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Current State of Research on the Risk of Morbidity and Mortality Associated with Air Pollution in Korea

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Purpose: The effects of air pollution on health can vary regionally. Our goal was to comprehensively review previous epidemiological studies on air pollution and health conducted in Korea to identify future areas of potential study.

Materials and Methods: We systematically searched all published epidemiologic studies examining the association between air pollution and occurrence of death, diseases, or symptoms in Korea. After classifying health outcomes into mortality, morbidity, and health impact, we summarized the relationship between individual air pollutants and health outcomes.

Results: We analyzed a total of 27 studies that provided 104 estimates of the quantitative association between risk of mortality and exposure to air pollutants, including particulate matter with aerodynamic diameter less than 10 μm, particulate matter with aerodynamic diameter less than 2.5 μm, sulfur dioxide, nitrogen dioxide, ozone, and carbon monoxide in Korea between January 1999 and July 2018. Regarding the association with morbidity, there were 38 studies, with 98 estimates, conducted during the same period. Most studies examined the short-term effects of air pollution using a time series or case-crossover study design; only three cohort studies that examined long-term effects were found. There were four health impact studies that calculated the attributable number of deaths or disability-adjusted life years due to air pollution.

Conclusion: There have been many epidemiologic studies in Korea regarding air pollution and health. However, the present review shows that additional studies, especially cohort and experimental studies, are needed to provide more robust and accurate evidence that can be used to promote evidence-based policymaking.

Key Words: Air pollution, mortality, morbidity, environmental medicine, Korea

INTRODUCTION

The effect of air pollution on mortality and the burden of disease increases as air pollution increases, although estimates can vary from region to region. According to the Global Burden of Disease Study, ambient air pollution accounted for 7.5% of deaths globally in 2016 and was the sixth leading contributor to attributable disability-adjusted life years (DALYs) in that year.[1] Korea has experienced rapid economic growth in the last century, and the quality of the atmosphere has worsened. Air pollution reduction policies, such as the Special Law on Air Quality in the Seoul metropolitan area, have had limited effect on particulate matter (PM) pollution, and the overall air quality remains poor. Concentrations of PM with aerodynamic diameter less than 10 μm (PM_{10}) have improved over the past decade, reaching the lowest national average of 45 μg/m^3 in 2012, and then rebounding to a level of 47 μg/m^3 in 2016. However, the concentration of nitrogen dioxide (NO_2) has remained relatively constant, with no large changes. The average values of ozone (O_3) concentration are continuously increasing.[2]

Epidemiological studies on the health effects of air pollution have been actively conducted in many countries. In particular, time series studies to examine the short-term effects of air pollution have been conducted worldwide and have yielded relatively consistent results.[3,4] However, cohort studies to assess the long-term effects of air pollution have been primar-

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ily conducted in Western countries that have relatively low concentrations of air pollutants. Due to a lack of direct evidence at higher global concentrations, the integrated expose–response (IER) model was developed. The IER combines information on PM-mortality associations from non-outdoor sources, including secondhand smoke, active smoking, and household air pollution,[5] and has been used to estimate the disease burden attributable to PM with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$).[1] As the use of IER requires a strict assumption of equal toxicity per unit dose across these non-outdoor sources, cohort studies are needed that reflect the different air pollution concentrations in different regions.[6]

The health effects of air pollution can vary regionally depending on the composition of pollutants or characteristics of the population at risk. The regional differences in $PM_{2.5}$ mortality risk estimates can likely be attributed to geographic variation in particle composition or the spatial heterogeneity of constituents,[7] as well as differences in the total air pollution mixture.[8] Regional differences of topography, which may lead to regional differences of exposure error, can contribute to regional differences in PM risk estimates.[9]

To accurately understand the impact of air pollution on health in Korea, the results of research performed specifically for Korea are needed. Since the publication of time series research starting in 1999 in Korea,[10] many epidemiological studies have been conducted; however, the results of these studies have not been systematically summarized. To accurately assess the impact of air pollution in Korea and to clarify future research directions, systematic sorting of epidemiological studies on air pollution conducted in Korea is required. The aim of the present analysis was to comprehensively review previous epidemiological studies on air pollution and health conducted in Korea to identify future study needs.

LITERATURE SEARCH

We conducted a literature search in PubMed using the search terms (“air pollution”[MeSH Terms] OR (“air”[All Fields] AND “pollution”[All Fields]) OR “air pollution”[All Fields]) AND (“mortality”[Subheading] OR “mortality”[All Fields] OR “mortality”[MeSH Terms]) AND (“Korea”[MeSH Terms] OR “Korea”[All Fields]) and ((“air pollution”[MeSH Terms] OR (“air”[All Fields] AND “pollution”[All Fields]) OR “air pollution” [All Fields]) AND (“epidemiology”[Subheading] OR “epidemiology” [All Fields] OR “morbidity”[All Fields] OR “morbidity” [MeSH Terms]) AND (“Korea”[MeSH Terms] OR “Korea”[All Fields])) NOT (“mortality”[Subheading] OR “mortality” [MeSH Terms]) to find published studies on the associations of air pollution with mortality and morbidity respectively in Korea, between January 1990 and July 2018.

We also searched for health impact assessment studies using the same search engine and the search terms (“number” [All Fields] AND (“death”[MeSH Terms] OR “death”[All Fields] OR “deaths”[All Fields])) OR “burden of disease”[All Fields] OR “health impact assessment”[All Fields] AND “Korea”[All Fields] AND (“air pollution”[All Fields] OR “ambient”[All Fields]).

After reviewing the title and abstract of each article, we selected epidemiological studies that reported associations between exposure to air pollution and mortality or morbidity. We then summarized these articles according to their characteristics and results.

The initial search for mortality and morbidity returned 87 and 195 results, respectively. After excluding articles that did not meet the inclusion criteria (Fig. 1), there remained 27 (Table 1) and 37 studies (Table 2) on mortality and morbidity, respectively. One of the mortality study also reported morbidity results, so a total of 38 studies were included in the present review. The search for health impact analyses returned 22 studies; four articles remained after a review of titles and abstracts.

