

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 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 [SO_x] and nitrogen oxides [NO_x]), 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 PM_{2.5} (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,

Les effets de la pollution de l'air atmosphérique sur la santé respiratoire des enfants canadiens : une analyse systématique d'études épidémiologiques

HISTORIQUE : La pollution de l'air atmosphérique est un problème mondial qui a de graves effets sur la santé humaine. Les enfants sont considérés comme très vulnérables aux effets de ce type de pollution.

OBJECTIF : Mener une analyse systématique complète et à jour des publications sur les effets de la pollution de l'air atmosphérique sur la santé respiratoire des enfants du Canada.

MÉTHODOLOGIE : Les chercheurs ont effectué des recherches dans quatre bases de données électroniques entre janvier 2004 et novembre 2014 pour évaluer l'effet de l'exposition aux polluants atmosphériques sur les symptômes respiratoires, les mesures de la fonction pulmonaire et l'utilisation des services de santé en raison de maladies respiratoires chez les enfants canadiens. Deux analystes ont procédé à l'analyse indépendante du processus de sélection et de l'évaluation de la qualité, au moyen de l'échelle de Newcastle-Ottawa.

RÉSULTATS : Les chercheurs ont colligé 27 études hétérogènes sur le plan de la méthodologie, de la population, des conséquences respiratoires et de l'exposition à la pollution atmosphérique. Dans l'ensemble, les études incluses portaient sur les effets indésirables de la pollution de l'air atmosphérique à des concentrations inférieures aux normes canadiennes et américaines. Les effets hétérogènes des polluants atmosphériques étaient déclarés selon la ville, le sexe, la situation socioéconomique et le caractère saisonnier du problème. La présente analyse décrit également les tendances de la recherche à l'égard de l'effet de la pollution atmosphérique sur les enfants canadiens depuis 25 ans.

CONCLUSION : La présente étude confirme de nouveau les effets indésirables de la pollution de l'air atmosphérique sur la santé respiratoire des enfants canadiens. Elle aidera les chercheurs, les cliniciens et les autorités en santé environnementale à repérer les données probantes sur les effets négatifs de la pollution de l'air atmosphérique ainsi que les lacunes et les limites de la recherche, et ce, en prévision de prochaines recherches.

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

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elsewhere. Air pollution levels in Canada are relatively low and most Canadian cities experience extreme low temperatures. Thus, Canadian studies offer a unique opportunity to examine the effects of more moderate doses of air pollution compared with those experienced in many other nations (13). In addition, Canada boasts one of the highest percentage of foreign-born citizens (14), being a society of mixed languages, cultures and genetic diversity. Recent findings suggest that the influence of genetic diversity on the population's susceptibility to air pollution is an important factor that should be considered in this field (15). In 2007, a systematic review of air pollution and children's health in Canada analyzed the results of epidemiological studies published between January 1989 and December 2004 (16). From 11 studies over a 15-year period, the review identified associations between respiratory health effects and at least some CAP measurements. These associations were, however, often weaker than those reported in studies conducted in other countries. This was believed to be due to the lower levels of air pollution in Canada, the lower number of hours spent outdoors during the colder Canadian winters, as well as reduced levels of outdoor air pollution infiltrating into homes, which could act to reduce personal exposure to outdoor air pollution.

The objective of the present study was to conduct a comprehensive systematic review of the literature reporting the effects of outdoor air pollution on the respiratory health of children in Canada. We focused on the literature published during the past 10 years to update 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.

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 design; publication date between January 1, 2004 and November 30, 2014; population included and reported data for children up to 18 years of age residing in Canada; exposure(s) included any nonbiological outdoor air pollutant whether measured directly or inferred (ie, by proximity to roadways), with special interest in the CAP (CO, NO₂, SO₂, O₃, and PM₁₀ and PM_{2.5}); and outcomes included health services use (HSU), lung function measurement or self-reported respiratory symptoms. Studies that included a subset or cohort of Canadian children in which the data for the Canadians were not presented separately were excluded. Two reviewers (LR-V and AM) independently screened the identified articles' titles and abstracts to select the articles for full review, and reviewed citations that were found to be potentially relevant for inclusion. A third reviewer (AO-V) resolved disagreement. Articles selected for full review were screened in a second round to confirm that the inclusion criteria were met. Agreement was measured using kappa (κ) statistics. Data extraction was performed by two reviewers (LR-V and AM) and summarized in standardized tables.

