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Review

Geographical Analysis of the Distribution of Publications Describing Spatial Associations among Outdoor Environmental Variables and Really Small Newborns in the USA and Canada

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Abstract: Newborns defined as being of "low birth weight" (LBW) or "small for gestational age" (SGA) are global health issues of concern because they are vulnerable to mortality and morbidity. Prenatal exposures may contribute to LBW/SGA. In this review, we searched peer-reviewed scientific literature to determine what location-based hazards have been linked with LBW/SGA in the industrialized nations of Canada and the USA. After selecting studies based on inclusion/exclusion criteria, we entered relevant details in to an evidence table. We classified and summarized 159 articles based on type of environment (built = 108, natural = 10, and social = 41) and general category of environmental variables studied (e.g., air pollution, chemical, water contamination, waste site, agriculture, vegetation, race, SES, etc.). We linked the geographic study areas by province/state to political boundaries in a GIS to map the distributions and frequencies of the studies. We compared them to maps of LBW percentages and ubiquitous environmental hazards, including land use, industrial activity and air pollution. More studies had been completed in USA states than Canadian provinces, but the number has been increasing in both countries from 1992 to 2018. Our geographic inquiry demonstrated a novel, spatially-focused review framework to promote understanding of the human 'habitat' of shared environmental exposures that have been associated with LBW/SGA.

Keywords: environmental health; adverse birth outcomes; small for gestational age; low birth weight; exposome; planetary health; Canada; USA

1. Introduction

An underlying premise of environmental health and epidemiology involves place—where one lives and where one starts out in life, even during in utero development, ultimately determines lifelong health [1,2]. The embryo and fetus are susceptible to toxicant exposure and other environmental influences on the mother during crucial stages of pregnancy [3–6], which may lead to babies being born too small, or too early. Because they are important markers of infant survival, development, and future health, newborns that are too small are a serious source of emotional and economic stress on society—hundreds of millions of dollars are spent on specialized equipment and treatments within the first several years of life [7,8]. The Barker hypothesis [9] evolved from studies on low birth weight (as well as premature birth and intrauterine growth restriction) that found significant associations with adult hypertension, coronary heart disease, and non-insulin-dependent diabetes [10–12]. The suspected exposures associated with these birth outcomes are widespread, thus heightening the importance of early life health impacts.

The World Health Organization identifies babies born too small as an issue of global health concern, and one that is to be monitored under Sustainable Developmental Goal (SDG) 3 to "ensure healthy lives and promote wellbeing for all at all ages" (www.who.int/sdg/targets). The definitions include:

- Small for gestational age (SGA), which are infants born with a birth weight <10th percentile of a reference population for sex-based gestational age (22 to 42 weeks gestation); and
- Low birth weight at term (LBWT), which are infants born with a birth weight <2500 g, and may or may not be at full term (37–42 weeks gestation) [13–15]. Figure 1 graphically defines SGA and LBW at term.

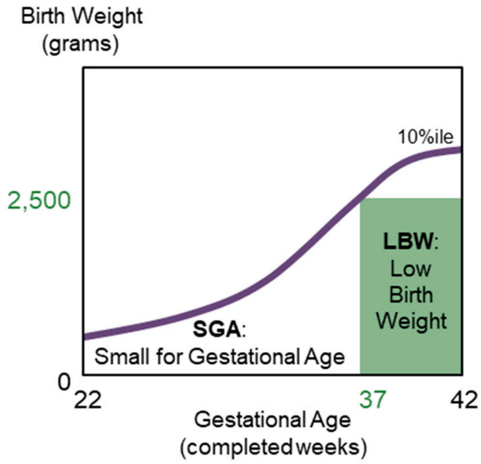
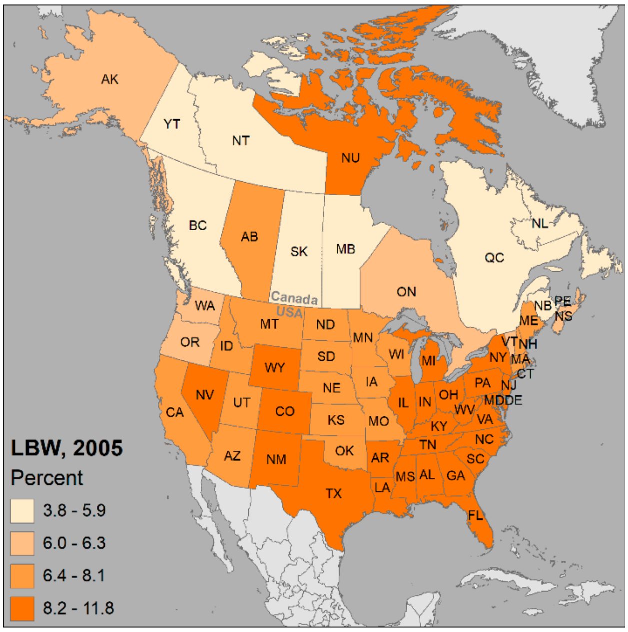


Figure 1. The set of birth weight–for–gestational age standards below the 10th percentile birth weights describes small for gestational age (SGA) in the purple curve; low birth weight at term (LBWT) is a subset of SGA in the green shaded rectangle.

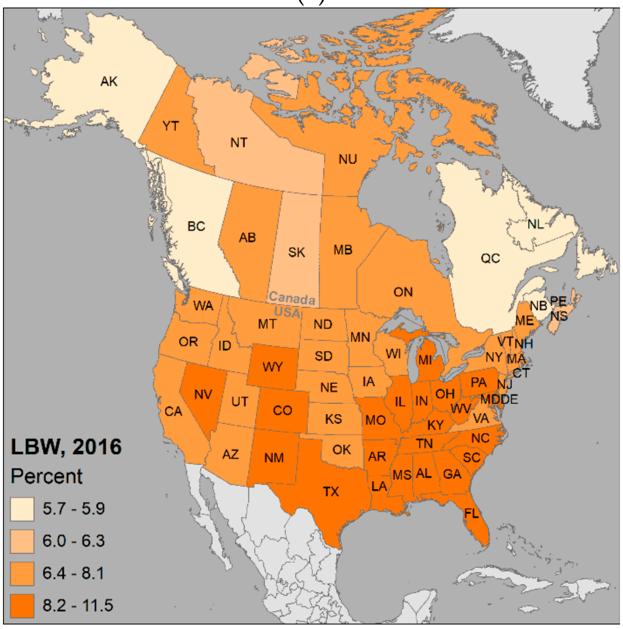
SGA and LBWT are not homogeneous pregnancy outcomes because they may consist of both infants born too early (known as preterm birth) or too small, (typically due to fetal growth restriction) [13,16]. The etiologies are multifactorial, where the most important maternal risk factors are tobacco smoking, nutrition, pre-pregnancy weight, ethnic origin, short maternal stature, and pre-existing health conditions [16–19]. Other risks include genetic and constitutional, demographic and psychosocial (e.g., socioeconomic status (SES) and stress), obstetric, antenatal care, and toxic exposures.

Globally, the rate of SGA in low- and middle-income countries is around 27% of all live births (varying between 1.2% to 41.5% in Sahelian countries of Africa and south Asia): in 2010, 32.4 million babies were SGA [20]. LBW (all gestational ages) occurred in 15% of all births, mostly in low- and middle-income countries (mostly south Asia) [21]. Of 18 million low-birthweight babies, 10.6 million were born at term. In the United States of America (USA) in 2005, SGA was 10% [22] and LBW was 8.2% [23]. In Canada in 2005, SGA was 8.4% [24] and LBW was 6.0% [25]. Although Canada is lower than the world and U.S., disorders related to short gestation and low birth weight are consistently ranked 2nd out of the 71 leading causes of infant death [26], and their prevalence has been increasing since 2000 [24].