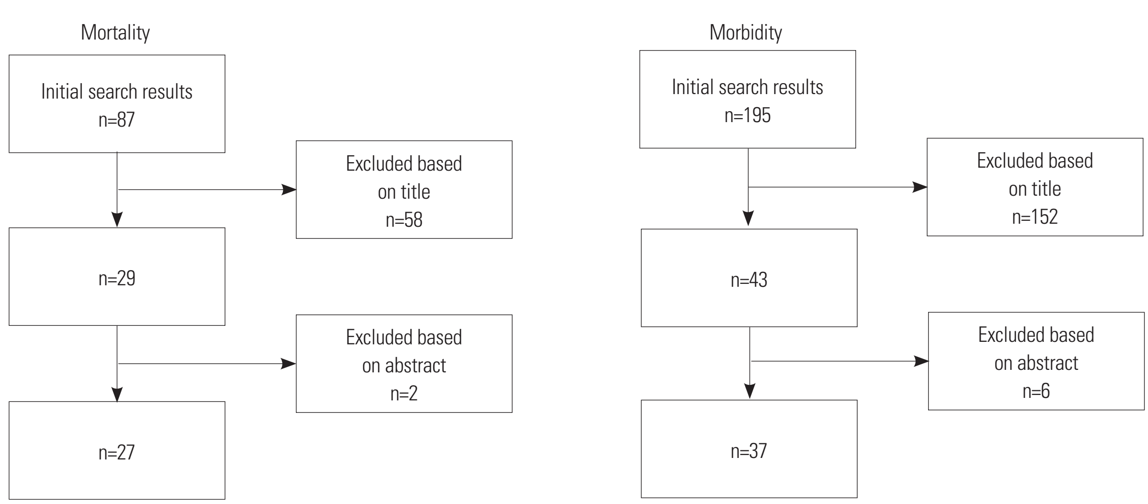

Fig. 1. Selection of papers.

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Table 1. Epidemiological Studies on Air Pollution and Mortality in Korea between 1999 and 2018

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
1	Lee, et al. (1999)[10]	Time series	1991–1995	Seoul	Non-accidental	SO_2	50 ppb	RR 1.078 (1.057, 1.099)
				Ulsan	Non-accidental	SO_2	50 ppb	RR 1.051 (0.991, 1.115)
				Seoul	Non-accidental	TSP	100 μg/m^3	RR 1.051 (1.031, 1.072)
				Ulsan	Non-accidental	TSP	100 μg/m^3	RR 0.999 (0.961, 1.039)
				Seoul	Non-accidental	1 hr max O_3	50 bbp	RR 1.015 (1.005, 1.025)
				Ulsan	Non-accidental	1 hr max O_3	50 bbp	RR 1.020 (0.889, 1.170)
2	Hong, et al. (1999)[13]	Time series	1995	Incheon	Total	TSP	10 μg/m^3	1.2% (0.2, 2.2)
					Total	PM_{10}	10 μg/m^3	1.2% (0.2, 2.1)
3	Lee, et al. (1999)[12]	Case-crossover		Seoul	Non-accidental	SO_2	50 ppb	RR 1.023 (1.016, 1.084)
					Non-accidental	Maximum O_3	50 ppb	RR 1.023 (0.999, 1.048)
					Non-accidental	TSP	100 μg/m^3	RR 1.010 (0.988, 1.032)
4	Hong, et al. (1999)[11]	Time series	1995–1996	Incheon	Total	PM_{10}	10 μg/m^3	RR 1.007 (1.001, 1.0013)
					Total	NO_2		RR 1.0026 (1.0006, 1.0046)
					Total	SO_2		RR 1.0023 (0.9996, 1.0051)
					Total	CO		RR 1.0019 (0.9990, 1.0049)
					Total	O_3		RR 0.9951 (0.9908, 0.9994)
5	Lee, et al. (2000)[59]	Time series	1991–1997	7 cities	Total	TSP	100 μg/m^3	0.5–4%
					Total	SO_2	50 ppb	RR 1.03 (1.01, 1.05)
6	Kwon, et al. (2001)[20]	Time series	1994–1998	Seoul	Total	PM_{10}	IQR (42.1 μg/m^3)	OR 1.014 (1.006, 1.022)
					Total	CO	IQR (0.59 ppm)	OR 1.022 (1.017, 1.029)
					Total	NO_2	IQR (14.6 ppb)	OR 1.021 (1.014, 1.029)
					Total	SO_2	IQR (9.9 ppb)	OR 1.020 (1.012, 1.028)
					Total	O_3	IQR (20.5 ppb)	OR 1.010 (1.002, 1.017)
7	Hong, et al. (2002)[60]	Time series	1995–1998	Seoul	Stroke	PM_{10}	IQR	1.5% (1.3, 1.8)
					Stroke	O_3	IQR	2.9% (0.3, 5.5)
					Stroke	NO_2	IQR	3.1% (1.1, 5.1)
					Stroke	SO_2	IQR	2.9% (0.8, 5.0)
					Stroke	CO	IQR	4.1% (1.1, 7.2)
8	Hong, et al. (2002)[21]	Time series	1991–1997	Seoul	Ischemic stroke	TSP	IQR	RR 1.03 (1.00, 1.06)
					Ischemic stroke	SO_2	IQR	RR 1.04 (1.01, 1.08)
					Ischemic stroke	NO_2	IQR	RR 1.04 (1.01, 1.07)
					Ischemic stroke	CO	IQR	RR 1.06 (1.02, 1.09)
					Ischemic stroke	O_3	IQR	RR 1.06 (1.02, 1.10)
9	Ha, et al. (2003)[61]	Cohort			Total (postneonates)	PM_{10}	IQR (42.9 μg/m^3)	RR 1.142 (1.096, 1.190)
					Respiratory (postneonates)	PM_{10}	IQR (42.9 μg/m^3)	RR 2.018 (1.784, 2.283)
10	Kim, et al. (2003)[15]	Time series	1995–1999	Seoul	Non-accidental	PM_{10}	IQR (43.12 μg/m^3)	3.7% (2.1, 5.4)
					Respiratory	PM_{10}	IQR (43.12 μg/m^3)	13.9% (6.8, 21.5)
					Cardiovascular	PM_{10}	IQR (43.12 μg/m^3)	4.4% (-1.0, 9.0)
					Cerebrovascular	PM_{10}	IQR (43.12 μg/m^3)	6.3% (2.3, 10.5)
11	Kim, et al. (2004)[62]	Time series	1997–2004	Seoul	Non-accidental	PM_{10} (mean)	IQR (42.11 μg/m^3)	RR 1.021 (1.009, 1.035)
					Non-accidental	PM_{10} (SD)	IQR (11.93 μg/m^3)	RR 1.025 (1.000, 1.028)
12	Lee, et al. (2007)[63]	Time series	2000–2004	Seoul	Non-accidental	Asian dust event		Larger effect sizes in the model without Asian dust event
13	Cho, et al. (2008)[64]	Time series	2001	Seoul	Respiratory	Fine particle count	IQR (10.221 number/cm^3)	5.73% (5.03, 6.45)
					Respiratory	Respiratory particle count	IQR (10.38 number/cm^3)	5.82% (5.13, 6.53)

