A Neighborhood Stress Index was measured at the census tract level, while other variables from the birth record were measured at the individual level. Traffic, O_3, and $PM_{2.5}$ were linked to each mother-fetal dyad based on the centroid of the census block. Multilevel logistic regression was performed from the multiply-imputed data using SAS Proc GLIMMIX. We employed a test for trend for traffic density.

Results

Descriptive statistics. Mothers who resided the City of Milwaukee were proportionately younger, less likely to have graduated from high school, and much more likely to be unmarried and non-Hispanic black or Hispanic compared to suburban mothers (data not shown). Low birth weight was higher in Milwaukee County and the City (nearly equal) for all infants. Smoking during pregnancy was slightly more common among mothers living in the City. Mothers in the City were less likely to begin prenatal care in the 1st or 2nd trimester or to have had adequate care based on the Kotelchuck

Index compared to suburban mothers. Sexually transmitted diseases (STDs) were recorded on the birth record almost twice as often for city mothers as suburban mothers, however, weight gain by race and prevalence of diabetes and hypertension were nearly identical. City mothers were much more likely to be attended by a certified nurse midwife and slightly less likely to have cesarean delivery or induction. The calculated male:female sex ratio was considerably lower for infants of City mothers (1.034) compared to suburban mothers (1.058). Although the proportion of multiple births were nearly identical (data not shown), City mothers were more likely to have LBW infants than county or suburban mothers (Chapter 1, Table 3). Overall, infants born in the Milwaukee suburbs fared better than infants in Wisconsin and the U.S. Hispanic infants were less likely to be LBW than infants of non-Hispanic white mothers. In contrast, the prevalence of LBW was greater among infants of non-Hispanic black mothers who lived in the City of Milwaukee compare to those who lived in the suburbs. Whereas the prevalence of LBW for infants of non-Hispanic white mothers was similar to the state as a whole and to the nation, it was worse for infants of non-Hispanic black mothers.

The prevalence of LBW for infants of non-Hispanic black mothers was twice that of non-Hispanic white mothers. Infants of Hispanic mothers fared better than other groups of mothers regardless of where they lived in Milwaukee County.

The distribution of traffic data values throughout the county was very skewed, as expected (Appendix D). Traffic changed over time. For blocks with decreasing traffic, the average percentage decrement was 10%, while the average for those increasing was 11%. The map of traffic density and LBW shows that they were concentrated on the near north side of the City (Appendix K). There were more highways through neighborhoods on the near north side, as well.

Based on the Neighborhood Stress Index (a composite measure of low income, no vehicle, and greater than ½ mile to a full grocery store), 34% of the census tracts in the City were stressed. In the suburbs, neighborhood stress was much less common (11.5%). The map of neighborhood stress and LBW illustrates they were most strongly correlated in neighborhoods on the near north side, and to a lesser extent, on the northwest side (Appendix K).

Missing data. Questions about alcohol and demographic characteristics of fathers had substantial missing data for both city and suburban parents. Missing data on City fathers is comparable to national data for non-marital births during the same period (Martin et al., 2012). City fathers were more likely to be non-Hispanic black, Hispanic, or other race than suburban fathers and to have had less education.

Multilevel logistic regression findings for LBW. Weighted ozone levels had no effect on the risk of LBW in the unadjusted model, or in the models that adjusted for $PM_{2.5}$, traffic density, and independent risk factors (Table 6). The crude ORs associated with $PM_{2.5}$ exposure was weakly elevated (3-4%) in the 2nd trimester and all trimesters. Traffic density was associated with a 14% - 35% increased risk of LBW, which showed a dose response (χ^2 = 64.37, p < 0.0001). However, when traffic density was adjusted for other factors (Models 1-3), no statistically significant effect was observed. Neighborhood stress, in contrast, demonstrated a small, but significant effect on LBW in the crude and final models.

Multilevel logistic regression findings for LBW at Full Term. There also was no evident effect for the weighted ozone models on risk of LBW at full term in any of the models (Table 7). Exposure to $PM_{2.5}$ in the unadjusted analysis, and in adjusted Models 2 and 3, showed a slight increased risk (4%) for each model) for LBW at term. A dose response was evident only in the unadjusted model (χ^2 = 33.36, p < 0.0001). Neighborhood stress was associated with approximately a 50% increased risk for LBW at full term in the unadjusted and final models, which were statistically significant.

Table 6. Multilevel logistic regression, Low Birth Weight, Milwaukee County (2005-2010)

	Unadjusted Model		**Full Model 1**		**Model 2**		**Final Model 3**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Neighborhood Stress	1.465	1.388 - 1.546	1.049	0.988 - 1.113	1.041	0.983 - 1.103	1.443	1.294 - 1.609
$PM_{2.5}$[3] Trimester 1	1.021	0.995 - 1.047	0.991	0.948 - 1.035	0.996	0.954 - 1.038	0.994	0.953 - 1.036
$PM_{2.5}$ Trimester 2	1.040	1.013 - 1.067	0.999	0.955 - 1.050	0.998	0.954 - 1.043	0.995	0.952 - 1.040
$PM_{2.5}$ All Trimesters	1.027	1.012 - 1.042	0.992	0.960 - 1.026	0.990	0.958 - 1.022	0.989	0.958 - 1.021
Ozone[4] Trimester 1	0.996	0.971 - 1.022	1.005	0.969 - 1.043	0.993	0.958 - 1.029	0.993	0.958 - 1.029
Ozone Trimester 2	0.969	0.945 - 0.993	0.996	0.941 - 1.055	0.988	0.934 - 1.045	0.989	0.935 - 1.045
Ozone All Trimesters	0.980	0.964 - 0.996	1.021	0.979 - 1.064	1.024	0.983 - 1.066	1.025	0.984 - 1.068
Traffic[5]4Quintile 2	1.143	1.049 - 1.245	1.028	0.940 - 1.123	1.019	0.935 - 1.112	1.014	0.925 - 1.111
Traffic Quintile 3	1.256	1.155 - 1.366	1.050	0.962 - 1.147	1.051	0.964 - 1.145	1.059	0.965 - 1.163
Traffic Quintile 4	1.351	1.244 - 1.468	1.061	0.972 - 1.158	1.078	0.990 - 1.173	1.090	0.994 - 1.156
Traffic Quintile 5	1.345	1.238 - 1.461	1.036	0.949 - 1.131	1.037	0.952 - 1.129	1.074	0.978 - 1.180

[1]Particulate matter ($PM_{2.5}$)
[2]Weighted ozone (W126)
[3]Cumulative average traffic
[4]Test for trend $p < 0.0001$
[5]Unadjusted model (crude Odds Ratios)
[6]*Full model* adjusted for maternal age, unmarried, race, low education, pregnancy interval, no prenatal visits, diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child, smoking, sexually transmitted diseases, weight gain risk, neighborhood stress, PM2.5, ozone, traffic density, birth year.
[7]*Final model 2 adjusted for variables in the full model excluding:* diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child.
[8]*Final model 3 adjusted for variables in full model 2 excluding:* maternal age, unmarried, race, low education.

Table 7. Multilevel logistic regression results, Low Birth Weight at Term, 2005-2010

	Unadjusted Model[5]		**Full Model 1[6]**		**Final Model 2[7]**		**Final Model 3[8]**	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Neighborhood Stress	1.569	1.441 - 1.708	1.093	0.998 - 1.197	1.085	0.991 - 1.188	1.510	1.324 - 1.722
PM 2.5[1] Trimester 1	1.026	0.985 - 1.068	0.993	0.929 - 1.062	0.996	0.932 - 1.064	0.996	0.932 - 1.064
PM 2.5 Trimester 2	1.054	1.012 - 1.098	0.981	0.914 - 1.053	0.979	0.912 - 1.050	0.978	0.912 - 1.049
PM 2.5 All Trimesters	1.039	1.015 - 1.063	0.993	0.943 - 1.045	0.995	0.946 - 1.047	0.991	0.941 - 1.043
Ozone[2] Trimester 1	1.019	0.978 - 1.062	0.994	0.938 - 1.054	0.987	0.931 - 1.046	0.989	0.933 - 1.048
Ozone Trimester 2	0.966	0.928 - 1.005	1.039	0.950 - 1.136	1.044	0.955 - 1.141	1.043	0.955 - 1.140
Ozone All Trimesters	0.992	0.966 - 1.018	0.982	0.920 - 1.048	0.978	0.916 - 1.043	0.980	0.919 - 1.046
Traffic[3,4] Quintile 2	1.273	1.109 - 1.461	1.133	0.985 - 1.033	1.125	0.979 - 1.293	1.165	1.009 - 1.346
Traffic Quintile 3	1.382	1.207 - 1.583	1.137	0.990 - 1.307	1.134	0.988 - 1.302	1.197	1.035 - 1.384
Traffic Quintile 4	1.462	1.278 - 1.673	1.139	0.992 - 1.308	1.138	0.992 - 1.306	1.231	1.065 - 1.423
Traffic Quintile 5	1.457	1.274 - 1.667	1.096	0.955 - 1.259	1.092	0.952 - 1.253	1.211	1.046 - 1.401

[1]Particulate matter ($PM_{2.5}$)
[2]Weighted ozone (W126)
[3]Cumulative average traffic
[4]Test for trend $p < 0.0001$
[5]Unadjusted model (crude Odds Ratios)
[6]*Full model* adjusted for maternal age, unmarried, race, low education, pregnancy interval, no prenatal visits, diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child, smoking, sexually transmitted diseases, weight gain risk, neighborhood stress, PM2.5, ozone, traffic density, birth year.
[7]*Final model 2 adjusted for variables in the full model excluding:* diabetes, hypertension, labor seizures, congenital anomalies, febrile, amniocentesis, labor induction, premature rupture of membranes (PROM), incompetent cervix, abruptio placenta, placenta previa, previous preterm birth, previous death of child.
[8]*Final model 3 adjusted for variables in full model 2 excluding:* maternal age, unmarried, race, low education.

Discussion

Traffic and air pollution findings. In this study of LBW in Milwaukee County, we applied the grid method developed by Schwartz and colleagues (Kloog et al., 2012; Zeka et al., 2008) to assign traffic exposures to birth outcomes. In the unadjusted analyses, we observed a small effect on LBW and LBW at full term at all levels of traffic density. These effects were not evident in the multilevel models except for the final model for LBW at full term. Despite these modest results in the regression modeling, the maps illustrate a higher concentration of traffic density and highways through neighborhoods on the City of Milwaukee's near north side where LBW outcomes also were concentrated. Similarly, $PM_{2.5}$ was associated with a small increased risk of LBW and LBW at full term, but only in the unadjusted model. The final model (Model 3), which examined traffic density in relation to neighborhood stress and other factors (but excluding maternal age, unmarried status, race, and educational attainment), showed a small (17% - 23%) stable increased risk associated with LBW in full term infants.

These findings are similar to those of other researchers who have been studying the effect of traffic- and air pollution-related exposures on low birth weight (Brauer et al. [regarding SGA], 2008; Gray, Edwards, & Miranda, 2010; Miranda, Edwards, Chang, & Auten, 2013; Kloog et al., 2012; van den Hooven et al., 2009; Wilhelm & Ritz, 2003 (LBW, LBW at term); Wilhelm et al., 2012 (LBW, LBW at term); Zeka et al., 2008). Additionally, there is some, albeit inconsistent evidence, that also links traffic density and air pollution to adverse effects such as impaired glucose tolerance (i.e., pre-diabetes) (Fleisch et al., 2014) and fatal cardiac events (Madrigano et al., 2013).