Figure 2 shows the geographic distribution of LBW by Canadian province and U.S. state for the years 2005 and 2016 (values for SGA unavailable). The above nationwide 2005 statistics are relevant for Figure 2a, where it can be observed that Alberta (AB), Ontario (ON), and Nunavut (NU) are higher than Canada overall, and the majority of the southern and eastern states (n = 27) are higher than USA overall.



(**a**)



(**b**)

Figure 2. Percentage births considered low birth weight (LBW (all gestational ages)) in Canada and the USA for: (**a**) the year 2005; (**b**) the year 2016.

Given that many areas are close to or exceeding the overall national percentages, and are increasing over time as indicated by the higher number of provinces and states above 6.4 % in Figure 2, it is valuable from a public health perspective to understand the patterns and processes involved in being born too small.

SGA/LBW and their association with the environment necessitate an interdisciplinary research approach with integration of knowledge from medicine and geography. Medical geography is a holistic investigation of health using concepts and methodologies from geography, which also encompasses the social, physical, and biological sciences [27].

Informed by the earlier work of May—who stated that to understand disease as a biological expression of maladjustment, an ecological (i.e., ecosystem-based) study must involve the environment, the host, and the culture [28]—Meade proposed the triangle of human ecology as the framework for the state of human health [27,29]. Meade's vertices are therefore anchored to:

- Habitat—the natural, social, and built environments where people live.
- Population—people (hosts) as biological organisms structured by age, gender, and genetics.
- Behavior—visible part of culture including beliefs, social organization, and technology.

These three points influence each other and the state of health, as can be seen when modelling and summarizing what is known about neonatal outcomes and maternal exposure to outdoor pollution (Figure 3). The primary population consists of pregnant mothers and their defining individual characteristics of varied ages, pre-existing health conditions and genetic makeup, with the location of where they live and work depending on their social and economic behaviors (i.e., nutritional status, access to quality health services). More research is needed that focuses on the lesser-studied habitat vertex, more specifically, the outdoor environment, since much less attention has been given to integrating ecological factors for understanding disease [27]. The location aspect of habitat (i.e., geography)—where mothers live, where industry and services are situated, where demographic groups congregate, and for many scales—is important to clinicians and specialists in environmental health, and to exposure assessment, epidemiologists, biostatisticians, and health analysts.

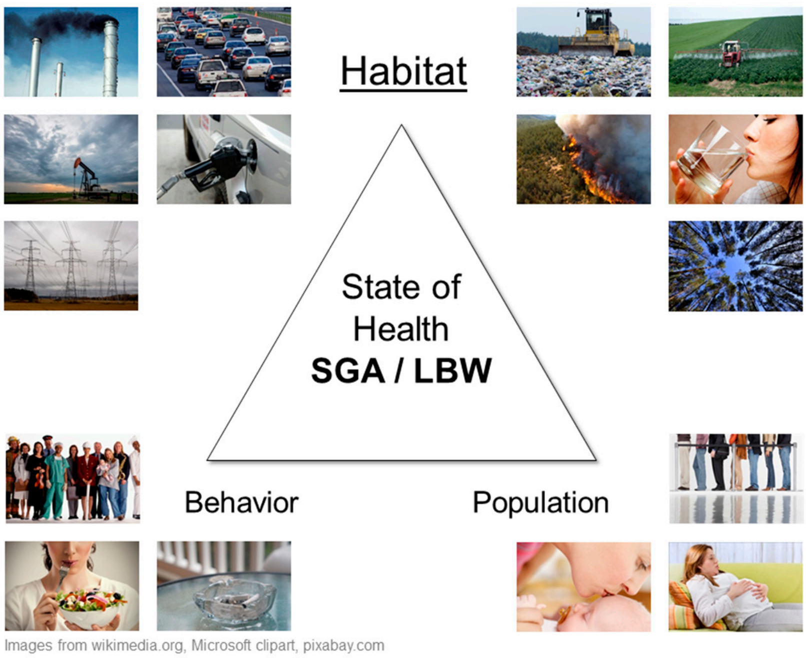


Figure 3. Meade's triangle of human ecology for maternal exposures and small for gestational age (SGA) and low birth weight (LBW).

Geography and environmental health are inextricably linked. Environmental health, as defined by the World Health Organization, "comprises those aspects of human health and disease that are determined by factors in the environment, and includes both the direct pathological effects of chemicals, radiation and some biological agents, and the effects (often indirect) on health and wellbeing of the broad physical, psychological, social and aesthetic environment, which includes housing, urban development, land use and transport" [30]. Environmental human health is implicit in the all-encompassing planetary health, "formally defined by the invivo Planetary Health network as the interdependent vitality of all natural and anthropogenic ecosystems (social, political and otherwise)" [31,32]. These concepts are not new—Hippocrates, the father of medicine, c. 460–c. 370 BC, understood the important interconnections of environment and health, in his "Airs, Waters, and Places" [33]. Hazards in those airs, waters, and places comprise the chemical, physical, and biological aspects that insult human health [27]. Many hazards have been known for centuries (e.g., lead, radiation, microorganisms), but they are only effective in altering health if an individual is exposed to them.

Exposure is the occurrence of a person coming into contact (via air, water, or skin) with a dose (requisite amount) of a toxicant (substance that produces a health effect) and may be isolated, repeated, or continual [34]. The health outcome can only occur if a person is exposed to the integral dose of a hazard for the crucial amount of time. These ideas are directly applicable to being born too small; the system can be simplified as follows:

$$Hazard_{\ (environment)} \rightarrow Exposure_{\ (prenatal)} \rightarrow Outcome_{\ (SGA/LBW)}$$

The measure of the total environmental exposures of an individual in a lifetime, and how those exposures relate to health, contribute to the human exposome. Evaluating the impact of the exposome is a concept of planetary health, and illuminating the exposures may contribute to understanding disease prevention [32]. This interdependence between human health and place brings us full-circle to early-life location-based exposures on pregnant mothers that may lead to really small newborns.

Mechanisms that trigger adverse birth outcomes, such as being born too small, among mothers exposed to hazards and pollutants are not well understood, but are suspected to include inflammation, direct toxic effects on the placenta and the fetus, interruption of oxygen-hemoglobin interaction, and damage to DNA [35–37]. Environmental associations differ among SGA and LBW, enhanced by temporal variations in exposures, personal characteristics (mothers' health, nutrition, and demographics) and external factors such as region and socioeconomic status (SES), [3,4,38].

Reviewing the published literature allows us to identify where information gaps exist, and also to determine whether the prevalence of the problem matches the number of existing published studies. This review serves to highlight environmental hazards, specifically, the shared exposures of the outdoor environment that have been associated with LBW and/or SGA newborns in Canada and the USA. Mapping the results will characterize where and how much LBW/SGA has been studied in the majority of industrialized North America and what and where the environmental factors are found to be important. The interested reader may use the maps as guides to what and where potential research gaps warrant further medical geographic inquiry.

