



Research Article

Health Impacts from PM_{2.5} Exposure Using Environmental Epidemiology and Health Risk Assessment: A Review

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Abstract

Exposure to PM_{2.5} has been known to cause a variety of serious health consequences. Quantifying and investigating the health effects of PM_{2.5} pollution are imperative to understand and collect scientific evidence for supporting policies and associated actions. In this paper, we reviewed published environmental epidemiological studies and health risk assessments evaluating the health impacts of PM_{2.5} exposure in the PubMed database to identify the attributes of each method and aggregate the health impact results to perform analyses and summaries. Forty-two studies were identified after applying our search strategy, inclusion, and exclusion criteria. The epidemiological studies found an increased risk of several diseases from short- and long-term exposure, such as cardiovascular and respiratory diseases, lung cancer, stroke, pneumonia, depression, and diabetes. However, several conditions remain to be explored as the associations remain unclear, such as asthma, bronchitis, breast cancer, Parkinson's disease for long-term exposure, chronic obstructive pulmonary disease, stillbirth, and hypertension for short-term exposure. Health risk assessment (HRA) studies at a global scale found more than 4 million deaths from diseases associated with PM_{2.5} exposure. These studies also emphasized the importance and benefits of health guidelines that demonstrated to help avoid the number of fatalities significantly, especially guidelines from the World Health Organization (WHO) that showed the highest benefit. HRA studies in Thailand also showed that the country's air quality needs to be improved to avoid deaths and hospital admission cases. We also found that cohort studies for the Thai population are required to improve the quality of data and limit overestimation from using global estimates. Finally, the benefits and limitations of each study approach were collated to assist future studies in determining the most suited instruments for their purposes.

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Introduction

PM_{2.5} is a fine particulate matter with an aerodynamic diameter equal to or less than 2.5 μm . The damages to human health caused by this ambient air pollutant could result in a wide array of health effects [1]. It is also critically hazardous to patients and susceptible individuals with pre-existing respiratory conditions, as acute exacerbation can result from short exposure to PM_{2.5} [2]. Thailand, especially in the Bangkok Metropolitan Region (BMR), has been recurrently affected by PM_{2.5} for years, primarily due to heavy congestion in traffic and the resulting pollutant emissions from vehicle exhausts [3]. In 2020, the concentrations of PM_{2.5} in BMR were at a concerning level, with the 24-hour average PM_{2.5} concentrations of 22–398 $\mu\text{g m}^{-3}$ with 107 $\mu\text{g m}^{-3}$ on average, which is two times higher than the national standards [4]. The global burden of disease linked with air pollution, including PM_{2.5}, has taken a massive toll on human health and the economy worldwide as exposure to air pollution is estimated to cause around 7 million deaths, hundreds of millions of disability-adjusted life years (DALYs), and a loss of around US\$ 3.6 trillion annually [5]. Meanwhile, an estimation of more than 5,500 deaths, 47,513 DALYs, and 28 billion baht annually attributed to PM_{2.5} exposure was found in BMR [6–7]. Increasing attention is also being given to illnesses such as depression, suicide, neurodegenerative diseases, and stillbirth suspected to be associated with PM_{2.5} exposure [8–10]. Recognizing various adverse health effects of PM_{2.5}, many epidemiological studies have been conducted to investigate the relationship and impacts of PM_{2.5} on human health. Recently, there has also been an increase in the number of health risk assessments (HRA). It helps estimate and communicate health impacts from exposure to air pollution under various socioeconomic, environmental, and policy circumstances by utilizing concentration-response functions derived from epidemiological studies. However, thus far, the outcomes and methodologies of existing studies have rarely been reviewed. Therefore, our study aims to conduct a comparative analysis of the health risks of PM_{2.5} exposure from meta-analysis studies using environmental epidemiological tools and original studies of health risk assessment. The health outcomes were summarized and compared with Thai case studies to understand the situation in Thailand in relation to global circumstances. The comparison could help identify significant issues that Thai policymakers should focus and improve on. Finally, the strengths and shortcomings of these tools were researched and compiled to support users as a

knowledge resource before making decisions to utilize these tools.