A small elevation in risk attributable to a common exposure can have a substantial effect at the population level (Freis & Sellers, 2004). Although our findings are neither strong nor consistent, the small effect demonstrated with these imprecisely measured environmental exposures may be linked to substantial effects on a large proportion of the population. More precisely measured factors that reflect larger individual impacts (e.g., crude odds ratios in this study: lack of any prenatal care [3.79], previous PTB [3.25], hypertension [2.98], non-Hispanic black race [2.44]], unmarried status [2.28], smoking [2.16], and neighborhood stress [1.47]) can readily obscure the effect of $PM_{2.5}$ and traffic density. Low birth weight and LBW at full term are among the problems associated with traffic-related issues.

One potential confounder controlled for in this study, but not in California, is the smoking history. Our multilevel findings are comparable to Wilhelm and Ritz (e.g., 2003; 2012). Although we were able to control for environmental stress and cigarette smoking, as well as other pregnancy-related risk factors, we cannot rule out the effect of additional factors not included in this study, such as noise, exposures to chemical pollutants (e.g., from current industrial operations and brownfields), inadequate public transportation, unemployment, and racism. Future research should take these factors into account.

In describing the mother-infant dyads, a noticeable difference in sex ratios was discovered between infants of City mothers (1.034) and suburban mothers (1.058), which raises questions about potential differential exposure to endocrine disrupting agents (James, 1998; James, 2001; Weisskopf, Anderson, & Hanrahan, 2003). Air pollution and polychlorinated hydrocarbons are suspected of altering endocrine signaling (James, 1998; Weisskopf et al., 2003) and is an area for further research. This serendipitous finding merits further attention regarding sex ratios in birth outcome studies, and potentially, research to determine if biomarkers can be used to detect endocrine disrupting targets associated with traffic, air pollution, and other sources.

Strengths and limitations. Several strengths of this study pertain to the methods used. For the traffic analyses, we replicated methods of Schwartz and colleagues (Kloog et al., 2012; Zeka et al., 2008), which used a discrete grid pattern that accommodated the street network in Milwaukee County. This method was more precise for the geography and available data (traffic and birth records) because it summarized all area traffic within the four closest grid squares to the block centroid of the mothers' addresses. Another strength of this study was the novel use of a weighted metric for O_3. This method placed emphasis on the higher levels of O_3 by trimester and displayed markedly reduced variance compared to unweighted ozone. The lack of association with LBW is most likely attributable to the sparse ozone data (approximately only ½ the year and its timing with respect to conception and the 33 weeks of each gestation to which data were linked. This is a reality of a northern climate.

Traffic and air pollutant data in the third trimester were truncated at 63 days. This procedure controlled for greater exposures that term infants may experience due to longer gestation as compared to that of preterm infants (Hewitt, 1997). In a case-control study, Wilhelm and Ritz (2011) used a similar approach that matched gestational exposure windows.

Another strength of this study is that we were able to control for neighborhood stress factors. We applied an index of neighborhood stress from an existing U.S.D.A. database, which to the best of our knowledge, has not been used before in health outcomes research. In our study, the Neighborhood Stress index controlling for other factors had a small stable effect (44% and 51%) on risk of LBW and LBW at full term, respectively. When used as an adjustment factor, traffic density had a small but statistically significant effect on LBW at full term. There is widespread recognition of the role that neighborhood factors may have on birth outcomes (IOM, 2007), but they are infrequently examined. An exception is the study by Miranda et al. (2012). They tested 7 indices of the built environment at the neighborhood level and found small, statistically significant effects on risk of PTB only in the unadjusted models.

Random misclassification. The major limitation of this study concerns imprecision in measuring exposure and outcome data. There is inherent imprecision in measuring exposures for both traffic and criteria air pollutants. Imprecision occurred in estimating the date of conception, and the related, calculation of trimesters, due to having only the month and year of birth in addition to issues in recalling LMP (Mathews & MacDorman, 2013; VandenHooven, et al., 2012). These errors are expected to bias the odds ratios towards the null.

According to the EPA (http://www.epa.gov/airquality/greenbk), as of 2013, the greater Milwaukee area was listed as a non-attainment area for $PM_{2.5}$ and for 1-hour O_3. When regulatory standards under the Clean Air Act have been met for three years, there is no requirement to continue monitoring these regulated pollutants. As a result, there is discontinuity in data for surveillance and research purposes. Furthermore, it is based on an erroneous assumption that once attainment has been achieved it will be sustained indefinitely. The current exemption for continued surveillance obviates the ability to determine if problems with non-attainment reemerge. In turn, the lack of air pollution surveillance data thwarts environmental health research.

Recommendations and Conclusion

Policy. The Precautionary Principle recommends policies and action based on available evidence (Grandjean, 2004). Findings from this study and other evidence of the broad array of adverse impacts, warrant policies to reduce traffic and air pollution. This can be done by facilitating transport to work, school, shopping, and other destinations through the use of public transit and other multimodal transportation such as walking and bicycling (Ewing, 2006). Incentivized use of public transit and carpooling would have the effect of diverting traffic away from neighborhoods where people live. Public transportation funds should be used to support the enhancement and cost effectiveness of using public transit. Additionally, equitable maintenance of roads in all neighborhoods is needed to reduce noise, stress, and the need for vehicle repairs. In addition, quality, affordable food needs to be available in all neighborhoods year round.

This can be accomplished by developing an array of strategies to supplement grocery stores such as farmers markets, food cooperatives, mobile food venues, and local agriculture.

There is a need for ongoing surveillance of criteria air pollutants. A minimum number of pollutants ought to be measured regardless of attainment status. The optimal number of monitoring sites should be used especially in locations that have demonstrated significant problems (e.g., Los Angeles area). Data that measure environmental and social factors, as well as human health, must be made available for community health assessment and research.

Research. Robust multidisciplinary research is an effective strategy to examine underlying determinants (include both physical and social environments) for their potential impact on birth outcomes and infant mortality. There is an urgent need to better understand the effect of the environment on human health, especially the very youngest. This requires human and technological resources to extract information from available data to inform decision-making. The Institute of Medicine (2007) recommends further research on the role of neighborhood conditions including environmental toxicants to understand the causes of adverse birth outcomes.

CHAPTER 5
CONCLUSIONS

Historic wisdom and contemporary evidence show that it is insufficient to attribute health problems of epidemic proportions such as infant mortality, preterm birth, and low birth weight solely to individual behavior independent of the environment and public policies. To address environmentally-induced problems requires shifting attention to the whole community.

Close examination of gene variants between Caucasians and African Americans has led other researchers to conclude that unmeasured genetic or environmental factors also affect these birth outcomes (Menon et al., 2011). At the same time, exposure to such toxicants is disproportionately borne by persons of color and those who are economically disadvantaged (Ahern, Pickett, Selvin, & Abrams, 2003; Dole, D. et al., 2003; Dole, N. et al., 2004; Llop et al., 2011; Schempf, Kaufman, Messer, & Mendola, 2011).

Consistent with the recommendations advanced by the *Institute of Medicine (IOM), Committee on Understanding Premature Birth and Assuring Health Outcomes,* this study engaged multidisciplinary collaboration and utilized all available data for an epidemiologic investigation to inform public policy (IOM, 2007).

Multidisciplinary approach

The study team consisted of a public health nurse researcher, environmental and occupational epidemiologist, statistician and geographer, geographic information systems (GIS) specialists, meteorologist, toxicologists, urban planner, and civil engineer.

Research, with improved data and epidemiologic investigations

For at least a decade, the World Health Organization (WHO, 2005) has expressed concern about the effect of increasing vehicular traffic on health. This global perspective on public health is enacted at the local level.

Traffic conditions. In this study, the traffic data used to assess transportation and related issues of traffic density were the average daily traffic (ADT) maintained by the Wisconsin Department of Transportation (WISDOT). These counts were comparable to those used by Wilhelm and Ritz (2003). Although the counts were updated annually, they were not necessarily all measured during that year. This data set provided count estimates for many of the side streets as well. Our GIS specialist meticulously interpolated traffic counts on side streets that were missing data; only 1.3% had to be assigned a random value. Data for the freeways and ramps were summarized in longer segments, which reflected traffic patterns. If resources were available, more detailed analyses of these exposures would be useful to further refine the traffic assessment in relation to health impacts.

This study provides additional support for the urgent need to redirect available resources to address the environmental determinants of health. Even after controlling for the commonly reported factors such as race, other diseases, and health care access, we found evidence that higher traffic burden in neighborhoods was associated with slightly increased risk in birth outcomes. Moreover, the finding of a dose-response between traffic and birth outcomes, albeit without adjustment for other factors, is intriguing. The individual effects of the factors may be distinguished further with sensitivity analyses in future studies.

Recent evidence from New York City demonstrated that policy-driven changes in transportation can affect better birth outcomes (Jung et al., 2014). This exemplifies the effectiveness of a population-level approach to policy and practice. Frumkin (2010) described the effect of traffic density noting that increased ridership of transit has multiple positive health and social benefits, and that several transportation demand management (TDM) strategies are worth consideration. TDM strategies, otherwise known as traffic calming measures, are designed to reduce traffic volume and speed.

Frumkin (2005) suggested the possibility of comparing risks introduced by available travel modes. He advocates for a holistic approach to understanding the natural, built, social, and cultural and spiritual environments, an approach that resonates with the concept of environmental justice.

Air Pollution. Due to sparse monitoring, data were not available for all of the criteria air pollutants. In fact, in a recent study Milwaukee County (and other counties in Wisconsin) rated in the 20% worst counties in the nation, having insufficient air monitoring surveillance for the population (Miranda, Edwards, Keating, & Paul, 2011). The impact of air pollution is far broader than many realize as these pollutants settle directly onto land and water, as well as pollute water through runoff from land surfaces.

Measures of criteria air pollutants are crude indicators of biological uptake of various airborne toxicants. Biomonitoring is feasible only for exposure research puposes, to correlate biological uptake with interpolated air pollution data. However, biomonitoring is not feasible for many epidemiological studies at this time. Therefore, the ability to detect an effect on health is reduced. Methods need to be developed in which sampling is accomplished closer to the breathing zone of individuals in the community. This holds true for for other pollutants such as noise. More research is needed to optimize data collection to study the impact of air pollutants on birth outcomes.

We speculate that other environmental factors, which are associated with traffic and air pollution, such as noise, may account for the weak and inconsistent effect demonstrated in this study. Future studies should examine these factors more precisely. In the meantime, transportation and air pollution policies are needed, nonetheless, to address the impact these factors have *on the entire population* producing many adverse health effects that are costly, debilitating, mostly chronic, and often fatal. Notably, these exposures in Milwaukee (and elsewhere) are disproportionately borne by economically disadvantaged groups and racial/ethnic minorities (Collins, 2011).

Neighborhood Stress. The biologic bases for the association of stress to PTB and LBW were presented in Chapter 1 (Bolten et al., 2011; Hadley, 2000; Pearce et al., 2010; Sandman et al., 1994; Figure 5). In summary, stressors stimulate the HPA axis and excretion of hormones that then interfere with circulation to the developing fetus. The chemicals in air pollutants additionally may mimic the endocrine system which can affect birth outcomes in future generations.

An additional strength of this study were the analyses related to effects of stress on birth outcomes. To do this, we utilized the Neighborhood Stress Index which is based on low income, access to transportation and to full grocery stores (http://www.ers.usda.gov/data-products/food-access-research-atlas.aspx). Although others have begun to study the effects of neighborhood features and conditions (Miranda, 2011), to our knowledge the Neighborhood Stress Index has not been tested previously in relation to birth outcomes. Notably, as measured by this index, approximately three times more City neighborhoods were stressed neighborhoods compared to Milwaukee County suburbs. Overall, 8.8% of all housing units in the United States do not have a vehicle, and 4.2% of all housing units are at least 0.5 mile from a store and without a vehicle. Here, the City prevalence is about quadruple the national average (USDA, 2012). These indicators correlate strongly with the areas of the City where the residents are predominantly non-Hispanic black.

