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REVIEW

Challenges of Air Pollution and Health in East Asia

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Abstract

Purpose of Review Air pollution has been a serious environmental and public health issue worldwide, particularly in Asian countries. There have been significant increases in epidemiological studies on fine particulate matter ($PM_{2.5}$) and ozone pollution in East Asia, and an in-depth review of epidemiological evidence is urgent. Thus, we carried out a systematic review of the epidemiological research on $PM_{2.5}$ and ozone pollution in East Asia released in recent years.

Recent Findings Recent studies have indicated that $PM_{2.5}$ and ozone are the most detrimental air pollutants to human health, resulting in substantial disease burdens for Asian populations. Many epidemiological studies of $PM_{2.5}$ and ozone have been mainly performed in three East Asian countries (China, Japan, and South Korea).

Summary We derived the following summary findings: (1) both short-term and long-term exposure to $PM_{2.5}$ and ozone could raise the risks of mortality and morbidity, emphasizing the need for continuing improvements in air quality in East Asia; (2) the long-term associations between $PM_{2.5}$ and mortality in East Asia are comparable to those observed in Europe and North America, whereas the short-term associations are relatively smaller in magnitude; and (3) further cohort and intervention studies are required to yield robust and precise evidence that can promote evidence-based policymaking in East Asia. This updated review presented an outline of the health impacts of $PM_{2.5}$ and ozone in East Asia, which may be beneficial for the development of future regulatory policies and standards, as well as for designing subsequent investigations.

Keywords Air pollution · East Asia · Health · Shot-term effect · Long-term effect

Introduction

Air pollution has become a crucial worldwide scientific and political issue [1, 2•]. Nearly all of the global population (99%) is exposed to air pollutants that surpass the World Health Organization (WHO) guideline limits and contains elevated levels of air pollutants [3]. In 2021, ample evidence of air pollutants exposure-induced adverse health effects prompted the WHO to tighten the air quality guidelines (AQG) for both fine particulate matter ($PM_{2.5}$) and ozone [4••]. The highest burden of air pollution falls on low- and middle-income countries [5]. According to recent estimates, air pollution exposure worldwide leads to 7 million premature deaths per year [6]. A considerable proportion of the population (92%), approximately 4 billion individuals, confront air pollutants that pose significant health risks in Asia and the Pacific region [6].

Over the last decade, $PM_{2.5}$ and ozone pollution have become a widespread health concern in Asia. Notably, the State of Global Air Report 2020 revealed that five Asian countries (India, Nepal, Qatar, Bangladesh, and Pakistan) were among the top 10 countries with the highest $PM_{2.5}$ pollution exposure [7•]. Ozone is also an air pollutant that poses risks to human health. Ozone reacts with the lining of the lungs and other surfaces in the respiratory system, which could affect cardiorespiratory function when inhaled [8]. Mounting epidemiological studies of $PM_{2.5}$ and ozone have been mainly performed in three East Asian countries (China, Japan, and South Korea). These studies have suggested that

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$PM_{2.5}$ and ozone are the most detrimental air pollutants to human health, resulting in substantial disease burdens for Asian populations.

Thus, in the current study, we aimed to perform a comprehensive review of the latest epidemiological research concerning the impact of air pollution exposure on human health in East Asia. We focused on $PM_{2.5}$ and ozone, as they were both included in the Global Burden of Disease Study. The systemic review includes the following key sections: (1) evaluating the epidemiological evidence regarding both short-term and long-term associations between $PM_{2.5}$ and ozone and adverse health outcomes; (2) exploring the intricate relationship between air pollution and climate change in East Asia; and (3) summarizing the challenges, significance, and perspectives in this area.

Levels and Trends of Air Pollution in East Asia

The rapid growth of the economy in Asia has led to a significant increase in air pollutant emissions over the past few decades. In 2019, the highest annual average $PM_{2.5}$ was predominantly observed in Asia [7•]. For example, inhalable particle pollution in Mongolia is relatively higher than in most of the Asian countries. There are some urban emission-controlling methods used such as fuel switching to gas and low-sulfur coal to reduce air pollution. However, there are a large number of combustion sources that may be difficult to control, and the efficiency of these technologies and levels of emission control remain low in Mongolia [9]. Notably, some regions have witnessed great improvements in air quality in recent years, particularly in Southeast and East Asia, led by China, Vietnam, and Thailand. In recent decades, the Chinese, Japanese, and South Korean governments have embarked on rigorous policies and measures to address and mitigate air pollution (Figure S1). Specifically, prominent initiatives in China include the implementation of the Air Pollution Prevention and Control Action Plan (CAP) from 2013 to 2017, as well as the Three-Year Action Plan spanning from 2018 to 2020. These initiatives played a central role in the government's efforts to tackle air pollution challenges in China. These measures have resulted in significant progress in improving the air quality of China (Figure S1A). However, it should be acknowledged that these air pollutant concentrations in China are still well beyond the global means (Fig. 1). Specifically, in 2021, the annual $PM_{2.5}$ in 339 major cities across China was recorded at 30 μg/m^3. Although this level slightly falls below the existing air quality standards (AQS) in China, which stipulates the threshold of $PM_{2.5}$ at 35 μg/m^3, it still surpasses the updated AQG established by the WHO (5 μg/m^3). Despite the ever-increasing numbers of premature deaths and disability-adjusted life years associated with $PM_{2.5}$ in East Asia (Fig. 2), the rate is somewhat moderate in comparison to the average growth rate worldwide.