Methodology

We performed a comprehensive search on online databases for existing peer-reviewed meta-analyses of environmental epidemiological studies investigating the association between PM_{2.5} and human health and case studies of health risk assessment of PM_{2.5}. Details about epidemiological studies and health risk assessment are described in the following sub-sections. Moreover, original studies were retrieved for case studies conducted in Thailand to make a comparative analysis with the meta-analysis studies. The primary database for this literature search is PubMed (MEDLINE), which is a leading source for biomedical research and one of the most widely accessible resources. The search period is set to studies published from 2010 to January 2022. Hand-searching was also done for further studies on the reference lists for additional relevant publications eligible for this study. The languages of published articles were limited to English and Thai. The search keywords include PM_{2.5}, particulate matter, meta-analysis, epidemiological study, cohort study, long-term, time series, case-crossover, short-term, health risk assessment, BenMAP, and AirQ+. The following items were included for inclusion criteria: meta-analyses reporting short-term and long-term effects of PM_{2.5} exposure on morbidity or mortality if the study presented the effect estimates based on the continuous exposure variables. Studies that applied health risk assessment tools to estimate the health impacts were also included in this review. Data extraction was done to retrieve information regarding the first author, year of publication, risk factors, exposure unit, study design, study period, population, health outcome, number of included studies, risk estimates, 95% confidence interval, p-value, and heterogeneity score. The strengths of outcomes from the meta-analysis studies were evaluated by considering two indicators, including estimate precision (p-value) and result inconsistency or heterogeneity (I^2), where the I^2 values of 25%, 50%, and 75% mean low, moderate, and high heterogeneity respectively [11].

1) Environmental epidemiological studies

Epidemiology is the study of the distribution and determination of specific health outcomes or diseases. As for environmental epidemiology, the main focuses are on the distribution of physical, chemical, and biological agents in the environment, which might be the main contributor to the development of certain

diseases. Environmental epidemiology studies seek to investigate the causality and identification of the environmental causes of diseases in various contexts such as air pollution, water, and dietary contamination. These studies could be categorized into three main groups: firstly, descriptive studies, which characterize emerging health-related events to environmental agents, emphasizing the person, place, and time of these different hypotheses for the correlation. Secondly, inferential studies using individual-level data such as cohort and case-control studies investigate specific diseases and exposure to certain environmental agents in phases including the design, implementation, and analysis phases. Lastly, ecological studies, in which group-level designs can also be defined as correlational studies since they compare the frequencies of a specific disease in the groups exposed to certain environmental agents at different degrees. The study groups could be based on a particular geography or period, known as time-series studies. Finally, the research outcomes from these studies would enable the generation of mitigation plans and policy implementation to reduce health impacts with environmental causes [12].

2) Air pollution health risk assessment (AP-HRA)

AP-HRA aims to estimate and communicate health impacts from exposure to air pollution under different socio-economic, environmental, and policy factors. This method enables quantitative assessments, which will be helpful for countries that lack such scientific advances and are limited to only qualitative evaluation. AP-HRAs are often required to be conducted in many countries to aid decision-making for new policies and regulations regarding air pollution mitigation. The procedure to perform an AP-HRA contains three main steps; First, assessing the level of exposure to specific air pollutants in the affected population based on data obtained from monitoring stations or air quality modeling. These data can vary based on the socioeconomic and environmental circumstances of the study area in case monitoring data are unavailable. Secondly, estimating the association between health risks and exposure to air pollution. In this process, concentration-response functions (CRFs), which quantify the health impact per concentration unit of a specific air pollutant, are derived from the relative risk (RR) of epidemiological studies (cohort study) representing the risk of a health effect of the highly exposed population in relation to lowly exposed population as shown in Eq. 1.

$$RR = \exp(\beta \times \Delta C) \quad (\text{Eq. 1})$$

where β represents the excess incidence rate of health effects per increment of pollutant, ΔC is the concentration change of air pollutants. The β coefficient can be used to determine the relationship between the concentration change of air pollutants (ΔC) and the change in health effects in terms of an incidence or mortality rate (Δy), as shown in Eq. 2.

$$\Delta y = y_0 - y_c = \beta \times (C_0 - C) = \beta \times \Delta C \quad (\text{Eq. 2})$$

where y_0 is health status before exposure, y_c is health effect after exposure, C_0 is the initial concentration of pollutants, and C is the final pollutant concentration [56]. The results of AP-HRA can be expressed as the number of attributable mortalities, cases of diseases, year of life lost (YLL), DALY, or change in life expectancy. These health impacts can be further interpreted into economic costs and benefits in the scenario where policy implementation successfully reduces air pollution and, therefore, health impacts. Thirdly, quantifying and expressing the uncertainty in the health impact estimates obtained from the assessment helps open an opportunity for valuable recommendations to be provided by technical experts for tool improvement. Currently, there are multiple kinds of AP-HRA tools available, each of which has different goals and, thus different data, workloads, expertise requirements, and limitations. Hence, in choosing a tool, it is crucial to identify the policy question that needs answering and the target audiences who will receive the information [13]. The most popular and comprehensive tools used widely are AirQ+ and BenMAP, developed and regularly updated by WHO and U.S. EPA [14]. Comparing and analyzing these two tools by identifying their differences, strengths, and weaknesses could help facilitate a tool selection process suitable for a specific policy question.