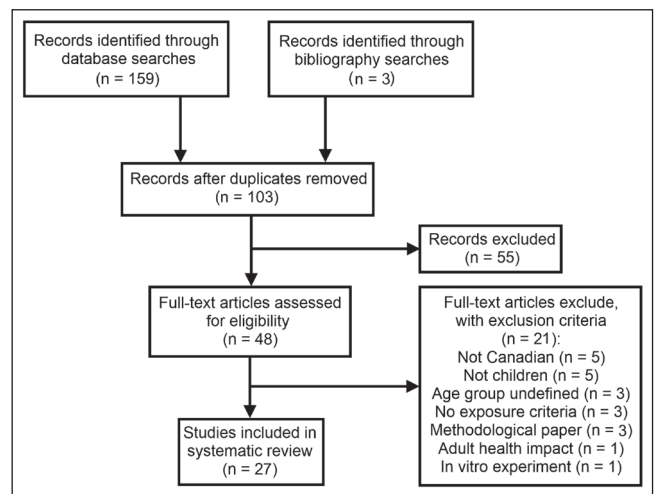


Figure 1) PRISMA flow diagram for selection of studies

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.

Data analysis

Descriptive results of the included studies are provided. While quantitative analyses using pooled measures and random effect models were planned, they could not be conducted due to heterogeneity among study populations (children's age), outcomes and study designs. Kappa statistics and 95% CIs were generated using Stata version 11.1 (StataCorp, USA).