2. Methods

2.1. Data Sources

Following the methodology proposed by Arksey and O'Malley [39], we searched bibliographic databases (PubMed, Web of Science, Scopus, Google Scholar, Taylor and Francis, and environmental health journal websites) to identify English-language, peer-reviewed, original research articles on outdoor environment and really small newborns. The Venn diagram in Figure 4 displays the search keywords that were used for the health outcome: (low) birth weight, small for gestational age; environmental variable: air pollution, agriculture (herbicide, pesticide, fertilizer), lead, mine, natural gas, road, traffic, (power) transmission, waste, water (contamination), socioeconomic, greenness; and any geographic extent within Canada or the USA (we read titles, abstracts and methods sections to ascertain the study country). We limited the study years to between 1990 (geographic-type analyses were rare prior) and 2018 (current year).

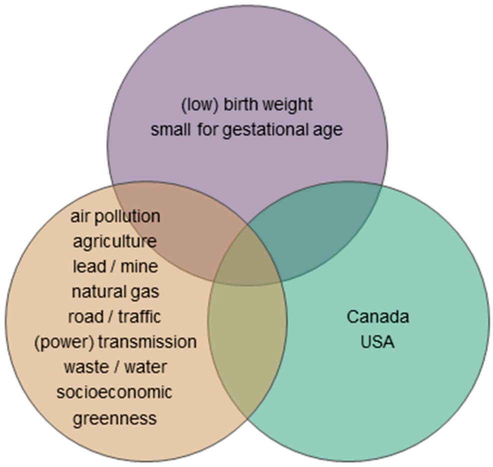


Figure 4. The keywords used in the literature search for studies associating outdoor environment and really small newborns are grouped by topic: health outcome (top), environmental variable (left), and geographic extent (right).

2.2. Study Selection and Data Extraction

We entered the articles with abstracts including both ABO and any environmental variable keywords in to Mendeley reference manager (www.mendeley.com), and tagged to identify 1 = North American and 2 = ABO. We read full articles that met the inclusion/exclusion criteria—must be Canada/USA, LBW/birth weight/SGA, and outdoor environment—and extracted the following data to a spreadsheet, formatted as the evidence table: year; study identifier; health outcome; detailed variable(s); and geography. To aid in mapping, we standardized the geography to the province or state level using the abbreviations shown in Appendix A (Table A1), regardless of whether the study was in a city, county/region, or larger administrative unit. We classified the variables in to general categories similar to the keywords, and then further generalized the environment as built, social, natural, or none. We summarized frequency statistics for the various studies. Then, we replicated records where there was more than one state or province involved in the study (e.g., a study on BC, Alberta, Manitoba, and Ontario [40] was copied to four rows in the table, one for each province) and generated a pivot table for each category or environment so that we could reliably map these for all locations.

2.3. Mapping

Using ArcGIS 10.6 [41], we joined the pivot table to the map of political boundaries provided by the Commission for Environmental Cooperation (CEC) [42] and created choropleth maps using four categories for the number of studies from all the selected articles—1, 2, 3, and 4 or more—labeled hereafter as frequency maps. We also mapped land use, pollution release transfer reporting (PRTR) industrial facilities [42], and satellite-based particulate matter [43]. To identify future research opportunities, these maps are compared with the 2005 and 2016 LBW percentages in Figure 2. Similarly, we visualized the frequency of studies on the built, natural, social environment, as well as those for studies related to air pollution, agriculture, chemical, vegetation, and individual factors.

3. Results and Discussion

The number of articles we selected for inclusion are documented in Figure 5. From the 159 included studies, associations were examined for built (n = 108), natural (n = 10), and social (n = 41) environmental variables.

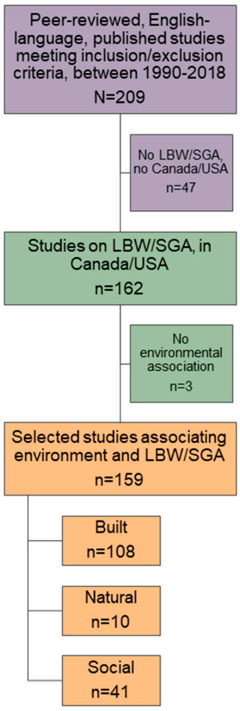


Figure 5. Flow diagram documenting the selection of published studies within Canada and the USA, between 1990 and 2018, for examining associations of the outdoor environment with low birth weight (LBW), birth weight (BW), and small for gestational age (SGA).

3.1. Outcomes and Variables

Table A2 lists all 159 studies selected for inclusion. The environmental hazards were identified as the following general categories of variables (from most-to-least frequent): air pollution (n = 53), SES (n = 17), chemical (n = 16), race (n = 11), individual (n = 10), water contamination (n = 9), waste site (n = 8), vegetation (n = 8), agriculture (n = 6), roads (n = 3), urban-rural (n = 3), food (n = 2), mining (n = 2), neighborhood (n = 2), weather (n = 2), immigration (n = 2), alcohol (n = 1), noise (n = 1), power (n = 1), transmission lines (n = 1), health care (n = 1). Note that we also included articles that studied birth weight (BW; n = 38) and intrauterine growth restriction (IUGR; n = 4) because they are interrelated with LBW (n = 72) and SGA (n = 27). There were also studies on both LBW and SGA (n = 18). Figure 6 shows how published research has increased over time from 1992 to 2018, with a peak in the year 2012. Individual states (n = 110) had more studies than Canadian provinces (n = 32), while all of USA (n = 8) and all of Canada (n = 8) were equal, with one study that included both countries.

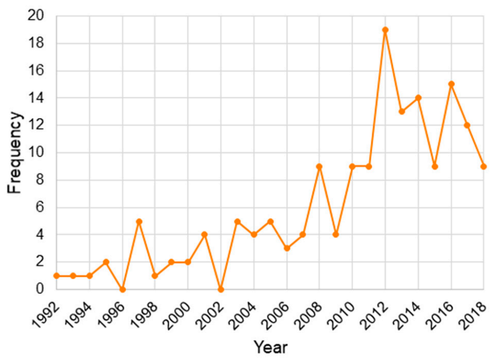


Figure 6. Yearly distribution of the selected studies, published on associations of the outdoor environment with low birth weight (LBW), birth weight, and small for gestational age (SGA), within Canada and the USA.

3.2. Spatial Associations

The following maps summarize findings from the included studies. Figure 7 maps locations and frequencies of the selected studies across North America; the distribution shows that LBW/SGA research has been conducted in six provinces and 41 states. Upon visually comparing Figure 7 with Figure 2 percentages, we observe that, despite the efforts, there are many regions with LBW and very low numbers of studies on the topic.