Results and discussion

After identification, inclusion, and exclusion processes by title and abstract screenings, a total of 42 articles were included in this review, with 22 meta-analyses of epidemiological studies and 18 AP-HRA studies, and 3 epidemiological studies conducted in Thailand. Among the meta-analysis of epidemiological studies, 12 were those of long-term exposure studies and 11 of short-term exposure studies, namely time-series and case-crossover studies. We also identified 3 time-series original studies which were included in the current review. However, we found no published cohort studies conducted in Thailand. The overall selection process is shown in Figure 1.

1) Environmental epidemiological studies

The meta-analyses for epidemiological studies were published between 2014-2021. Most of the studies included populations from all age groups. Several articles also studied the health effects of other pollutants such as PM₁₀, O₃, and more. However, only the health effects of PM_{2.5} exposure were included in this study. Most studies reported the effect estimates of PM_{2.5} on mortality or hospital admission cases for every 10 µg m⁻³ increase. The characteristics of the selected studies are presented in Table 1. Health impacts from long-term PM_{2.5} exposure were reported for the following diagnoses and causes of death: respiratory tract diseases, asthma, wheezing, cough, bronchitis, lower respiratory infection (LRI), lung cancer (LC) [15-18], breast cancer [17], cardiovascular disease [18, 19], natural deaths [18], Parkinson's disease [10], All-cancer mortality [20], type 2 diabetes mellitus [21], hemorrhagic stroke [22], stillbirth [8], hypertension [23]. The diseases that contain the highest relative risk (RR) are cardiovascular mortality and lung cancer, with the RR of 1.20 (95% CI: 1.09-1.31) and 1.16 (95% CI: 1.19-1.23) respectively. For short-term exposure, the diagnoses and causes of death were childhood asthma [24], All-cause mortality, cardio-vascular disease, ischemic heart disease (IHD), stroke, chronic obstructive pulmonary disease (COPD), respiratory disease [25-27], cardiac arrhythmia [28], cerebrovascular mortality [26], pneumonia [29], asthma and stillbirth [8], depression and suicide [9], and cardiac arrest [30]. In comparison with long-term effects, short-term exposure cases demonstrate lower RR with asthma admission and hypertension containing the highest RRs of 1.07 (95% CI: 1.02-1.09) and 1.069 (95% CI: 1.003-1.141) respectively. Although, it should note that these RRs of different diseases are not comparable if population groups are different. The overall results found in these studies showed an increased risk of disease incidence/prevalence and death related to PM_{2.5} exposure. However, an association of certain diseases, such as asthma, bronchitis, breast cancer, Parkinson's disease, and hypertension for long-term exposure; and COPD and stillbirth for short-term exposure, remains unclear as indicated by

its 95% confidence interval crossing 1. The majority of the meta-analysis studies have high heterogeneity or low consistency ($I^2 > 75$) of the results. Only a few studies have low ($I^2 < 25$) or moderate ($I^2 < 50$) inconsistency including [8, 9, 22]. Although the studies [8, 22] exhibited minimal inconsistency, their association strength appears to be statistically insignificant ($p > 0.05$), suggesting that these studies may, in fact, contain a large degree of heterogeneity. Other research including [18, 25, 28] did not report p-values for heterogeneity, but a comparison could be made based on their I^2 values, which also contain high inconsistencies for all the studied diseases, except for mortality from stroke and respiratory diseases that have moderate and low heterogeneity respectively.

For studies in Thailand, no cohort study results were found. The primary impediment to conducting epidemiological studies on the health effects of PM_{2.5} in Thailand is the lack of necessary data as a result of the limited monitoring stations [54]. On the other hand, a time-series study in Chiang Mai found significant associations of an increased risk of non-accidental death, COPD, coronary artery disease, and sepsis at lag day 6. However, the associations between PM_{2.5} and asthma, community-acquired pneumonia (CAP), heart failure, and stroke were not statistically significant ($p > 0.05$). Another study in northern Thailand, Mae Sot, also reported a slightly significant risk of PM_{2.5} exposure and asthma admission with a RR of 1.012 ($p = 0.046$). In another national-level study, an increased risk of hospital admission and mortality by cardio-vascular and respiratory diseases were also found to be significantly associated with PM_{2.5} exposure at lag day 0. It should be noted that each time-series and case-crossover study focuses on a different lag day depending on the period when the highest effect estimate was observed. Although it is not yet conclusive which lag day should be selected as the standard in Thailand, a study observed higher mortality and hospital admission cases during lag day 0-1 [31], suggesting that PM_{2.5} has a short latent period causing acute effects on human health as the previous studies [32-33].