RESULTS

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

Reference; study location; and study period	Study design; study population and size	Pollutants (mean or median levels*) and methods assessing exposure	Respiratory outcome	Study findings	Adjustment for confounding factors
Lin et al, 2004 (34); Vancouver area; 1987–1998	Time series study; hospitalizations of 6–12 year olds; from BC Linked Health Dataset (n=3822)	Mean CO (960), SO ₂ (4.77), NO ₂ (18.65), O ₃ (28.02), PM ₁₀ (NS), PM _{2.5} (NS) from 1995–1998; from monitoring stations	Hospitalizations for asthma	RR of asthma hospitalizations in low SES group associated with: NO ₂ (male, 1-day lag): 1.16 (95% CI 1.06–1.28), NO ₂ (male 4-day lag): 1.18 (95% CI 1.03–1.34), SO ₂ (female 4-day lag): 1.17 (95% CI 1–1.37), and SO ₂ (female 6-day lag): 1.19 (95% CI 1–1.42)	Sex, temperature, relative humidity, SES, day of the week
Yang et al, 2004 (46); Greater Vancouver; 1995–1999	Case-crossover, case-control and time-series analyses; first hospital admis- sions of 0–3 year olds, excluding birth-related admissions (n=1610)	Mean CO (700), O ₃ (14.3), NO ₂ (16.8), SO ₂ (3.5), PM ₁₀ (13.3) and PM _{2.5} (7.7); from local monitors	Hospitalizations for respiratory disease (includ- ing asthma)	OR of respiratory hospitalizations associated with 3-day lag mean and max PM _{10-2.5} : 1.22 (95% CI 1.02–1.48) and 1.14 (95% CI 0.99–1.32), respectively; time-series analysis gave weaker associations	Sex, SES, day of the week, season, study year, sea- son and influenza hospitalizations
Lin et al, 2005 (35); Toronto; 1998–2001	Case-crossover design; hospitalizations of 0–14 year olds (n=6782)	Mean PM ₁₀ (20.41), PM _{2.5} (9.59), PM _{10-2.5} (10.86), CO (1160), SO ₂ (4.73), NO ₂ (24.54), O ₃ (38.06); from monitoring stations	Hospitalization for respiratory infections	OR of hospitalizations for 6-day average exposure to: PM _{10-2.5} : boys 1.15 (95% CI 1.02–1.3), girls 1.18 (95% CI 1.01–1.36); PM ₁₀ : boys 1.25 (95% CI 1.01–1.54); NO ₂ : girls 1.31 (95% CI 1.05–1.63); PM _{2.5} , O ₃ and SO ₂ showed no associations	Sex, temperature, pollutant interac- tions and season- ality
Luginaah et al, 2005 (37); Windsor; 1995–2000	Time series and case- crossover design; hospitalizations 0–14 year olds (n=1602)	Mean NO ₂ (38.9), SO ₂ (27.5), CO (1300), PM ₁₀ (50.6), TRS (8), and coefficient of haze (0.5); from monitoring stations	Hospitalizations for respiratory disease	Time Series RR: NO ₂ : female 2-day lag: 1.19 (95% CI 1.002–1.411); SO 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)	Temperature, sex, humidity, baromet- ric pressure, seasonality
Dales et al, 2006 (25); 11 of the largest Canadian cities; 1986–2000	Time series study; hospitalizations of 0–27 day olds (n=8586)	Mean NO ₂ (21.8), SO ₂ (4.3), CO (1.0), O ₃ (17.0), and PM ₁₀ (NS); from monitoring stations (population weighted average)	Hospitalizations for respiratory disease	The percentage of variation for IQR increase for all gasses combined was 9.61% (95% CI 4.52–14.7); individually: O ₃ : 2.67 (95% CI 0.98– 4.39); NO ₂ 2.48 (95% CI 1.18–3.8); SO ₂ : 1.41 (95% CI 0.35–2.47); CO: 1.3 (95% CI 0.13–2.49)	Long-term temporal trends, day of week effects, weather variables, other gases and PM ₁₀
Villeneuve et al, 2007 (45); Edmonton; 1992–2002	Case-crossover design (time stratified); ED visits of 2–14 year olds (n=20,392)	Summer/winter median PM ₁₀ (22.0/19.0), PM _{2.5} (7.0/7.3), CO (600/900), SO ₂ (2.0/3.0), NO ₂ (17.5/28.5), O ₃ (38.0/24.3); from monitoring stations	ED visits for asthma	Positive association were observed in warm season and higher in 2–4 years: OR 5-day average: NO ₂ 1.50 (95% CI 1.31–1.71), CO 1.48 (95% CI 1.27–1.72), PM _{2.5} : 1.16 (95% CI 1.04–1.28) and PM ₁₀ : 1.16 (95% CI 1.05– 1.28); For 5–14 years: OR 5-day average: NO ₂ : 1.13 (95% CI 1.02–1.24), O ₃ : 1.14 (95% CI 1.05–1.24), PM _{2.5} : 1.10 (95% CI 1.02–1.17), 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	Temperature, relative humidity, season, aeroallergens, and ED visits for influenza
Szyszkowicz et al, 2008 (43); Edmonton; 1992–2002	Longitudinal study; 0–10 years ED visits (n=18,891)	Mean/median CO (700/600), NO ₂ (21.9/19.7), SO ₂ (2.6/2.2), O ₃ (18.6/17.8), PM ₁₀ (22.6/19.4), PM _{2.5} (8.5/6.2); from monitoring stations	ED visits for asthma	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 ₂ (2-day lag) male: 19.2% (95% CI 11.4–27.6), O ₃ (same day) female: 17.8% (95% CI 7.1–29.5), PM ₁₀ (2-day lag) male: 7.4% (95% CI 3.1–11.9), PM _{2.5} (same-day) female: 7.7% (95% CI 5.2– 10.3), O ₃ (1-day lag), PM ₁₀ (same-day), and PM _{2.5} (2-day lag) showed positive variations for some age/sex/season combinations	Sex, temperature, relative humidity, day of the week
Burra et al, 2009 (20); Toronto; 1992–2001	Longitudinal study; family physician and specialists service claim records for 1–17 year olds (n=1,146,215)	Mean SO ₂ (9.7), NO ₂ (39.2), O ₃ (33.3) and PM _{2.5} (17.9); from monitoring stations	Asthma physician visits	RR for pollutants by SES quintiles (Q1/Q5) were: SO ₂ : 1.005 (95% CI 1.000–1.010), NO ₂ : 1.002 (95% CI 0.995–1.008), and PM _{2.5} : 1.006 (95% CI 0.997–1.015); low SES groups had higher RR in SO ₂ and PM _{2.5} models	SES, temperature, barometric pres- sure, 24 h mean relative humidity, day of the week

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TABLE 1 – CONTINUED
Characteristics and results of included studies with health services use outcomes