As the USDA (2012) data show, areas of food deserts (i.e., lack of accessible food) are not randomly distributed. A survey of local food markets in the affected neighborhoods would verify the need for affordable, quality food in all areas of the community.

Birth record data. This study used Wisconsin Vital Records based on the 1989 standard birth certificate (Freedman, Gay, Brockert, Potrzebowski, & Rothwell, 1988). We only had information on the mother's residence at the time of birth, and linked exposure data throughout the pregnancy to the census block. We assume that change in residence had minimal effect on assignment of traffic and air pollution exposures as research shows that people tend to relocate in close proximity (Chen, Bell, Caton, Druschel, & Lin, 2010). Further research should test this assumption on a local level. WI Vital Records excluded records where mailing addresses were listed as PO Boxes, which resulted in loss of 1.4% of the births during the time period. Presumably these were high risk mothers, but the very small proportion is likely to have introduced negligible selection bias.

No information was included in the data set regarding payment source, parental occupations, and unmarried fathers. To partially address the lack of information on income, we selected a neighborhood-level variable that included data on the census tract-level income compared to the rest of the metropolitan area. The 1989 birth record form lacked items on mothers' pre-pregnancy weight and height (separately, as height is an independent risk factor for PTB) to calculate BMI, to evaluate ideal weight gain, and to examine short stature as an independent risk factor. These important data may become available for future Wisconsin studies, since the Wisconsin Division of Public Health has adopted the revised 2003 Standard Birth Certificate as of 2011.

We analyzed all available individual-level variables that have been implicated in relation to preterm birth and low birth weight. The construction of a correlation matrix for the socioeconomic variables informed the development of models while avoiding hypercollinearity, and to more clearly recognize effects. Relevant independent variables were used to control for confounding when available on the electronic birth record.

Public policy

Traffic conditions. Public concern about the social and economic effects of the transportation system is not new. The issues have been raised by others for more than half a century (Jacobs, 1961). However, now that epidemiological studies have been conducted, we are beginning to understand the effects on human health and disease, as well.

Although transportation represents 28% of U.S. greenhouse gas (second only to the industrial sector), highway vehicles represent 82% of U.S. transportation greenhouse gas (Burbank & Brinckerhoff, 2009). The U.S. consumption of oil for individually occupied vehicles is staggering compared to other countries (Falconer & Newman, 2008). Heavy traffic is noisy and stressful (Litman & Burwell, 2006). The relative lack of access to transportation that is convenient and affordable for all is also stress-producing.

Further research to distinguish local from commuter traffic, examine transit ridership and schedules would assist with program planning and policy development. However based on these preliminary findings, we recommend using TDM strategies to reduce traffic in the places where people live. A comprehensive policy would address both cleaner, more energy-efficient vehicles that reduce per-mile emissions, and mobility management to reduce total vehicle travel. (Burbank & Brinckerhoff, 2009; Frank, Greenwald, Kavage, & Devlin, 2011). An emphasis on sustainability requires a major shift in priorities, including travel (Litman & Burwell, 2006). These strategies reduce congestion, as well as improve traffic safety, consumer savings and mobility for non-drivers.

Air pollution. Based on the findings of this study and others', we question the validity of the policy that permits an exemption from criteria air pollutant monitoring after three years of attainment with respect to the Clean Air Act. Surveillance of criteria air pollutants should never be waived. Future research should incorporate available biomonitoring methods to verify air pollutants as close to the breathing zone as possible.

Transportation and air pollution control policies are needed, nonetheless, to address the impact these factors have *on the entire population* producing many adverse health effects that are costly, debilitating, mostly chronic, and often prematurely fatal.

Neighborhood stress. There were three components of stress within the Index we applied, which are amalgamated, thus it is impossible to disentangle the issues of lack of transportation, income, and food using the USDA data. Instead sensitivity analyses can only be done with the original sources of data on poverty and transportation from the U.S. Census Bureau and the food desert data from the USDA. These factors, of course, are interrelated. Transportation is essential to access jobs and food; income is needed to have personal vehicles and to purchase food; jobs and grocery stores are sited in locations that are inaccessible to persons with low income. Food accessibility is necessary (though not sufficient) to ensure good nutrition and health.

The quality of food that is available has been questioned. Specifically, nutritional content in our available food sources is receiving more attention (Guidotti & Gitterman, 2007) and merits transparency about the nutritional and toxicant content of foods transported long distances from industrial farming operations, compared to locally grown food (Smith et al., 2005).

Birth record data. Electronic birth record data should be used for public health surveillance of PTB, LBW, and infant mortality (when linked to death records) on an ongoing basis to examine trends and to understand the underlying determinants of health. This is needed to make evidence-based public health practice and policy decisions that affect the health of the whole population. These records should be readily available without cost to local and state health officials and to academic researchers. Epidemiologic investigation and multidisciplinary research should be encouraged as recommended by the IOM (2007).

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UNIVERSITY of WISCONSIN
UWMILWAUKEE
Department of University Safety & Assurances

Jessica Rice
IRB Administrator
Institutional Review Board
Engelmann 270
P. O. Box 413
Milwaukee, WI 53201-0413
(414) 229-3182 *phone*
(414) 229-6729 *fax*

http://www.irb.uwm.edu
ricej@uwm.edu

New Study - Notice of IRB Expedited Approval

Date: February 1, 2013

To: Jeanne Hewitt, PhD
Dept: Nursing

Cc: Deborah James Pasha

IRB#: 13.220
Title: Effects of Traffic and Air Pollution on Risk of Preterm Birth and Low Birth Weight Outcomes in Milwaukee County, 2005-2010

After review of your research protocol by the University of Wisconsin – Milwaukee Institutional Review Board, your protocol has been approved as minimal risk Expedited under Category 5 as governed by 45 CFR 46.110.

This protocol has been approved on **February 1, 2013** for one year. IRB approval will expire on **January 31, 2014**. If you plan to continue any research related activities (e.g., enrollment of subjects, study interventions, data analysis, etc.) past the date of IRB expiration, a continuation for IRB approval must be filed by the submission deadline. If the study is closed or completed before the IRB expiration date, please notify the IRB by completing and submitting the Continuing Review form found on the IRB website.

Unless specifically where the change is necessary to eliminate apparent immediate hazards to the subjects, any proposed changes to the protocol must be reviewed by the IRB before implementation. It is the principal investigator's responsibility to adhere to the policies and guidelines set forth by the UWM IRB and maintain proper documentation of its records and promptly report to the IRB any adverse events which require reporting.

It is the principal investigator's responsibility to adhere to UWM and UW System Policies, and any applicable state and federal laws governing activities the principal investigator may seek to employ (e.g., FERPA, Radiation Safety, UWM Data Security, UW System policy on Prizes, Awards and Gifts, state gambling laws, etc.) which are independent of IRB review/approval.

Contact the IRB office if you have any further questions. Thank you for your cooperation and best wishes for a successful project

Respectfully,

Jessica P. Rice
IRB Administrator

UNIVERSITY of WISCONSIN
UWMILWAUKEE
Department of University Safety & Assurances

Melissa Spadanuda
IRB Manager
Institutional Review Board
Engelmann 270
P. O. Box 413
Milwaukee, WI 53201-0413
(414) 229-3173 *phone*
(414) 229-6729 *fax*

http://www.irb.uwm.edu
spadanud@uwm.edu

Continuing Review - Notice of IRB Expedited Approval

Date: January 30, 2014

To: Jeanne Hewitt, PhD
Dept: College of Nursing

Cc: Deborah Pasha James

IRB#: 13.220
Title: Effects of Traffic and Air Pollution on Risk of Preterm Birth and Low Birth Weight Outcomes in Milwaukee County, 2005-2010

After review of your research protocol by the University of Wisconsin – Milwaukee Institutional Review Board, your protocol has received continuing approval as minimal risk Expedited under category 5 as governed by 45 CFR 46.110.

This protocol has been approved on **January 30, 2014** for one year. IRB approval will expire on **January 29, 2015**. If you plan to continue any research related activities (e.g., enrollment of subjects, study interventions, data analysis, etc.) past the date of IRB expiration, a Continuation for IRB Approval must be filed by the submission deadline. If the study is closed or completed before the IRB expiration date, please notify the IRB by completing and submitting the Continuing Review form found in IRBManager.

Any proposed changes to the protocol must be reviewed by the IRB before implementation, unless the change is specifically necessary to eliminate apparent immediate hazards to the subjects. The principal investigator is responsible for adhering to the policies and guidelines set forth by the UWM IRB, maintaining proper documentation of study records, and promptly reporting to the IRB any adverse events which require reporting. The Principal Investigator is also responsible for ensuring that all study staff receive appropriate training in the ethical guidelines of conducting human subjects research.

As Principal Investigator, it is also your responsibility to adhere to UWM and UW System Policies, and any applicable state and federal laws governing activities which are independent of IRB review/approval (e.g., FERPA, Radiation Safety, UWM Data Security, UW System policy on Prizes, Awards and Gifts, state gambling laws, etc.). When conducting research at institutions outside of UWM, be sure to obtain permission and/or approval as required by their policies.

Contact the IRB office if you have any further questions. Thank you for your cooperation and best wishes for a successful project

Respectfully,

Melissa C Spadanuda

Melissa C. Spadanuda
IRB Manager

Information Collected on the Birth Certificate Worksheet

- This form is only to be used to file births that occur in or en route to hospitals or clinics with authorized birth certificate designees. If the child and placenta are delivered elsewhere (*e.g.*, at home), the parent is responsible for filing the birth. If this is the case, please direct the parent to contact the State Vital Records Office (608/266-1939).
- The information on this worksheet (except signatures) must be typed, if possible. If a typewriter is not available, the information (including informant information) must be printed neatly in **BLACK INK**. Illegible worksheets will be returned for replacement.
- Item numbers reflect data entry order and are not always in consecutive order on this form.
- **INFORMANT/PARENT:** Read DPH 5103 Facts About Your Child's Birth Certificate before completing this form. Complete all shaded areas.

PENALTIES: Any person who willfully and knowingly supplies any false information to be used in the preparation of a birth certificate is guilty of a Class I felony [a fine of not more than $10,000 or imprisonment of not more than 3 years and 6 months, or both, per Chapter 69.24(1), Wisconsin Statutes]. Any person who willfully and knowingly obtains a birth certificate for fraudulent purposes is guilty of a Class I felony [a fine of not more than $10,000 or imprisonment of not more than 3 years and 6 months, or both, per s. 69.24(1), Wis. Stats.].

PART I RECORD FILER LEGAL INFORMATION
(RECORD FILER: Type or print child's name and re-verify with name given above by informant.)

CHILD'S NAME Read the information in DPH 5103, "Facts About Your Child's Birth Certificate," item D, "Naming Your Child" before completing this section. **Print the name as you want it to appear on the legal birth certificate.**

1. Child's Name
   - First
   - Middle
   - Last
   - Title (e.g., Jr., II, III, etc.)
2. Sex
   - Male
   - Female
3. Date of Birth (Month/Day/Year)
4. Time of Birth (Specify hour and minute and check appropriate box.)
   - AM
   - PM
   - Noon
   - Midnight

5a. Birth Facility
   - Clinic/Dr. Office
   - Residence
   - Hospital
   - Birth Center
   - Other

5b. Name of Hospital – If birth occurred at or en route to a hospital

5c. Street Address Where Birth Occurred – If not at or en route to a hospital (where the placenta was delivered).