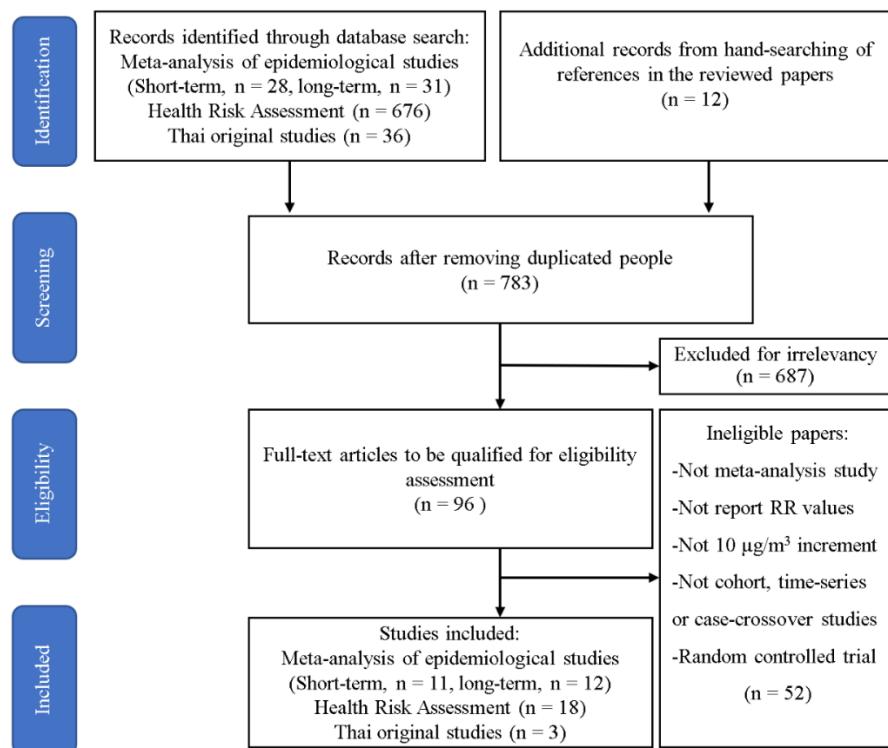


Figure 1 Flowchart of paper eligibility assessment.

2) Air pollution health risk assessment (AP-HRA)

The current review extracted HRA studies performed in several countries, Italy, Myanmar, Australia, Iran, Pakistan, South Korea, China, India, Colombia, Global, and Thailand, from 2007 to 2030 (Table 2) presents the study. Most HRAs in this review used Benefits Mapping and Analysis Program (BenMAP) and AirQ+ program as the study tools with a focus on the following health outcomes: all-cause mortality, cardiovascular and respiratory diseases, ischemic heart disease, stroke, LRI, COPD, lung cancer, diabetes, influenza, and pneumonia. The results were expressed as the number of deaths/hospital admissions attributable to PM_{2.5} based on the local air quality or avoided number of cases due to improved air quality by following available guidelines. The results showed that at the global scale, approximately 4.58 million deaths from any causes, followed by LRI, COPD, IHD, stroke, cancer, and diabetes of about 0.89, 1.00, 1.39, 0.68, 0.35, and 0.28 million deaths, respectively, were attributed to PM_{2.5} exposure [34]. The guideline for air quality standards that provided the most benefits in increasing the number of avoided hospital admission or mortality was the WHO 2005 guideline ($<10 \mu\text{g m}^{-3}$), followed by National Ambient Air Quality Standards (NAAQS), which depends on each country. For instance, India could avoid 2.18 million deaths from any illnesses from PM_{2.5} exposure if the WHO guideline was successfully

followed, while only 1.04 million deaths could be avoided if NAAQS ($<25 \mu\text{g m}^{-3}$) was achieved. For HRA studies in Thailand, there are 4 existing published studies in Chiang Mai, Songkhla, Saraburi, Bangkok, and the whole country. The studies found a similar trend for the severity of causes of death in the following order, all-cause, cardiovascular and respiratory diseases, and lung cancer. However, each study reported a different number of deaths due to the data inputs retrieved from various sources. For instance, the study [35] used the Global Exposure Mortality Model (GEMM) risk estimate, which is based on cohort studies derived predominantly from European and North American countries. Hence, when applying this model to the Thai population, the study results might not represent and be specific to the actual conditions in Thailand. This highlights the insufficiency of available local data necessary to conduct high-quality research. Moreover, it is relatively challenging to compare studies in Thailand as the reported units, diseases, and air quality guidelines are different among the published studies. As a result, it may be beneficial for researchers conducting similar studies to publish their findings in a way that is more consistent with the current ones, enabling meaningful comparison. Finally, to aid decision-making for tool selection, Table 3 displays the pros and cons of various assessment methods widely used to evaluate health risks and health impacts from PM_{2.5} exposure.