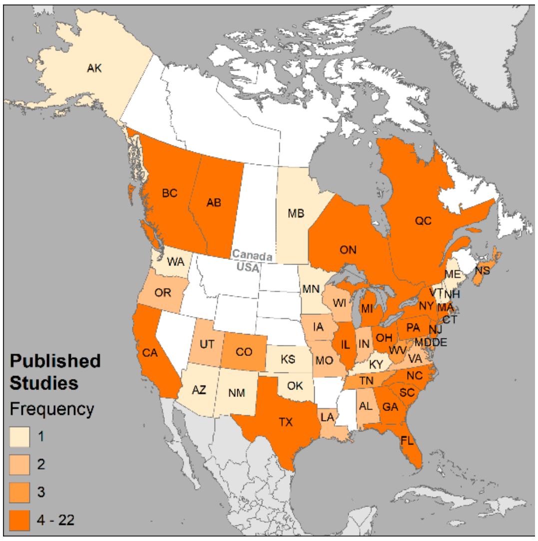
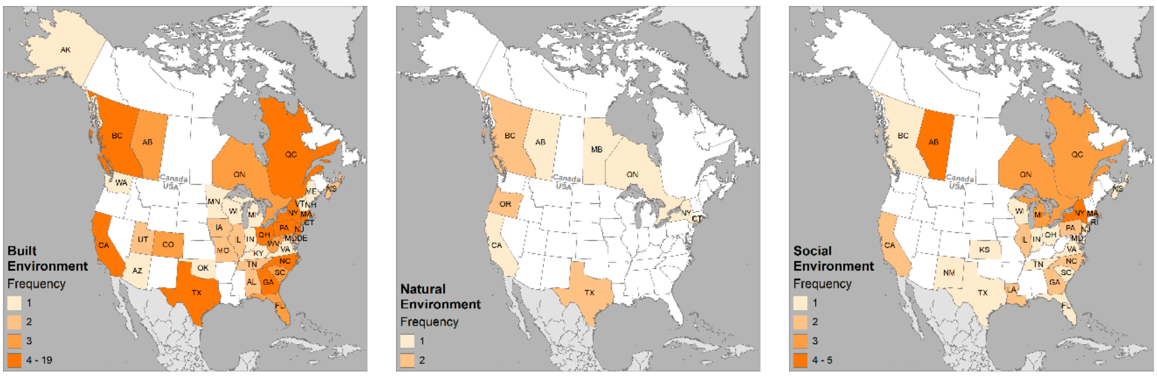


Figure 7. Geographic distribution and number of studies in provinces/states for the 159 candidate studies across Canada and the USA. Frequency classes standardized across all maps to intuit where the health issue is of interest (1), emerging (2), concern (3), or potential problem (4 or more).

The distributions of the types of environment (built, natural, and social) are shown in Figure 8. Figure 9 displays the most frequently studied categories.



(**a**) (**b**) (**c**)

Figure 8. Geographic distribution of published studies by environment: (**a**) built; (**b**) natural; and (**c**) social. Frequency classes standardized across all maps to intuit where the health issue is of interest (1), emerging (2), concern (3), or potential problem (4 or more).

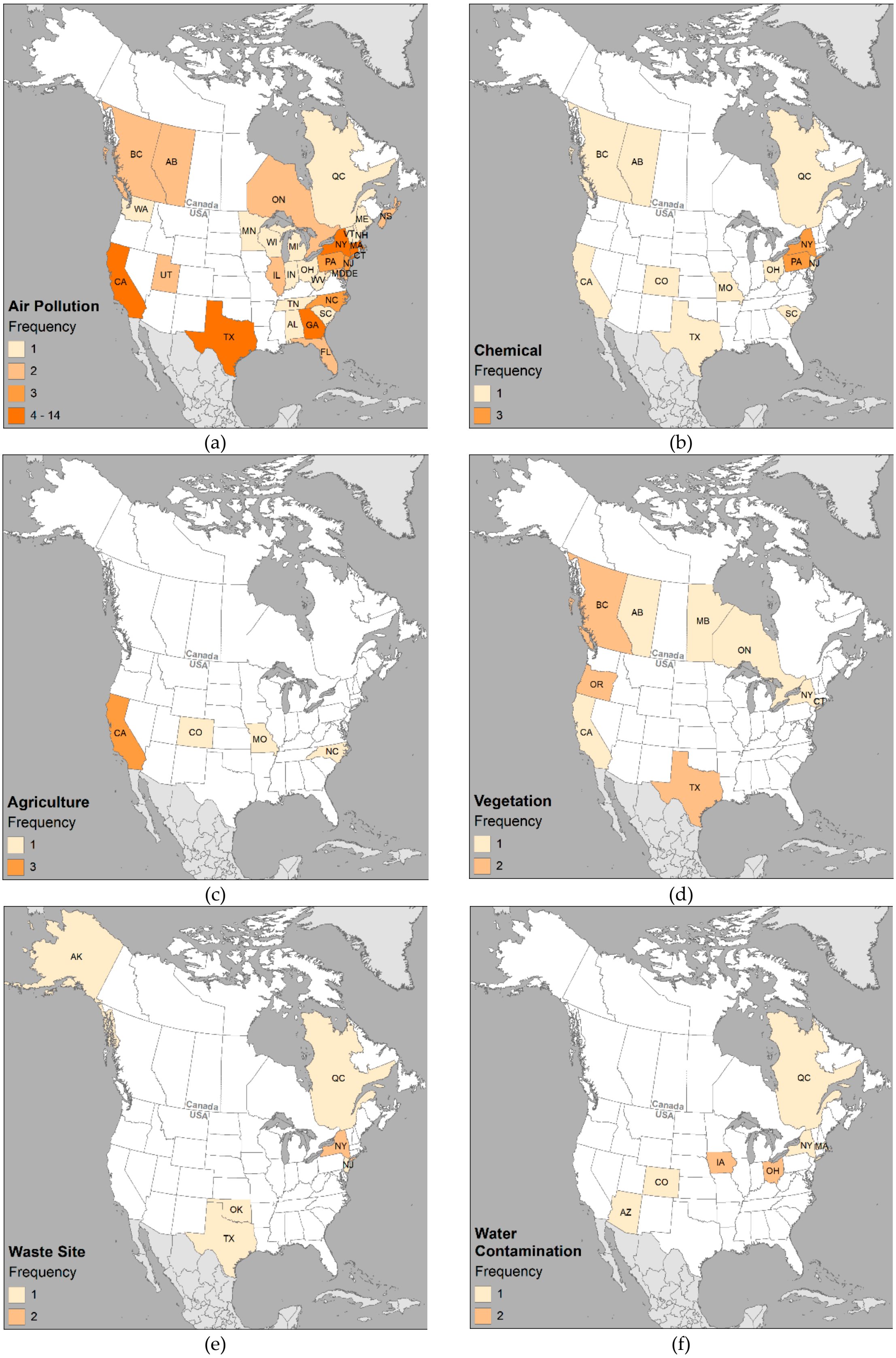
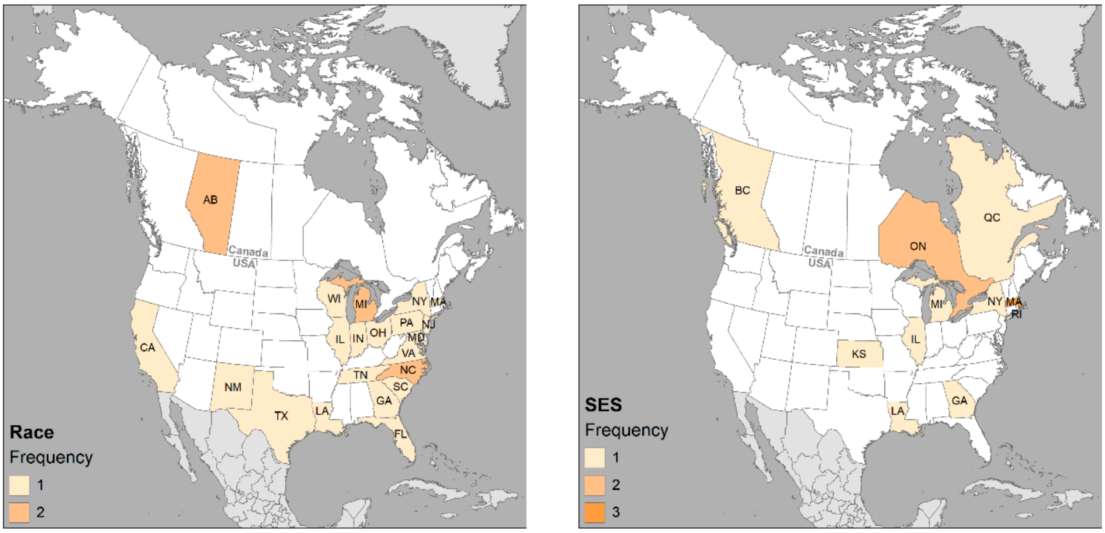


Figure 9. *Cont.*



(g) (h)

Figure 9. Geographic distribution of the most frequently published categories of (**a**) air pollution; (**b**) chemical; (**c**) agriculture; (**d**) vegetation; (**e**) waste site; (**f**) water contamination; (**g**) race; and (**h**) SES. Frequency classes standardized across all maps to intuit where the health issue is of interest (1), emerging (2), concern (3), or potential problem (4 or more).