Reference; study location; and study period	Study design; study population and size	Pollutants (mean or median levels*) and methods assessing exposure	Respiratory outcome	Study findings	Adjustment for confounding factors
Smargiassi et al, 2009 (41); Montreal (Quebec); 1996-2004	Case-crossover design (time stratified); 2–4 year olds living near a refinery (n=1579)	Daily peak mean SO ₂ (east/southwest of refineries) using monitor- ing stations (23.8/12.8); and AERMOD dispersion model (19.2/16.0)	Asthma ED visits or hospital admissions	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)	Temperature, relative humidity, regional/ background air pollutant levels
Henderson et al, 2011 (30); Southeast corner of BC 92 days: July to September 2003	Cohort study; Residents at the southeast area of BC with a reliable geocodable residen- tial address in health databases; included newborns (n=281,711; 21.6% <20 years old)	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)	Respiratory or cardiovascular physician visits and hospital admissions	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)	Age, sex, SES
Lavigne et al, 2012 (32); Windsor (Ontario); 2002-2009	Case-crossover design (time strati- fied); 2–14 year olds hospitalized for asthma (n=3728)	Mean summer/winter SO (2.1/1.7), NO ₂ (9.8/7.4), CO (400/300), PM _{2.5} (7.1/7.4), O ₃ (13.2/26.0); from monitoring stations	Asthma ED visits	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	Daily number of influenza ED visits, temperature and relative humidity.
Lewin et al, 2013 (33); Shawinigan (Quebec); 1999-2008	Case-crossover design (time strati- fied); hospitalized 0–4 year olds living near aluminium smelter (n=396)	Exposure calculated by: % of hours/day each residence was downwind of the smelter; and daily mean SO ₂ (6.3) and PM _{2.5} (13.5) from moni- toring station	Hospitalization for asthma or bronchiolitis	OR of hours downwind of a smelter on same-day hospitalization of 2–4-year-old chil- dren: 1.27 (95% CI 1.03–1.56), and PM _{2.5} exposure: 1.22 (95% CI 1.03–1.11)	Average daily wind direction and speed
To et al, 2013 (44); Ontario; 2003-2006	Longitudinal study; All Ontario residents with asthma registered at the (OASIS) database	Canada 2003/2004/2005/2006 mean AQHI (3.87/3.64/3.83/3.34), NO ₂ (NS), O ₃ (NS), and PM _{2.5} (NS) measures; from monitoring stations	Asthma-attributed hospitaliza- tions, ED and outpatient visits	RR for 1-unit increase in the AQHI by same-day outpatient visits: 1.056 (95% CI 1.053–1.058) and hospitalization: 1.0256 (95% CI 1.053– 1.058), and 2-day lag ED visits: 1.013 (95% CI 1.010–1.017)	Age group, season, residence area, and year
Szyszkowicz et al, 2014 (42); Windsor (Ontario); 2004-2010	Case-crossover design (time strati- fied); ED visits for 2–14 year olds; (n=2151)	AQHI for Canada; hourly AQHI calculations. NO ₂ , O ₃ , and PM _{2.5} measures from two monitoring sta- tions	Asthma ED visits	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])	Ambient tempera- ture, relative humidity and daily counts of ED visits for influ- enza

*Parts per billion for gasses, µg/m³ for particulate matter (PM). AQHI Air Quality Health Index; BC British Columbia; CO Carbon monoxide; ED Emergency department; IQR Interquartile range; NO₂ Nitrogen dioxide; NS Not stated; O₃ Ozone; OASIS Ontario Asthma Surveillance Information System; RR Relative risk; SES Socioeconomic status; SO₂ 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 (Quebec). 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).

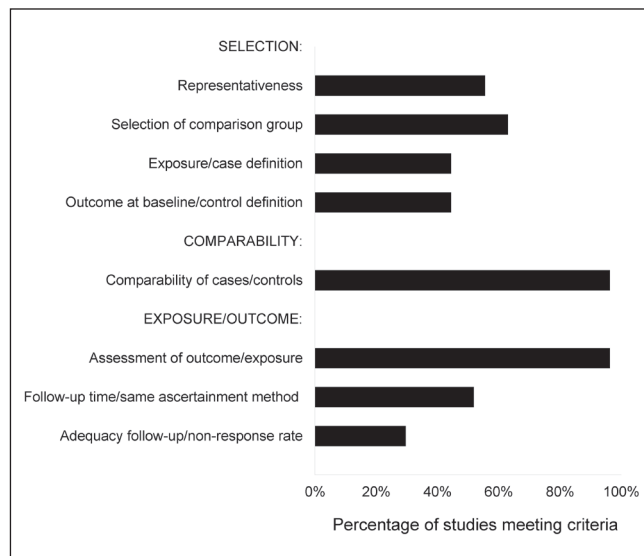


Figure 2 Quality assessment of the 27 included studies using the Newcastle-Ottawa Scale, which assess three main groups of criteria consisting of a total of eight items. All criteria are assessed in a binary fashion (0 or 1), except for 'comparability of cases/controls', which was scored as 0, 1 or 2. 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 (\pm 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 PM_{2.5-10} 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 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 PM_{2.5-10} (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, PM_{2.5} 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 PM_{2.5} 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, PM₁₀, 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) reconfirm 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 PM_{2.5} 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