6. Location of Birth – County
7. Location of Birth – City, Village, or Township
8. Check one.
   - City
   - Village
   - Township

9a. Attendant Name

9b. Wisconsin License No.
10. Title
    M.D.
    D.O.
    C.N.M..
    Other Midwife
    Other
11a. Name and Title – Filing Party
11b. Signature – Filing Party
12. Date Completed (Month/Day/Year)
13. Mailing Address – Filing Party (Check box, if same as hospital)
    Same as Hospital
14. Local Information
15. Local Information

PART I INFORMANT LEGAL INFORMATION

16. Mother's Current Name
    First
    Middle
    Last
17. Mother's Birth Name (Maiden Name)
    First
    Middle
    Surname (As it appears on her birth certificate)
18. Mother's Date of Birth (Month/Day/Year)
19. Mother's State of Birth (If not in the U.S.A., name the country).

For items 20-23, enter the mother's legal residence (the physical location where the mother lives). Name the city, village or township where the home is located. This may **differ from** the post office's mailing address for your location. **Do not name an unincorporated place or neighborhood.**

20. Residence – State
21. Residence – County
22. Residence – City, Village, Township
23. Check one.
    City
    Village
    Township

HUSBAND INFORMATION. Read the information in DPH 5103, "Facts About Your Child's Birth Certificate," item E, "Husband/Father Information on the Birth Certificate" before completing any items on the worksheet pertaining to the husband and before completing item 35, "Is Mother Married?"

24. Husband's Name
    First
    Middle
    Last (As it appears on his birth certificate)
25. Husband's Date of Birth (Month/Day/Year)
26. Husband's State of Birth (If not in U.S.A., name the country.)
27. Birthweight (Original unconverted)
    Grams OR
    Pounds
    Ounces
28. Crown-Heel Length (Original unconverted)

Centimeters OR
Inches

29. Date – Infant Died (Month/Day/Year)
30. Plurality (Single, Twin, Triplet, etc.)
31. If not Single Birth (Born first, second, third, etc.)
32. Informant's Name
33. Relation to Child (Do not enter "Father" if informant is not listed as husband in item 24.)

PART II INFORMANT CONFIDENTIAL LEGAL INFORMATION
(This information does not appear on certified copies of the birth certificate.)

34a. Mother's Mailing Address (Street, RFD or Post Office Box / City, Village or Township / State / Zip Code) The Birth Notification form will be sent to this address. If the infant is being placed for adoption or this possibility is under consideration, check the box and do NOT provide the address.
Child may/will be placed for adoption

Read the information in DPH 5103, "Facts About Your Child's Birth Certificate," item G, "Social Security Number Requested," before completing items 34b-34d. The infant must be named and the mother's mailing address must be complete if the box is checked "Yes."

34b. Social security Number Requested by Parents?
Yes
No

34c. Mother's Social Security Number
34d. Husband's Social Security Number

Read the information in DPH 5103, "Facts About Your Child's Birth Certificate," item E, "Husband/Father Information" before completing item 35.

35. Mother's Marital Status (Check 'Yes' if either or both statements are true.)
Is the mother either (1) married now OR (2) married to someone at any time from conception to the birth of this child?
Yes
No

PART III CONFIDENTIAL MEDICAL/STATISTICAL INFORMATION

The information from this page is only available to the mother and to the public health offices and selective research programs which must treat this information as confidential material. The information is collected throughout the nation for health and population research. It is used to promote healthy births and to identify present and future health needs and populations of certain groups or areas. This information does not appear on the legal portion of the birth certificate, BUT MUST BE COMPLETED for the birth certificate to be filed. Medical records, if available, are the only primary source of this information. Obtain the information from the mother or other informant only if there is no other medical record source of the information.

INSTRUCTIONS (Items 36-39)

36. RACE - Enter the race of the mother and husband (if listed in item 24) on the appropriate line. Enter both (or more) races if of "mixed" race. Do not enter "Hispanic" here.
If "Native American," enter "American Indian." If Asian or Southeast Asian, specify the national origin, such as "Hmong," Cambodian," "Chinese," "Japanese," etc.

37. HISPANIC ORIGIN - "Hispanic" refers to people whose origins are from Spain, Mexico or the Spanish-speaking countries of Central or South America. If you are of Hispanic origin, specify the national origin. If not of Hispanic origin, check the "No" box.

38. EDUCATION - Enter the number of years of schooling completed. Do not count partial years (For example, if the freshman year of college is not completed, enter "12" under "Elementary/Secondary.") Do not include years in technical or specialty schools unless college transferable academic credits were received.

39. EMPLOYMENT ONE YEAR AGO - Enter the occupation and type of firm or agency worked at one year prior to this birth. Be as specific as possible in these items. (See examples below.) Avoid the use of a firm or agency name. Instead, describe the type of business in which the firm or agency is involved. Do not use abbreviations for job titles.

	OCCUPATION	TYPE OF FIRM OR AGENCY
Enter:	**Clerk Typist**	**City Health Department**
Not:	*Office Worker*	*City of Madison*
Enter:	**Math Teacher**	**High School**
Not:	*Teacher*	*Public School*
Enter:	**Auto Mechanic**	**Self-Employed**
Not:	*Mechanic*	*Own*

	OCCUPATION	TYPE OF FIRM OR AGENCY
Enter:	**Disabled**	**None**
Not:	*None*	*None*
Enter:	**Unemployed**	**None**
Not:	*Never Worked*	*None*
Enter:	**Student**	**High School**
Not:	*None*	*None*

Enter:	Sales Clerk	Hardware Store
Not:	*Clerk*	*Smith's Store*

Enter:	Homemaker	Own Home
Not:	*None*	*None*

36a. Race of Mother (White, Black, American Indian, etc. Do not enter Hispanic.)
36b. Race of Husband (White, Black, American Indian, etc. Do not enter Hispanic.)
37a. Hispanic Origin of Mother (Specify Mexican, Puerto Rican, Cuban, etc.)
No
a. write in
37b. Hispanic Origin of Husband (Specify Mexican, Puerto Rican, Cuban, etc.)
No
a. write in
38a. Education of Mother (Highest Grade Completed)
a. Elementary/Secondary (0-12)
b. College (1-4 or 5+)
38b. Education of Husband (Highest Grade Completed)
a. Elementary/Secondary (Enter 0-12)
b. College (Enter 1-4 or 5+)
39a. Employment One Year Ago of Mother – Occupation
39b. Employment One Year Ago of Mother – Type of Firm or Agency
39c. Employment One Year Ago of Husband – Occupation
39d. Employment One Year Ago of Husband – Type of Firm or Agency
40a. Pregnancy History (Obtain from informant only) Live Births (Exclude this child.) Now Living
a. write in
None
40b. Pregnancy History (Obtain from informant only) Live Births (Exclude this child.) Now Dead
a. write in
None
40c. Pregnancy History (Obtain from informant only) Live Births (Exclude this child.) Date of Last Live Birth (Month/Year)
40d. Pregnancy History (Obtain from informant only) Other Terminations (Spontaneous or Induced) Less Than 20 Weeks Gestation
d. write in
None
40e. Pregnancy History (Obtain from informant only) Other Terminations (Spontaneous or Induced) 20 Weeks or More
e. write in
None
40f. Pregnancy History (Obtain from informant only) Other Terminations (Spontaneous or Induced) Date of Last Other Termination (Month/Year)
41. Clinical Estimate of Gestation (Weeks)
42. Date Last Normal Menses Began (Month/Day/Year)
43. Month of Pregnancy in Which Prenatal Care Began (Months 1-9, not Trimester)
44. Total Number of Prenatal Visits
Number
None

45. APGAR Score
    a. 1 Minute
    b. 5 Minutes
46. Mother Transferred Prior to Delivery
    Yes
    No
47. Infant Transferred to Intensive Care or Another Hospital?
    Yes
    No
    If yes, name of facility and city
    Date of Transfer (Month/Day/Year)

Cigarette use and alcohol use (Items 48a-48c). If the mother smoked cigarettes and/or consumed alcohol at any time during the pregnancy, check the "Yes" box in items 48a and/or 48b. Enter the average number of cigarettes smoked per day and/or the average number of alcoholic drinks consumed per week. If the average is less than "1," enter "0" (zero). If the mother did not smoke cigarettes or drink alcohol at any time during the pregnancy, check "No" for the appropriate item(s).

48a. Cigarette Use During Pregnancy?
    Yes
    No
    If yes, average number of cigarettes per day
48b. Alcohol Use During Pregnancy?
    Yes
    No
    If yes, average number of drinks per week
48c. Weight Gain/Loss During Pregnancy
    Net pounds gained OR
    Net pounds lost

CHECK ALL THAT APPLY.

49. Medical History for This Pregnancy
    Anemia (Hct.< 30/Hgb.< 10)
    Cardiac disease
    Acute or chronic lung disease
    Pre-existing diabetes
    Gestational diabetes
    Genital herpes
    Other STD (chlamydia, GC)
    Hydramnios/Oligohydramnios
    Hemoglobinopathy
    Hypertension, chronic
    Hypertension, pregnancy associated
    Eclampsia
    Incompetent cervix
    Previous infant 4000+ grams
    Previous preterm or small-for-gestational-age infant
    Renal disease
    Rh sensitization
    Uterine bleeding

None
Other (Specify.)

50. Obstetric Procedures
    - Amniocentesis
    - Electronic fetal monitoring
    - Induction of labor
    - Stimulation of labor
    - Tocolysis
    - Ultrasound
    - Postpartum sterilization
    - None
    - Other (Specify.)
51. Events of Labor and/or Delivery
    - Febrile (>100F or 38C)
    - Meconium, moderate/heavy
    - Premature rupture of membranes (>12 hrs)
    - Abruptio placenta
    - Placenta previa
    - Other excessive bleeding
    - Seizures during labor
    - Precipitous labor (<3 hrs)
    - Prolonged labor (>20 hrs)
    - Dysfunctional labor
    - Breech
    - Other malpresentation
    - Cephalopelvic disproportion
    - Cord prolapse
    - Anesthetic complications
    - Fetal distress
    - None
    - Other (Specify.)
52. Method of Delivery
    - Vaginal
    - Vaginal after previous C-section
    - Primary C-section
    - Repeat C-section
    - Forceps
    - Vacuum
53. Abnormal Conditions of the Newborn
    - Anemia (Hct. < 39/Hgb. < 13)
    - Birth injury

Hyaline membrane disease/RDS
Meconium aspiration syndrome
Assisted ventilation (< 30 min)
Assisted ventilation (≥ 30 min)
Seizures
None
Other (Specify.)

54. Congenital Anomalies of Child

Anencephalus
Spina Bifida/Meningocele
Hydrocephalus
Microcephalus
Other central nervous sys. Anomalies (Specify.)
Heart malformations
Other circulatory/respir. Anomalies (Specify.)
Rectal atresia/stenosis
Tracheo-esophageal fistula/Esophageal atresia
Omphalocele/Gastroschisis
Other gastrointestinal anomalies (Specify.)
Malformed genitalia
Renal agenesis
Other urogenital anomalies (Specify.)
Cleft lip/palate
Polydactyly/Syndactyly/Adactyly
Club Foot
Diaphragmatic hernia
Other musculoskeletal/integumental anomalies (Specify.)
Down syndrome
Other chromosomal anomalies (Specify.)
None
Other (Specify.)

Appendix C. Institute of Medicine Weight Gain Guidelines.