For comparison purposes, the major land use classes, industrial facilities, and particulate matter distributions are mapped in Figure 10. Visual assessment highlights that the states and provinces having higher percentages of LBW in Figure 2 coincide with the same areas having relatively more proportions of urban, agriculture, industry, and $PM_{2.5}$. Inspection of the distribution of studies in Figure 7 through Figure 10 with Figure 4 shows there are clearly areas requiring future research, especially Canada's northern territories and the states bordering the Mississippi River.

3.3. Environmental Variables

The cumulative evidence suggested associations among outdoor environmental hazards and LBW/SGA in Canada and the USA. Most of the studies found that LBW/SGA varied with air pollution gases and/or particles depending on the trimester/gestation. Anthropogenic air pollution originates from industrial/traffic emissions and includes gaseous components—sulfur dioxide (SO_2), carbon monoxide (CO), nitrogen oxide (NO), nitrogen dioxide (NO_2), ozone (O_3)—and particulate matter (PM)—$PM_{2.5}$ particles with aerodynamic diameter $\leq$ 2.5 μm and PM_{10} particles $\leq$ 10 μm. Electromagnetic frequencies from powerlines was not found to be important, nor was proximity to gas stations, but proximity to roads and waste sites were. The strength of association in the studies varied greatly and had limitations due to sampling, spatial resolution, availability of confounding factors, and inability to quantify duration and intensity of exposures.

Many of the previous studies linked individual or small subsets of factors; however, all factors can be modelled as vertices of the triangle of human ecology, synthesizing the complex disease ecology and advancing hypotheses [27]. As Table A2 exemplifies, the majority of air pollutants under investigation consisted of traffic-related air contaminants. A handful of studies targeted agricultural activities, heavy metals and/or industrial activities. More research is needed on assessing the spatial relationships of the actual chemicals involved in those industrial activities, especially the known or suspected developmental toxicants. Similarly, the combined effect of multipollutant exposures are still relatively unknown. Water contamination was another challenging variable, and King et al. [44] stressed the importance of household rather than distribution system sampling, making it difficult to efficiently study at a population level. Socioeconomic inequalities in LBW showed strong associations, and was larger in the United States than Canada, likely due to differing health care systems [45].

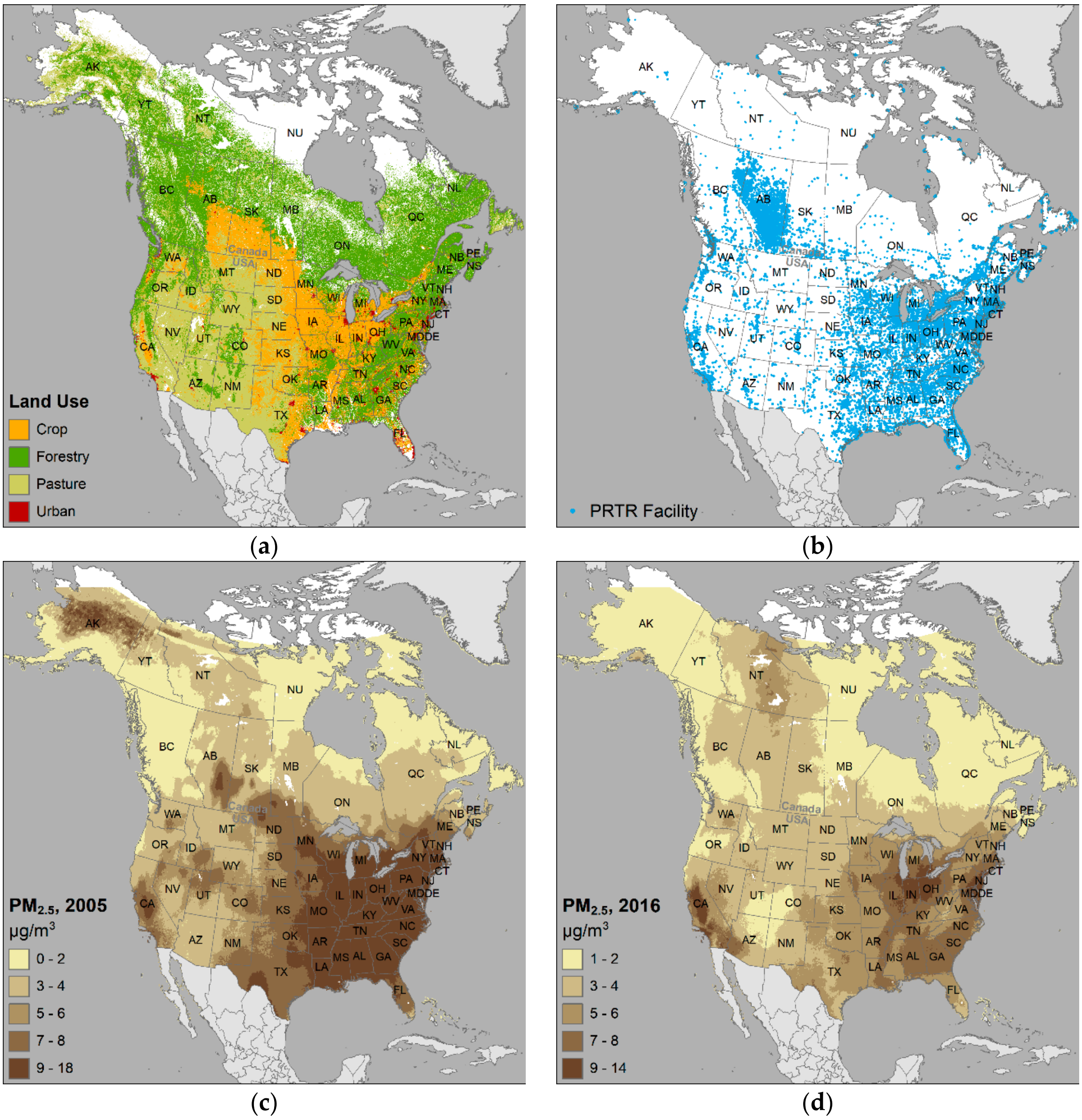


Figure 10. Selected environmental variables of interest in the SGA/LBW studies for Canada and USA of: (**a**) land use classes; (**b**) industrial facilities in pollutant release transfer reporting (PRTR); (**c**) common air pollutant – particulate matter particles with aerodynamic diameter $\leq$ 2.5 µm, ($PM_{2.5}$) for 2005; and (**d**) $PM_{2.5}$ for 2016.