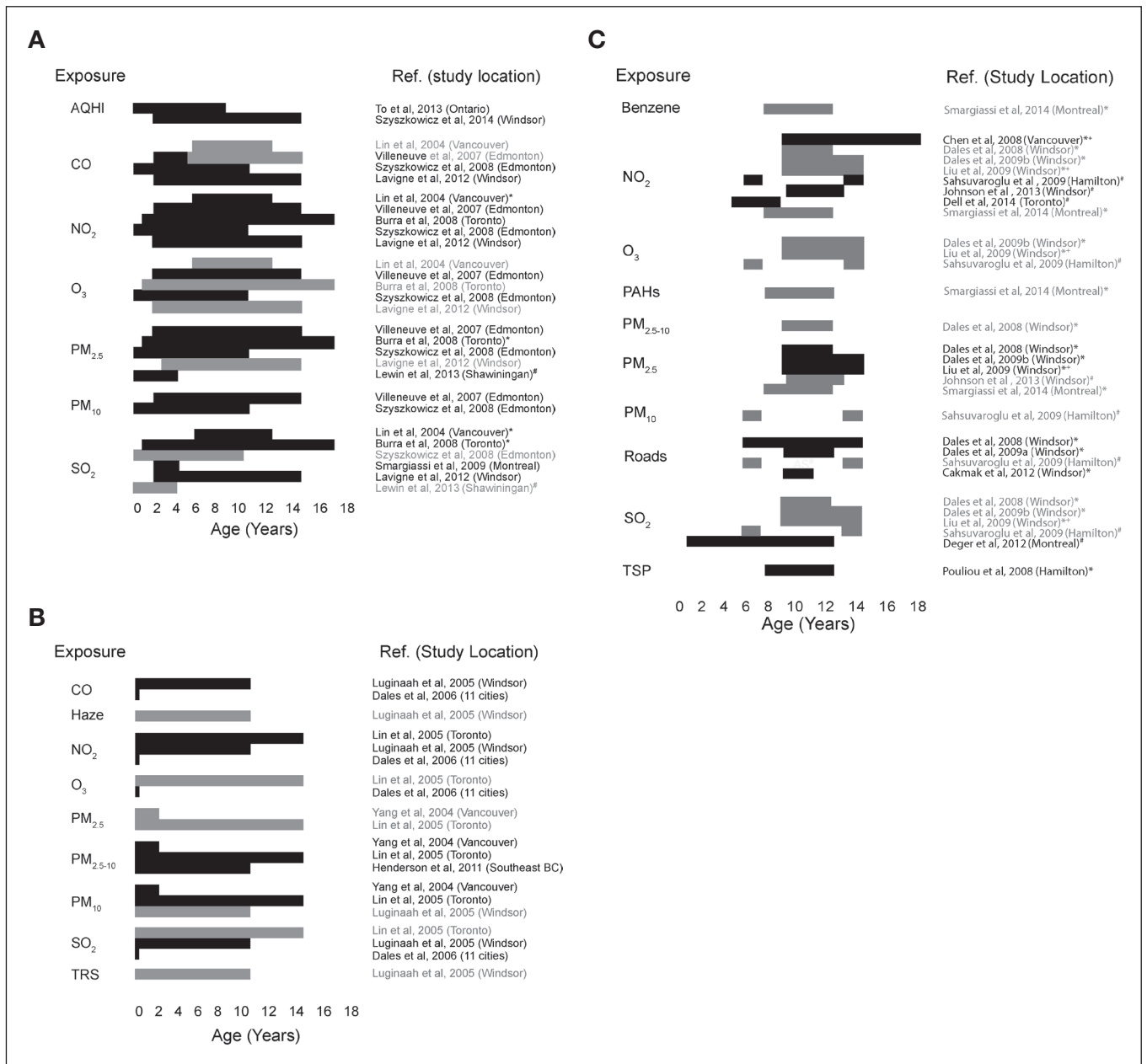


Figure 3) Respiratory health outcomes according to air pollutant and children's age range. The age groups of children tested by each reference were plotted for each air pollutant measure tested. Bars indicate either a statistically significant ($P < 0.05$, black) or nonsignificant ($P > 0.05$, grey) 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; PM_{2.5}/PM₁₀ Particulate matter size $\leq 2.5 \mu\text{m}$ / $\leq 10 \mu\text{m}$ in aerodynamic diameter; SO₂ Sulphur dioxide; TRS Total reduced sulphur; TSP Total suspended particles

government agencies), and the development of epidemiology, 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).

