The effects of outdoor air pollution on the respiratory health of Canadian children: A systematic review of epidemiological studies

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BACKGROUND: Outdoor air pollution is a global problem with serious effects on human health, and children are considered to be highly susceptible to the effects of air pollution.

OBJECTIVE: To conduct a comprehensive and updated systematic review of the literature reporting the effects of outdoor air pollution on the respiratory health of children in Canada.

METHODS: Searches of four electronic databases between January 2004 and November 2014 were conducted to identify epidemiological studies evaluating the effect of exposure to outdoor air pollutants on children's respiratory symptoms, lung function measurements, and the use of health services due to respiratory conditions in Canadian children. The selection process and quality assessment, using the Newcastle-Ottawa Scale, were conducted independently by two reviewers.

RESULTS: Twenty-seven studies that were heterogeneous with regard to study design, population, respiratory outcome and air pollution exposure were identified. Overall, the included studies reported adverse effects of outdoor air pollution at concentrations that were below Canadian and United States standards. Heterogeneous effects of air pollutants were reported according to city, sex, socioeconomic status, and seasonality. The present review also describes trends in research related to the effect of air pollution on Canadian children over the past 25 years.

CONCLUSION: The present study reconfirms the adverse effects of outdoor air pollution on the respiratory health of children in Canada. It will help researchers, clinicians, and environmental health authorities identify the available evidence of the adverse effect of outdoor air pollution, research gaps, and the limitations for further research.

Key Words: Air pollution; Asthma; Children; Health effects; Respiratory tract diseases

Outdoor air pollution is a global problem with serious effects on human health (1). In fact, it has been estimated that in 2011, approximately 80% of the world’s population was exposed to air pollution levels that exceeded WHO guidelines (2,3). Air pollution is a complex mixture of compounds that vary greatly depending on the emission sources. Typically, the so-called criteria air pollutants (CAP, which include particulate matter [PM], ozone [O₃], lead [Pb], carbon monoxide [CO], sulphur oxides [SOx] and nitrogen oxides [NOx]), are monitored in surveillance air-quality networks. Interestingly, PM itself represents a complex mixture of particles of various sizes and concentrations of soil, metals, organics, inorganics, elemental carbon, ions and endotoxins, among other contaminants (4). Recently, the PM2.5 (PM size ≤2.5 μm in aerodynamic diameter) has been the focus of most outdoor air pollution and health studies due to its ability to penetrate the lung tissue and induce local and systemic effects (4).

Based on findings for lung and bladder cancer, the International Agency for Research on Cancer recently classified outdoor air pollution, as a whole, as a group 1 carcinogen (5). In addition, well-documented associations exist between outdoor air pollution and other health conditions including asthma, cardiovascular diseases, respiratory infections, adverse birth outcomes and additional cancers, such as leukemia (1,6,7). Children are considered to be highly susceptible to the effects of air pollution due to the immaturity of their immune system, the potential for developmental disruption, greater amount of time spent outdoors and, therefore, higher exposure levels, and a relatively high volume of air exchange relative to body mass (8,9). In fact, outdoor air pollution consistently shows an adverse effect on childhood respiratory health, especially on asthma outcomes, with a total estimated health care cost (among 34 countries, including Canada) of approximately US$1.7 trillion in 2010 (10,11).

Asthma is one of the top 10 causes of years lost due to disability in male children worldwide (12). The effects of outdoor air pollution on asthma and other respiratory conditions have been the subject of study involving many adult and children populations in Canada and...
Air pollution and children’s respiratory health

METHODS
An a priori systematic literature review protocol was developed. The research question addressed in the present review was: what is the effect of outdoor air pollution exposure on respiratory conditions in Canadian children? Respiratory conditions included respiratory symptoms, lung function measurements and the use of health services due to respiratory disease.

Search strategy
To increase sensitivity, the search strategy used in the previous review (16) was modified. Specifically, four electronic bibliographic databases (MEDLINE, CINAHL, Scopus and CAB abstracts) were searched (Appendix 1). In general, databases were searched with a combination of terms and derived key words including variation to the following basic terms: “air pollution”, “outdoor air pollution”, “asthma”, “respiratory disorders”, “respiratory health”, “respiratory symptoms”, “child”, “adolescent”, “youth” and “Canada”. In the MEDLINE search, the names of 16 specific Canadian cities were included to increase search sensitivity. The search strategy was not restricted by language or publication type. A Google Scholar web search was conducted and references of relevant studies were scanned and selected as a complementary search strategy.

Study selection and data extraction
The criteria for selecting studies included: any observational analytic studies were scanned and selected as a complementary search strategy. Google Scholar web search was conducted and references of relevant studies were scanned and selected as a complementary search strategy. The search strategy was not restricted by language or publication type. To increase sensitivity, the search strategy used in the previous review, identify new findings on types of associations between air pollutants and childhood respiratory health, and evaluate differences in those associations across Canadian cities.

Quality assessment
Study quality was assessed using the Newcastle-Ottawa Scale (NOS), which uses an eight-item rating system to evaluate the method of selection of participants, the exposure/outcome assessment, and comparability among study groups (17). Comparability was evaluated by controlling for potential confounders in terms of study design and the type of health effects under evaluation. The Cochrane Non-Randomized Studies Methods Working Group recommends the use of the NOS, although the study of its psychometric properties remains in progress (18). The NOS quality scores range from 0 to 9 (0 to 4 = poor quality; 5 to 7 = moderate quality; 8 to 9 = high quality). The NOS has specific formats for cohort and case-control studies only. The cohort study form was used to evaluate noncohort longitudinal studies and the case control form to evaluate case-crossover and cross-sectional studies. Two reviewers (LR-V and AM) independently performed the quality assessment of the included studies and disagreements were discussed and resolved by consensus.