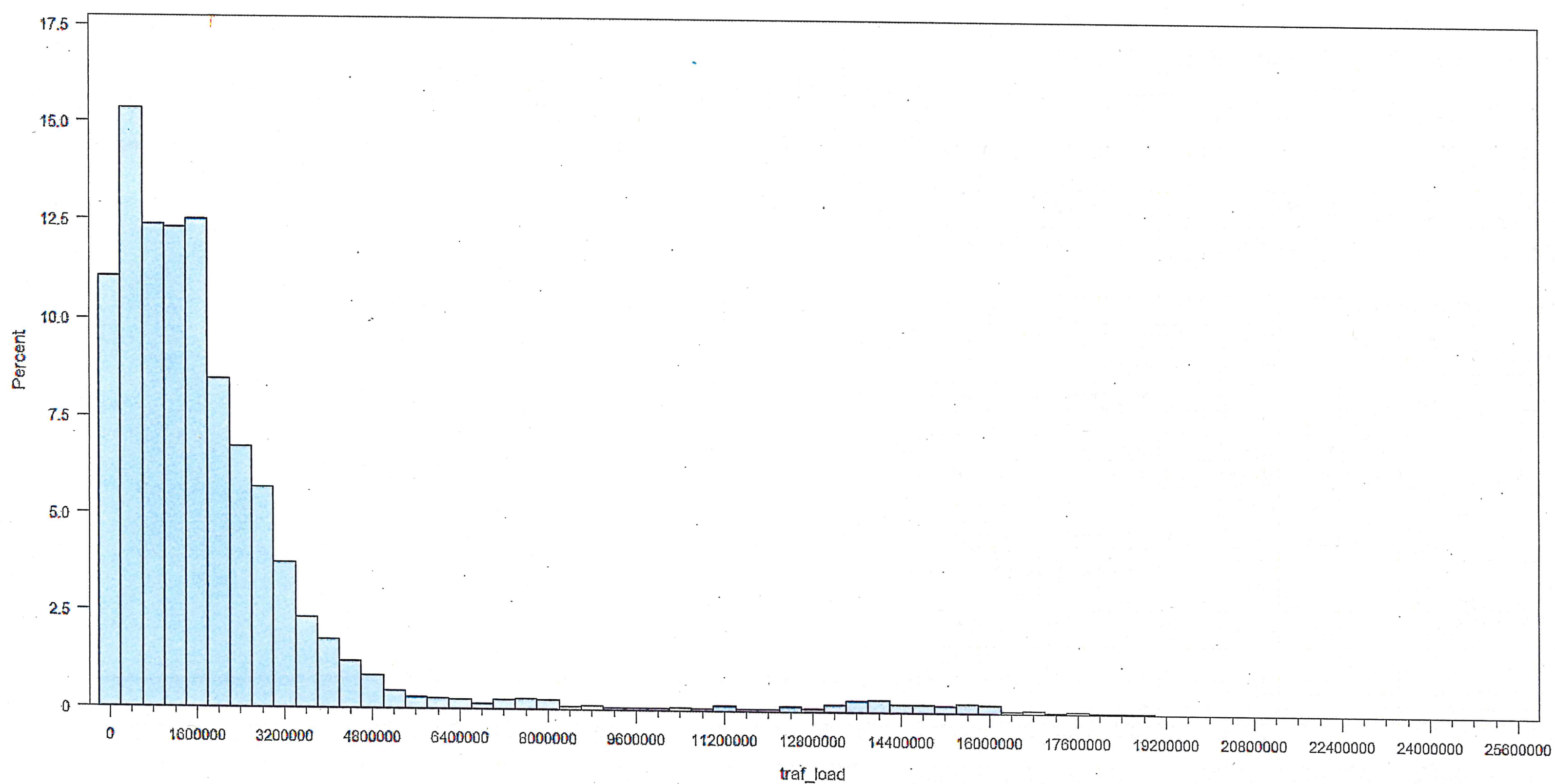
TABLE S-1 New Recommendations for Total and Rate of Weight Gain During Pregnancy, by Prepregnancy BMI

	Total Weight Gain		Rates of Weight Gain* 2nd and 3rd Trimester	
Prepregnancy BMI	Range in kg	Range in lbs	Mean (range) in kg/week	Mean (range) in lbs/week
Underweight (< 18.5 kg/m^2)	12.5-18	28-40	0.51 (0.44-0.58)	1 (1-1.3)
Normal weight (18.5-24.9 kg/m^2)	11.5-16	25-35	0.42 (0.35-0.50)	1 (0.8-1)
Overweight (25.0-29.9 kg/m^2)	7-11.5	15-25	0.28 (0.23-0.33)	0.6 (0.5-0.7)
Obese (≥ 30.0 kg/m^2)	5-9	11-20	0.22 (0.17-0.27)	0.5 (0.4-0.6)

* Calculations assume a 0.5-2 kg (1.1-4.4 lbs) weight gain in the first trimester (based on Siega-Riz et al., 1994; Abrams et al., 1995; Carmichael et al., 1997).

Rasmussen, K.M., & Yaktine, A.L. (Eds). (2009). Weight gain during pregnancy: Reexamining the guidelines. Washington, DC: National Academies Press. (p. 2)

Appendix D. Traffic Distribution Milwaukee County, 2005-2010.



Appendix E. National Ambient Air Quality Standards.

National Ambient Air Quality Standards (NAAQS)

The Clean Air Act, which was last amended in 1990, requires EPA to set National Ambient Air Quality Standards (40 CFR part 50) for pollutants considered harmful to public health and the environment. The Clean Air Act identifies two types of national ambient air quality standards. ***Primary standards*** provide public health protection, including protecting the health of "sensitive" populations such as asthmatics, children, and the elderly. ***Secondary standards*** provide public welfare protection, including protection against decreased visibility and damage to animals, crops, vegetation, and buildings.

EPA has set National Ambient Air Quality Standards for six principal pollutants, which are called "criteria" pollutants. They are listed below. Units of measure for the standards are parts per million (ppm) by volume, parts per billion (ppb) by volume, and micrograms per cubic meter of air (µg/m³).

Pollutant [final rule cite]		Primary/ Secondary	Averaging Time	Level	Form
Carbon Monoxide [76 FR 54294, Aug 31, 2011]		primary	8-hour	9 ppm	Not to be exceeded more than once per year
			1-hour	35 ppm	
Lead [73 FR 66964, Nov 12, 2008]		primary and secondary	Rolling 3 month average	0.15 µg/m³ (1)	Not to be exceeded
Nitrogen Dioxide [75 FR 6474, Feb 9, 2010] [61 FR 52852, Oct 8, 1996]		primary	1-hour	100 ppb	98th percentile, averaged over 3 years
		primary and secondary	Annual	53 ppb (2)	Annual Mean
Ozone [73 FR 16436, Mar 27, 2008]		primary and secondary	8-hour	0.075 ppm (3)	Annual fourth-highest daily maximum 8-hr concentration, averaged over 3 years
Particle Pollution Dec 14, 2012	$PM_{2.5}$	primary	Annual	12 µg/m³	annual mean, averaged over 3 years
		secondary	Annual	15 µg/m³	annual mean, averaged over 3 years
		primary and secondary	24-hour	35 µg/m³	98th percentile, averaged over 3 years
	PM_{10}	primary and secondary	24-hour	150 µg/m³	Not to be exceeded more than once per year on average over 3 years
Sulfur Dioxide [75 FR 35520, Jun 22, 2010] [38 FR 25678, Sept 14, 1973]		primary	1-hour	75 ppb (4)	99th percentile of 1-hour daily maximum concentrations, averaged over 3 years
		secondary	3-hour	0.5 ppm	Not to be exceeded more than once per year

as of October 2011

(1) Final rule signed October 15, 2008. The 1978 lead standard (1.5 µg/m3 as a quarterly average) remains in effect until one year after an area is designated for the 2008 standard, except that in areas designated nonattainment for the 1978, the 1978 standard remains in effect until implementation plans to attain or maintain the 2008 standard are approved.

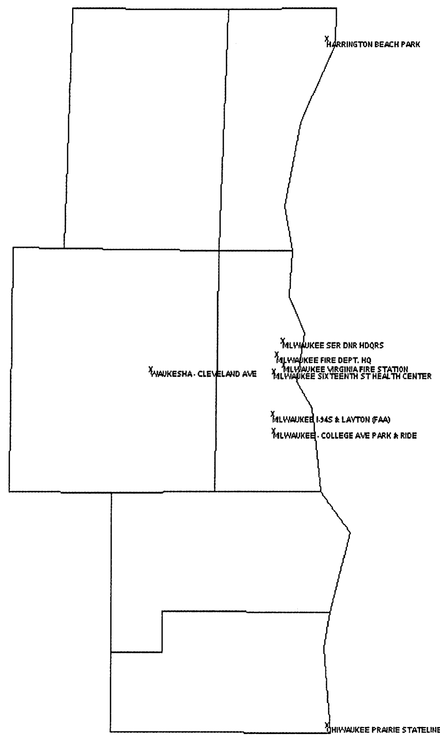
(2) The official level of the annual NO2 standard is 0.053 ppm, equal to 53 ppb, which is shown here for the purpose of clearer comparison to the 1-hour standard.

(3) Final rule signed March 12, 2008. The 1997 ozone standard (0.08 ppm, annual fourth-highest daily maximum 8-hour concentration, averaged over 3 years) and related implementation rules remain in place. In 1997, EPA revoked the 1-hour ozone standard (0.12 ppm, not to be exceeded more than once per year) in all areas, although some areas have continued obligations under that standard ("anti-backsliding"). The 1-hour ozone standard is attained when the expected number of days per calendar year with maximum hourly average concentrations above 0.12 ppm is less than or equal to 1.

(4) Final rule signed June 2, 2010. The 1971 annual and 24-hour SO2 standards were revoked in that same rulemaking. However, these standards remain in effect until one year after an area is designated for the 2010 standard, except in areas designated nonattainment for the 1971 standards, where the 1971 standards remain in effect until implementation plans to attain or maintain the 2010 standard are approved.

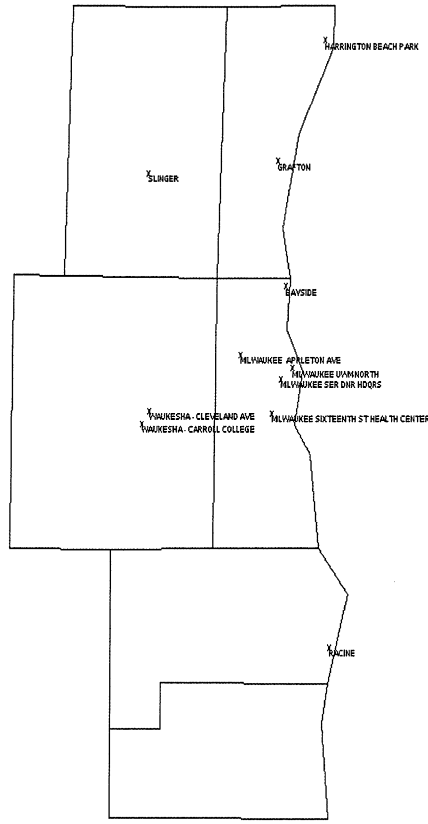
Appendix F. Criteria air pollutant monitoring sites, Milwaukee County, 2004-2010.