Table 1. Epidemiological Studies on Air Pollution and Mortality in Korea between 1999 and 2018 (Continued)

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
14	Son, et al. (2008)[22]	Case-crossover	1999–2003	Seoul	Infant	PM_{10}	1 μg/m^3	OR 1.000 (0.998, 1.002)
					Infant	NO_2	1 unit	OR 1.002 (0.994, 1.009)
					Infant	SO_2	1 unit	OR 1.015 (0.973, 1.058)
					Infant	CO	1 unit	OR 1.029 (0.833, 1.271)
					Infant	O_3	1 unit	OR 0.984 (0.977, 0.992)
15	Yi, et al. (2010)[75]	Case-crossover	2000–2006	Seoul	Non-accidental	PM_{10}	10 μg/m^3	0.28% (0.12, 0.44)
					Cardiovascular	PM_{10}	10 μg/m^3	0.51% (0.19, 0.83)
					Respiratory	PM_{10}	10 μg/m^3	0.59% (-0.08, 1.26)
16	Kim, et al. (2010)[19]	Case-crossover	2004	7 cities	Suicide	PM_{10}	IQR	9.0% (2.4, 16.1)
					Suicide	$PM_{2.5}$	IQR	10.1% (2.0, 19.0)
17	Park, et al. (2011)[65]	Time-series	1999–2007	Seoul	Non-accidental (high temp. ≥26.2°C)	SO_2	0.5 ppb	0.83% (0.42, 1.25)
					Non-accidental (low temp. <26.2°C)	SO_2	0.5 ppb	0.21% (0.07, 0.36)
18	Son, et al. (2011)[66]	Birth cohort	2004–2007	Seoul	All-cause infant	TSP	IQR	HR 1.44 (1.06, 1.97)
					All-cause infant	PM_{10}	IQR	HR 1.65 (1.18, 2.31)
					All-cause infant	$PM_{2.5}$	IQR	HR 1.53 (1.22, 1.90)
					All-cause infant	$PM_{10-2.5}$	IQR	HR 1.19 (0.83, 1.70)
					Respiratory infant	TSP	IQR	HR 3.78 (1.18, 12.13)
					Respiratory infant	PM_{10}	IQR	HR 6.20 (1.50, 25.66)
					Respiratory infant	$PM_{2.5}$	IQR	HR 3.15 (1.26, 7.85)
					Respiratory infant	$PM_{10-2.5}$	IQR	HR 2.86 (0.76, 10.85)
19	Son, et al. (2012)[14]	Case-crossover	2000–2007	Seoul	Total	PM_{10}	IQR	0.94% (0.25, 1.62)
					Total	NO_2	IQR	2.27% (1.03, 3.53)
					Total	SO_2	IQR	1.94% (0.80, 3.09)
					Total	CO	IQR	2.21% (1.00, 3.43)
					Total	O_3	IQR	Positive/NS
					Cardiovascular	PM_{10}	IQR	1.95% (0.64, 3.27)
					Cardiovascular	NO_2	IQR	4.82% (2.18, 7.54)
					Cardiovascular	SO_2	IQR	3.64% (1.46, 5.87)
					Cardiovascular	CO	IQR	4.32% (1.77, 6.92)
					Cardiovascular	O_3	IQR	Positive/NS
20	Heo, et al. (2014)[67]	Time-series	2003–2007	Seoul	Non-accidental, cardiovascular, respiratory	$PM_{2.5}$ and components		Percentage of excess risk by $PM_{3.5}$ and components
21	Lim, et al. (2014)[68]	GWR	2008–2010	Seoul	Cardiovascular	PM_{10}		Mean β (SE) 0.956 (0.102)
22	Ha, et al. (2015)[69]	Case-crossover	2002–2008	7 cities	Unintentional injury	PM_{10}	IQR (48.3 μg/m^3)	NS
					Unintentional injury	SO_2	IQR (0.005 ppm)	OR 1.119 (1.022, 1.226)
					Unintentional injury	NO_2	IQR (0.02 ppm)	OR 1.208 (1.043, 1.400)
					Unintentional injury	O_3	IQR (0.03 ppm)	NS
					Unintentional injury	CO	IQR (0.36 ppm)	OR 1.012 (1.000, 1.024)
23	Kim, et al. (2017)[16]	Time-series	1993–2009	7 cities	Non-accidental	PM_{10}	10 μg/m^3	0.51% (0.01, 1.01)
24	Kim, et al. (2018)[70]	Time-series	1993–2009	7 cities	Non-accidental	PM_{10}	Daily concentrations of ≥75 μg/m^3	0.48% (0.30, 0.60)
					Cardiovascular	PM_{10}	Daily concentrations of ≥75 μg/m^3	0.48% (0.14, 0.82)
					Respiratory	PM_{10}	Daily concentrations of ≥75 μg/m^3	1.13% (0.37, 1.89)

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Table 1. Epidemiological Studies on Air Pollution and Mortality in Korea between 1999 and 2018 (Continued)