Global ozone exposures range from a low level of approximately 12.2 parts per billion (ppb) to a high level of 67.2 ppb across the world.

Over the last decade, ozone pollution has emerged as an increasingly severe environmental problem and an important contributor of disease burden in major cities of East Asia (Figs. 3 and 4). China's rapid economic development has led to an increased demand for energy and higher utilization of fossil fuels. Consequently, ozone pollution is severe in metropolitan regions of China, where daily maximum 8-h average ozone concentrations routinely surpass the recommended level of 80 parts ppb [8]. China has devoted substantial resources to reducing air pollution, but ambient ozone levels remained or even increased. Research studies have reported a decrease in ozone concentrations year-by-year in most countries of Asia, except

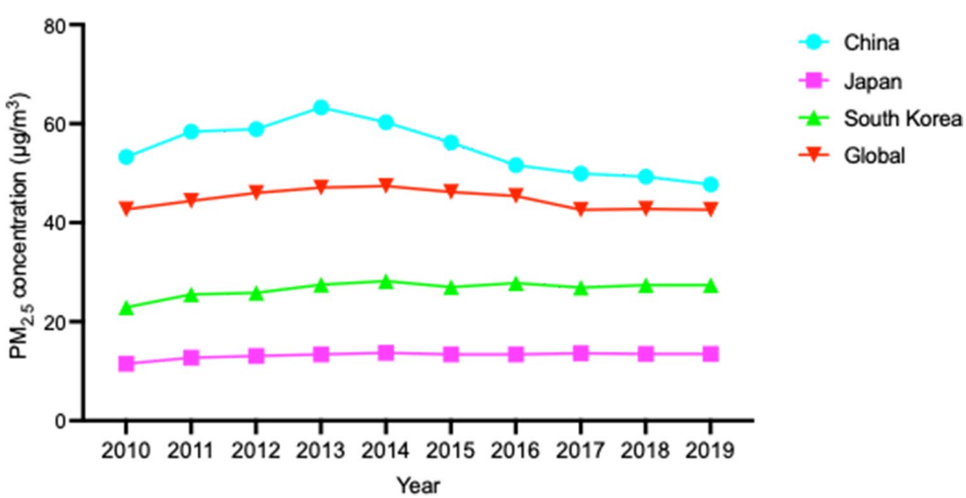

Fig. 1 Average annual population-weighted $PM_{2.5}$ concentration in China, Japan, and South Korea compared with global data from 2010 to 2019 (source: derived from State of Global Air 2020)

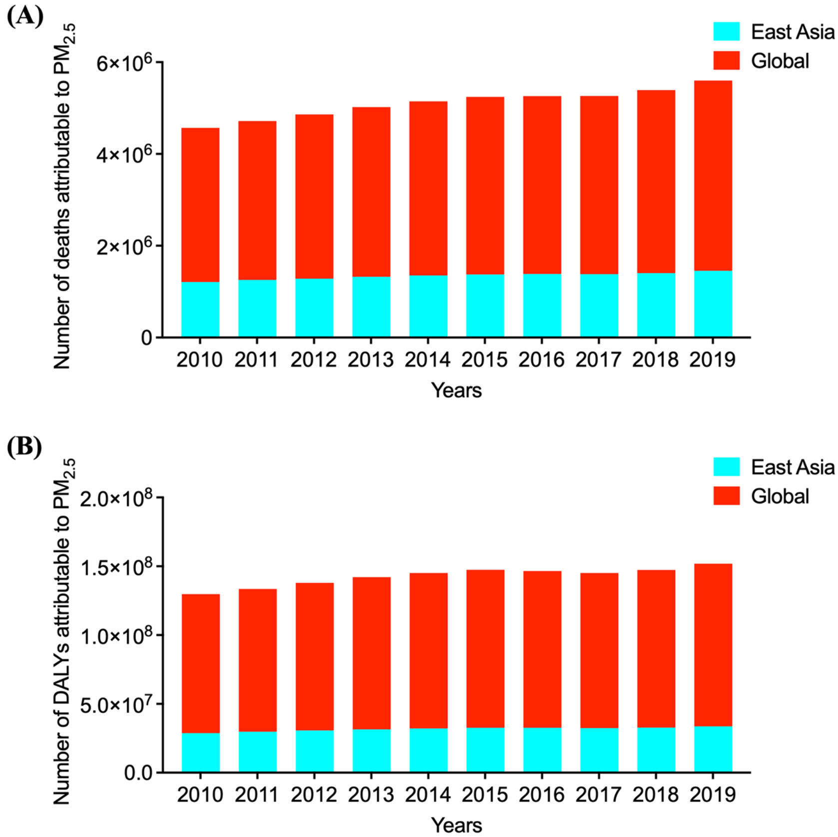

Fig. 2 Number of deaths and disability-adjusted life years (DALYs) attributable to $PM_{2.5}$ in East Asia compared with global data from 2010 to 2019 (data source: derived from Global Burden of Disease Study 2019)