Table 1 Summary of selected epidemiological studies health outcomes from long- and short-term PM_{2.5} exposure

Exposure temporality	Study design	Study region	Studies included	Study period	Health outcome	Risk estimate	Effect size *	LCI	UCI	I ² (%)	p-value	Reference
Cohort	18 NA, 1 SA, 11 EU, 2 Asia, 3 Oceania	35	1983-2012		Respiratory tract diseases in children incidence	RR	1.08	1.05	1.10	94	0.000	[15]
					Asthma incidence	RR	1.07	0.99	1.16	98	0.000	
					Wheezing incidence	RR	1.07	1.02	1.13	72	0.000	
					Cough incidence	RR	1.05	1.00	1.10	58	0.004	
					Bronchitis incidence	RR	1.12	0.96	1.29	89	0.000	
					Lower respiratory infection incidence	RR	1.15	1.03	1.29	89	0.000	
					Lung cancer incidence	RR	1.08	1.05	1.10	94	0.000	
	8 NA, 3 EU, 5 Asia	16	1982-2016		Lung cancer mortality	RR	1.16	1.09	1.23	89	0.000	[16]
	11 NA, 6 EU, 4 Asia	21	1980-2016		Lung cancer mortality	RR	1.16	1.10	1.23	81	0.01	[17]
	5 NA, 5 EU, 2 Asia	12	1974-2011		Breast cancer mortality	RR	1.18	0.81	1.73	70	0.02	
Long-term	11 NA, 5 EU, 3 Asia	19	1982-2011		CVDs mortality	HR	1.12	1.08	1.16	92	0.01	[19]
	6 NA, 3 EU, 1 Asia	10	1976-2012		All-cancer mortality	RR	1.17	1.11	1.24	97	0.001	[20]
	1 NA, 2 EU, 4 Asia	7	1990-2015		Type 2 diabetes incidence	HR	1.11	1.03	1.19	56	0.012	[21]
					Hemorrhagic stroke incidence or mortality	HR	1.13	1.09	1.17	29	0.197	[22]
Cohort/ Case-control	4 NA, 6 EU, 1 Asia	11	1977-2009		Cardiovascular mortality	RR	1.20	1.09	1.31	98	NR	[18]
					Respiratory mortality	RR	1.05	1.01	1.09	61	NR	
					Natural mortality	RR	1.05	1.01	1.09	87	NR	
Cohort/ Case-control	5 NA, 1 EU	6	1990-2013		Parkinson disease admission	RR	1.06	0.99	1.14	86	0.000	[10]
Cohort/ Case-control	4 NA, 1 Africa, 2 Asia	8	1998-2017		Stillbirth mortality	OR	1.10	1.07	1.13	62	0.015	[8]
Mixed ¹	2 NA, 9 EU, 3 Asia, 1 Mixed	15	1992-2016		Depression EMS	OR	1.18	1.05	1.32	46	0.026	[9]
Mixed ²	2 Asia, 2 NA, 1 EU	5	1995-2011		Hypertension case	OR	1.07	0.97	1.12	68	0.020	[23]

Table 1 Summary of selected epidemiological studies health outcomes from long- and short-term PM_{2.5} exposure (*continued*)