3.4. Exposure Assessment

Note that only English-language, peer-reviewed journal articles were selected; other literature sources have not been included here. Missing publications in other languages causes a conceptual bias, as they contribute to the overall understanding of birth weight and the environment; here, the geographic attention provides an up-to-date review on the predominantly English-publishing countries of Canada and the USA. The focus on shared sources of exposures from the outdoor environment allowed the researchers to incorporate spatial methods (i.e., GIS) in their studies, which was advantageous, especially because they facilitated several steps in exposure assessment [46]. GIS can define epidemiologic study populations, identify source and potential routes of exposure, estimate environmental levels of target contaminants, and estimate personal exposure. The studies reviewed here applied the spatial methods of coincidence, proximity, and surface predictions to identify and estimate exposures at different scales. Postal code/zip code and county-level geography was helpful for understanding broad population patterns, but it will be worthwhile for future studies to analyze all scales with greater detail. Woodruff et al. [47] hypothesized that geographic scale was important in adverse birth outcome studies, proposing that smaller scales are useful to better understand biological mechanisms and apply to local policies, and larger scales are useful to look at population-level factors and apply to regional policy. For many of the studies, the proximity measures would benefit from increased resolution as well. An increasing number of studies are incorporating land-use regression modelling, a promising method for advancing the knowledge of exposures assessment. Analyses should also more fully integrate the socioeconomic and maternal/paternal factors, improve methods for quantifying duration and intensity of exposure, and adjust for residential mobility [35,48–50]. As previous non-spatial reviews have also stated, biological mechanisms still remain to be fully understood.

3.5. Protective Variables

Overall, the studies contribute to the evolving evidence that maternal exposure during pregnancy to varying levels of ambient air pollutants is associated with LBW/SGA. An interesting finding is the increase in studies on protective exposures, such as greenness—natural environments promote resiliency and prevent disease, further supporting the concept of planetary health.

4. Conclusions

We compiled previous spatial research on the outdoor environment and really small newborns, and through the use of maps, we presented the parameters that help with understanding how important the ambient environment is and the correspondingly valuable question of location. Such a spatially-focused review, to our knowledge, has not been seen in the literature, and we hope we have provided a useful framework for other countries to better understand environmental associations with the important global health issue of LBW and SGA newborns. North American researchers may consult these maps to aid in understanding their particular study areas.

It is hoped that our review and maps may assist healthcare professionals, in Hippocrates-style, by providing them with what location-based variables may be associated with their patients' health issues, as well as informing the public that where they live is as important to their current and future family health as what they eat and do. Our focus on environmental associations was not able to account for nutrition, maternal health, or occupation, but those studies conversely rarely accounted for outdoor exposures. Each contributes pieces to the exposome puzzle. Medical researchers are provided with more motivation for studying which components of outdoor environmental exposures may cause reduction in neonatal weight, a condition that, if prevented, will diminish future adverse health, such as adult cardiac disease, diabetes, and other non-communicable diseases that require a strong healthy start in life. Policy makers and planners (health, urban, transportation, industrial) may use this information for mitigating developments to reduce environmental effects on places where pregnant mothers (and everyone else) live. For example, existing land use may need to be altered over time depending on the proximity of industrial activities and residential areas.

May this research add to the many needed arguments for reducing the most widespread source of hazardous exposures—outdoor environmental pollution—in the places where one lives and starts out in life, to promote a more positive state of planetary health for all.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. Abbreviations for Canadian provinces and USA states.

Country	Province/State	Abbreviation
Canada	Alberta	AB
	British Columbia	BC
	Manitoba	MB
	New Brunswick	NB
	Newfoundland and Labrador	NL
	Northwest Territories	NT
	Nova Scotia	NS
	Nunavut	NU
	Ontario	ON
	Prince Edward Island	PE
	Quebec	QC
	Saskatchewan	SK
	Yukon Territory	YT
USA	Alabama	AL
	Alaska	AK
	Arizona	AZ
	Arkansas	AR
	California	CA
	Colorado	CO
	Connecticut	CT
	Delaware	DE
	District of Columbia	DC
	Florida	FL
	Georgia	GA
	Hawaii	HI
	Idaho	ID
	Illinois	IL
	Indiana	IN
	Iowa	IA
	Kansas	KS
	Kentucky	KY
	Louisiana	LA
	Maine	ME
	Maryland	MD
	Massachusetts	MA
	Michigan	MI
	Minnesota	MN
	Mississippi	MS
	Missouri	MO
	Montana	MT
	Nebraska	NE
	Nevada	NV
	New Hampshire	NH
	New Jersey	NJ
	New Mexico	NM
	New York	NY
	North Carolina	NC
	North Dakota	ND
	Ohio	OH
	Oklahoma	OK
	Oregon	OR
	Pennsylvania	PA
	Rhode Island	RI
	South Carolina	SC
	South Dakota	SD

Table A1. *Cont.*

Country	Province/State	Abbreviation
	Tennessee	TN
	Texas	TX
	Utah	UT
	Vermont	VT
	Virginia	VA
	Washington	WA
	West Virginia	WV
	Wisconsin	WI
	Wyoming	WY

Appendix B

Table A2. List of 159 identified studies examining birth outcomes and the environment.

Year	Study	Outcome [1]	Environment	Category	Variable(s)	Geography [2]
2000	Xiang et al. 2000 [51]	LBW	built	agriculture	crops	CO
2010	Fenster et al. 2010 [52]	LBW, BW	built	agriculture	agricultural occupation	CA
2010	Sathyanarayana et al. 2010 [53]	LBW	built	agriculture	pesticides	NC
2013	Gemmill et al. 2013 [54]	BW	built	agriculture	methyl bromide	CA
2014	Almberg et al. 2014 [55]	LBW	built	agriculture	crops	MO
2017	Larsen et al. 2017 [56]	BW	built	agriculture	pesticides	CA
1999	Ritz et al. 1999 [57]	LBW	built	air pollution	CO	CA
2000	Rogers et al. 2000 [58]	LBW	built	air pollution	SO_2, TSP	GA, SC
2001	Maisonet et al. 2001 [59]	LBW	built	air pollution	CO, SO_2, PM_{10}	CT, MA, PA, DC
2001	Vassilev et al. 2001 [60]	SGA	built	air pollution	polycyclic organic matter	NJ
2003	Liu et al. 2003 [61]	LBW, IUGR	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}	Canada
2004	Basu et al. 2004 [62]	BW	built	air pollution	$PM_{2.5}$	CA
2004	Lederman et al. 2004 [63]	BW	built	air pollution	urban disaster	NY
2005	Salam et al. 2005 [64]	LBW, IUGR	built	air pollution	CO, NO_2, O_3, PM_{10}	CA
2006	Dugandzic et al. 2006 [65]	LBW	built	air pollution	PM_{10}, SO_2, O_3	NS
2007	Bell et al. 2007 [66]	BW	built	air pollution	CO, NO_2, SO_2, PM_{10}, $PM_{2.5}$	CT, MA
2007	Liu et al. 2007 [67]	IUGR	built	air pollution	CO, NO_2, SO_2, O_3, $PM_{2.5}$	AB, QC
2007	Williams et al. 2007 [68]	BW	built	air pollution	Pb, SO_2	TN
2008	Brauer et al. 2008 [69]	LBW, SGA	built	air pollution	traffic	BC
2008	Choi et al. 2008 [70]	SGA	built	air pollution	PAHs	NY
2009	Currie et al. 2009 [71]	LBW	built	air pollution	industrial releases	USA
2010	Morello-Frosch et al. 2010 [72]	BW	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}, $PM_{2.5}$	CA
2011	Darrow et al. 2011 [73]	BW	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}, $PM_{2.5}$	GA
2012	Berrocal et al. 2012 [74]	BW	built	air pollution	$PM_{2.5}$	NC
2012	Ebisu et al. 2012 [75]	LBW	built	air pollution	$PM_{2.5}$	CT, DE, MD, MA, NH, NJ, NY, PA, RI, VT, VI, DC, WV
2012	Geer et al. 2012 [76]	BW	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}, $PM_{2.5}$	TX
2012	Ghosh et al. 2012 [77]	LBW	built	air pollution	traffic	CA
2012	Holstius et al. 2012 [78]	BW	built	air pollution	wildfires	CA
2012	Kloog et al. 2012 [79]	BW	built	air pollution	$PM_{2.5}$	MA
2012	Kumar et al. 2012 [80]	LBW	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}, $PM_{2.5}$	IL
2012	Le et al. 2012 [81]	SGA	built	air pollution	CO, NO_2, SO_2, O_3, PM_{10}	MI
2012	Padula et al. 2012 [82]	LBW	built	air pollution	traffic	CA
2012	Sathyanarayana et al. 2012 [83]	SGA	built	air pollution	NO_2, $PM_{2.5}$	WA