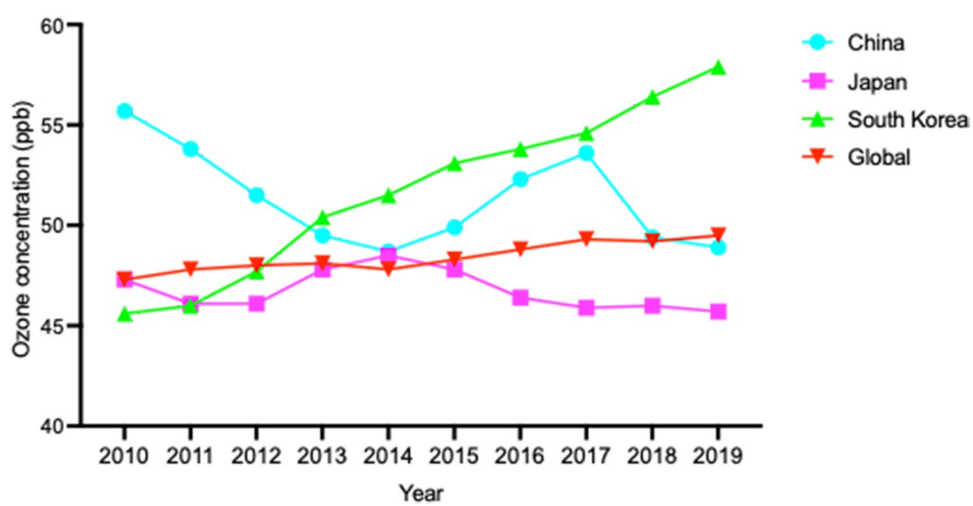

Fig. 3 Average annual population-weighted ozone concentration in China, Japan, and South Korea compared with global data from 2010 to 2019 (source: derived from State of Global Air 2020)

for South Korea [10, 11]. The combustion of fossil fuels releases air pollutants such as nitrogen oxides and volatile organic compounds into the environment, resulting in harmful ozone formation. In Japan, ozone concentrations have been decreasing annually due to source regulations. However, it is believed that cross-border air pollution is the main reason ground-level ozone does not decrease significantly. In South Korea, surface ozone has become a severe air quality issue over the past decades [12]. In the Seoul metropolitan area, where 50% of South Korea's population resides, ozone levels often exceed 90 ppb [13]. In addition to China, both Japan and South Korea are committed to improving air quality and have implemented a range of policies and regulations to address air pollution issues and protect public health [e.g., Establishment of the Air Pollution Control Act (Japan), the first and second Comprehensive Plans for Air Quality Improvement (South Korea)] (Figure S1B and C). These policies focused on

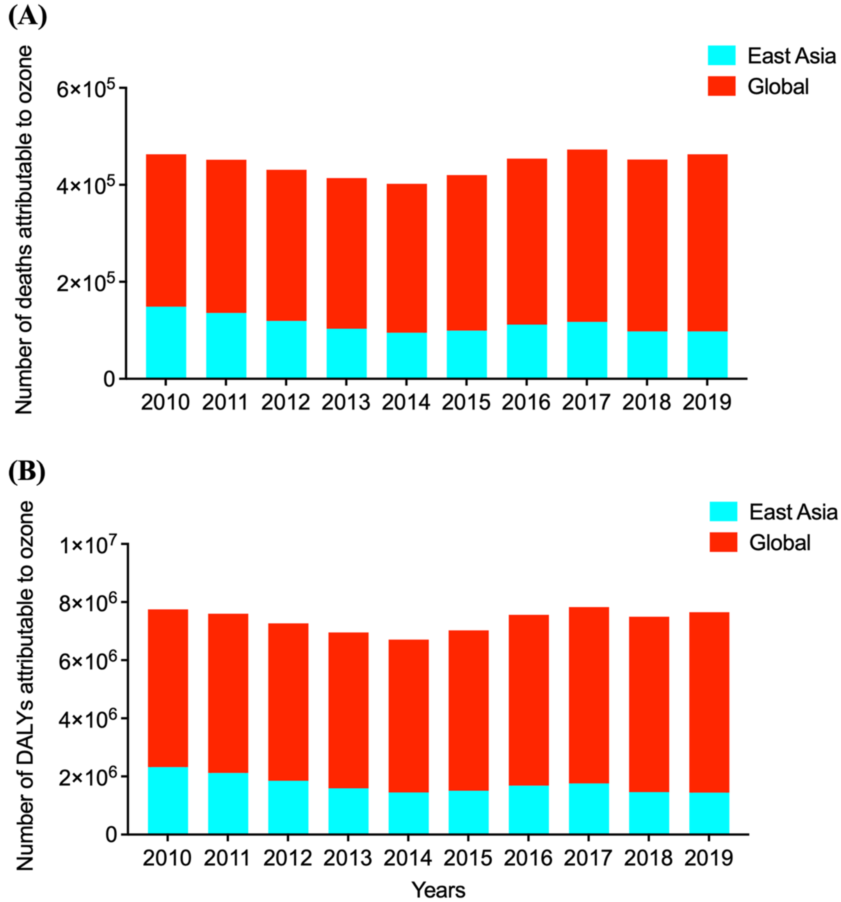

Fig. 4 Number of deaths and disability-adjusted life years (DALYs) attributable to ozone in East Asia compared with global data from 2010 to 2019 (data source: derived from Global Burden of Disease Study 2019)

reducing emissions from industrial processes, vehicles, and other sources while promoting cleaner energy and transportation options.