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

TABLE 2
Characteristics and results of included studies with respiratory symptoms, lung function measures and incidence of asthma diagnosis outcomes

Author (reference), year; location; study period	Study design; study population and size	Pollutants (mean or median levels*) and methods assessing exposure	Respiratory outcome	Study findings	Adjustment for confounding factors
Pouliou et al (38), 2008; Hamilton (Ontario); 1978-1985	Reanalysis of cohort study; 9–12 year olds identified by postal code (n=1164)	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	FEV ₁ , FVC, MEF, PF; survey used for respiratory symptoms	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 ₁ (0.002), FVC (0.003), MEF _{75%} (0.002), and FEF _{25-75%} (0.099); LUR performed better than Kriging	Height, sex, previous hospitalizations, medical history of siblings, SES, parental smoking, use of gas for cooking and heating
Dales et al (27), 2008; Windsor (Ontario); study period not stated	Cross-sectional; 9–12-year-old school children (n=2328)	Roadway density and mean/median annual SO ₂ (5.39/5.28), NO ₂ (13.58/13.15), PM _{10-2.5} (7.25/7.27), PM _{2.5} (15.62/15.42), and black smoke (0.75/0.75 10 ⁻⁵ /m); LUR model assigned exposures at postal code level	FVC, FEV ₁ , eNO	3.9% eNO increase associated with 1 µg/m ³ increase in PM _{2.5} ; each km of road within 200 m associated with 6.8% increase in eNO, and 0.70% decrease in FVC	Previous respiratory infection, asthma medication usage, cigarette exposure and house pets
Chen et al (22), 2008; Vancouver (British Columbia); study period not reported	Longitudinal study for symptoms and lung function measures; 9–18-year-old asthmatic children (n=73)	NO ₂ concentrations; LUR model assigned exposures for the entire study area at a resolution of 10 m.	Daily PEF measurements and asthma symptoms reported by parents and children (diary). Baseline inflammatory markers measured	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.	Asthma severity, asthma medication use, and demographic characteristics (age, sex, ethnicity, time of year of study visit).
Dales et al (26), 2009; Windsor (Ontario); September 2004	Cross-sectional; 6–14-year-old school children (n=12,693)	Exposure to roadways; total length of local roadways within 200 m radius around postal code of each house	Respiratory symptoms and illnesses (cough, wheezing, chest illness)	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)	Age, sex, parental history of asthma and allergy, parental education, household income, home smokers, number of bedrooms, siblings, pets, stove type, visible indoor moulds
Dales et al (24), 2009; Windsor (Ontario); October to December 2005	Cross-sectional; 9–14-year-old asthmatic school children (n=182)	Mean PM _{2.5} (7.8), NO ₂ (19.1), O ₃ (14.1), O _{3max} (27.3), and SO ₂ (6.0); from monitoring stations	Acute (daily) FEV ₁	IQR increase (6.0 µg/mm ³) in the previous 24 h mean PM _{2.5} associated with a 0.54% (95% CI 0.06–1.02) decrease in bedtime FEV ₁	Daily mean temperature, relative humidity, day of the week, number of hours spent on outdoor activities, sex, and study period
Sahsuvargolu et al (39), 2009; Hamilton (Ontario); 1994-1995	Cross-sectional; 6–7 and 13–14-year-old school children (n=1467)	Air pollution in 4 ways: distance from roadways 50 m-100 m; mean interpolated surfaces of O ₃ (20.12), SO ₂ (5.81), PM ₁₀ (20.90), NO _x (31.77) from monitoring stations; Krigged NO ₂ (15.36) surface based on a network of 100 monitors; and LUR for NO ₂ (14.84) derived from the same monitoring network	Asthma symptoms	Effects were observed for the association of asthma without hay fever and NO ₂ 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	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

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TABLE 2 – CONTINUED
Characteristics and results of included studies with respiratory symptoms, lung function measures and incidence of asthma diagnosis outcomes