RESULTS
The present review follows the PRISMA recommendations (19). As indicated in Figure 1, the systematic search identified 162 studies. After removing duplicates, initial screening with inclusion/exclusion criteria and full-text review, 27 studies were included. Studies were excluded for a variety of reasons, primarily because they did not report results on Canadian children. Reviewer agreement was substantial for identifying potentially relevant studies (disagreement 22%; \(\kappa = 0.73\) [95% CI 0.70 to 0.75]) and excellent for identifying included/excluded studies in full-text review (\(\kappa = 0.91\) [95% CI 0.78 to 1.00]).

Search results
The present review follows the PRISMA recommendations (19). As indicated in Figure 1, the systematic search identified 162 studies. After removing duplicates, initial screening with inclusion/exclusion criteria and full-text review, 27 studies were included. Studies were excluded for a variety of reasons, primarily because they did not report results on Canadian children. Reviewer agreement was substantial for identifying potentially relevant studies (disagreement 22%; \(\kappa = 0.73\) [95% CI 0.70 to 0.75]) and excellent for identifying included/excluded studies in full-text review (\(\kappa = 0.91\) [95% CI 0.78 to 1.00]).

Study characteristics
The 27 studies that met the selection criteria varied in design, study location, number and type of air pollutants considered, age of children, population and respiratory outcome. Tables 1 and 2 summarize the main characteristics and results of the individual studies grouped according to respiratory outcome examined (20-46).

Fifteen of the 27 studies included data from Ontario (20,21,24,26,27,29,31,32,35-39,42,44), five used British Columbia (BC) data (22,23,30,34,46), four used Quebec data (28,33,40,41),...
## TABLE 1
Characteristics and results of included studies with health services use outcomes