Epidemiological Evidence on Health Impacts of $PM_{2.5}$ and Ozone Exposure in East Asia

$PM_{2.5}$ and Health

Short-Term Associations Between $PM_{2.5}$ and Mortality

Short-term health effects typically refer to adverse outcomes that occur as a result of exposures lasting only a few days or weeks. Indeed, many studies have been performed to investigate the associations between short-term $PM_{2.5}$ and various health outcomes in East Asia, including mortality and morbidity. Multi-city studies in East Asia have played a crucial role in providing more robust evidence for the health effects of $PM_{2.5}$ and generating exposure–response (E-R) curves that are more representative of the population's health outcomes.

The most serious and conclusive health endpoint is death. Extensive investigations into the associations of short-term $PM_{2.5}$ with daily mortality have been conducted in East Asia, with a particular focus on countries such as China, Japan, and South Korea. In 2013, China built the National Urban Air Quality Real-time Publishing Platform, which has given researchers a beneficial chance to perform extensive studies across several cities on $PM_{2.5}$ and its impacts on population health. Epidemiological studies in China have provided abundant evidence regarding the health effects in response to $PM_{2.5}$ exposure, as well as the representative E-R curves. For example, Sun et al. performed a time-series analysis that included data from 250 counties in China. Their findings revealed that $PM_{2.5}$ had independent impacts on daily mortality, including mortality from all causes and mortality from circulatory and respiratory disorders [14]. Based on nationwide data in China, Chen et al. found that per 10 μg/m^3 increase in $PM_{2.5}$ was significantly associated with increases of 0.22% in all-cause mortality, 0.27% in cardiovascular mortality, and 0.29% in respiratory mortality, respectively [15]. Another nationwide study reported even higher mortality risks associated with $PM_{2.5}$ in China. They found that per 10 μg/m^3 increase in $PM_{2.5}$ was linked to significant increases of 0.44% in all-cause mortality, 0.59% in respiratory mortality, and 0.50% in cardiovascular mortality [16].

In the developed countries of this area, Kim et al. found that per 10 μg/m^3 increase in $PM_{2.5}$ concentrations was significantly associated with an increase of 1.18%, 0.34, and 0.43% in all-cause mortality in the cities of Busan, Seoul, and Incheon in South Korea from 2006 to 2012, respectively [17]. In Japan, Michikawa et al. reported that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with an increase of 1.30% (95% CI, 0.90, 1.60) in total mortality based on a nationwide dataset.

Furthermore, in a comprehensive study covering 11 cities across three East Asian countries (China, South Korea, and Japan), Lee et al. observed the noteworthy associations between $PM_{2.5}$ and adverse health outcomes. Specifically, they found that each 10 μg/m^3 increase in $PM_{2.5}$ was linked to a 0.38% [95% confidence interval (CI): 0.21, 0.55] increase in all-cause mortality and a 0.96% (95% CI: 0.46, 1.46) increase in cardiovascular mortality [18]. In general, these studies identified an apparent plateauing trend at high concentrations of $PM_{2.5}$ in the E-R curves. Overall, the coefficients of E-R relationships in East Asia were smaller than those reported in Europe and North America. For example, according to a meta-analysis of 68 studies, an increase in $PM_{2.5}$ concentration of 10 μg/m^3 was substantially linked to increases in all-cause, respiratory, and cardiovascular mortality of 1.23%, 3.81%, and 2.26% in Europe and 0.94%, 1.39%, and 0.84% in North America [19].

Short-Term Associations Between $PM_{2.5}$ and Morbidity

Morbidity indicators may be more accurate in capturing the immediate negative impact of air pollution exposure on health than death metrics. Many studies conducted in East Asia have focused on investigating the associations between $PM_{2.5}$ and daily hospital admissions, emergency room visits, or outpatient visits. For example, Gu et al. indicated that per 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 0.29% increase in daily hospital admissions for respiratory diseases based on a national registration database [20]. Another time-series research of 248 Chinese cities reported that for every 10 μg/m^3 rise in $PM_{2.5}$, the hospital admissions for total cerebrovascular illness and ischemic stroke increased by 0.19% and 0.26%, respectively [21].

In a nationwide study of Japan, according to Zhao et al., for every 10 μg/m^3 rise in $PM_{2.5}$, there was a higher probability of having an out-of-hospital cardiac arrest [odds ratio (OR) 1.02 (95% CI 1.01, 1.023)] [22]. Tasmin et al. found that per 10 μg/m^3 increase in $PM_{2.5}$ was associated with a combined relative risk (RR) of 1.008 (95% CI 1.007, 1.010) for ambulance dispatches related to acute illnesses in four prefectures of Japan [23]. Hasegawa et al. found that an interquartile range (IQR) increase in $PM_{2.5}$ was associated with a 0.90% (95% CI 0.35, 1.45) increase in hospital admissions for ischemic stroke in 97 Japanese cities [24]. Jo et al. observed that a 10 μg/m^3 rise in $PM_{2.5}$ concentration was significantly associated with a 0.26% increase in overall hospital visits using the National Health Insurance Service database of South Korea [25]. In another study conducted in Busan, South Korea, the authors revealed that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 0.25% increase in hospital admission rates for acute bronchitis, a 0.14% increase for allergic rhinitis, and a 0.01% increase for asthma [26].