PM25 monitoring sites



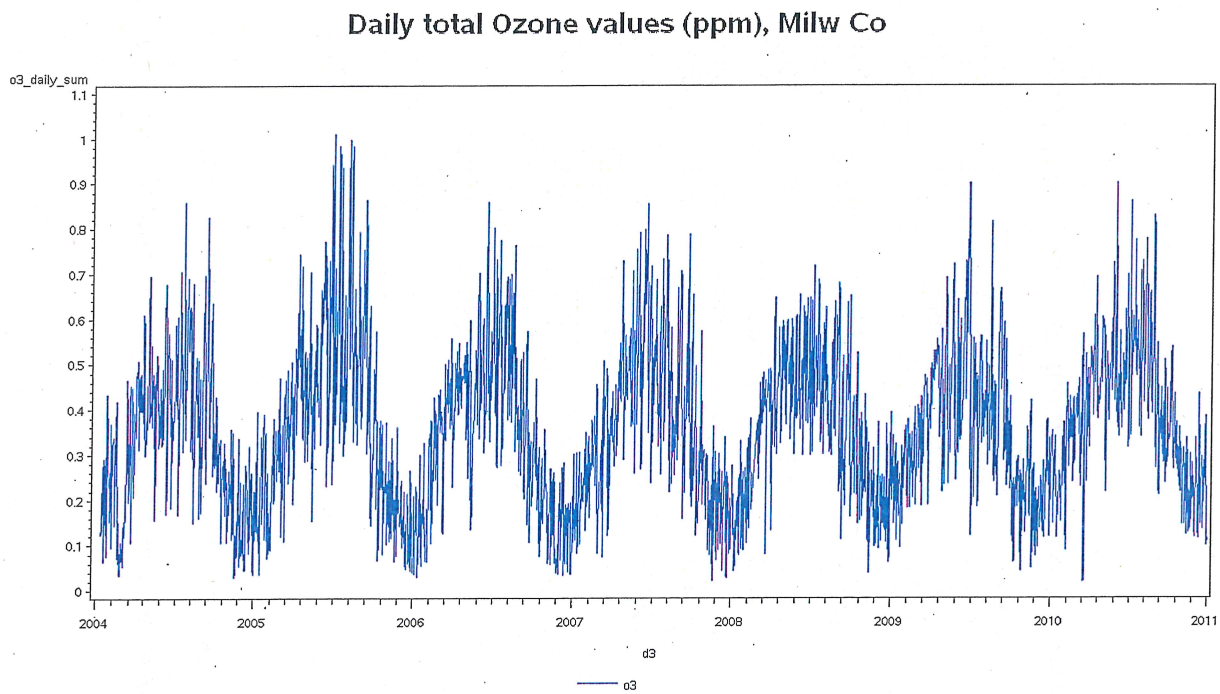
Air Monitoring Station	count	start	end
(19) Chiwaukee Prairie Stateline	892	01Jan2004	31Dec2010
(10) Milwaukee Sixteenth Street Health Center	916	01Jan2004	31Dec2010
(26) Milwaukee Southeast DNR Headquarters	915	01Jan2004	31Dec2010
(43) Milwaukee Virginia Fire Station	781	01Jan2004	31Dec2009
(58) Milwaukee - College Ave Park & Ride	93	03Nov2009	28Dec2010
(59) Milwaukee I-94 & Layton (FAA)	547	01Jan2004	28Oct2009
(99) Milwaukee Fire Department Headquarters	746	01Jan2004	30Dec2009
(9) Harrington Beach Park	857	01Jan2004	31Dec2010
(27) Waukesha - Cleveland Ave	910	01Jan2004	31Dec2010

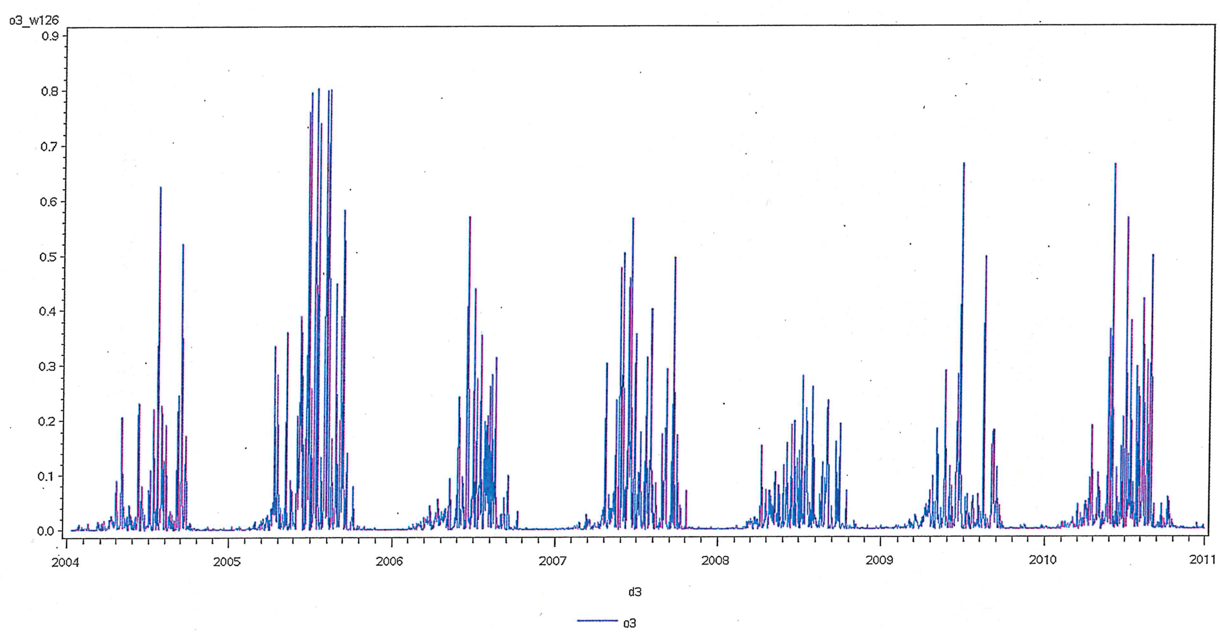
Ozone monitoring sites



Air Monitoring Station	count	start	end
(10) Milwaukee Sixteenth Street Health Center	1337	09MAR2004	20OCT2010
(26) Milwaukee Southeast DNR Headquarters	2549	06JAN2004	31DEC2010
(41) milwaukee uwm-north	1150	15APR2004	21OCT2009
(44) milwaukee appleton ave	394	15APR2004	17OCT2005
(85) bayside	1355	15APR2004	22OCT2010
(8) grafton	1327	15APR2004	18OCT2010
(9) harrington beach park	1337	15APR2004	20OCT2010
(17) racine	1318	15APR2004	18OCT2010
(9) slinger	1328	15APR2004	18OCT2010
(17) waukesha - carroll college	336	15APR2004	07SEP2005
(27) waukesha - cleveland ave	1327	29APR2004	21OCT2010

Appendix G. Weighted Ozone (W126), Milwaukee County, 2004-2010.



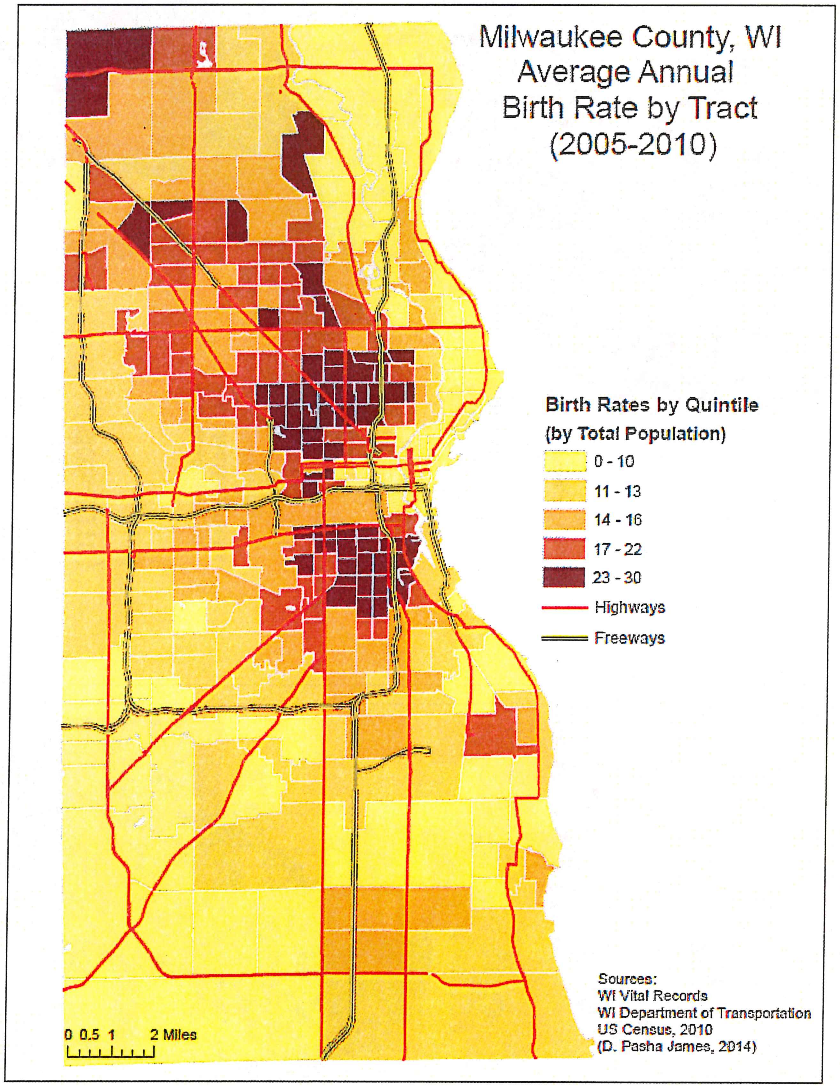


Appendix H. Correlation matrix of select variables that reflect single variable imputations, $N = 85{,}038$.

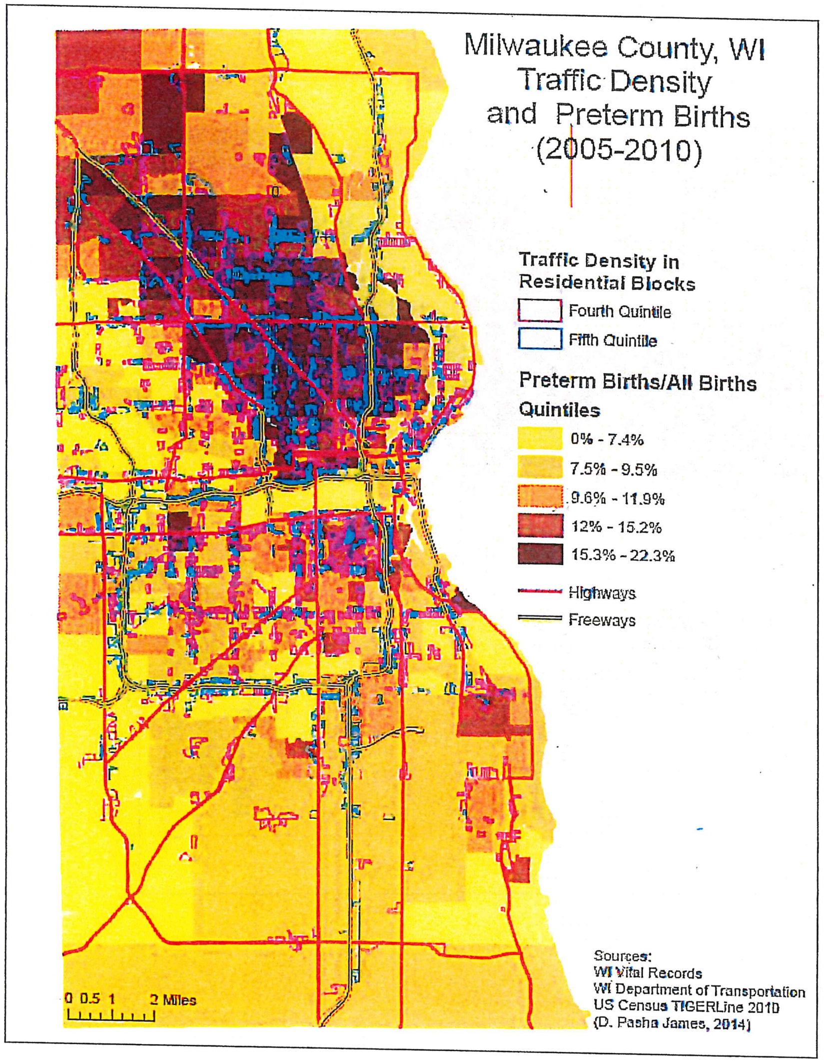
	PTB	LBW	Stress	Weight Risk	Unmarried	MAge Risk	MBlack	MHispanic	MOtherRace	MEducLo	No PNC
PTB	1.0										
LBW	0.447 <.0001	1.0									
Stress	0.041 <.0001	0.048 <.0001	1.0								
Weight Risk	0.034 <.0001	0.030 <.0001	0.033 <.0001	1.0							
Unmarried	0.090 <.0001	0.100 <.0001	0.219 <.0001	0.066 <.0001	1.0						
MAge Risk	0.010 .0045	0.004 .2005	-0.069 <.0001	-0.008 0.0254	-0.179 <.0001	1.0					
MBlack	0.099 <.0001	0.119 <.0001	0.336 <.0001	0.067 <.0001	0.464 <.0001	-0.097 <.0001	1.0				
MHispanic	-0.009 .0095	-0.036 <.0001	-0.078 <.0001	-0.005 0.1246	0.042 <.0001	-0.024 <.0001	-0.349 <.0001	1.0			
MOtherRace	-0.008 .0258	-0.008 0.0267	-0.015 <.0001	-0.012 0.0004	-0.119 <.0001	-0.005 0.1293	-0.041 <.0001	-0.120 <.0001	1.0		
MEducLo	0.053 <.0001	0.0444 <.0001	0.061 <.0001	0.035 <.0001	0.281 <.0001	-0.041 <.0001	0.122 <.0001	-0.041 <.0001	-0.023 <.0001	1.0	
No PNC	0.069 <.0001	0.071 <.0001	0.026 <.0001	0.020 <.0001	0.068 <.0001	-0.000 0.9624	-0.041 <.0001	-0.014 <.0001	0.004 0.2243	0.060 <.0001	1.0