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
25	Kim, et al. (2017)[18]	Cohort	2007–2013	Seoul	Composite cardiovascular events	$PM_{2.5}$	1 μg/m^3	HR 1.41 (1.32, 1.50)
					All-cause	$PM_{2.5}$	1 μg/m^3	HR 1.32 (1.22, 1.43)
					Cardiovascular	$PM_{2.5}$	1 μg/m^3	HR 1.36 (1.11, 1.66)
					Composite cardiovascular events	CO	IQR (0.25 ppm)	HR 1.79 (1.61, 1.99)
					All-cause	CO	IQR (0.25 ppm)	HR 1.72 (1.52, 1.94)
					Cardiovascular	CO	IQR (0.25 ppm)	HR 2.96 (2.12, 4.14)
					Composite cardiovascular events	SO_2	IQR (2.54 ppb)	HR 1.94 (1.78, 2.11)
					All-cause	SO_2	IQR (2.54 ppb)	HR 1.73 (1.55, 1.92)
					Cardiovascular	SO_2	IQR (2.54 ppb)	HR 1.50 (1.14, 1.96)
					Composite cardiovascular events	NO_2	IQR (18.4 ppb)	HR 2.30 (2.08, 2.55)
					All-cause	NO_2	IQR (18.4 ppb)	HR 1.79 (1.59, 2.03)
					Cardiovascular	NO_2	IQR (18.4 ppb)	HR 2.67 (1.94, 3.69)
					Composite cardio-vascular events	O_3	IQR (15.9 ppb)	HR 0.63 (0.63, 0.73)
					All-cause	O_3	IQR (15.9 ppb)	HR 0.68 (0.63, 0.73)
					Cardiovascular	O_3	IQR (15.9 ppb)	HR 0.59 (0.49, 0.71)
26	Kim, et al. (2017)[17]	Cohort	2002–2014	Korea	Non-accidental	PM_{10}	10 μg/m^3	HR 1.05 (0.99, 1.11)
					Cardiovascular	PM_{10}	10 μg/m^3	HR 1.02 (0.90,1.16)
					Cerebrovascular	PM_{10}	10 μg/m^3	HR 1.14 (0.93, 1.39)
					Respiratory	PM_{10}	10 μg/m^3	HR 1.19 (0.91, 1.57)
					Cancer	PM_{10}	10 μg/m^3	HR 1.02 (0.95, 1.10)
					Lung cancer	PM_{10}	10 μg/m^3	HR 0.96 (0.82,1.13)
27	Lee, et al. (2018)[71]	Case-crossover	2002–2013	26 cities	Suicide	PM_{10}	IQR	Increased OR 1.2% (0.2, 2.3)
						NO_2	IQR	Increased OR 4.3% (1.9, 6.7)
						SO_2	IQR	Increased OR 2.2% (0.7, 3.8)
						CO	IQR	Increased OR 2.4% (0.9, 3.8)
						O_3	IQR	Increased OR 1.5% (-0.3, 3.2)

TSP, total suspended particles; IQR, interquartile range; OR, odds ratio; RR, relative risk; HR, hazard ratio; NS, not significant; GWR, geographically weighted regression; 7 cities, Seoul, Incheon, Daejeon, Gwangju, Daegu, Busan, Ulsan.

Air pollution and mortality

Among the included studies, the earliest reports regarding an association between air pollution and mortality in Korea were published in 1999.[10-13] Three of these were time series studies and one was a case-crossover study. Both time series and case-crossover designs are suitable for analysis of acute effects (in days) of short-term exposure to air pollution. One time series analysis was conducted in Seoul and Ulsan. That study reported that the daily variation of ambient concentrations of sulfur dioxide (SO_2), total suspended particles (TSP), and O_3 in Seoul were significantly associated with increased non-accidental mortality.[10] In the same year, the results of reanalysis of Seoul data from the previous time series using a case-crossover approach, in which each participant became its own control, were reported, showing that only SO_2 was significantly associated with non-accidental mortality.[12] Another time series study conducted in Incheon showed that, in addition to TSP, a 10-μg/m^3 increase in the daily mean concentration of PM_{10} was also associated with a 1.2% increase in total mortality.[13] The remaining study was the first to examine the effects of all five criteria pollutants [PM_{10}, SO_2, NO_2, carbon monoxide (CO), and O_3] on mortality in Seoul. That study reported that the previous day's concentrations of PM_{10} and NO_2 were significantly associated with increased daily mortality [relative risks (RRs) of 1.0007 and 1.0026 for PM_{10} and NO_2, respectively].[11]

After 1999, most subsequent studies examined the associations between air pollutants and total or non-accidental mortality using time series analysis and a case-crossover design. However, the effect sizes varied according to different studies. For instance, the percent increase in mortality for an interquartile range (IQR) increment in PM_{10} ranged between 0.9%[14] and 3.7%.[15] This may be due to different factors of these studies, including the study period and area, and a multi-city study may provide more robust effect size. There were few multi-city studies and even fewer reported associations with total mortality. The most recent such study stated that a 10-μg/m^3 increase in daily ambient PM_{10} was associated with a 0.51% increase in mortality.[16]

The effects of air pollution are not only acute but also chronic, and long-term exposure is generally expected to have a much higher effect size than short-term exposure. However, the chronic effect of air pollution has rarely been examined in Korea. In fact, there were only two studies reporting long-term effects of PM exposure on mortality among our search results, one each for PM_{10} and $PM_{2.5}$. Kim, et al.[17] analyzed a sample cohort of the National Health Insurance Service and reported a marginally significant 5% increase in mortality per a 10-μg/m^3 increase in annual PM_{10} concentration. Another study reported a hazard ratio (HR) of 1.32 for all-cause mortality with an increment of 1 μg/m^3 in $PM_{2.5}$.[18] Long-term exposure to other gaseous pollutants was also found to be associated with increased risk of mortality, and CO, SO_2, and NO_2 showed HRs of 1.72, 1.73, and 1.79 for each IQR increase, respectively.

The effect of air pollution exposure on mortality is cause-specific, and the related cardiovascular and respiratory effects are well known. There have been several reports on cardiovascular and respiratory mortality owing to air pollution in Korea. An interesting cause of death that shows an association with air pollution is suicide. In a case-crossover study conducted using data from seven metropolitan cities in Korea (Seoul, Incheon, Daejeon, Gwangju, Daegu, Busan, and Ulsan), the authors reported that an IQR increase of $PM_{2.5}$ was associated with a 10.1% increase in the number of suicides.[19]

Most gaseous air pollutants (SO_2, NO_2, and CO) showed consistently significant associations with increased mortality. For acute exposure, an IQR increase of SO_2, NO_2, and CO increased daily mortality about 2%, and an IQR increase in chronic exposure to those three pollutants showed consistent RRs of around 1.7 (Table 1). However, the association between ambient O_3 concentration and mortality seems inconclusive. Two studies reported significant positive associations of O_3 concentration with total mortality[20] and ischemic stroke mortality.[21] However, we also found reports of significant negative associations with all-cause,[13,18] cardiovascular,[18] and infant mortality.[22]

Air pollution and morbidity

Asthma and respiratory diseases were among the first specific disorders analyzed in Korea. A time series analysis conducted in Seoul reported that an IQR increase in PM_{10}, SO_2, NO_2, CO, and O_3 showed significant RRs for children's asthma hospitalization of 1.07, 1.11, 1.15, 1.16 and 1.12, respectively.[23] Another study reported the results of a children's panel for NO_2 exposure showing an OR of 1.12 for upper respiratory symptoms and ORs for lower respiratory symptoms of 1.18, 1.12, and 1.16 for increased exposures to NO_2, SO_2, and CO, respectively.[24] O_3 was also associated with children's asthma hospitalization, especially in groups with lower socioeconomic status (RR: 1.32, 95% CI: 1.11, 1.58).[25] In a cohort study, O_3 concentration was associated with a 12-month prevalence of wheeze[26] and airway hyperresponsiveness[27] in children. Other allergic disorders, such as allergic rhinitis and atopic dermatitis, were also associated with air pollution (Table 2).