In addition to cardiorespiratory disorders, short-term $PM_{2.5}$ exposure has been associated with untraditional health conditions (e.g., mental disorders) in East Asia [20, 27, 28, 29•]. For instance, Gu et al. observed that a per 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 0.52% increase in hospital admissions related to depression in 75 Chinese cities [30]. In a case-crossover research conducted in 26 Chinese cities, Wang et al. found significant associations between $PM_{2.5}$ and hospital admissions for depression, with a 2.92% increase per IQR rise of $PM_{2.5}$ [31].

Long-Term Associations Between $PM_{2.5}$ and Mortality

Long-term associations pertain to chronic health effects resulting from exposures lasting between months and decades. In assessing long-term effects in response to $PM_{2.5}$ exposure, both cross-sectional and cohort studies have been utilized in East Asia. Annual $PM_{2.5}$ exposures have been linked in cross-sectional studies to a variety of health outcomes. However, these studies have limitations in establishing causal relationships. In contrast, cohort studies are seen to be more trustworthy for giving epidemiological information on the health impacts following long-term $PM_{2.5}$ exposures. Even at very low concentrations, long-term $PM_{2.5}$ exposure has been shown to have negative health impacts by several cohort studies done in North America and Europe. It is still unclear whether East Asia fits within the relationships observed in these nations. There might be regional differences in exposure levels, population characteristics, and other contributing factors that could impact the health effects in response to $PM_{2.5}$ exposure.

In recent years, several prospective cohort studies have produced important data addressing the long-term impact of $PM_{2.5}$ exposure on the health of Asians. For example, based on the Chinese Male Cohort, Yin et al. revealed significant associations between long-term $PM_{2.5}$ exposure and mortality risk for various health outcomes in the population. Specifically, they reported that per 10 μg/m^3 increase in $PM_{2.5}$ was with hazard ratio (HR) of 1.09 for nonaccidental causes, 1.09 for cardiovascular disease (CVD), and 1.12 for chronic obstructive pulmonary disease (COPD) [32]. Similarly, using the China-PAR database, the authors found that there was a substantially greater risk of nonaccidental mortality (HR 1.11), cardio-metabolic mortality (HR 1.22), and CVD mortality (HR 1.16) for every 10 μg/m^3 rise in $PM_{2.5}$ [33]. Using the Chinese Longitudinal Healthy Longevity Survey, Li et al. reported that per 10 μg/m^3 increase in 3-year average $PM_{2.5}$ concentration was associated with higher all-cause mortality (HR 1.08) [34]. Guo et al. reported that each 10 μg/m^3 increase in $PM_{2.5}$ was associated with increased HR of 1.09 (95% CI 1.03, 1.16) and 1.13 (95% CI 1.02, 1.24) in mortality from gastrointestinal and liver cancers, respectively [35]. In addition, several cohort studies in China also revealed significant associations between $PM_{2.5}$ and mortality from various causes, including all-cause, stroke, cancer, renal failure, etc. [36–38].

In South Korea and Japan, several studies also investigated the long-term effects of $PM_{2.5}$ exposure on mortality. For example, Lim et al. performed a study on the elderly populations of seven cities in South Korea and found that the overall HR for a 10 μg/m^3 increase in a 3-year average $PM_{2.5}$ was 1.02 (95% CI 1.01, 1.04) [39]. In Japan, using data from the Japan Public Health Center-based Prospective Study, Sawada et al. found a positive association between per 1 μg/m^3 increase in $PM_{2.5}$ and mortality from CVD (HR 1.23) [40].

In general, these cohort studies consistently estimated similar mortality risks associated with long-term $PM_{2.5}$ exposure in East Asia, which are comparable to those reported in developed countries, including North America and Europe [41, 42].

Long-Term Associations Between $PM_{2.5}$ and Morbidity

Chronic exposure to $PM_{2.5}$ is associated with elevated risks of a broad spectrum of various diseases. Several cross-sectional studies have indicated positive associations between $PM_{2.5}$ and the prevalence of various chronic conditions, such as CVD, COPD, and metabolic syndromes [43, 44], but the causality for these associations was limited by the nature of the cross-sectional design.

Several cohort studies in Asian countries have investigated the impact of long-term $PM_{2.5}$ exposure on morbidity. For example, a cohort study reported that per 10 μg/m^3 increase in $PM_{2.5}$ associated with increased risks of incident CVD (HR 1.25) [33], coronary heart disease (CHD) (HR 1.43) [45], and stroke (HR: 1.13) based on the China-PAR database [46]. Exposure to high-level $PM_{2.5}$ (> 29.98 μg/m^3) was associated with an increased risk of global cognitive impairment (OR = 4.56) based on a four-year prospective cohort study in Taiwan, China [47]. Guo et al. reported that every 5 μg/m^3 increment in $PM_{2.5}$ was associated with a decrease of 1.18% for forced vital capacity (FVC), 1·46% for forced expiratory volume in 1 s (FEV_1), 1.65% for maximum mid-expiratory flow, and 0·21% for FEV_1:FVC ratio based on the Taiwan MJ Health Management Institution cohort [48]. Additionally, it has been discovered that $PM_{2.5}$ raises the morbidity risk of metabolic disorders including diabetes and obesity. Xue et al. conducted a quasi-experimental study on 20,000 adults using the China Health and Retirement Longitudinal Study (CHARLS) database from 2013 to 2017. The CHARLS database conducted three waves of surveys in 2011 (before), 2013, and 2015 (after CAP). By employing a difference-in-differences approach, they found a significant association of $PM_{2.5}$ reduction with decreased risk of depression [49] and increased risk of dyslipidemia [50]. Furthermore, increasing evidence from cross-sectional and cohort studies (e.g., birth cohorts) studies has indicated that long-term $PM_{2.5}$ exposure may impair maternal, reproductive, and children's health. For example, it has been suggested that exposure to $PM_{2.5}$ during pregnancy or infancy may have an effect on children's health, including increased risk of respiratory diseases [51], overweight or obesity [52], and autism [53].