Exposure temporality	Study design	Study region	Studies included	Study period	Health outcome	Risk estimate	Effect size*	LCI	UCI	I ² (%)	p-value	Reference
Time-series/ Case-crossover	NA (majority) SA EU Other	110	1961-2008		All cause-mortality	%increase	1.04	0.52	1.56	93	NR	[25]
					CVDs mortality	%increase	0.84	0.41	1.28	76	NR	
					IHD mortality	%increase	3.36	0.68	6.10	90	NR	
					Stroke mortality	%increase	1.85	0.74	2.97	50	NR	
					Respiratory diseases mortality	%increase	1.51	1.01	2.01	0	NR	
	7 NA, 14 EU, 5 Asia 1 Australia	27	1984-2015		COPD mortality	%increase	2.86	-0.12	5.93	72	NR	[26]
					All-cause mortality	RR	1.007	1.004	1.009	NR	NR	
					Cardiovascular mortality	RR	1.009	1.006	1.012	NR	NR	
					Respiratory mortality	RR	1.007	1.003	1.011	NR	NR	
					Cerebrovascular mortality	RR	1.007	1.001	1.013	NR	NR	
	6 NA, 1 SA, 3 EU, 7 Asia	17	1992-2017		Pneumonia admission	OR	1.01	1.005	1.015	70	0.01	[29]
	2 NA, 1 Asia	3	1998-2017		Stillbirth mortality	OR	1.000	0.997	1.003	0	0.513	[8]
	4 NA, 4 Australia	8	1994-2010		Asthma admission	RR	1.06	1.02	1.09	61	0.01	[36]
	6 NA, 3 Australia	9	1994-2010		Asthma ED	RR	1.07	1.04	1.09	82	0	
Short-term	12 NA, 2 EU, 5 Asia	19	1980-2011		Cardiac arrhythmia admission or mortality	RR	1.015	1.006	1.024	78	NR	[28]
	14 NA, 8 EU, 3 Asia	26	1981-2011		Childhood asthma admission	RR	1.05	1.03	1.07	96	0.000	[24]
	6 NA, 3 Asia	9	1992-2016		Depression EMS	OR	1.02	1.01	1.03	62	0.001	[9]
	1 NA, 2 SA and NA, 3 Asia	6	1992-2016		Suicide Mortality	OR	1.02	1.01	1.03	0	0.001	
	7 EU, 6 Asia	13	1974-2015		COPD hospitalization	OR	1.03	1.02	1.03	94	0.000	[27]
	2 NA, 1 Asia	3	1992-2011		Hypertension case	OR	1.069	1.003	1.141	78	0.004	[23]
	5 NA, 4 EU, 4 Asia, 2 Australia	12	1985-2013		Out-of-hospital cardiac arrest EMS	RR	1.04	1.01	1.07	71	0.001	[30]
Time-series	Chiang Mai, Thailand*	1	2016-2018		Non-accidental mortality	RR ³	1.016	1.001	1.032	<0.05		[37]
					COPD mortality	RR ³	1.089	1.016	1.167	<0.05		
					Asthma mortality	RR ³	0.946	0.891	1.092	NR		
					CAP mortality	RR ³	0.996	0.934	1.061	NR		
					CAD mortality	RR ³	1.086	1.002	1.117	<0.05		
					Heart failure mortality	RR ³	0.990	0.935	1.049	NR		
					Stroke mortality	RR ³	0.983	0.936	1.032	NR		
					Sepsis mortality	RR ³	1.059	1.006	1.116	<0.05		
	Thailand*	1	2017-2020		CVD and respiratory diseases admission	RR ⁴	1.012	1.007	1.018	NR		[31]
					CVD and respiratory diseases mortality	RR ⁴	1.022	1.014	1.030	NR		
	Mae Sot, Thailand**	1	2017		Asthma admission	OR	1.012	1.000	1.024	0.046		[5]

Remark 1-cohort, cross-sectional, case-crossover, time-series, 2-cohort, cross-sectional, case-control, 3-lag day 6 for worst-case scenario, 4-lag day 0 for worst-case scenario.

Abbreviation CAP: community acquired pneumonia, CAD: Coronary, COPD: chronic obstructive pulmonary disease, artery, CVDs: cardiovascular diseases, EU: Europe, ED: emergency department, EMS: emergency medical service, IHD: Ischemic heart disease, disease, LCI: lower confidence interval, NA: North America, NR: not report, SA: South America, UCI: Upper confidence interval.

* Effect size per 10 µg/m³ increase. **Effect size per 1 µg/m³ increase

Table 2 Summary of selected AP-HRA studies of PM_{2.5} exposure and health impacts

