The Long-Term Effect of Exposure to Particulate Matter Air Pollution on the Incidence of Myocardial Infarction: A Systematic Review and Meta-Analysis

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Abstract

This study systematically reviews the long-term impact of exposure to particulate matter (PM) air pollution with aerodynamic diameter ≤ 10 μm on the incidence of myocardial infarction (MI).

The relevant databases were searched with appropriate keywords on February 29, 2020. A random-effects model through a generic inverse-variance method was used to calculate the pooled hazard ratio (HR) and 95% confidence interval (CI) of MI. The number of 17 cohort studies with more than 18 million participants and 800,000 cases of MI were included. A significantly higher risk of MI was observed per 1 μg/m^3 increment of PM with aerodynamic diameter ≤ 10 μm (HR= 1.02,95 % CI = 1.01, 1.03). Subgroup analysis according to the study population indicates subjects with cardiovascular diseases history had a significantly greater risk of MI per 1 μg/m^3 increase in PM with aerodynamic diameter ≤ 10 μm level (HR= 1.05,95% CI= 1.01, 1.08). Subgroup analysis according to aerodynamic diameter of PM showed only a significant stronger risk of MI per 1 μg/m^3 increase in PM with aerodynamic diameter < 2.5 μm (HR= 1.01,95% CI= 1.00, 1.02).

The pooled result confirms a significant association between the long-term exposure to PM air pollution and the developing of MI.

1. Introduction

Air pollution is a growing challenge in the world that seriously threatens health of people. According to the World Health Organization (WHO), more than 90% of the world's population, especially in low-income and middle-income countries lives in areas with inappropriate air pollution quality [1]. Although Air pollution is a complex cocktail of chemicals, more attentions are focused on particulate matter (PM) component mainly due to its high toxicity for lung and cardiovascular system [2]. According to recent data, from 1990 to 2017, global age-standardized summary exposure value for ambient PM air pollution raised by 41.2% averagely making it the first environmental risk factor in 2017 [3].

A large number of adverse health effects can be associated with PM air pollution. Previous epidemiological studies indicted exposure to PM air pollution increased risk of lung disturbances involving mainly chronic obstructive pulmonary disease (COPD) [4], asthma [5], and lung cancer [6] and cardiovascular diseases, including heart failure [7], hypertension [8], arthrosclerosis [9], arrhythmia [10], carotid intima-media thickness [11], and stroke [12–13]. Furthermore, metabolic dysfunctions such as diabetes [14–15], neurological disorders [16], including Parkinson's disease, dementia, Alzheimer's disease depression and Autism spectrum disorder (ASD) were reported. What is more, some studies indicated PM can be associated with the stronger risk of depression [17] and kidney disease [18]. The Other studies showed a significant association between PM air pollution and incidence of cancers [6, 19]. What is more, both short and long- term exposure to PM air pollution were showed increased risk of mortality and largely respiratory and cardiovascular mortality [20–21]. From 1990 to 2017, the number of deaths attributed to PM air pollution was increased nearly by 68 % and reached to about 5 % of all deaths [3].

To current date, many studies have assessed the short-term effect of exposure to PM on MI. According to recent meta-analysis studies, short-term exposure to PM can be significantly associated with the stronger risk of MI [22–25]. However, the long-term effect of exposure to PM on MI is inconclusive or even contradictory. Although some studies showed the greater risk of MI per increase in PM levels [26–33], others did not find a significant association [34–42]. We designed this systematic and meta-analysis with the aim of synthesizing the current evidence to investigate the long-term association between PM air pollution and the incidence of MI.

2. Methods

1.2. Protocol and registration

We acted upon the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [43]. Also, the elaboration and explanation of PRISMA statement were considered [44]. This study was approved by Research Deputy and Technology of Kermanshah University of Medical Sciences.

2.2. Eligibility criteria

Study population was defined any subjects whose exposure to PM determined and then followed by time for MI occurrence. The hazard ratio (HR) of both primary and secondary MI defined by ICD-9 code 410 or ICD-10 codes I21 to I23 was considered outcome. It should be noted we excluded studies with including ICD-10 codes I20, I24, and I25 under name of ischemic heart disease (IHD) or coronary heart disease (CHD) if did not provide an independent HR for MI. Given that the focus of this study was in clarifying the long-term effect of PM on MI, we included only prospective cohort studies. No publication date restriction was considered, however, we entered studies with English language.

3.2. Information sources

On July 14, 2019, we searched PubMed (https://www.ncbi.nlm.nih.gov/pubmed/), Scopus (https://www.scopus.com/), and Web of Science (https://www.webofknowledge.com/) to trace any relevant publication. The last updating for new articles was performed on February 29, 2020. We also screened references of included studies to find any relevant publication that may not be detected by the searching.