Ozone and Health

Short-Term Associations Between Ozone and Mortality

Many epidemiological studies have indicated that short-term exposure to ozone was associated with an elevated risk of daily mortality and main cardiopulmonary diseases in East Asia. For example, Chen et al. reported an IQR increase in ozone which was associated with a 1.44% [95% posterior interval (PI) 1.08, 1.80] increase in the daily total mortality across 21 cities in East Asia [54]. Yin et al. reported that per 10 μg/m^3 increase in ozone was significantly associated with higher daily mortality from all nonaccidental causes (0.24%), CVD (0.27%), hypertension (0.60%), coronary diseases (0.24%), and stroke (0.29%) based on a national database in China [55]. Similarly, Chen et al. observed that a 10 μg/m^3 increase in ozone was associated with increases of 0.12% in mortality risk from non-accidental disease, 0.11% from circulatory disease, and 0.09% from respiratory disease, respectively, in China [56]. Guo et al. found that per increment of 10 μg/m^3 in ozone concentration was associated with 0.68% (95% CI 0.49, 0.86) higher mortality from CVD based on a meta-analysis in China [57]. Bae et al. observed a non-linear E-R relationship between ozone and daily non-accidental mortality in Japan and South Korea with thresholds (ranging from 11 to 34 ppb) [58].

Short-Term Associations Between Ozone and Morbidity

Many studies suggested that short-term ozone exposure was significantly associated with higher risks of hospitalizations or mortality, particularly cardiorespiratory diseases [59]. For example, in Beijing, Li et al. found the significant effects of short-term ozone exposures on cardiopulmonary function which were found over time based on a panel study [60].

Jiang et al. found that per 10 μg/m^3 increase in ozone was associated with elevated admission risks of 0.46% (95% CI 0.28, 0.64) in CHD, 0.75% (95% CI 0.38, 1.13) in acute myocardial infarction, and 0.50% (95% CI: 0.24, 0.77) in heart failure in 70 Chinese cities [61]. Chen et al. reported that significant associations were observed between the number of hospital admissions for hypertension and ozone levels on warm and cool days, with OR of 1.20 (95% CI 1.03, 1.4) and 1.20 (95% CI 1.02, 1.42), respectively, using the National Health Insurance program in Taipei, China [62].

Based on another nationwide time-series data from South Korea from 2011 to 2015, Kim et al. reported that there was a greater incidence of pneumonia hospital admissions in children aged 0 to 4 years (RR 1.02) and 5 to 9 years (RR 1.06) for every 10 ppb rise in ozone [63]. Phosri et al. reported that per 10 ppb increase in ozone was associated with a 0.80% (95% CI 0.25, 1.35) increase in the risk of emergency ambulance dispatch for acute illnesses in Japan [64]. Yorifuji et al. found that an IQR increase in ozone was associated with OR of 1.40 (95% CI 1.02, 1.92) of cardiac arrest in Okayama, Japan [65].

To date, evidence for the health impact of ozone (particularly CVD) is far less than that for $PM_{2.5}$ in East Asia, and most of the available research on ozone exposure was based on hospital admission data. It should be highlighted that the majority of earlier research either assessed a few CVD subtypes or was carried out in a single city, resulting in significant heterogeneity based on the available evidence.

Long-Term Associations Between Ozone and Mortality

Recent epidemiological research has found a link between long-term ozone exposure and mortality in East Asia. For example, using data from a sizable Chinese cohort, Liu et al. discovered that the association between ozone and cause-specific CVD mortality was independent of $PM_{2.5}$ and other CVD risk variables. They found that per 10 μg/m^3 ozone increase was significantly associated with overall CVD mortality (HR 1.22), ischemic heart disease (IHD) (HR 1.08), and overall stroke (HR 1.28) [66]. Similarly, using China Chronic Disease and Risk Factors Surveillance project, Niu et al. reported that per 10 μg/m^3 increase in ozone was significantly associated with overall CVD (HR 1. 09), IHD (HR 1.18), and stroke (HR 1.06), respectively [67•]. Besides China, Byun et al. revealed that per 10 ppb increase in ozone was significantly associated with both circulatory (HR 1.03) and respiratory (HR 1.11) mortalities based on a cohort study in South Korea [68].