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<tr>
<th>Reference; study location; and study period</th>
<th>Study design; study population and size</th>
<th>Pollutants (mean or median levels*) and methods assessing exposure</th>
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<tr>
<td>Lin et al, 2004 (34); Vancouver; 1987–1998</td>
<td>Time series study; hospitalizations of 6–12 year olds; from BC Link Health Dataset (n=3822)</td>
<td>Mean PM$<em>{10}$ (20.41), PM$</em>{2.5}$ (9.59), NO$<em>{2}$ (10.86), CO (1160), SO$</em>{2}$ (4.73), NO$<em>{2}$ (24.54), O$</em>{3}$ (38.06); from monitoring stations</td>
<td>Hospitalizations for respiratory disease (including asthma)</td>
<td>Time Series RR: NO$<em>{2}$: male: 17.7% (95% CI 10.2–25.6), NO$</em>{2}$: boys 1.15 (95% CI 1.02–1.3), girls 1.18 (95% CI 1.01–1.36); PM$<em>{10}$: boys 1.25 (95% CI 1.01–1.54); NO$</em>{2}$: girls 1.31 (95% CI 1.05–1.63); PM$<em>{2.5}$: O$</em>{3}$ and SO$_{2}$ showed no associations</td>
<td>Sex, temperature, pollutant interactions and seasonality</td>
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<tr>
<td>Yang et al, 2004 (46); Greater Vancouver; 1995–1999</td>
<td>Case-crossover, case-control and time-series analyses; first hospital admissions of 0–3 year olds, excluding birth-related admissions (n=1610)</td>
<td>Mean NO$<em>{2}$ (38.9), SO$</em>{2}$ (27.5), CO (1300), PM$_{10}$ (50.6), TRS (8), and coefficient of haze (0.5); from monitoring stations</td>
<td>Hospitalizations for respiratory infections</td>
<td>Time Series RR: NO$<em>{2}$: female 2-day lag: 1.19 (95% CI 1.002–1.411); SO$</em>{2}$: female Current-Day: 1.11 (95% CI 1.011–1.221); CO: female 2-day lag: 1.07 (95% CI 1.001–1.139); Cross-over design OR: CO: female current day, 2-day lag and 3-day lag: 1.15 (95% CI 1.006–1.307), 1.19 (95% CI 1.020–1.379) and 1.22 (95% CI 1.022–1.459)</td>
<td>Temperature, sex, humidity, barometric pressure, seasonality</td>
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<td>Lin et al, 2005 (35); Toronto; 1998–2001</td>
<td>Case-crossover design; hospitalizations of 0–14 year olds (n=6782)</td>
<td>Mean NO$<em>{2}$ (21.8), SO$</em>{2}$ (4.3), CO (1.0), O$<em>{3}$ (17.0), and PM$</em>{10}$ (NS); from monitoring stations (population weighted average)</td>
<td>Hospitalizations for respiratory disease</td>
<td>The percentage of variation for IQR increase for all gases combined was 9.61% (95% CI 4.52–14.7); individually: O$<em>{3}$: 2.67 (95% CI 0.98–4.39); NO$</em>{2}$: 4.52–14.7); individually: NO$<em>{2}$: 4.52–14.7); O$</em>{3}$: 1.10 (95% CI 1.05–1.15); PM$_{10}$: 1.14 (95% CI 1.06–1.22); many of the 1- and 3-day lags were also significant during the warm season for various pollutants</td>
<td>Long-term temporal trends, day of the week, weather variables, other gases and PM$_{10}$</td>
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<td>Luginaah et al, 2005 (37); Windsor; 1995–2000</td>
<td>Time series and case-crossover design; hospitalizations of 0–14 year olds (n=1692)</td>
<td>Mean NO$<em>{2}$ (38.9), SO$</em>{2}$ (27.5), CO (1300), PM$_{10}$ (50.6), TRS (8), and coefficient of haze (0.5); from monitoring stations</td>
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<td>Dales et al, 2006 (25); 11 of the largest Canadian cities; 1986–2000</td>
<td>Time series study; hospitalizations of 0–27 day olds (n=8586)</td>
<td>Mean NO$<em>{2}$ (21.8), SO$</em>{2}$ (4.3), CO (1.0), O$<em>{3}$ (17.0), and PM$</em>{10}$ (NS); from monitoring stations (population weighted average)</td>
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<td>Villeneuve et al, 2007 (45); Edmonton; 1992–2002</td>
<td>Case-crossover design (time stratified); ED visits of 2–14 year olds (n=20,392)</td>
<td>Summer/ winter median PM$<em>{10}$ (22.0/19.0), PM$</em>{2.5}$ (7.0/7.3), CO (600/900), SO$<em>{2}$ (2.3/3.0), NO$</em>{2}$ (17.5/28.5), O$_{3}$ (38.0/24.3); from monitoring stations</td>
<td>ED visits for asthma</td>
<td>Positive association were observed in warm season and higher in 2–4 years: OR 5-day average: NO$<em>{2}$: 1.50 (95% CI 1.31–1.71); CO: 1.48 (95% CI 1.27–1.72); PM$</em>{10}$: 1.16 (95% CI 1.04–1.28) and PM$<em>{2.5}$: 1.16 (95% CI 1.05–1.28); For 5–14 years: OR 5-day average: NO$</em>{2}$: 1.13 (95% CI 1.02–1.24), O$<em>{3}$: 1.14 (95% CI 1.05–1.24), PM$</em>{10}$: 1.10 (95% CI 1.02–1.17), PM$_{2.5}$: 1.14 (95% CI 1.06–1.22); many of the 1- and 3-day lags were also significant during the warm season for various pollutants</td>
<td>Temperature, relative humidity, season, aeroallergens, and ED visits for influenza</td>
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<td>Szymczokicz et al, 2008 (43); Edmonton; 1992–2002</td>
<td>Longitudinal study; 0–10 years ED visits (n=18,891)</td>
<td>Mean/median CO (700/600), NO$<em>{2}$ (21.9/19.7), SO$</em>{2}$ (2.6/2.2), O$<em>{3}$ (18.6/17.8), PM$</em>{10}$ (22.6/19.4), PM$_{2.5}$ (8.6/6.2); from monitoring stations</td>
<td>ED visits for asthma</td>
<td>Many positive associations were observed in the warm season; the higher percentage increase for each pollutant was: CO (2-day lag) male: 17.7% (95% CI 10.2–25.6), NO$<em>{2}$ (2-day lag) male: 19.2% (95% CI 11.4–27.6), O$</em>{3}$ (same day) female: 17.8% (95% CI 7.1–29.5), PM$<em>{10}$ (2-day lag) male: 7.4% (95% CI 3.1–11.9), PM$</em>{2.5}$ (same-day) female: 7.7% (95% CI 5.2–10.3), O$<em>{3}$ (1-day lag), PM$</em>{10}$ (same-day), and PM$_{2.5}$ (2-day lag) showed positive variations for some age/sex/season combinations</td>
<td>Sex, temperature, relative humidity, day of the week</td>
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<td>Burra et al, 2009 (20); Toronto; 1992–2001</td>
<td>Longitudinal study; family physician and specialists service claim records for 1–17 year olds (n=1,146,215)</td>
<td>Mean SO$<em>{2}$ (9.7), NO$</em>{2}$ (39.2), O$<em>{3}$ (33.3) and PM$</em>{2.5}$ (17.9); from monitoring stations</td>
<td>Asthma physician visits</td>
<td>RR for pollutants by SES quintiles (Q1/Q5) were: SO$<em>{2}$: 1.005 (95% CI 1.000–1.010), NO$</em>{2}$: 1.002 (95% CI 0.995–1.008), and PM$<em>{2.5}$: 1.006 (95% CI 0.997–1.015); low SES groups had higher RR in SO$</em>{2}$ and PM$_{2.5}$ models</td>
<td>SES, temperature, barometric pressure, 24 h mean relative humidity, day of the week</td>
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<td>Smargiassi et al, 2009 (41); Montreal (Quebec); 1996-2004</td>
<td>Case-crossover design (time stratified); 2–4 year olds living near a refinery (n=1579)</td>
<td>Daily peak mean SO$_2$ (east/southwest of refineries) using monitoring stations (23.8/12.8) and AERMOD dispersion model (19.2/16.0)</td>
<td>Asthma ED visits or hospital admissions</td>
<td>OR for same-day ED visits: 1.10 (95% CI 1.00–1.22), and hospital admissions: 1.42 (95% CI 1.10–1.82)</td>
<td>Temperature, relative humidity, regional/ background air pollutant levels</td>
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<tr>
<td>Henderson et al, 2011 (30); Southeast corner of BC 92 days: July to September 2003</td>
<td>Cohort study; Residents at the southeast area of BC with a reliable geocodable residential address in health databases; included newborns (n=281,711; 21.6% &lt;20 years old)</td>
<td>Mean PM$_{10}$ during days of smoke coverage from forest fires; Comparison of two methods: TEOM monitoring stations (45.9); and CALPUFF dispersion model (44.2)</td>
<td>Respiratory or cardiovascular physician visits and hospital admissions</td>
<td>OR change due to 10 μg/m$^3$ increase in total PM$_{10}$ (TEOM) in respiratory hospital admissions: 1.05 (95% CI 1.00–1.10), and cardiovascular admissions: 1.00 (95% CI 0.96–1.05)</td>
<td>Age, sex, SES</td>
</tr>
<tr>
<td>Lavigne et al, 2012 (32); Windsor (Ontario); 2002-2009</td>
<td>Case-crossover design (time stratified); 2–14 year olds hospitalized for asthma (n=3728)</td>
<td>Mean summer/winter SO$_2$ (2.1/1.7), NO$<em>2$ (9.8/7.4), CO (400/300), PM$</em>{2.5}$(7.1/7.4), O$_3$ (13.2/8.0); from monitoring stations</td>
<td>Asthma ED visits</td>
<td>Increased risk of warm season asthma ED visit of 19%, 25% and 36% associated with increases in IQR of 1-day lagged exposure to SO$_2$, NO$_2$ and CO levels, respectively</td>
<td>Daily number of influenza ED visits, temperature and relative humidity.</td>
</tr>
<tr>
<td>Lewin et al, 2013 (33); Shawinigan (Québec); 1999-2008</td>
<td>Case-crossover design (time stratified); hospitalized 0–4 year olds living near aluminium smelter (n=396)</td>
<td>Exposure calculated by: % of hours/day each residence was downwind of the smelter; and daily mean SO$<em>2$ (6.3) and PM$</em>{2.5}$ (13.5) from monitoring station</td>
<td>Hospitalization for asthma or bronchiolitis</td>
<td>OR of hours downwind of a smelter on same-day hospitalization of 2–4-year-old children: 1.27 (95% CI 1.03–1.56), and PM$_{2.5}$ exposure: 1.22 (95% CI 1.03–1.11)</td>
<td>Average daily wind direction and speed</td>
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<tr>
<td>To et al, 2013 (44); Ontario; 2003-2006</td>
<td>Longitudinal study; All Ontario residents with asthma registered at the OASIS database</td>
<td>Canada 2003/2004/2005/2006 mean AQHI; (3.87/3.64/3.83/3.34), NO$_2$ (NS), O$<em>3$ (NS), and PM$</em>{2.5}$ (NS) measures; from monitoring stations</td>
<td>Asthma-attributed hospitalizations, ED and outpatient visits</td>
<td>RR for 1-unit increase in the AQHI by same-day outpatient visits: 1.056 (95% CI 1.053–1.058), and 2-day lag ED visits: 1.013 (95% CI 1.010–1.017)</td>
<td>Age group, season, residence area, and year</td>
</tr>
<tr>
<td>Szyszkowicz et al, 2014 (42); Windsor (Ontario); 2004-2010</td>
<td>Case-crossover design (time stratified); ED visits for 2–14 year olds; (n=2151)</td>
<td>AQHI for Canada; hourly AQHI calculations, NO$_2$, O$<em>3$, and PM$</em>{2.5}$ measures from two monitoring stations</td>
<td>Asthma ED visits</td>
<td>Positive and statistically significant associations were observed for same-day and 9-day lag exposure (both OR 1.11 [95% CI 1.01–1.21]) and 3-day lag exposure (OR 1.09 [95% CI 1.00–1.18])</td>
<td>Ambient temperature, relative humidity and daily counts of ED visits for influenza</td>
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*Parts per billion for gasses, μg/m$^3$ for particulate matter (PM); AQHI Air Quality Health Index; BC British Columbia; CO Carbon monoxide; ED Emergency department; IQR Interquartile range; NO$_2$ Nitrogen dioxide; NS Not stated; O$_3$ Ozone; OASIS Ontario Asthma Surveillance Information System; RR Relative risk; SES Socioeconomic status; SO$_2$ Sulphur dioxide; TEOM Tapered element oscillating microbalance; TRS Total reduced sulphur