Study method	Location	Study period	Health outcome	Parameter	Value	Unit	LL	UL	Reference
BenMAP	Turin, Italy	2025-2030	All-cause mortality	Avoided death ^h	297	Cases	224	369	[38]
			Cardiovascular diseases mortality	Avoided hospital admissions ^h	496		337	652	
			Respiratory diseases mortality	Avoided hospital admissions ^h	170		-142	468	
	Yangon, Myanmar	2019	All-cause mortality	Avoided death WHO ^b	1,200	Cases	NR	NR	[39]
			ischemic heart disease mortality	Avoided death WHO ^b	144		NR	NR	
			Lung cancer mortality	Avoided death WHO ^b	48		NR	NR	
	Sydney, Australia	2007	Premature mortality	Avoided death ^g	71	Cases	NR	NR	[40]
			Cardiovascular diseases mortality	Avoided hospital admissions ^g	46		NR	NR	
			Respiratory diseases	Avoided hospital admissions ^g	25		NR	NR	
GBD	Tehran, Iran	2017	All-cause mortality	Avoided death WHO ^b	4,335	Cases	NR	NR	[41]
			ischemic heart disease mortality	Avoided death WHO ^b	2,261		NR	NR	
			Stroke mortality	Avoided death WHO ^b	653		NR	NR	
			Lower respiratory infection mortality	Avoided death WHO ^b	409		NR	NR	
			COPD mortality	Avoided death WHO ^b	253		NR	NR	
	Pakistan	2017	Lung cancer mortality	Avoided death WHO ^b	196	10 ⁶ Cases	NR	NR	[42]
			All-cause mortality	Avoided death ^f	2.02		NR	NR	
			ischemic heart disease mortality	Avoided death ^f	1.94		NR	NR	
	Seoul metropolitan region, Korea	2013	lung cancer mortality	Avoided death ^f	0.08		NR	NR	[43]
			All-cause mortality	Death	1,631	Case	NR	NR	
Global	China	2014-2018	All-cause mortality	Death	1.47	10 ⁶ cases	1.12	1.64	[44]
				Avoided death ^d	0.23		142	241	
			All-cause mortality	Avoided death NAAQS ^e	1.04		NR	NR	
				Avoided death WHO ^b	2.18		NR	NR	
			Ischemic Heart Disease mortality	Avoided death NAAQS ^e	0.34		NR	NR	
	India	2019		Avoided death WHO ^b	0.68	10 ⁶ cases	NR	NR	[45]
			COPD mortality	Avoided death NAAQS ^e	0.20		NR	NR	
				Avoided death WHO ^b	0.39		NR	NR	
			Stroke mortality	Avoided death NAAQS ^e	0.17		NR	NR	
				Avoided death WHO ^b	0.34		NR	NR	
Global	Medellin, Colombia	2016	Lung cancer mortality	Avoided death NAAQS ^e	0.01	Case	NR	NR	[46]
				Avoided death WHO ^b	0.03		NR	NR	
			All-cause mortality	Death	605 (15.6%)		NR	NR	
			Ischemic heart disease mortality	Death	230 (38.0%)		NR	NR	
			COPD mortality	Death	169 (27.9%)		NR	NR	
	Global	2017	Influenza and pneumonia mortality	Death	108 (17.9%)	10 ⁶ cases	NR	NR	[34]
			Cancer mortality	Death	64 (10.6%)		NR	NR	
			Cerebrovascular disease mortality	Death	33 (5.5%)		NR	NR	
			All-cause mortality	Death	4.58		4.13	5.03	
			Lower respiratory infections mortality	Death	0.89		0.75	1.04	
			COPD mortality	Death	1.00		0.68	1.28	
			Ischemic heart disease mortality	Death	1.39		1.23	1.55	
			Stroke mortality	Death	0.68		0.55	0.81	
			Cancer mortality	Death	0.35		0.25	0.45	
			Diabetes mortality	Death	0.28		0.19	0.33	

Table 2 Summary of selected AP-HRA studies of PM_{2.5} exposure and health impacts (*continued*)

Study method	Location	Study period	Health outcome	Parameter	Value	Unit	LL	UL	Reference
AirQ+	Tehran, Iran	2015-2016	Natural mortality	Death	4,819	Case	3,201	6,270	
			Chronic obstructive pulmonary disease	Death	150	Case	61	237	[47]
			Lung cancer Death	Death	135	Case	37	205	
	Turkey	2018	All-cause mortality	Death	44,617	Case	29,882	57,709	[48]
	Kuwait	2016	All-cause mortality adult	Death	2,685	Case	NR	NR	
			All-cause mortality Infant	Death	86	Case	NR	NR	[49]
	10 major cities, India	2017	All-cause mortality	Death	127,014	Case	NR	NR	[50]
HRA in Thailand	Chiang Mai, Thailand	2017		DALY	-		33	176	
			Overall causes: cancers, eye diseases, cardiovascular diseases, respiratory diseases	DALY	-	For every 10 ³ people	151	264	[51]
				DALY	-		78	317	
	Bangkok, Thailand	2016	Non-accidental mortality	Death	4,240		1,219	6,938	[7]
				Avoided death NAAQS ^a	1,393		593	2,691	
				Avoided death WHO ^b	3,159		893	5,248	
			Cardiopulmonary diseases mortality	Death	1,317		1,065	1,551	
				Avoided death NAAQS ^a	360	Case	284	434	
				Avoided death WHO ^b	959		769	1,140	
			Lung cancer mortality	Death	370		175	530	
	Thailand	2009		Avoided death NAAQS ^a	102		45	156	
				Avoided death WHO ^b	270		125	397	
			All-cause mortality	Death	269.9				
Thailand	Thailand	1996-2016	Cardiovascular disease mortality	Death	153.6	10 ² cases	NR	NR	[52]
				Avoided death ^c	34.0				
			Lung cancer mortality	Death	24.6				
	Thailand	1996-2016		Avoided death ^c	5.4				
			All-cause mortality	Death	50,019		42,189	57,849	
			Lower respiratory infections mortality	Death	16,419		9,154	21,544	
			Ischemic heart disease mortality	Death	15,489		14,266	16,661	
			Stroke mortality	Death	7,411		3,731	10,628	
			Lung cancer mortality	Death	5,701		3,537	7,596	
			COPD mortality	Death	4,999		2,480	7,166	