Nevertheless, it is essential to note that the associations between long-term exposure to ozone and mortality (particularly CVD) show inconsistency when compared with several studies conducted in North America and Europe. The varying epidemiological findings on the cardiovascular effects of ozone could be attributed to various factors such as exposure estimation accuracy, follow-up duration, population characteristics, and levels of ozone. Further evidence from extended and large-scale cohort studies is crucial to gain a better understanding of the chronic health effects of ozone exposure on human health in East Asia.

Long-Term Associations Between Ozone and Morbidity

Only a few studies have examined the associations between long-term ozone exposure and prevalence/morbidity in East Asia. In China, Niu et al. reported significant associations between ozone and impaired small airway function, as well as higher odds of small airway dysfunction (SAD) [69]. They found that for an SD (4.90 ppb) rise in ozone concentrations, the OR of SAD was 1.09 (95% CI, 1.06, 1.11). Guo et al. discovered that per 1 μg/m^3 rise in ozone was associated with a 4.57% (95% CI 4.32, 16.16) increase in female lung cancer incidence in 436 Chinese counties [70]. According to Zhou et al., higher levels of ozone were strongly related to an elevated risk of allergic rhinitis and bronchitic symptoms; they reported an IQR rise in ozone; the ORs were 1.13 (95% CI 1.07, 1.18), 1.10 (95% CI 1.06, 1.16), and 1.12 (95% CI 1.05, 1.20) for allergic rhinitis, persistent cough, and persistent phlegm in Chinese children [71]. Several recent research also reported that long-term ozone exposure has a substantial effect on hypertension, blood pressure, and Alzheimer disease. For example, Niu et al. found that per 10 μg/m^3 rise in ozone concentration was associated with a 13.70% (95% CI 4.80, 23.3) increase in the incidence of hypertension based on a national cross-sectional investigation in China [72]. Jung et al. reported an increased risk of 2.11 (95% CI: 2.92, 3.33) of Alzheimer's disease with per increase of 10.91 ppb in ozone using the data from the Taiwan Environmental Protection Agency during 2000–2010 [73].

In Japan, Michikawa et al. reported that high ozone exposure was associated with an increased risk of hypertensive problems in pregnancy, with an OR of 1.05 (95% CI 1.00, 1.11) per 10 ppb increase in ozone [74]. In addition, several studies have also revealed that exposure to ozone was associated with overweight, obesity, and diabetes [75–77]. For example, based on a countrywide study of 13,548 Chinese people, Wang et al. reported that a 10 μg/m^3 increase in 1-year average ozone was associated with a 1.06 (95% CI 1.00, 1.11) increase in the risk of incident diabetes [77].

In comparison to the well-established connection of ozone with respiratory illness in East Asia, the long-term effects of ozone exposure on CVD were inconsistent [72, 78, 79]. This might be because a large portion of prior research was conducted in developed nations and among the general population, but just a few studies were undertaken in developing countries with poor air quality and among middle-aged or older persons [80].

Air Pollution and Climate Change in East Asia

Air quality and climate change are strongly related. Climate change can impact public health in multiple ways, such as heatwaves, food insecurity, and the prevalence of infectious diseases [81]. Climate change will also affect local and regional air quality. There is a strong association between high temperatures and higher ozone concentrations in polluted cities [82, 83]. Under the highest emission scenario, Lee et al. predicted increases of 9 ppb in annual ozone concentration at the end of the century [84]. According to this modeling study, the change in ozone levels in China is primarily dependent on changes in precursor emissions, whereas the change in ozone levels in Japan is more dependent on climate change [84].

Understanding how $PM_{2.5}$ and ozone pollution will change as the climate changes is challenging and fraught with uncertainties. According to worldwide research, changes in air circulation caused by global warming would increase the frequency of stagnation occurrences throughout the majority of the world [85]. More high-resolution and local research is needed to better understand how climate change effect $PM_{2.5}$ and ozone pollution in different locations of Asia on a regional to local scale.

Considering in Revising Air Quality Standard in East Asia

AQS is the foundation of air quality management for China, Japan, and South Korea (Table S1). For instance, the Ministry of Ecology and Environment of China is responsible for updating the AQS on a regular basis. The current Chinese AQS was released in 2012, with some changes made in 2018. The Ministry of Ecology and Environment is debating whether and when to begin a fresh round of standard changes. South Korea sets ambient air quality standards for seven major pollutants including PM_{10}, $PM_{2.5}$, and ozone. The current air quality standards of South Korea that have been applicable since 2011 are presented in Table S1. Air quality is monitored in Japan according to the Basic Environment Law, which introduced the first standards for several air pollutants in 1973. However, it should be noted that several AQSs in these countries, when comparable, are set at concentration levels higher than those suggested by the WHO AQG.

The publication of the revised WHO AQG has obviously sparked more debate. As suggested by the WHO, countries throughout the world, including China, Japan, and South Korea, could employ the AQG in a variety of ways based on local technological skills, air quality control policies, and other political and social variables.

The basis for setting/revising the AQS is primarily scientific studies on the health impacts of air pollution exposure. When upgrading AQS for East Asia, the most recent knowledge on the relationship between air pollution and health should be thoroughly reviewed, with a specific emphasis on epidemiological data wherever possible. Local evidence is especially crucial when modifying AQS. Some factors, such as demographic characteristics, climate, and the degree and source of air pollution, may alter the E-R connection.