two used Alberta data (43,45) and one study used data from 11 Canadian cities (25). At least one of the two Ontario cities – Windsor and Hamilton – were represented in 13 of the articles analyzed. The most common study designs used were longitudinal (n=7), cross-sectional (n=7) and case-crossover (n=6). All studies included children <15 years of age, except for one that included children up to 17 years of age (20). Twelve (44%) studies received funding support from provincial or federal government agencies. Eighteen studies focused on exposures to at least one of the CAP; two used proximity to roads as the exposure source, two used Air Quality Health Index (AQHI) as the tested exposure, and four examined CAP as well as proximity to roads or industrial facilities. One study measured exposure to total suspended particles (TSP) in Hamilton, and other polycyclic aromatic hydrocarbon (PAH) and volatile organic compounds in Montreal (Québec). Of the 23 studies tracking CAP or TSP, the majority (n=13) used fixed ambient air monitoring stations to assess exposures, two modelled exposures, seven used a combination of measurements and models, and one used personal monitoring devices. Regarding respiratory outcomes, 14 studies relied on health services use for respiratory conditions as the main health outcome (Table 1), while five used lung function measures based on spirometry; four used self-report of respiratory symptoms; three used a combination of lung function measures and symptoms; and one calculated incidence of asthma diagnosis (23) (Table 2).
NO2 was exacerbated among female children of low socioeconomic status (from 0 to 17 years of age). There was also evidence that the effect of NO2 results, showing a positive association with HSU at different ages generally differed according to age and city studied, as well as the study period. Two studies using the AQHI as an air pollution indicator also showed positive associations with HSU.