Table A2. *Cont.*

Year	Study	Outcome [1]	Environment	Category	Variable(s)	Geography [2]
2012	Wilhelm et al. 2012 [84]	LBW	built	air pollution	$PM_{2.5}$, NO, NO_2, PAHs	CA
2013	Lee et al. 2013 [85]	SGA	built	air pollution	PM_{10}, $PM_{2.5}$, O_3	PA
2013	Meng et al. 2013 [86]	LBW	built	air pollution	traffic	ON
2013	Trasande et al. 2013 [87]	LBW	built	air pollution	CO, NO_2, SO_2, PM_{10}, $PM_{2.5}$, Pb, VOCs	USA
2013	Warren et al. 2013 [88]	LBW	built	air pollution	O_3	TX
2014	Basu et al. 2014 [89]	LBW	built	air pollution	$PM_{2.5}$	CA
2014	Gray et al. 2014 [90]	BW	built	air pollution	PM_{10}, $PM_{2.5}$	NC
2014	Ha et al. 2014 [91]	LBW	built	air pollution	$PM_{2.5}$, O_3	FL
2014	Harris et al. 2014 [92]	LBW	built	air pollution	$PM_{2.5}$	CT, ME, MN, NJ, NY, UT, WI
2014	Hyder et al. 2014 [93]	LBW, SGA	built	air pollution	$PM_{2.5}$	CT, MA
2014	Porter et al. 2014 [94]	LBW	built	air pollution	industrial releases	AL
2014	Vinikoor-Imler et al. 2014 [95]	LBW, SGA	built	air pollution	$PM_{2.5}$, O_3	NC
2015	Coker et al. 2015 [96]	LBW	built	air pollution	$PM_{2.5}$	CA
2015	Poirier et al. 2015 [97]	LBW	built	air pollution	SO_2, NO_2, benzene, toluene, PM_{10}, $PM_{2.5}$	NS
2016	Coker et al. 2016 [98]	LBW	built	air pollution	NO, NO_2, $PM_{2.5}$	CA
2016	Erickson et al. 2016 [99]	BW	built	air pollution	$PM_{2.5}$, social	BC
2016	Laurent et al. 2016 [100]	LBW	built	air pollution	PM_{10}, $PM_{2.5}$	CA
2016	Lavigne et al. 2016 [101]	LBW, SGA	built	air pollution	$PM_{2.5}$, NO_2, O_3	ON
2016	Stieb et al. 2016 [102]	LBW, SGA, BW	built	air pollution	NO_2, $PM_{2.5}$	Canada
2016	Tu et al. 2016 [103]	BW	built	air pollution	O_3, $PM_{2.5}$	GA
2016	Twum et al. 2016 [104]	LBW	built	air pollution	$PM_{2.5}$	GA
2017	Ha et al. 2017 [105]	LBW, SGA	built	air pollution	11 criteria air contaminants and PM	CA, DC, DE, FL, UT, IL, IN, MA, MD, NY, OH, TX
2017	Jedrychowski et al. 2017 [106]	BW	built	air pollution	$PM_{2.5}$, PAH	NY
2017	Ng et al. 2017 [107]	LBW	built	air pollution	$PM_{2.5}$	CA
2017	Nielsen et al. 2017 [108]	LBW, SGA	built	air pollution	industrial releases, built	AB
2018	Gong et al. 2018 [109]	LBW	built	air pollution	industrial releases	TX
2018	Seabrook et al. 2018 [110]	LBW	built	alcohol	alcohol	ON
1992	Shaw et al. 1992 [111]	BW	built	chemical	chemical	CA
1997	Philion et al. 1997 [112]	SGA, IUGR	built	chemical	lead	BC
2004	Lawson et al. 2004 [113]	BW	built	chemical	occupational TCDD	NJ, MO
2005	Perera et al. 2005 [114]	BW	built	chemical	ETS, PAH, pesticides	NY
2008	Wolff et al. 2008 [115]	BW	built	chemical	phenols, phthalates	NY
2010	Hamm et al. 2010 [116]	BW	built	chemical	perfluorinated acids	AB
2010	Zhu et al. 2010 [117]	BW	built	chemical	metals: Pb	NY

Table A2. *Cont.*

Year	Study	Outcome [1]	Environment	Category	Variable(s)	Geography [2]
2012	Aelion et al. 2012 [118]	BW	built	chemical	metals: As, Pb	SC
2012	Rauch et al. 2012 [119]	BW	built	chemical	pesticides	OH
2014	Mckenzie et al. 2014 [120]	LBW	built	chemical	natural gas	CO
2015	Stacy et al. 2015 [121]	SGA, BW	built	chemical	natural gas	PA
2015	Thomas et al. 2015 [122]	SGA	built	chemical	metals: Pb, Hg, Cd, As	Canada
2016	Casey et al. 2016 [123]	SGA, BW	built	chemical	natural gas	PA
2017	Whitworth et al. 2017 [124]	SGA, BW	built	chemical	natural gas	TX
2018	Ashley-Martin et al. 2018 [125]	BW	built	chemical	metals: Mn	QC
2018	Hill et al. 2018 [126]	SGA	built	chemical	natural gas	PA
2008	Lane et al. 2008 [127]	LBW	built	food	food, social	NY
2016	Ma et al. 2016 [128]	LBW, BW	built	food	food	SC
2011	Ahern et al. 2011 [129]	LBW	built	mining	coal	WV
2017	Ferdosi et al. 2017 [130]	SGA	built	mining	coal	KY, TN, VA, WV
2011	Vinikoor-Imler et al. 2011 [131]	LBW	built	neighborhood	neighborhood	NC
2012	Miranda et al. 2012 [132]	LBW, SGA	built	neighborhood	neighborhood	NC
2014	Gehring et al. 2014 [133]	LBW, BW	built	noise	noise, traffic	BC
2015	Ha et al. 2015 [134]	LBW	built	power	power plants	FL
2003	Wilhelm et al. 2003 [135]	LBW	built	roads	roads	CA
2008	Généreux et al. 2008 [136]	LBW, SGA	built	roads	roads, social	QC
2012	Miranda et al. 2012 [137]	LBW, SGA	built	roads	roads	NC
2011	Auger et al. 2011 [138]	LBW, SGA	built	transmission lines	transmission lines	QC
1997	Larson et al. 1997 [139]	LBW	built	urban-rural	urban	USA
2009	Auger et al. 2009 [140]	LBW, SGA	built	urban-rural	urban, social	QC
2013	Kent et al. 2013 [141]	LBW	built	urban-rural	urban, social	AL
1994	Sosniak et al. 1994 [142]	LBW	built	waste site	waste site	USA
1995	Goldberg et al. 1995 [143]	LBW, SGA	built	waste site	waste site	QC
1997	Berry et al. 1997 [144]	BW	built	waste site	waste site	NJ
2003	Baibergenova et al. 2003 [145]	LBW	built	waste site	waste site	NY
2006	Gilbreath et al. 2006 [146]	LBW, IUGR	built	waste site	waste site	AK
2011	Austin et al. 2011 [147]	LBW	built	waste site	waste site	NY
2014	Thompson et al. 2014 [148]	LBW	built	waste site	waste site	TX
2016	Claus et al. Henn et al. 2016 [149]	BW	built	waste site	waste site	OK
1997	Munger et al. 1997 [150]	IUGR	built	water contamination	herbicides	IA
1998	Gallagher et al. 1998 [151]	LBW	built	water contamination	trihalmethanes	CO
2005	Hinckley et al. 2005 [152]	LBW, IUGR	built	water contamination	trihalomethane, haloacetic acid	AZ
2008	Aschengrau et al. 2008 [153]	BW	built	water contamination	tetrachloroethylene	MA