Similar to the association between air pollution and cardiovascular mortality, the morbidity of cardiovascular and cerebrovascular diseases, such as stroke, myocardial infarction, and hypertension, were also significantly associated with increased exposure to air pollution. A time series analysis reported that NO_2 increased stroke (RR=1.2, p-value=0.001),[28] and a cohort study reported that long-term exposure to $PM_{2.5}$, CO, SO_2, and NO_2 increased the risk of acute myocardial infarction, congestive heart failure, and stroke (Table 2).[18]

We found two studies examining the association of air pollution with cancer. In these recent studies, indoor radon concentrations were associated with an increased risk of male lung cancer and non-Hodgkin's lymphoma in girls,[29] and conventional air pollutants (PM_{10} and NO_2) were associated with lung cancer with marginal significance.[30]

Similar to the association of suicide with air pollution, depressive symptoms were also found to be associated with air pollution in Korea. A panel study examining air pollution and depressive symptoms was one of the first to report such an association.[31] An association between $PM_{2.5}$ and major depressive disorder was also found in a community-based urban cohort.[32]

Birth outcome has been another subject of analysis. PM_{10}, SO_2, and CO exposures were reported to have significant associations with low birth weight in a cohort study.[33,34]

Health impact assessment

Among four studies (Table 3), two calculated the attributable number of deaths,[35,36] one calculated the attributable number of deaths and morbidity,[37] and a fourth calculated DALYs.[38]

There were substantial differences in the attributable number of deaths among the study results. For instance, Leem, et al.[37] estimated the number of deaths attributable to $PM_{2.5}$ to be 15346 in the Seoul metropolitan area, whereas Han, et al.[36] estimated this number to be 1763. Yorifuji, et al.[35] estimated the number of deaths attributable to PM_{10} over 20 μg/m^3 at 5840 in Seoul. These numbers are substantially different, even when considering the differences in study area, study period, and pollutants investigated.

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Table 2. Epidemiological Studies on Air Pollution and Morbidity in Korea between 1999 and 2018

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
1	Lee, et al. (2002)[23]	Time series		Seoul	Asthma hospitalization	PM_{10}	IQR (40.4 μg/m^3)	RR 1.07 (1.04, 1.11)
					Asthma hospitalization	SO_2	IQR (4.4 ppb)	RR 1.11 (1.06, 1.17)
					Asthma hospitalization	NO_2	IQR (14.6 ppb)	RR 1.15 (1.10, 1.20)
					Asthma hospitalization	O_3	IQR (21.7 ppb)	RR 1.12 (1.07, 1.16)
					Asthma hospitalization	CO	IQR (1.0 ppm)	RR 1.16 (1.10, 1.22)
2	Lee, et al. (2005)[24]	Panel study	2003	Seoul	Upper respiratory symptoms	NO_2		OR 1.12 (1.01, 1.24)
					Lower respiratory symptoms	NO_2		OR 1.18 (1.06, 1.31)
					Lower respiratory symptoms	SO_2		OR 1.12 (1.01, 1.25)
					Lower respiratory symptoms	CO		OR 1.16 (1.02, 1.32)
3	Son, et al. (2006)[25]	Time series	2002	Seoul	Asthma hospitalization (highest SES)	O_3		RR 1.12 (1.00, 1.25)
					Asthma hospitalization (moderate SES)	O_3		RR 1.24 (1.08, 1.43)
					Asthma hospitalization (lowest SES)	O_3		RR 1.32 (1.11, 1.58)
4	Lee, et al. (2007)[72]	Natural experiment	2002	Busan	Childhood asthma hospitalization		RR post Asian game period/ RR baseline	0.73 (0.49, 1.11)
5	Lee, et al. (2006)[73]	Time series	2002	Seoul	Asthma hospitalization	PM_{10}	IQR	31% (14, 51)
					Asthma hospitalization	SO_2	IQR	29% (8, 53)
					Asthma hospitalization	NO_2	IQR	29% (5, 58)
6	Seo, et al. (2007)[33]	Cohort	2002–2003	Seoul	Low birth weight	CO	IQR	RR 1.081 (1.002, 1.166)
					Low birth weight	SO_2	IQR	RR 1.145 (1.036, 1.267)
					Low birth weight	PM_{10}	IQR	RR 1.053 (1.002, 1.108)
					Low birth weight	NO_2	IQR	RR 1.003 (0.954, 1.055)
7	Moon, et al. (2009)[74]			4 cities	Respiratory symptoms	5 criteria pollutants		Significant positive association with SO_2 and NO_2
8	Seo, et al. (2010)[34]	Cohort	2004	Seoul	Low birth weight	PM_{10}		OR 1.08 (0.99, 1.18)
				Busan	Low birth weight	PM_{10}		OR 1.24 (1.02, 1.52)
				Daegu	Low birth weight	PM_{10}		OR 1.19 (1.04, 1.37)
				Incheon	Low birth weight	PM_{10}		OR 1.12 (0.98, 1.28)
				Gwangju	Low birth weight	PM_{10}		OR 1.22 (0.98, 1.52)
				Daejeon	Low birth weight	PM_{10}		OR 1.06 (1.00, 1.11)
				Ulsan	Low birth weight	PM_{10}		OR 1.19 (1.03, 1.38)
9	Yi, et al. (2010)[75]*	Case-crossover	2001–2006		Cardiovascular hospitalization	PM_{10}	10 μg/m^3	0.77% (0.53, 1.01)
					Respiratory hospitalization	PM_{10}	10 μg/m^3	1.19% (0.94, 1.44)
10	Kim, et al. (2011)[26]	Cohort			12-month prevalence of wheeze	O_3	5 ppb	OR 1.372 (1.016, 1.852)
11	Lim, et al. (2012)[31]	Panel study		Seoul	Depression (SGDS-K)	PM_{10}	IQR	17.0% (4.9, 30.5)
					Depression (SGDS-K)	NO_2	IQR	32.8% (12.6, 65.6)
					Depression (SGDS-K)	O_3	IQR	43.7% (11.5, 85.2)
12	Kim, et al. (2012)[76]	Panel study		Seoul	Insulin resistance	PM_{10}, O_3, NO_2	IQR	Significantly increased
13	Kim, et al. (2013)[77]	Cross sectional			Allergic diseases	Traffic related pollutants	Polluted vs. non-polluted school	OR 2.12 (1.41, 3.19)
14	Kim, et al. (2013)[27]	Cohort			Airway hyperresponsiveness	O_3		OR 1.60 (1.13, 2.27)
					New episodes of wheezing	O_3		OR 1.92 (0.96, 3.83)