Figure 2) Quality assessment of the 27 included studies using the Newcastle-Ottawa Scale, which assess three main groups of criteria consisting of a total of eight items. All criteria are assessed in a binary fashion (0 or 1), except for ‘comparability of cases/controls’, which was scored as 0, 1 or 2. Percentages indicate the total score of all the articles in the indicated categories out of the total possible score

Quality assessment
The overall methodological quality assessment of the studies was moderate, with a mean (± SD) NOS score of 6.04±1.3 from a maximum score of 9. Figure 2 summarizes the methodological quality of the studies based on the NOS items. All studies clearly defined outcomes and most (96.3%) of the studies controlled for potential confounding variables; however, the nonexposed group definition, the follow-up criteria (especially for noncohort longitudinal studies), and the report of nonparticipation (in cross-sectional studies) were not met in >50% of the articles.

HSU as a result of air pollution exposure
Nine studies focused on HSU for the treatment of asthma symptoms. A variety of age ranges and pollutants had positive associations with asthma-related HSU (Figure 3A). Higher adverse effects were reported consistently during the warm season in different cities. The highest percentage increase of emergency department (ED) visits for asthma (up to 36%) was reported in one-day lag exposures to CO, SO2, and NO2 in Windsor during the warm season (32), and the highest percentage increase of asthma hospitalization (up to 42%) was reported in children exposed to SO2 in refinery areas in Montreal (41). Studies examining NO2 produced the most consistent results, showing a positive association with HSU at different ages (from 0 to 17 years of age). There was also evidence that the effect of NO2 was exacerbated among female children of low socioeconomic status (20,34). Two pollutants (CO, O3) gave conflicting results among studies; however, it is important to note that the studies generally differed according to age and city studied, as well as the study period. Two studies using the AQHI as an air pollution indicator also showed positive associations with HSU.

Five studies examined HSU for general respiratory conditions (which could include, but were not limited to, asthma) and infections. As with HSU for asthma, several positive associations were demonstrated (Figure 3B). In this case, CO, NO2, and PM2.5,10 were positively associated with HSU for respiratory ailments. Conflicting results were demonstrated for O3, PM10 and SO2, depending on the city and age of the children studied.

Air pollution effects on lung function and asthma symptoms/diagnosis
A variety of pollutants was tested for an association with increased asthma symptoms (AS) or decreased lung function (LF) (Figure 3C). LF was typically assessed using forced expired vital capacity (FVC) and/or forced expiratory volume in 1 s (FEV1) measures. The most consistent null effects were reported for O3, when either LF or AS were examined in children, in Windsor and Hamilton. Associations with reduced LF were also apparent for PAH (Montreal) and TSP (Hamilton). No associations with reduced lung function were seen with benzene (Montreal) or PM2.5,10 (Windsor); and no increased AS were apparent with increased PM10 exposure (Hamilton). While proximity to roadways had no association with AS in Hamilton, it did show an effect on LF in three Windsor-based studies (21,26,27). Inconsistent results were observed for NO2, PM2.5, and SO2, even though the contradictory studies often examined similar health effects and age groups in the same cities. For NO2, most LF data failed to demonstrate an association (Montreal and Windsor), while one showed the opposite (Windsor), as did one study using AS (Hamilton). There was no clear pattern in the PM2.5 data, with three Windsor articles identifying effects on LF and/or inflammation, and two from Montreal and Windsor showing no effect on LF. For SO2, four studies using either LF, AS, or LF and inflammation failed to demonstrate an effect in Hamilton and Windsor, while a single study in Montreal detected an association with AS. Two studies showed effect modification of NO2 on asthma symptoms by chronic psychosocial stress and other allergic disease (20,27).

Only one study examined increases in asthma diagnosis, as a consequence of exposure to CAPs, wood smoke and black carbon (soot), or industrial and road proximity in children <5 years of age from southwest BC (23). Positive associations were seen with CO, NO, NO2, PM2.5, SO2, black carbon and industrial proximity (Table 2).

DISCUSSION
The present systematic review summarizes the evidence available from epidemiological studies exploring the association of outdoor air pollution on Canadian children’s respiratory in the past 10 years. From 2004 to 2014, 27 new studies were identified; all but one (40) confirm the adverse effects of outdoor air pollution on respiratory symptoms, lung function and HSU at different CAP concentrations, almost all of which were below United States and Canadian (available only for PM2.5 and O3) standards (47). The present review also identified that the increase in respiratory-related ED visits and hospitalizations were demonstrated in higher proportions than the outpatient visits, and that those effects are even higher in places near industrial facilities or refinery areas in Windsor and Montreal, respectively. The findings showed more consistent associations of adverse respiratory outcomes for traffic-related exposures of PM and NO2, especially related to health services use. Some studies also report differential effects of gases and particles on female and socially disadvantaged children.