Author (reference), year; location; study period	Study design, study population and size	Pollutants (mean or median levels*) and methods assessing exposure	Respiratory outcome	Study findings	Adjustment for confounding factors
Liu et al (36), 2009; Windsor (Ontario); 4 weeks: October to December 2005	Longitudinal repeated measures study; 9–14-year-old asthmatic children (n=182)	1-day/2-day/3-day median SO ₂ (4.5/5.0/5.6), NO ₂ (19.8/18.3/18.3), O ₃ (13.0/14.1/14.0), and PM _{2.5} (6.5/6.6/6.9); from two fixed monitors in study area	Pulmonary function, airway oxidative stress and inflammation in asthmatic children	IQR increases in 3-day average SO ₂ , NO ₂ , and PM _{2.5} were associated with decreases in forced expiratory flow with changes between –2.8% and 3.1%. SO ₂ , NO ₂ and PM _{2.5} were associated with increases in TBARS but not FeNO, 8-isoprostane or interleukin 6; O ₃ was not associated with health outcomes	Testing period, interactions of pollutant concentrations with sex and use of inhaled corticosteroids
Clark et al (23), 2010; British Columbia Southwest; 1999-2003	Case-control population-based study; children born in 1999 and 2000 in the study location; (n=3482)	IDW/LUR modelled exposures for NO, NO ₂ , CO, O ₃ , PM ₁₀ , PM _{2.5} , black carbon, SO ₂ , and road proximity In utero and in first year of life based on monitor data (see source data)	Asthma diagnosis (incidence)	Highest OR for asthma diagnosis was associated with increased early life exposures to CO (100 µg/m ³ increase OR 1.10; 95% CI 1.06–1.13), NO (10 µg/m ³ increase OR 1.08; 95% CI 1.04–1.12) and NO ₂ (10 µg/m ³ increase OR 1.12; 95% CI 1.07–1.17); PM ₁₀ , SO ₂ , black carbon and proximity roads and pollution point sources also showed significant associations with asthma diagnosis	Age, sex, birth weight, gestational age, maternal smoking, maternal age, # siblings, intention to breast-feed, First Nation status, income quintiles and maternal education quartiles by dissemination area to approximate SES
Cakmak et al (21), 2012; Windsor (Ontario); February to June (year NS)	Cross-sectional; 9–11-year-old school children; (n=2328)	Annual volume of vehicles within 200 m radius of child's neighbourhood; used sensors to measure traffic counts and turning movements	Respiratory symptoms; FCV, FEV ₁ , and eNO	OR associated with IQ increase of turning movements: chest congestion 1.20 (95% CI 1.06–1.35), FEV ₁ decline 1.84% (95% CI 0.007–3.61); 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	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
Deger et al (28), 2012; Montreal (Quebec); April to July 2006	Cross-sectional; 6 month to 12 year olds exposed to refinery emissions (n=482)	Yearly mean ambient SO ₂ exposures in children (with active asthma/no active asthma/poor asthma control/active asthma with acceptable control/no asthma/controlled asthma) (1.68/1.55/1.90/1.61/1.56); SO ₂ exposure levels estimated using AERMOD dispersion model	Symptoms of active asthma and poor asthma control	Adjusted PR for IQR increase of SO ₂ exposure on increased: active asthma: 1.14 (95% CI 0.94–1.39); poorly controlled asthma: 1.39 (95% CI 1.00–1.94)	Age, sex, parental history of asthma or rhinitis or eczema, household income, maternal educational level, house tobacco smoke; for SO ₂ models longitude, latitude, emission temperature, height and exit velocity for each vent and stack used
Johnson et al (31), 2004-2005	Longitudinal repeated measures study; asthmatic 10–13 year olds; (n=45)	Daily outdoor house levels of NO ₂ and PM _{2.5} ; Comparison of home monitoring data and LUR temporally refined models based on monitoring site data	FEV ₁ and PEF	Daily home NO ₂ associated with 7%–8% decrement in FEV ₁ /IQR; LUR temporally adjusted models better predicts spatial and temporal variability in lung function models in asthmatic children	Environmental tobacco smoke, height and weight; home: temperature and relative humidity
Dell et al (29), 2014; Toronto (Ontario); June to September 2006	Cross-sectional; School children grades 1–2 (5–9 year olds); (n=1497)	Cumulative NO ₂ exposures; estimations using LUR and IDW models including lifetime addresses (birth, moving, daycare/school and current addresses)	Current and lifetime asthma and wheeze	In children with other allergic disease, birth, cumulative and 2006 NO ₂ were associated with lifetime asthma and wheeze; no or weaker effects were seen without other allergic diseases	Presence of other allergic diseases was tested for effect modification; other variables include ETS and other household exposures, family history of asthma and demographics.