Table 2. Epidemiological Studies on Air Pollution and Morbidity in Korea between 1999 and 2018 (Continued)

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
15	Han, et al. (2013)[78]				Hemorrhagic fever with renal syndrome	PM_{10}	1 μg/m^3	0.013 increase of monthly cases
16	Son, et al. (2013)[79]		2003–2008	8 cities	Allergic disease hospital admission	PM_{10}	IQR (30.7 μg/m^3)	2.2% (0.5, 3.9)
					Asthma hospital admission	PM_{10}	IQR (30.7 μg/m^3)	2.8% (1.3, 4.4)
					Respiratory hospital admission	PM_{10}	IQR (30.7 μg/m^3)	1.7% (0.9, 2.6)
					Cardiovascular hospital admission	PM_{10}	IQR (30.7 μg/m^3)	0.7% (0.0, 1.4)
					Allergic disease hospital admission	NO_2	IQR (12.2 ppb)	2.3% (0.6, 4.0)
					Asthma hospital admission	NO_2	IQR (12.2 ppb)	2.2% (0.3, 4.1)
					Respiratory hospital admission	NO_2	IQR (12.2 ppb)	2.2% (0.6, 3.7)
					Cardiovascular hospital admission	NO_2	IQR (12.2 ppb)	2.2% (1.1, 3.4)
17	Park, et al. (2013)[80]	Time series		7 cities	Asthma admission	PM_{10}, CO, O_3, NO_2	Children vs. adult	Lower risk in children for PM_{10} and CO
18	Kim, et al. (2014)[81]	Cohort			Neurodevelopment (MDI)	PM_{10}		β=-2.83; p=0.003
					Neurodevelopment (PDI)	PM_{10}		β=-3.00; p=0.002
19	Hwang, et al. (2014)[82]	Retrospective cohort		Seoul	Tuberculosis	SO_2	IQR	RR 1.07 (1.03, 1.12)
20	Han, et al. (2015)[28]	Time series	2004–2013		Stroke	NO_2		RR 1.262, p=0.001
21	Kim, et al. (2015)[83]	Case-crossover		Korea	Hourly asthma ED visit	$PM_{10\text{-}2.5}$	IQR	OR 1.05 (1.00, 1.11)
					Hourly asthma ED visit	O_3	IQR	OR 1.10 (1.04, 1.16)
22	Jang, et al. (2015)[84]	Ecological		Korea	Monthly malaria incidence	NO_2		β=-0.884, p<0.01
23	Shim, et al. (2016)[85]	Cross sectional	2010–2013	Korea	Benign prostate hyperplasia	NO_2		OR 2.23 (1.55, 2.39)
					Benign prostate hyperplasia	SO_2		OR 2.02 (1.42, 2.88)
24	Kang, et al. (2016)[86]	Time series	2006–2013	Seoul	Cardiac arrest	$PM_{2.5}$	10 μg/m^3	1.30% (0.20, 2.41)
25	Kim, et al. (2016)[87]	Cross sectional			Allergic rhinitis	CO (during the first year of life)	100 ppb	OR 1.10 (1.03, 1.19)
					Atopic dermatitis	CO (past 12 months)	1 ppm	OR 8.11 (1.06, 62.12)
26	Kim, et al. (2016)[88]	Cross sectional			Asthma	NO_2		OR 1.67 (1.03, 2.71)
					Allergic rhinitis	Black carbon		OR 1.60 (1.36, 1.90)
					Allergic rhinitis	SO_2		OR 1.09 (1.01, 1.17)
					Allergic rhinitis	NO_2		OR 1.18 (1.07, 1.30)
27	Han, et al. (2016)[89]	Time series	2004–2014	Seongdong-gu, Seoul	Intracerebral hemorrhage	PM_{10}		RR 1.09 (1.02, 1.15)
					Subarachnoid hemorrhage	O_3		RR 1.32 (1.10, 1.58)
28	Kim, et al. (2016)[32]	Cohort	2002–2010	Korea	Major depressive disorder	$PM_{2.5}$	10 μg/m^3	HR 1.44 (1.17-1.78)
29	Lee, et al. (2016)[90]	Cross sectional	2008–2010	Korea	Hypertension	PM_{10}	10 μg/m^3	OR 1.042 (1.009, 1.077)
					Hypertension in >30 years old	PM_{10}	10 μg/m^3	OR 1.044 (1.009, 1.079)
					Stroke	PM_{10}	10 μg/m^3	OR 1.044 (0.979, 1.114)
					Angina	PM_{10}	10 μg/m^3	OR 0.977 (0.901, 1.059)
					Hypertension	NO_2	10 ppb	OR 1.077 (1.044, 1.112)
					Hypertension in >30 years old	NO_2	10 ppb	OR 1.080 (1.043, 1.118)
					Stroke	NO_2	10 ppb	OR 1.073 (0.994, 1.157)
					Angina	NO_2	10 ppb	OR 1.047 (0.968, 1.134)
					Hypertension	CO	10 ppb	OR 1.123 (0.963, 1.310)
					Hypertension in >30 years old	CO	10 ppb	OR 1.129 (0.963, 1.387)
					Stroke	CO	10 ppb	OR 1.336 (0.987, 2.011)

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Table 2. Epidemiological Studies on Air Pollution and Morbidity in Korea between 1999 and 2018 (Continued)