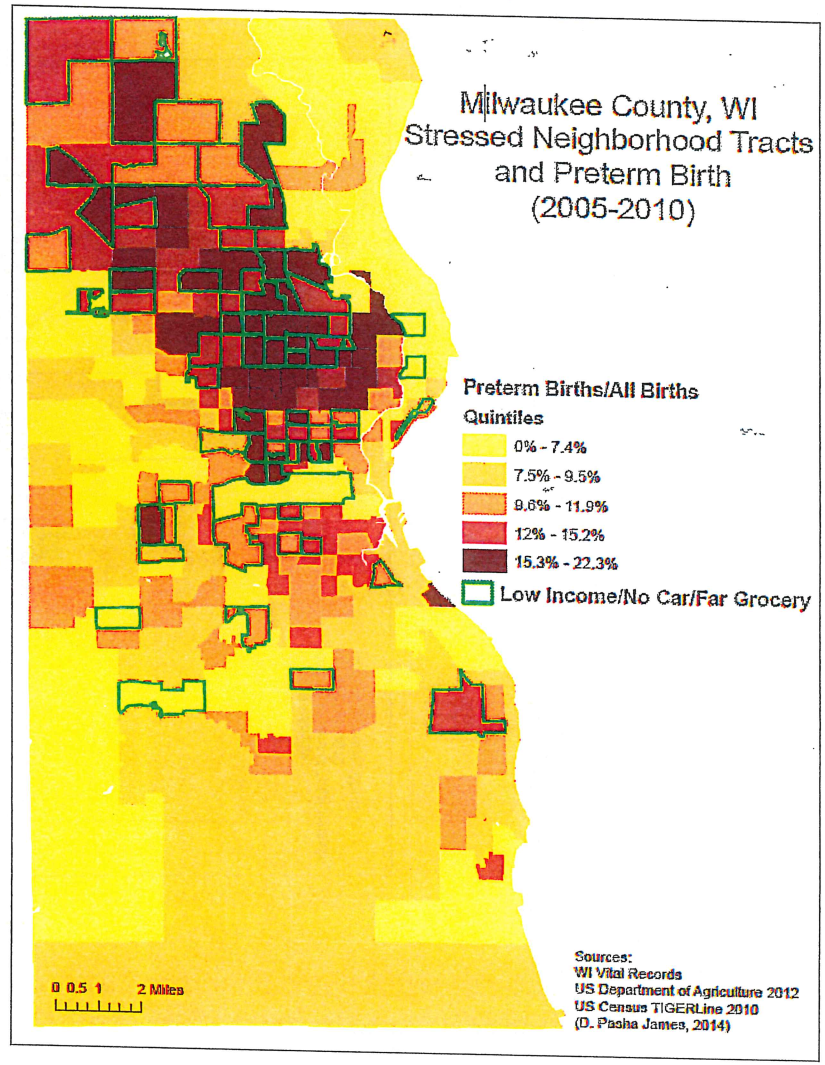
Decision: Run a multi-level model with the Stress Index and without Race, Unmarried, and Maternal Education.

Appendix I. Map of Average Annual Birth Rate by Tract, Milwaukee County, 2005-2010

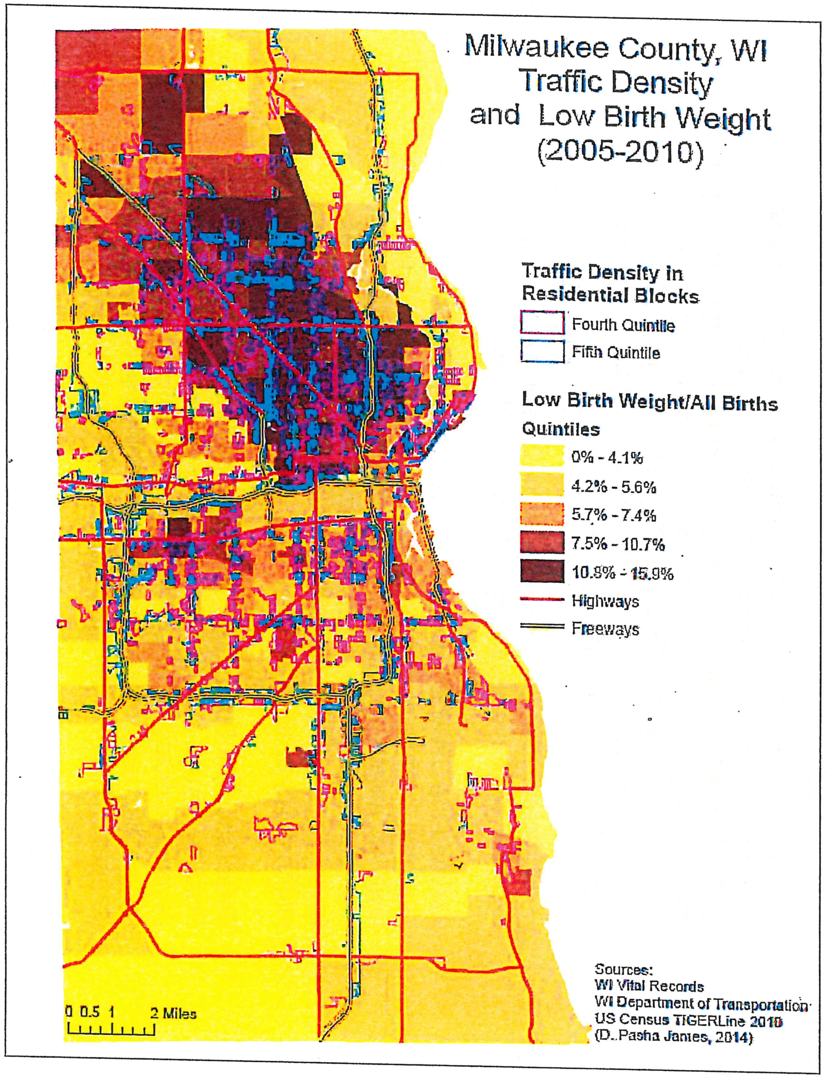


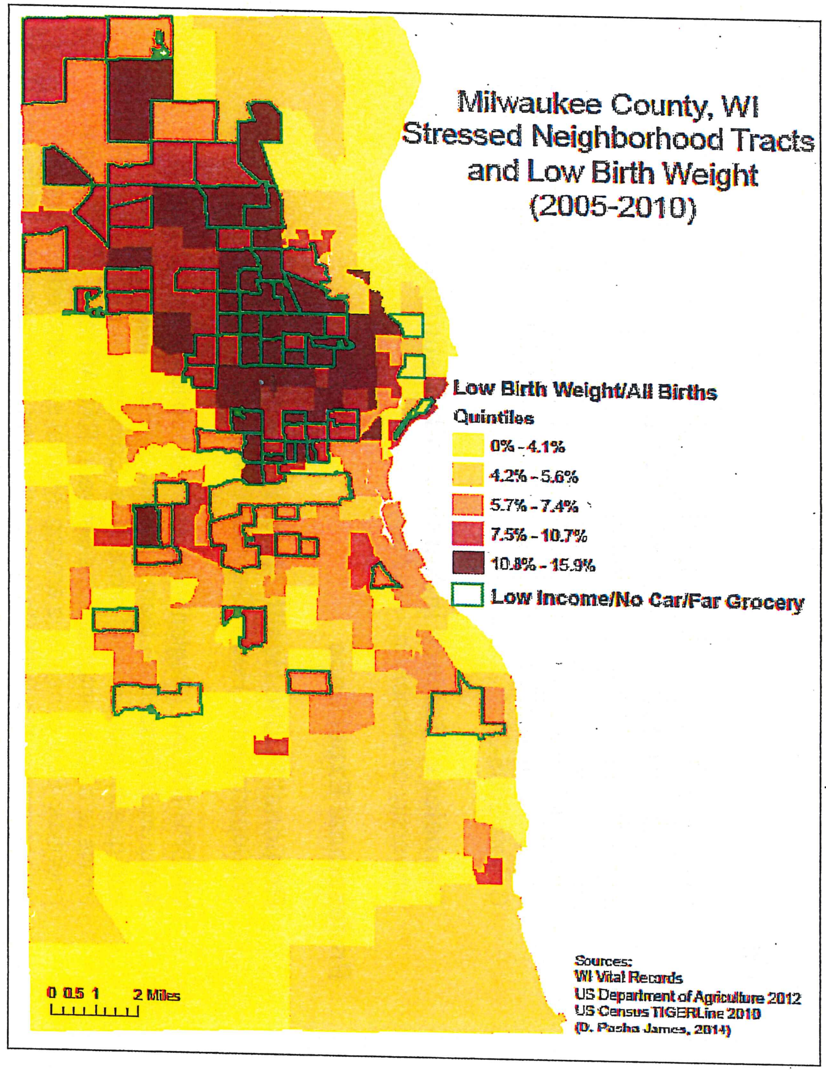
Appendix J. Maps of Cumulative Traffic Density, Stressed Neighborhood Tracts, and PTB, Milwaukee County, 2005-2010.





Appendix K. Maps of Cumulative Traffic Density, Stressed Neighborhood Tracts, and LBW, Milwaukee County, 2005-2010.