Our review updates a similar study covering 1989 to 2004 (16), enabling us to compare publications and describe trends in the research related to the effect of air pollution on Canadian children over the past 25 years. There are differences, mainly in terms of the number of publications, type of study designs, exposure measurement and study locations. Compared with publications from 1989 to 2004, the publications in the past decade were: more than twofold more frequent, over a shorter period of time studied; conducted mainly in Windsor and Hamilton rather than in Toronto and Vancouver; most commonly used cross-sectional, longitudinal and case-crossover study designs rather than time-series analysis; and increasingly introduced air pollutant exposure assessment using model-based small area estimations (eg, land-use regression models), in addition to data from fixed ambient air monitoring stations. These changes could be explained by several factors, such as the increase in funding for the study of environmental-related health conditions in Canadian children (48), the increased access to high quality administrative data, growing societal concern for the potential health effects of industrial development around cities (12 of 27 studies between 2004 and 2014 were supported by provincial or federal
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Figure 3) Respiratory health outcomes according to air pollutant and children's age range. The age groups of children tested by each reference were plotted for each air pollutant measure tested. Bars indicate either a statistically significant (P<0.05, black) or nonsignificant (P>0.05, grey) association between the indicated pollutant and the health effect, for each age group studied by the indicated study. A The incidence of emergency department (ED) visits and hospitalizations for asthmatic symptoms and pollution exposure. *Effect was present or stronger in populations with low socioeconomic status. #ED visits and hospitalizations for bronchiolitis were also included as relevant health outcomes in the study. B Associations between pollution exposure and health services use for conditions other than asthma. C Lung function measurements and symptoms of affected lung function (eg, wheezing and other asthma-like symptoms) were tested for associations with differing levels of pollutant exposure. *Lung function was measured; +Lung inflammation was measured; #Asthmatic symptoms were measured. AQHI Air Quality Health Index; CO Carbon monoxide; NO₂ Nitrogen dioxide; O₃ Ozone; PAHs Polycyclic aromatic hydrocarbons; PM₂.₅/PM₁₀ Particulate matter size ≤₂.₅ µm/≤₁₀ µm in aerodynamic diameter; SO₂ Sulphur dioxide; TRS Total reduced sulphur; TSP Total suspended particles

National air pollution surveillance data have shown that the concentration of CAP gases decreased slightly over time in Canada (53), and mean Canadian CAP levels are lower than those in most of the major cities of the world (54-58). Even at current Canadian levels, however, they are associated with adverse health effects in children, as well as cardiovascular, respiratory and gastrointestinal effects in adults (mainly linked to SO₂ and PM) (59,60). Moreover, several of the studies referenced herein suggest heterogeneous effects of the current levels of gases and particles on children according to sex, socioeconomic status and seasonality; however, none of them included an analysis of government agencies), and the development of epidemiologic, spatial and statistical methods applicable to air pollution research (49).

Conversely, similarities across time included the preference for reporting asthma-related outcomes and the use of CAP concentrations as the metric to assess outdoor air pollution exposure. These similarities can be explained by the persistent high prevalence of asthma in Canadian children (50), the availability of high-quality administrative health data, especially for acute asthma-related conditions (51) and detailed CAP data from the air quality monitoring surveillance systems in many densely populated Canadian cities (52).
### TABLE 2
Characteristics and results of included studies with respiratory symptoms, lung function measures and incidence of asthma diagnosis outcomes