Conclusions, Challenges, and Future Research Directions

There has been a significant rise in epidemiological studies studying the association between $PM_{2.5}$ and ozone and human health during the last decade in East Asia. These studies have produced robust evidence associating air pollution with a variety of negative health consequences (Table 1). By summarizing the epidemiological studies conducted in Asia, we derived the following conclusions. Specifically, (1) both short-term and long-term exposure to $PM_{2.5}$ and ozone could raise the risk of mortality and morbidity, emphasizing the need for continuing improvements in air quality in East Asia; (2) the long-term associations between $PM_{2.5}$ and mortality in East Asia are comparable to those observed in Europe and North America, whereas the short-term associations are relatively smaller in magnitude; and (3) further cohort and intervention studies are required in East Asia to yield robust and precise evidence that can promote evidence-based policymaking.

The implications arising from these findings bear significance for policy development and future research improvements. Firstly, the absence of a discernible “safe” threshold for the adverse effects of $PM_{2.5}$ underscores the ongoing necessity for sustained improvements in future AQS revisions across Asia. Secondly, the E-R associations exhibit apparent spatial variability, emphasizing the importance of considering local contextual factors in revising AQS, conducting health risk assessments, estimating disease burdens, and formulating effective policies. Thirdly, the identification of vulnerable populations, including individuals with chronic respiratory or cardiovascular conditions, children, and the elderly, highlights the need to implement protective measures and investigate

Table 1 Overall summary of epidemiological evidence on the health effects of $PM_{2.5}$ and ozone air pollution in Asia

	Short-term (hours to days)			Long-term (months to years)		
	Number	Quality	Consistency	Number	Quality	Consistency
Mortality						
All-cause	† † †	† † †	† † †	† †	† † †	† † †
Respiratory disease	† † †	† † †	† † †	† †	† †	† † †
Cardiovascular disease	† † †	† † †	† † †	† †	† † †	† † †
Morbidity						
Respiratory disease	† †	† †	† †	† †	† † †	† † †
Cardiovascular disease	† †	† †	† †	† †	† †	† † †
Mental disorders	–	† †	† †	† †	† † †	† † †
Lung cancer	–	–	–	† †	† † †	† † †
Metabolic syndrome	–	–	–	† †	† †	† † †
Adverse reproductive outcomes	–	–	–	† †	† † †	† † †
Chronic kidney disease	–	–	–	† †	† †	† †

† † † refers to many relevant studies (> 10), † † refers to several relevant studies (3–10), and † refers to only 1 to 2 relevant studies

Quality: † † † high (≥ 3 multi-cities studies for short-term effects or ≥ cohort studies for long-term effects), † † moderate (1–2 multi-cities studies for short-term effects or 1 to 2 cohort studies for long-term effects), and † low (no multi-cities studies)

Consistency: † † † almost completely consistent, † † † partly consistent, and † completely inconsistent. –, no relevant studies. The above studies are derived from China, Japan, and South Korea

the underlying mechanisms of susceptibility. Fourthly, exploring the adverse impact of $PM_{2.5}$ and ozone on diverse human systems contributes to an enhanced understanding of various diseases caused by these pollutants. Future endeavors should prioritize epidemiological and toxicological studies to further elucidate the underlying causal relationships. Lastly, air pollution can influence climate change, while climate conditions could in turn affect air quality. Both factors directly or indirectly impact human health. Given the strong interplay between climate and air quality, there is an urgent need to investigate these complex interactions and mechanisms. China announced the climate commitment to achieve carbon neutrality by 2060, which may be the means by which long-term air quality improvement is brought about in China [86]. By 2060, the low-carbon policies driven by the carbon neutrality target are expected to contribute to more than 80% of reductions in $PM_{2.5}$ and ozone-8 h 90th concentrations relative to the 2020 levels [87].

Despite the well-established knowledge regarding the adverse health outcomes of $PM_{2.5}$ and ozone, several unresolved questions and challenges remained for human-based studies. Firstly, evidence from prospective cohort studies is crucial for establishing causal relationships, formulating regulatory standards, and assessing disease burdens. While several cohort studies in developed countries have shown different health risks linked with long-term $PM_{2.5}$ exposure, it is unclear whether these relationships are valid in the setting of East Asia. Despite recent cohort studies in China that investigated the long-term effects of $PM_{2.5}$ exposure on total and cardiopulmonary mortality or morbidity, there is currently a paucity of information from cohort studies assessing mortality and morbidity across a wide variety of disorders. Secondly, studies that evaluated the health benefits of clean air policies are essential for understanding the cessation effects of air pollution exposure. Implementing more advanced approaches, such as the difference-in-difference method and randomized crossover design, could further enhance causal inference in this context. Thirdly, controlled-exposure experiments are crucial in proving the biological plausibility of air pollution's negative health impacts. These trials could provide an opportunity to directly examine the potential causation between exposure to specific pollutants and subsequent health outcomes, thus offering valuable insights into the pathophysiological processes involved and the identification of sensitive biomarkers. Lastly, the current body of human-based evidence on the effects of air pollution remains in its preliminary stages. Evidence from large-scale prospective cohort studies and intervention studies is crucial in improving our understanding on these areas.

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Data Availability Data are available on request from the corresponding author.

Declarations

Competing interests The authors declare no competing interests.

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- • Of importance
- •• Of major importance

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