CURRICULUM VITAE

Deborah L. Pasha James

Education

Doctor of Philosophy – Multidisciplinary
Built Environment and Public Health
University of Wisconsin - Milwaukee
May, 2014
Milwaukee, WI

Dissertation Title: Effects of Traffic and Air Pollution on Risk of Preterm Birth and Low Birth Weight Outcomes in Milwaukee County 2005-2010

Bachelor of Science in Nursing with Distinction
University of Wisconsin - Madison
1977
Madison, WI

Professional Experience

Regional Public Health Nursing Consultant
WI Department of Health Services/Division of Public Health
2000 - present
Milwaukee, WI

WI DPH RADAR (Regional Assessment policy Development Assurance Response) team, focused on Performance management and quality improvement processes. Convened meeting of all DPH PHNs to discuss intersections between RADAR team and program priorities. Built consensus among internal staff and administrators to incorporate the PHN Competencies and Standards of Practice in new position descriptions and orientation.

Healthy WI Leadership Institute (HWLI) Regional CHIPPs team. Collaborated with other WI DPH employees and other organizations to improve coordination and uniformity of Community Health Improvement Processes and Plans (CHIPPs) in WI. Assisted a multijurisdictional health department to locate environmental, educational and health outcomes data for their community health assessment.

DPH Accreditation gaps analysis team. Collaborated with Bureaus to gather DPH evidence to meet PHAB standards.

Assisted the UWM Environmental Health Sciences Core Center (National Institute of Environmental Health Sciences) to prepare a town hall meeting for the national director. Facilitated community members' ability to articulate their concerns (representing all factions of the City of Milwaukee) to officials, which continue to inform policy at all levels.

Established the Southeast Public Health Nurse (PHN) Academic-Practice Forum. Provided leadership between organizations to develop matrixes for clear direction, optimum impact, and to avoid supplanting resources to increase practicing public health nurses' competencies. Provided guest lectures for nursing classes.

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Deborah L. Pasha James

Assisted Waukesha County Public Health Division and Waukesha Memorial Hospital in achieving the first in the state multi-year combined grant from two sources (MCH-CYSHCN and PHHS) to pilot a program to address the obesity issue in the local Hispanic community. The program received a 5-star rating as a CDC Prevention Success story and the successful results have been published in the medical literature.

Initiated the Milwaukee Safe Routes Campaign together with the Milwaukee Safety Division (Police Department) and Wisconsin Walks to apply for and receive one of three National Highway Transportation Safety Administration (NHTSA) grants awarded nationwide that year. City elected officials allocated city funds for safer walking conditions. The school system pledged to continue Safe Routes programs—which has been ongoing. Provided evidence about the health and economic benefits related to multimodal transportation, which the Bicycle Federation of Wisconsin utilized to gain bike racks on all Milwaukee County Transit Service (MCTS) buses. Ridership increased with 1,000 bike users per month (MCTS, 2009).

Administered more than $1,000,000 of federally-funded grants, annually, comprised of individual contracts that range from $50,000 to $200,000; and consulted with DPH colleagues on use of funds for their assigned agencies.

Respond to community emergencies as needed—public health preparedness training includes HSEEP Exercise Design, Risk and Crisis Communication, Emergency Planning for Special Needs Communities, Strategic National Stockpile Mobile Preparedness, ICS-400 Advanced Command and General Staff, and NIMS-700.

Public Health Nurse 1989 - 2000
Milwaukee Health Department Milwaukee,WI
Addressed individual and population-based concerns related to communicable and other diseases, substance abuse, neglect/abuse, lead poisoning and other environmental issues in home visits (mostly inner city), schools, Travel Clinic and Breast Cancer Awareness Project. Recertified staff in American Heart Association blood pressure assessment. Implemented system-level changes in schools such as an asthma prevention program and a medication administration policy and procedure by working with school administration and parent groups.

Nurse Coordinator 1987-1988
IntraCorp Milwaukee, WI
Negotiated out-of-contract provisions for the insured, with the goal of achieving overall cost savings as measured by the returns-on-investment for the insurance companies

CURRICULUM VITAE

Deborah L. Pasha James

Medical Case Management Supervisor — 1986 - 1987, Green Bay, WI
IntraCorp
Serviced companies for lines of coverage such as Major Medical, Self-insured, and Workers Compensation, including supervision of others' cases locally and nationwide. Recruited and interviewed regional nurse applicants, oriented and supervised several regional nursing staff

Rehabilitation/Utilization Review Specialist — 1985 - 1986, Green Bay, WI
IntraCorp
Assessed health care/vocational needs and recommended cost-effective care alternatives. Audited hospital bills.

Assistant Head Nurse — 1979 - 1985, Fond du Lac, WI
St. Agnes Hospital
Assisted in clinical supervision of 45-bed medical teaching unit. Provide collaborative coverage of the unit and oversight of approximately 70 staff persons during the Head Nurses medical leave-of-absence. Retained during unit mergers as one of the mid-level managers for the newly formed management of the unit. Administered chemotherapy and hospice care for patients with cancer throughout the continuum of the disease. Assisted other professional staff with their assignments. Worked with the faculty of the local college to precept nursing students.

Staff Nurse — 1978 - 1979, Neenah, WI
Theda Clark Regional Medical Center
Advocated with the nursing administration and the medical chief of staff regarding the need for increased staffing on this and similar units, which was implemented. Directed and provided patient care for 36-bed Medical/Surgical/Orthopedic unit. Oriented graduate nurses.

Staff Nurse — 1977 - 1978, Oklahoma City, OK
Bone & Joint Hospital
Directed and provided patient care for 18-bed orthopedic unit.
Managed industrial injuries and critical care during emergency department rotations.

Other Experience and Professional Memberships

Public Health Forum: The Value of Prevention and a Competent Workforce — April, 2011, Wauwatosa, WI
Facilitated statewide discussion to inform Susan M. Swider, PhD, APHN-BC, who was recently appointed by President Obama to the advisory committee on Prevention, Health Promotion, Integrative and Public Health.

Stakeholders' Advisory Board and Steering Committees, Children's Environmental Health Sciences Core Center, funded by the National Institute of Environmental Health Sciences. — 2010 - present, Milwaukee, WI

Association of State and Territorial Directors of Nursing (ASTDN)/Environmental Committee — 2009 - 2011

CURRICULUM VITAE
Deborah L. Pasha James

American Public Health Association (APHA)	2009 - 2011
Association of Pedestrian and Bicycle Professionals (APBP)	2009 - 2011
MAPP Built Environment committee, City of Milwaukee Health Department	2009
Wisconsin Physical Activity Nutrition Coalition, Environmental Committee (WIPAN)	2007 - present
Wisconsin Asthma Coalition/Environmental subcommittee	2007 - present
Fight Asthma Milwaukee Allies/Environmental subcommittee	2007 - present
Organizer, Southeast Wisconsin PHN Academic Practice Collaborative (SEWEAP)	2005 - present
President, Alameda Place Neighborhood Association	2005 - present Milwaukee, WI
Milwaukee Bicycle-Pedestrian Task Force, appointed by Mayor John Norquist, re-appointed by Mayor Tom Barrett	2003 - 2007
Board of Directors, Wisconsin Walks	2003 - 2007
Organizer, The Pedestrian/Traffic Safety Venture (state pilot)	2003-2006 Milwaukee, WI
Planner, *Creating Active Community Environments,* regional workshops	2004 (Statewide)
Planner and moderator, *Mobilizing to Meet Public Health Challenges,* Wisconsin Public Health Association (WPHA) annual meeting	2003 Milwaukee, WI

Awards/Honors

Community Health Education Memorial Scholarship, second award	2013
Invited to co-chair Built Environment Committee, APHA Built Environmental Section	2011
UW-Milwaukee Graduate School Travel Award	2010
American Public Health Association Environmental Section Student Scholarship Award	2009
Invited to submit alternative (sustainable) transportation action steps for inclusion in the Wisconsin Asthma Coalition Plan.	2008

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Deborah L. Pasha James

Community Health Education Memorial Scholarship, (Wisconsin Association of Local Health Departments and Boards: The University of Wisconsin Foundation maintains an endowment with additional funds added by the Wisconsin Public Health Association, Wisconsin Home Care Organization, and other contributors).	2004

Selected Publications

McMullen, P., & Pasha, D., "Alternative Transportation Makes Sense (and Saves Cents!)", Fight Asthma Milwaukee Allies/Environmental Committee white paper, 2007.

Pasha, D. "Public health nursing matters to everyone," Nursing Matters, 2007.

Working Papers

Pasha James, D., & Hewitt, J.B. (2011). Historic and contemporary role of public health nurses in building safer, healthier communities.

Pasha James, D. (2011). Prevention success stories in Wisconsin, examples for the Public Health Forum: deploying a workforce for prevention.

Selected Presentations

Hewitt, J. B., Pasha James, D., Backus, A. S., & Delgado, L. V. (2013). Preparing PHNs for Population-Focused Practice, American Public Health Association Annual Meeting.	2013 Boston, MA
Bremer, J., Eide, Y., Pasha James, D.L., Raddatz, K., & Ringhand, T. (2013). Improving Public Health Nurse Orientation. Wisconsin Annual Public Health Nursing Conference.	2013 Stevens Point, WI
Pasha James, D., Hewitt, J.B., Simandl, G., & Mrochek, T. Southeast WI Education & Practice (SEWEAP): Public Health Nursing LEAPing to Excellence in Southeast Wisconsin [Public Health Nursing-Led Collaboration for Workforce Development (2005-2012)]. WPHA Annual Meeting.	2012 Wisconsin Dells, WI
Pasha James, D., & Hewitt, J.B. "Back to the Future: Public Health Nursing Practice in the 21st Century." WPHA Annual Meeting.	2011 Appleton, WI
Pasha James, D., & Hewitt, J.B. "Back to the Future: Public Health Nursing Practice in the 21st Century." APHA Annual Meeting.	2010 Denver, CO
Hewitt, J. B., Pasha, D. L., Weber, D. N., Boulanger, M. E., Backus, A. S., & Petering, D. H. "Public Health Nursing Practice: Finding Evidence to Apply to Environmental Health Issues." APHA Annual Meeting.	2008 San Diego, CA
Pasha, D. L. "$E^4 = mc^3$ Applying the energy of the public health system to the built environment." 2008 ProWalk ProBike.	2008 Seattle, WA

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Deborah L. Pasha James

Schmelzer, M. O., & Pasha, D. L. "Legal Aspects of Public Health Nursing."	2008 Wauwatosa, City of Milwaukee, Appleton, WI
Pasha, D. L. "Urban Built Environments—where public health nursing intersects with the transportation culture," *Public Health Nursing Practice: Finding Evidence to Apply to Environmental Issues.*	2008 Milwaukee, WI
Pasha, D. L. "Walking Together: Collaborative partnerships that assure community access to physical activity," *Building Evidence Through Evidence-based Nursing Practice.*	2004 Milwaukee, WI
Keller, K., & Pasha, D. L., & Roberts, P. "The Milwaukee Safe Routes to School Campaign," Department of Transportation-National Highway Traffic Safety Administration and the National Center for Bicycling & Walking.	2003 Washington, DC
Pasha, D. L. et al. "The Power of Walking Audit: Improving walkability and pedestrian safety," Governor's Highway Safety Conference.	2003 Appleton, WI

Research Experience

Ongoing Research Support

P30ES004184 — 10/2013-9/2014
UW-Milwaukee Children's Environmental Health Sciences Core Center — Role: Co-I
Jeanne B. Hewitt (PI)

Effects of traffic and air pollution on risk of preterm birth and low birth weight outcomes in Milwaukee County, 2005-2010. This study examines key environmental determinants of birth outcomes in a multi-racial community.

Completed Research

DTNH22-03-H-25078 — 9/15/03-9/04/05
Roberts/Dukes (PI) — Role: Co-I
Milwaukee Police Dept.
Milwaukee Safe Routes to School Education, Enforcement, & Encouragement Campaign, National Highway Traffic Safety Administration (NHTSA) Law Enforcement Pedestrian Safety Program implemented in all 7 police districts with schools (6) and downtown business district.