<table>
<thead>
<tr>
<th>Author (reference), year; location; study period</th>
<th>Study design; study population and size</th>
<th>Pollutants (mean or median levels*) and methods assessing exposure</th>
<th>Respiratory outcome</th>
<th>Study findings</th>
<th>Adjustment for confounding factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poulou et al (38), 2008; Hamilton (Ontario); 1978-1985</td>
<td>Reanalysis of cohort study; 9–12 year olds identified by postal code (n=1164)</td>
<td>TSP measured at 28 monitoring stations; exposures assigned to postal code using Kriging and LUR; mean of five stations (station/Kriging/LUR): 58.64/55.69/58.57</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;, FVC, MEF, PF; survey used for respiratory symptoms</td>
<td>OR for association between TSP and wheezy: 1.01 (95% CI 0.99–1.02). Cold usually goes to chest: 1.01 (95% CI 1.005–1.019), and having a cough: 1.56 (95% CI 1.35–1.80); coefficient for lung measures: FEV&lt;sub&gt;1&lt;/sub&gt; (0.002), FVC (0.003), MEF&lt;sub&gt;25%-75%&lt;/sub&gt; (0.002), and FEF&lt;sub&gt;25%-75%&lt;/sub&gt; (0.099); LUR performed better than Kriging</td>
<td>Height, sex, previous hospitalizations, medical history of siblings, SES, parental smoking, use of gas for cooking and heating</td>
</tr>
<tr>
<td>Dales et al (27), 2008; Windsor (Ontario); study period not stated</td>
<td>Cross-sectional; 9–12-year-old school children (n=2328)</td>
<td>Roadway density and mean/median annual SO&lt;sub&gt;2&lt;/sub&gt; (5.39/5.28), NO&lt;sub&gt;2&lt;/sub&gt; (13.58/13.15), PM&lt;sub&gt;10&lt;/sub&gt; (7.25/7.27), PM&lt;sub&gt;2.5&lt;/sub&gt; (15.62/15.42), and black smoke (0.75/0.75 10&lt;sup&gt;-3&lt;/sup&gt; m&lt;sup&gt;-3&lt;/sup&gt;/m); LUR model assigned exposures at postal code level</td>
<td>FVC, FEV&lt;sub&gt;1&lt;/sub&gt;, eNO</td>
<td>3.9% eNO increase associated with 1 µg/m&lt;sup&gt;3&lt;/sup&gt; increase in PM&lt;sub&gt;2.5&lt;/sub&gt;; each km of road within 200 m associated with 6.8% increase in eNO, and 0.70% decrease in FVC</td>
<td>Previous respiratory infection, asthma medication usage, cigarette exposure and house pets</td>
</tr>
<tr>
<td>Chen et al (22), 2008; Vancouver (British Columbia); study period not reported</td>
<td>Longitudinal study for symptoms and lung function measures; 9–18-year-old asthmatic children (n=73)</td>
<td>NO&lt;sub&gt;x&lt;/sub&gt; concentrations; LUR model assigned exposures for the entire study area at a resolution of 10 m.</td>
<td>Daily PEF measurements and asthma symptoms reported by parents and children (diary). Baseline inflammatory markers measured</td>
<td>Chronic exposure to traffic and psychosocial stress interact to predict both biological and clinical outcomes in children with asthma. The effect of psychosocial stress was more evident among children living in lower-pollution areas.</td>
<td>Asthma severity, asthma medication use, and demographic characteristics (age, sex, ethnicity, time of year of study visit)</td>
</tr>
<tr>
<td>Dales et al (26), 2009; Windsor (Ontario); September 2004</td>
<td>Cross-sectional; 6–14-year-old school children (n=12,693)</td>
<td>Exposure to roadways; total length of local roadways within 200 m radius around postal code of each house</td>
<td>Respiratory symptoms and illnesses (cough, wheeze, chest illness)</td>
<td>OR comparing the highest to the lowest exposure (roadway density) quintiles significant for wheeze: 1.23 (95% CI 1.07–1.41) and wheeze with dyspnea: OR 1.27 (95% CI 1.05–1.52), but not cough, chest illness or asthma; general OR lowest versus others quintiles was 1.08 (95% CI 1.012–1.149)</td>
<td>Age, sex, parental history of asthma and allergy, parental education, household income, home smokers, number of bedrooms, siblings, pets, stove type, visible indoor moulds</td>
</tr>
<tr>
<td>Dales et al (24), 2009; Windsor (Ontario); October to December 2005</td>
<td>Cross-sectional; 9–14-year-old asthmatic school children (n=182)</td>
<td>Mean PM&lt;sub&gt;2.5&lt;/sub&gt; (7.8), NO&lt;sub&gt;x&lt;/sub&gt; (19.1), O&lt;sub&gt;3&lt;/sub&gt; (14.1), O&lt;sub&gt;3&lt;/sub&gt;max (27.3), and SO&lt;sub&gt;2&lt;/sub&gt; (6.0); from monitoring stations</td>
<td>Acute (daily) FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>IQR increase (6.0 µg/m&lt;sup&gt;3&lt;/sup&gt;) in the previous 24 h mean PM&lt;sub&gt;2.5&lt;/sub&gt; associated with a 0.54% (95% CI 0.06–1.02) decrease in bedtime FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Daily mean temperature, relative humidity, day of the week, number of hours spent on outdoor activities, sex, and study period</td>
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<tr>
<td>Sahsuvaroglu et al (39), 2009; Hamilton (Ontario); 1994-1995</td>
<td>Cross-sectional; 6–7 and 13–14-year-old school children (n=1467)</td>
<td>Air pollution in 4 ways: distance from roadways 50 m-100 m; mean interpolated surfaces of O&lt;sub&gt;3&lt;/sub&gt; (20.12), SO&lt;sub&gt;2&lt;/sub&gt; (5.81), PM&lt;sub&gt;10&lt;/sub&gt; (20.99), NO&lt;sub&gt;x&lt;/sub&gt; (31.77) from monitoring stations; Krigged NO&lt;sub&gt;x&lt;/sub&gt; (15.36) surface based on a network of 100 monitors; and LUR for NO&lt;sub&gt;x&lt;/sub&gt; (14.84) derived from the same monitoring network</td>
<td>Asthma symptoms</td>
<td>Effects were observed for the association of asthma without hay fever and NO&lt;sub&gt;2&lt;/sub&gt; LUR in 6–7 and 13–14-year-old girls (OR 1.86 [95% CI 1.59–2.16]) and 13–14-year-old girls (OR 2.98 [95% CI 0.98–9.06]); refined exposure models produced the most robust associations</td>
<td>Income, dwelling value (Census), smoking data available, % houses built pre-1946, rate of repair of housing to account for mould and damp conditions (from Census 1996), Deprivation Index by using principal components analysis for income, education and employment variables</td>
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### TABLE 2 – CONTINUED
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<th>Study findings</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Liu et al (36), 2009; Windsor (Ontario); 4 weeks: October to December 2005</td>
<td>Longitudinal repeated measures study; 9–14-year-old asthmatic children (n=182)</td>
<td>1-day/2-day/3-day median SO2 (4.5/5/0.5/6), NO2 (19.8/18.3/18.3), O3 (13.0/14/14.0), and PM2.5 (6.5/6.6/6.9); from two fixed monitors in study area</td>
<td>Pulmonary function, airway oxidative stress and inflammation in asthmatic children</td>
<td>IQR increases in 3-day average SO2, NO2, and PM2.5 were associated with decreases in forced expiratory flow with changes between -2.8% and 3.1%. SO2, NO2 and PM2.5 were associated with increases in TBARS but not FeNO, 8-isoprostane or interleukin 6; O3 was not associated with health outcomes</td>
<td>Testing period, interactions of pollutant concentrations with sex and use of inhaled corticosteroids</td>
</tr>
<tr>
<td>Clark et al (23), 2010; British Columbia Southwest; 1999-2003</td>
<td>Case-control population-based study; children born in 1999 and 2000 in the study location; (n=3482)</td>
<td>IDW/LUR modelled exposures for NO, NO2, CO, O3, PM10, PM2.5, black carbon, SO2, and road proximity In utero and in first year of life based on monitor data (see source data)</td>
<td>Asthma diagnosis (incidence)</td>
<td>Highest OR for asthma diagnosis was associated with increased early life exposures to CO (100 μg/m3 increase OR 1.10; 95% CI 1.06–1.13), NO (10 μg/m3 increase OR 1.08; 95% CI 1.04–1.12) and NO2 (10 μg/m3 increase OR 1.12; 95% CI 1.07–1.17); PM10, SO2, black carbon and proximity roads and pollution point sources also showed significant associations with asthma diagnosis</td>
<td>Age, sex, birth weight, gestational age, maternal smoking, maternal age, # siblings, intention to breast-feed, First Nation status, income quintiles and maternal education quarters by dissemination area to approximate SES</td>
</tr>
<tr>
<td>Cakmak et al (21), 2012; Windsor (Ontario); February to June (year NS)</td>
<td>Cross-sectional; 9–11-year-old school children; (n=2328)</td>
<td>Annual volume of vehicles within 200 m radius of child’s neighbourhood; used sensors to measure traffic counts and turning movements</td>
<td>Respiratory symptoms; FVC, FEV1, and eNO</td>
<td>OR associated with IQ increase of turning movements: chest congestion 1.20 (95% CI 1.06–1.35), FEV1 decline 1.84% (95% CI 0.07–3.61); OR associated with IQ increase in traffic counts: FVC decrease 0.68% (95% CI 1.32–0.03); effects on asthmatic children were larger; traffic measures had association with effect on eNO</td>
<td>Ethnic background (Caucasian versus other), smokers at home, pets at home, acute respiratory illness in past 2 weeks, medication for wheezing/asthma in last 2 weeks, month or the year</td>
</tr>
<tr>
<td>Deger et al (28), 2012; Montreal (Quebec); April to July 2006</td>
<td>Cross-sectional; 6 month to 12 year olds exposed to refinery emissions (n=482)</td>
<td>Yearly mean ambient SO2 exposures in children (with active asthma/ no active asthma/ poor asthma control/ active asthma with acceptable control/ no asthma/ controlled asthma) (1.68/1.55/1.50/1.61/1.56); SO2 exposure levels estimated using AERMOD dispersion model</td>
<td>Symptoms of active asthma and poor asthma control</td>
<td>Adjusted PR for IQR increase of SO2 exposure on increased: active asthma: 1.14 (95% CI 0.94–1.39); poorly controlled asthma: 1.39 (95% CI 1.00–1.94)</td>
<td>Age, sex, parental history of asthma or rhinitis or eczema, household income, maternal educational level, house tobacco smoke; for SO2 models longitude, latitude, emission temperature, height and exit velocity for each vent and stack used</td>
</tr>
<tr>
<td>Johnson et al (31), 2013; Windsor (Ontario); 2004-2005</td>
<td>Longitudinal repeated measures study; asthmatic 10–13 year olds; (n=45)</td>
<td>Daily outdoor house levels of NO2 and PM2.5; Comparison of home monitoring data and LUR temporally refined models based on monitoring site data</td>
<td>FEV1 and PEF</td>
<td>Daily home NO2 associated with 7%–8% decrement in FEV1/IQR; LUR temporally adjusted models better predicts spatial and temporal variability in lung function models in asthmatic children</td>
<td>Environmental tobacco smoke, height and weight; home: temperature and relative humidity</td>
</tr>
<tr>
<td>Dell et al (29), 2014; Toronto (Ontario); June to September 2006</td>
<td>Cross-sectional; School children grades 1–2 (5–9 year olds); (n=1497)</td>
<td>Cumulative NO2 exposures; estimations using LUR and IDW models including lifetime addresses (birth, moving, daycare/school and current addresses)</td>
<td>Current and lifetime asthma and wheeze</td>
<td>In children with other allergic disease, birth, cumulative and 2006 NO2 were associated with lifetime asthma and wheeze; no or weaker effects were seen without other allergic diseases</td>
<td>Presence of other allergic diseases was tested for effect modification; other variables include ETS and other household exposures, family history of asthma and demographics.</td>
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Continued on next page
potential mechanisms explaining those differences, which may vary across populations (61).