No.	Author (year)	Study design	Study period	Location	Outcome	Pollutant	Unit	Effect size
30	Lee, et al. (2017)[91]	Cross sectional	2008–2011	Korea	Pterygium	PM_{10}	5 μg/m^3	OR 1.23 *p*=0.023
31	Chung, et al. (2017)[92]				Cardioembolic stroke	PM_{10}		Significantly increased
					Cardioembolic stroke	SO_2		Significantly increased
32	Kim, et al. (2016)[93]	Randomized intervention trial			Atopic dermatitis	Indoor VOC	Environmentally friendly vs. PVC wallpaper	More improvement in environmentally friendly wallpaper group
33	Ha, et al. (2017)[29]	Ecological	1999–2008		Male lung cancer	Indoor radon	10 Bq/m^3	1%
					Female children non-Hodgkin's lymphoma	Indoor radon	10 Bq/m^3	7%
34	Hwang, et al. (2017)[94]	Time series			Cardiovascular ED visit	NH4+ ($PM_{2.5}$ component)		RR 1.05 (1.01, 1.09)
35	Kim, et al. (2017)[18]*	Cohort	2007–2013	Seoul	Acute myocardial infarction	$PM_{2.5}$	1 μg/m^3	1.36 (1.19, 1.56)
					Congestive heart failure	$PM_{2.5}$	1 μg/m^3	1.44 (1.29, 1.61)
					Stroke	$PM_{2.5}$	1 μg/m^3	1.39 (1.27, 1.52)
					Acute myocardial infarction	CO	IQR (0.25 ppm)	2.12 (1.72, 2.61)
					Congestive heart failure	CO	IQR (0.25 ppm)	1.86 (1.56, 2.21)
					Stroke	CO	IQR (0.25 ppm)	2.00 (1.73, 2.30)
					Acute myocardial infarction	SO_2	IQR (2.54 ppb)	1.82 (1.52, 2.19)
					Congestive heart failure	SO_2	IQR (2.54 ppb)	2.00 (1.73, 2.32)
					Stroke	SO_2	IQR (2.54 ppb)	2.25 (2.00, 2.54)
					Acute myocardial infarction	NO_2	IQR (18.4 ppb)	1.81 (1.46, 2.25)
					Congestive heart failure	NO_2	IQR (18.4 ppb)	2.40 (2.02, 2.85)
					Stroke	NO_2	IQR (18.4 ppb)	2.65 (2.29, 3.06)
					Acute myocardial infarction	O_3	IQR (15.9 ppb)	0.71 (0.63, 0.82)
					Congestive heart failure	O_3	IQR (15.9 ppb)	0.64 (0.58, 0.71)
					Stroke	O_3	IQR (15.9 ppb)	0.60 (0.55, 0.65)
36	Lamichhane, et al. (2017)[30]	Case-control		Korea	Lung cancer	PM_{10}	10 μg/m^3	OR 1.09 (0.96, 1.23)
						NO_2	10 ppb	OR 1.10 (1.00, 1.22)
37	Yi, et al. (2017)[95]	Cross sectional	2010	Seoul	Children's atopic eczema	Road density		OR 1.08 (1.01, 1.15)
						Road proximity		OR 1.15 (1.01, 1.31)
38	Lamichhane, et al. (2018)[96]	Birth cohort			Fetal growth (BPD)	PM_{10}	10 μg/m^3	-0.26 mm (-0.41, -0.11)
						NO_2	10 μg/m^3	-0.30 mm (-0.59, -0.03)

SES, socioeconomic status; SGDS-K, Short Geriatric Depression Scale-Korean; MDI, mental developmental index; PDI, psychomotor developmental index; BPD, biparietal diameter; VOC, volatile organic carbon; PVC: polyvinyl chloride; IQR, interquartile range; OR, odds ratio; RR, relative risk; HR, hazard ratio; 7 cities, Seoul, Incheon, Daejeon, Gwangju, Daegu, Busan, Ulsan.
*From the search results of mortality studies.

DISCUSSION

Beginning in 1999, many studies have been conducted to elucidate the health effects of air pollution in Korea. These studies have reported associations with mortality (all-cause, respiratory, cerebrovascular, cardiovascular, infant, injury, and suicide) and morbidity (allergic, respiratory, cardiovascular, cerebrovascular, adverse birth outcomes, depression, and cancer). Most studies examined the short-term effects of air pollution using a time series or case-crossover study design; we found only three cohort studies that examined long-term effects. There were four studies that estimated the health impacts of air pollution, and except for one study that reported DALYs, three studies had inconsistent estimations of the attributable number of deaths.

Estimating health impacts is usually conducted later than other research as previously estimated associations between exposure and outcome, or concentration-response function (C-R function) are required.[39] Naturally, the estimated health impact depends on the C-R function used. We suspect that differences in the attributable number of deaths estimated in the three studies reviewed here is partly due to the different

Table 3. Studies Estimating Health Impact of Air Pollution Conducted in Korea

No.	Autor (year)	Study period	Location	Outcome	Pollutant	Health impact (person)
1	Leem, et al. (2015)[37]	2010	Seoul metropolitan area	Attributable number of deaths	$PM_{2.5}$	15346
				Attributable number of respiratory hospital admission	PM_{10}	12511
				Attributable number of cardiovascular hospital admission	$PM1_{0}$	12351
				Attributable number of lung cancer incidence	PM_{10}	1403
				Attributable number of asthma attack (children)	PM_{10}	11389
				Attributable number of asthma attack (adults)	PM_{10}	44006
				Attributable number of chronic bronchitis	PM_{10}	20490
				Attributable number of acute bronchitis	PM_{10}	278346
2	Yorifuji, et al. (2015)[35]	2009	Seoul	Attributable number of deaths	PM_{10} over 20 μg/m^3	5840
			Busan	Attributable number of deaths	PM_{10} over 20 μg/m^3	2465
			Daegu	Attributable number of deaths	PM_{10} over 20 μg/m^3	1466
			Incheon	Attributable number of deaths	PM_{10} over 20 μg/m^3	1931
			Daejeon	Attributable number of deaths	PM_{10} over 20 μg/m^3	599
			Gwangju	Attributable number of deaths	PM_{10} over 20 μg/m^3	698
			Ulsan	Attributable number of deaths	PM_{10} over 20 μg/m^3	539
3	Yoon, et al. (2015)[38]	2007	Korea	Disability-adjusted life years	Out door air pollution	6.89/1000 person
4	Han, et al. (2018)[36]	2015	Korea	Attributable number of deaths	$PM_{2.5}$	11924
			Seoul	Attributable number of deaths	$PM_{2.5}$	1763
			Busan	Attributable number of deaths	$PM_{2.5}$	947
			Daegu	Attributable number of deaths	$PM_{2.5}$	672
			Incheon	Attributable number of deaths	$PM_{2.5}$	309
			Gwangju	Attributable number of deaths	$PM_{2.5}$	657
			Daejeon	Attributable number of deaths	$PM_{2.5}$	342
			Ulsan	Attributable number of deaths	$PM_{2.5}$	222
			Sejong	Attributable number of deaths	$PM_{2.5}$	49

C-R functions applied by the authors. Specifically, Yorifuji, et al.[35] and Leem, et al.[37] used C-R functions for mortality derived from epidemiological studies conducted in the United States (U.S.), whereas Han, et al.[36] used an IER function developed for the Global Burden of Disease 2010 and 2013. The C-R function derived from U.S. studies only accounted for a relatively low level of PM; thus, it may be inadequate for estimation of health impacts in Korea where exposure to higher concentrations of PM is observed. The IER function was developed by integrating various C-R functions of other exposures, such as tobacco smoke and burning of indoor solid fuel, to fill the gap in exposure range.[36] However, it remains uncertain whether the C-R function is comparable to the higher exposure range observed in Korea. Considering this, it is important to produce C-R functions using Korean data to accurately estimate the health impacts of exposure to air pollution.