Remark: a- Thai National Ambient Air Quality Standards (NAAQS: 25 $\mu\text{g m}^{-3}$); b- WHO guidelines (10 $\mu\text{g m}^{-3}$); c-20% reduction of PM_{2.5} concentration; d-model prediction changes in concentration (52.2 $\mu\text{g m}^{-3}$ in 2014 to 34.4 $\mu\text{g m}^{-3}$ in 2018);

e-Indian National Ambient Air Quality Standards (NAAQS: 25 $\mu\text{g m}^{-3}$), f-reduction to 15 $\mu\text{g m}^{-3}$; g-10% reduction (0.6 $\mu\text{g m}^{-3}$); h-50% reduction

Table 3 Strengths and limitations of health assessment methods collated from previous studies [12-14, 42, 53]

Type of study	Methods	Strength	Limitation
Epidemiological method for long-term exposure	Cohort study: Observing and following the change in health conditions of participants from baseline until health endpoints	<ul style="list-style-type: none"> Consider the total impact of any type of health effects Include temporality between exposure and disease Have important individual-level data 	<ul style="list-style-type: none"> Costly and labor-intensive Several types of data needed e.g., spatial, temporal, and average concentration data
Epidemiological method for short-term exposure	Time-series: Studying the daily health effects under changing pollutant concentrations in the exposed population using the statistical model.	<ul style="list-style-type: none"> Reduce uncertainties from long-term variations: such as occupation and SES. Lower costs and time demand 	<ul style="list-style-type: none"> Health data uncertainties Not applicable for long-term effects from exposure
	Case-crossover: Assessing the risk of acute health effects after a short-exposure period	<ul style="list-style-type: none"> Limit confounders regarding time-independent factors Better causal inferences on the individual level 	<ul style="list-style-type: none"> Risk estimates from exposures with a time trend cannot be evaluated
Air Pollution Health Risk Assessment (AP-HRA)	Environmental Benefits Mapping and Analysis Program (BenMAP): Estimating the human health effects and economic value of a change in air quality to find benefits from improvements in health	<ul style="list-style-type: none"> Able to construct a new function with diverse demographic data by merging the CFRs with pooling strategies such as fixed effects and random effects 	<ul style="list-style-type: none"> Estimating health impacts is related to a single-year period The effects of mixtures of pollutants can be evaluated only in specific cases
	AirQ+: Quantifying the effects of exposure to air pollution to find estimates of reduction in life expectancy	<ul style="list-style-type: none"> Take into account both indoor/outdoor quantification Can quantify the risks of cancers from pollutants such as chromium (VI), arsenic, benzene, and more Available in many languages 	<ul style="list-style-type: none"> The strength of the evidence-based health effect relationships can be insufficient Unrefined spatial resolution compared to BenMAP
	Global Burden of disease: estimating the magnitude and distribution of disease burden from ambient air pollution	<ul style="list-style-type: none"> Consider the degree of overlap in exposures from household and ambient air pollution The estimates provide complete global coverage, reduced biases, high spatial resolution, and estimation of source contributions 	<ul style="list-style-type: none"> Uncertainties in the risk function Uncertainties in disease burden, pollution exposure level, response to pollution, and the counterfactual level of air pollution

Conclusions

The studies related to PM_{2.5} exposure were reviewed, analyzed, and summarized in this study. The reviewed environmental epidemiological studies frequently used time-series analysis for short-term exposure and cohort study for long-term exposure; and showed an increased risk for various kinds of diseases such as cardiovascular and respiratory diseases, lung cancer, diabetes, depression, etc. Moreover, emerging health concerns such as stillbirth, hypertension and Alzheimer's disease were also suspected to be related to PM_{2.5} exposure. However, more studies are required as the associations of these diseases are still unclear, particularly in Thailand. Health risk assessment studies were also explored and found that PM_{2.5} attributable deaths were estimated in many regions, accounting for almost 4.58 million deaths worldwide in 2017. Original studies in Thailand were also focused on and reviewed to summarize and compare the overall health effects of PM_{2.5}.

This study has a few limitations, most notably the search approach and the possibility of overlooking more relevant studies due to database selection. For the studies in Thailand, the paucity of cohort studies seems to be the most critical and urgent issue as it is needed to understand the health effects from long-term exposure to PM_{2.5}. Moreover, the results from these long-term studies are useful and valuable information, which is required in order to perform a more accurate health risk assessment with country-specific data. Hence, further research should focus on conducting cohort studies to acquire essential data that will be of use in the future. This study only explored the associations between PM_{2.5} exposure and health effects, but not the mechanisms behind how PM_{2.5} damages human health and the impacts of PM_{2.5} from different sources. More research on such areas is needed to acquire a thorough knowledge of PM_{2.5} exposure. Lastly, to assist decision-making for users in tool selection, the strengths and limitations of various methodologies were collated and presented in this study.

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