Limitations

The methodological quality of the studies included in the present review was relatively homogeneous, with a mean ‘moderate quality’ score according to the NOS tool. This ‘moderate’ score is lower than expected for most included articles because the NOS tool is designed only for classic cohort or case-control studies. Thus, we believe that properly assessing the quality of observational studies related to environmental health remains challenging.

To avoid selection bias in the present review, two independent reviewers conducted the screening and selection processes. Although efforts to undertake meta-analyses failed due to the high qualitative heterogeneity in the included studies, qualitative summary tables and graphs were developed to examine trends. Having more homogenous studies in terms of children’s age in studies would allow quantitative analysis in future reviews. Another limitation of the review was that unpublished studies in the formal scientific literature were not identified; therefore, there may be a chance of publication bias. However, the included studies showed both positive and null effects of different CAP for different cities. In fact, the common mixture of positive and null effects in many studies may be explained by the fact that air pollutants effects differ not only according to type of pollutant (alone or in combination), but also by the different physical and sociodemographic conditions of the places and populations under study. Finally, the scope of the present review was limited to the childhood population and the results and conclusions may be not generalizable to adults, even in Canada.

CONCLUSIONS

The present review provides researchers, clinicians and environmental health authorities with a current summary of the evidence linking the adverse effects of outdoor air pollution to children’s respiratory health in Canada. Further studies should fill knowledge and methodological gaps that are related but not restricted to: deepening the understanding of the ‘why’ of the differences in the observed adverse effects for some pollutants and socioeconomic conditions across cities; exploring the combined effect of various air pollutants; expanding the study of the health effects of non-CAP air toxics that are emitted in Canada, such as PAH or volatile organic compounds; strengthening the advances in epidemiological, spatial, statistical and social analysis as applied to air pollution studies, aiming for a more integrated approach between the physical and social environment; and developing and validating a tool for assessing the methodological quality of observational studies commonly used in environmental health studies, other than cohort and case control studies.

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