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TABLE 2 – CONTINUED
Characteristics and results of included studies with respiratory symptoms, lung function measures and incidence of asthma diagnosis outcomes

Author (reference); year, location; study period	Study design, study population and size	Pollutants (mean or median levels*) and methods assessing exposure	Respiratory outcome	Study findings	Adjustment for confounding factors
Smargiassi et al (40), 2014; Montreal (Quebec); 10 days between 2009- 2010	Longitudinal repeated measures; asthmatic 8-12 year olds living near two oil refineries; (n=72)	Daily personal monitoring of SO ₂ , NO ₂ , PAHs, VOCs and PM _{2.5} concentrations (data not shown); passive samplers for gases and real time monitor for PM _{2.5} (NS)	FVC, FEV ₁ and FEF _{25-75%}	No consistent associations were observed with PM _{2.5} , NO ₂ and benzene; suggestion of small decrease in respiratory function with PAHs (FVC: -9.9 mL per IQR PAH [95% CI -23.4 to 3.7])	Within-subject serial corre- lation, medication use, parent's or caregiver's education, ethnicity, temperature, relative humidity, age, height, sex, and the design variable month of study

*Parts per billion for gasses, µg/m³ for particulate matter (PM) and total suspended particles (TSP). CO Carbon monoxide; ED Emergency department; eNO Exhaled nitric oxide; ETS Environmental tobacco smoke; FEF_{25-75%} Forced expiratory flow between 25% and 75% of the forced vital capacity (FVC); FeNO Fractional exhaled nitric oxide; FEV₁ Forced expiratory volume in 1 s; IDW Inverse distance weighted; IQ Interquartile; IQR IQ range; LUR Land use regression; MEF_{75%} maximum expiratory flow after 75% of FVC has been exhaled; NO Nitrogen monoxide; NO₂ Nitrogen dioxide; NS Not stated; O₃ Ozone; PAH Polycyclic aromatic hydrocarbon; PEF Peak expiratory flow; PF Pulmonary function; PR Prevalence ratio; RR Relative risk; SES Socioeconomic status; SO₂ Sulphur dioxide; TBARS Thiobarbituric acid reactive substances; VOC Volatile organic compound

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 homogeneous 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 toxicants 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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APPENDIX 1 OVID MEDLINE, CINAHL Plus, Scopus and CAB search strategies

Ovid MEDLINE sequence and terms

1. Air Pollution/
2. air pollutants/ or gasoline/ or hydrogen sulfide/ or particulate matter/ or sulfur dioxide/ or vehicle emissions/
3. ("Air pollution" or "air pollutant").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
4. ("ambient air pollution" or "outdoor air pollution").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
5. 1 or 2 or 3 or 4
6. asthma/ or bronchitis/ or respiration disorders/
7. ("respiratory health" or "asthma" or "respiratory condition").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
8. ("respiratory symptoms" or "wheeze" or "respiratory function" or "pulmonary function").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
9. 6 or 7 or 8
10. Child/
11. ("child*" or "adolesc*" or "teen*" or "youth" or "pediat*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
12. 10 or 11
13. canada/ or alberta/ or british columbia/ or manitoba/ or new brunswick/ or "newfoundland and labrador"/ or north west territories/ or nova scotia/ or nunavut/ or ontario/ or prince edward island/ or quebec/ or saskatchewan/ or yukon territory/
14. ("Canada" or "Vancouver" or "Edmonton" or "Calgary" or "Victoria" or "Regina" or "Saskatchewan" or "Winnipeg" or "Toronto" or "Hamilton" or "Windsor" or "Mississauga" or "Montreal" or "Halifax" or "Ottawa" or "Kingston" or "London").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15. 13 or 14
16. 5 and 9 and 12 and 15
17. limit 16 to yr="2004 -Current"

CINAHL Plus sequence and string terms*

1. Air pollut*
2. (Respirat* OR Asthm* OR Pulmon*)
3. 1 and 2
4. (Child* OR adolescen*)
5. 3 and 4

Scopus exact string terms

TITLE-ABSKEY
(AIR POLLUT* AND (RESPIRAT* OR ASTHM* OR PULMON*) AND (CHILD* OR ADOLESCEN*) AND CANAD*)

AND SUBJAREA

(MULT OR AGRI OR BIOC OR IMMU OR NEUR OR PHAR OR MULT OR MEDI OR NURS OR VETE OR DENT OR HEAL)

AND PUBYEAR > 2003

CAB abstracts

("air pollut*" AND "respirat*" AND "child*" AND "Canada").

Indexes=CAB Abstracts Timespan=2004-2014

*Limiters - Published Date: 20040101-20140231; Geographic Subset: Canada; Age Groups: All Child

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