As mentioned above, the effect of air pollution exposure can be divided into short-term and long-term effects. Typically, short-term effects are examined using time series and case-crossover studies, and long-term effects are investigated in cohort studies. The most recent time series study in Korea reported a 0.51% increase in mortality for each 10-μg/m^3 increase in PM_{10}.[16] This is comparable to the results of a recent meta-analysis of studies from East Asian cities, including Seoul and Incheon, which reported a 0.47% increase in total mortality for the same amount of increase in PM_{10}.[40] Similarly, although we could not find health impact assessment studies regarding air pollutants other than PM, we believe that previous epidemiological studies can provide relatively robust C-R functions for NO_2 and SO_2 to estimate health impacts.

Previous studies have reported inconsistent associations between O_3 exposure and mortality. Some published studies have reported a negative association, and the cause of this negative association has been an intriguing subject for additional analysis. One hypothesis is that the C-R function between O_3 concentration and mortality is not linear.[41] Time series analyses conducted in Korea and Japan support this hypothesis in short-term associations.[42,43] However, such non-linearity has not been observed in other studies,[44,45] and the shape of the C-R function between O_3 concentration and acute mortality is still controversial. Nevertheless, studies analyzing the C-R function for long-term exposure of O_3 and mortality consistently report no evidence of a threshold.[46,47] However, these studies may not have accounted for lower concentrations of O_3; this may be the reason for not observing a non-linear association, as the reported threshold of non-linear associations tends to

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be at lower concentrations. The negative association reported in a cohort study conducted by Kim, et al.[18] may suggest the existence of a non-linear C-R function between long-term exposure to O_3 and mortality because Korea has lower concentrations of O_3 than the U.S.;[43] however, no analysis has been conducted using Korean data, as far as we know.

Among the two cohort studies on air pollution and mortality, one study examined the long-term health effects of $PM_{2.5}$ exposure. Although it is a valuable addition to the current knowledge, the results of that study seem inconsistent with previous reports. For instance, Kim, et al.[18] reported an HR of 1.32 for all-cause mortality for a 1-μg/m^3 increment of $PM_{2.5}$ in a cohort constructed using the National Health Insurance Service database, and a recent U.S. study analyzing a cohort constructed from a Medicare database reported an HR of 1.073 for a 10-μg/m^3 increment of $PM_{2.5}$.[47] Kim, et al.[18] suggested possible differences in the effect and composition of $PM_{2.5}$, genetic characteristics, and range of exposure between these studies, although we find a more than 30-fold greater HR difficult to explain. The largest difference between these two studies was in exposure assessment. Kim, et al.[18] linked the concentration measured at a fixed monitoring station to the addresses of participants, whereas Di, et al.[47] used a model-based estimation of individual exposure. Another cohort study examined the long-term effect of PM_{10} exposure.[17] Those authors reported similar effects for PM_{10} exposure, although the association was not statistically significant. However, this latter study applied an exposure assessment strategy, which could alleviate the effect of misclassification caused by participant mobility and exposure measurement at fixed monitoring stations.

Conventionally, air pollution studies use concentrations measured at fixed monitoring stations for exposure, which is an advantage for providing a large amount of data for a wide range of pollutants. However, data linked to study participants' addresses may not reflect individual exposure, especially when the mobility pattern of individuals is not accounted for.[48] This limitation may lead to misclassification, which may have substantial implications for the interpretation of results.[49] In recent years, advanced sensor and modeling technologies have facilitated individual exposure measurement in air pollution studies with the use of personal sensors and various exposure models based on dispersion models, geographical information, and satellite images.[48,50,51] Estimation of exposure using these methods in Korea has been reported recently,[52] and these individual exposure estimation methods should be applied in future studies to reduce uncertainty.

In addition to observational studies, there have been many intervention studies on air pollution and its health effects. Recent intervention studies have explored the benefits of exposure reduction using devices, such as an air purifier[53,54] and facemasks,[55] in randomized controlled trials. The strength of intervention studies is two-fold: First, intervention studies may provide more robust evidence regarding the health effects of exposure to air pollution. Second, these trials may provide evidence regarding the effectiveness of personal measures that can be used to reduce the effects of air pollution. However, due to ethical and practical limitations, randomized controlled trials can only be applied to evaluate acute effects of exposure to air pollution. For instance, it may be unfeasible and unethical to design a study in which a portion of study participants are asked to wear facemasks for a long period (e.g., years). Causal modeling is a method that has been proposed to mitigate the shortcomings of observational studies without the need to conduct a randomized trial. This approach includes marginal structure modeling, instrumental variable analysis, and negative exposure control.[56] The causal modeling approach provides associations that are free of confounding under certain assumptions, which can be interpreted as causal, similar to the results of a trial. To date, there had been reports on the causal associations of $PM_{2.5}$, black carbon, and NO_2 in various circumstances.[57,58] Such experimental studies are necessary so as to correctly assess the effects of air pollution on health and to facilitate more effective interventions through which to reduce exposure and to mitigate the health effects of air pollution.

Finally, despite our best efforts to comprehensively summarize the study results regarding the health effects of air pollution exposure in Korea, it is possible that we did not compile a complete list of all relevant research, which should be considered a limitation of the present review.

CONCLUSION

In the present review, we presented epidemiological studies conducted in Korea examining the health effects of exposure to air pollution. For the past 2 decades, there has been a considerable accumulation of knowledge regarding air pollution and health in Korea. However, the present review highlights that additional studies, especially cohort and experimental studies, are needed to provide more robust and accurate evidence that can be used to promote evidence-based policymaking.

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AUTHOR CONTRIBUTIONS

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