Table A2. *Cont.*

Year	Study	Outcome [1]	Environment	Category	Variable(s)	Geography [2]
2009	Ochoa-Acuña et al. 2009 [154]	SGA	built	water contamination	herbicides	IA
2012	Forand et al. 2012 [155]	LBW	built	water contamination	tetrachloroethylene and trichloroethylene	NY
2012	Savitz et al. 2012 [156]	LBW, SGA	built	water contamination	perfluorooctanoic acid	OH
2013	Darrow et al. 2013 [157]	LBW, BW	built	water contamination	perfluorooctanoic acid and perfluorooctane sulfonate	OH
2015	Ileka-Priouzeau et al. 2015 [158]	SGA	built	water contamination	haloacetaldehydes, haloacetonitriles	QC
2011	Donovan et al. 2011 [159]	SGA	natural	vegetation	greenness	OR
2013	Laurent et al. 2013 [160]	BW	natural	vegetation	greenness	CA
2014	Hystad et al. 2014 [161]	SGA, BW	natural	vegetation	greenness	BC
2016	Ebisu et al. 2016 [162]	LBW, SGA, BW	natural	vegetation	greenness, built: urban	CT
2017	Abelt et al. 2017 [163]	LBW, SGA, BW	natural	vegetation	greenness, blue space	NY
2017	Cusack et al. 2017 [164]	SGA, BW	natural	vegetation	greenness	TX
2017	Cusack et al. 2017 [165]	BW	natural	vegetation	greenness	OR, TX
2018	Cusack et al. 2018 [40]	BW	natural	vegetation	greenness	BC, AB, MB, ON
2012	Lin et al. 2012 [166]	BW	natural	weather	extreme weather	USA
2014	Thayer et al. 2014 [167]	LBW	natural	weather	UV-vitamin D, social: race	USA
2016	Savard et al. 2016 [168]	SGA	social	health care	health care	QC
2010	Urquia et al. 2010 [169]	BW	social	immigration	immigration	ON
2011	Janevic et al. 2011 [170]	SGA	social	immigration	immigration	NY
1995	Mclafferty et al. 1995 [171]	LBW	social	individual	social	NY
2001	Tough et al. 2001 [172]	LBW	social	individual	maternal health	AB
2003	English et al. 2003 [173]	LBW	social	individual	maternal health	CA
2005	Lasker et al. 2005 [18]	LBW	social	individual	maternal health	PA
2008	Grady et al. 2008 [174]	LBW	social	individual	maternal health	NY
2013	Heaman et al. 2013 [175]	SGA	social	individual	maternal health	Canada
2014	Aris et al. 2014 [176]	LBW, IUGR	social	individual	endometriosis	QC
2015	Chen et al. 2015 [177]	LBW, SGA	social	individual	interpregnancy interval	AB
2016	Shapiro et al. 2016 [178]	SGA	social	individual	individual	Canada
2018	Jain et al. 2018 [179]	SGA	social	individual	maternal health	NS
1999	Gorman et al. 1999 [180]	LBW	social	race	race	USA
2004	Wenman et al. 2004 [181]	LBW	social	race	race	AB
2008	Vinikoor et al. 2008 [182]	LBW	social	race	race	NC
2009	Reichman et al. 2009 [183]	BW	social	race	race	CA, TX, MD, MI, NJ, PA, VA, IN, WI, NY, MA, TN, IL, FL, OH, NM
2010	Grady et al. 2010 [184]	IUGR	social	race	race	MI

Table A2. *Cont.*

Year	Study	Outcome [1]	Environment	Category	Variable(s)	Geography [2]
2010	Nepomnyaschy et al. 2010 [185]	LBW	social	race	race	USA
2011	Anthopolos et al. 2011 [186]	LBW, BW	social	race	race	NC
2011	Kirby et al. 2011 [187]	LBW	social	race	race	GA, SC
2013	Wallace et al. 2013 [188]	LBW	social	race	race	LA
2016	Oster et al. 2016 [189]	LBW	social	race	race	AB
2018	Shapiro et al. 2018 [190]	SGA	social	race	race	Canada
1993	Kieffer et al. 1993 [191]	LBW	social	SES	SES	HI
2003	Krieger et al. 2003 [192]	LBW	social	SES	SES, blood Pb	MA, RI
2006	Farley et al. 2006 [193]	IUGR	social	SES	SES	LA
2007	Masi et al. 2007 [194]	BW	social	SES	SES, built	IL
2008	Zeka et al. 2008 [195]	SGA, BW	social	SES	SES, built	MA
2010	Young et al. 2010 [196]	BW	social	SES	SES	MA
2012	Tu et al. 2012 [197]	BW	social	SES	SES	GA
2013	Auger et al. 2013 [198]	SGA	social	SES	SES	QC
2013	Legerski et al. 2013 [199]	LBW	social	SES	SES	KS
2013	Meng et al. 2013 [200]	LBW	social	SES	SES	ON
2015	Chan et al. 2015 [201]	LBW, SGA	social	SES	SES	Canada
2015	Shmool et al. 2015 [202]	BW	social	SES	SES, NO_2	NY
2016	Martinson et al. 2016 [45]	LBW	social	SES	SES	Canada, USA
2017	Bushnik et al. 2017 [203]	SGA	social	SES	SES	Canada
2017	MacQuillan et al. 2017 [204]	LBW	social	SES	SES	MI
2018	Campbell et al. 2018 [205]	LBW	social	SES	SES	ON
2018	McRae et al. 2018 [206]	SGA	social	SES	SES	BC

[1] Outcomes included low birth weight (LBW), small for gestational age (SGA), birth weight (BW), and intrauterine growth restriction (IUGR). [2] Geography abbreviations are detailed in Table A1.

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