4.2. Search

We searched the mentioned databases by appropriate keywords and terms such as “myocardial infarction” ,”heart attack”, “acute coronary syndrome” as outcome, and “air pollution”, “air pollutants”, “particulate matter”, and “PM” as exposure. Then, Endnote files of records were obtained for further assessment.

5.2. Study selection

As illustrated in Fig. 1, after removing duplicate records, we screened documents by title and abstract then excluded studies did not investigated the association. Next, we retrieved the full text of potentially relevant studies and examined them carefully. According to the eligibility criteria, at first, studies did not investigated PM as an exposure or MI as an outcome were omitted. Second, studies assessed the short-term effect of air pollution on MI were removed. Third, we discarded studies assessed the effects of PM on MI mortality or studies mixed the incidence and death of MI. Forth, we removed studies with including ICD-10 codes I20, I24, and I25 under name of ischemic heart disease (IHD) or coronary heart disease (CHD) because did not provide an independent HR for MI. Finally, book chapters, conference papers, editorials, and review articles were eliminated.

6.2. Data collection process

We assessed carefully all included studies. The main characteristics of studies recorded in Microsoft excel version 2013. During the process of data collection whenever there was a problem, we solved it with team-based discussion or consulted with other available researchers or the relevant books.

8.2. Data items

The following items were extracted from each study: study ID (name and publication year), country that study was conducted, characteristics of study population (age, sex, and sample size), PM measurement methods and types of them, the way of diagnosing MI, and the estimated HR and 95% CI(confidence interval)of MI with adjusted variables (see Table 1).

Table 1
The summary characteristics of included studies.

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Miller et al. (2007)	The United Stated of America (USA)	**Target Population**: postmenopausal women **Sample size**: 58,610 **Follow up**:1994–2002 **Sex**: F **Age**: 50–79 years	**Source of data**: The Environmental Protection Agency's Aerometric Information Retrieval System **Exposure assessment**: The nearest monitor according to ZIP Code **Type**: Annual averages of $PM_{2.5}$	**Number of cases**: 584 **Diagnose**: Questionnaires and the review of medical records by physician adjudicators	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: age, race or ethnic group, educational level, household income, smoking status, systolic blood pressure, body-mass index, and presence or absence of diabetes, hypertension, or hypercholesterolemia	Good
Zanobetti et al. (2007)	USA	**Target Population**: Patients with myocardial infarction (MI) **Sample size**: 196,131 **Follow up**:1985–1999 **Sex**: M&F **Age**: ≥ 65 years	**Source of data**: The Environmental Protection Agency's Aerometric Information Retrieval System **Exposure assessment**: cities levels **Type**: Annual averages of PM_{10}	**Number of cases**: 22,522 **Diagnose**: Medical records based on ICD-9: 410	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: time period, age, sex, race, and type of MI. model controlled for days of coronary care and intensive care, previous diagnosis for atrial fibrillation, and secondary or previous diagnoses for COPD, diabetes, and hypertension	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Puett et al. (2008)	USA	**Target Population**: Nurses **Sample size**: 66,250 **Follow up**:1992–2002 **Sex**: F **Age**: 30–55 years	**Source of data**: The Environmental Protection Agency's Aerometric Information Retrieval System, the IMPROVE network, and Harvard University research studies. **Exposure assessment**: A geographic information system–based spatial smoothing model **Type**: Monthly averages of PM_{10}	**Number of cases**: 854 **Diagnose**: World Health Organization criteria through interview or confirmed cases by hospitals	**Index**: HR(95%CI) per 10 $\mu g/m^3$ increment of PM **Adjustment**: Stratifying by age in months, adjusting for state of residence, year, and season.	Good
Puett et al. (2009)	UAS	**Target Population**: Nurses **Sample size**: 66,250 **Follow up**:1992–2002 **Sex**: F **Age**: 30–55 years	**Source of data**: The Environmental Protection Agency's Aerometric Information Retrieval System, the IMPROVE network, and Harvard University research studies. **Exposure assessment**: A geographic information system–based spatial smoothing model **Type**: Monthly averages of $PM_{2.5}$ and $PM_{2.5–10}$	**Number of cases**: 854 **Diagnose**: World Health Organization criteria through interview or confirmed cases by hospitals	**Index**: HR(95%CI) per 10 $\mu g/m^3$ increment of PM **Adjustment**: Stratifying by age in months, adjusting for state of residence, year, and season.	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Lipsett et al.(2011)	USA	**Target Population**: Current and former public school professionals (Teachers) **Sample size**: 124,614 **Follow up**:1997–2005 **Sex**: F **Age**: ≥20 years	**Source of data**: Federal Reference Method monitors of California's State, the Local Air Monitoring Network and the Interagency Monitoring of Protected Visual Environments (IMPROVE) network **Exposure assessment**: Geocoded residential addresses with inverse distance-weighted **Type**: Monthly averages of $PM_{2.5}$ and PM_{10}	**Number of cases**: 722 **Diagnose**: Government mortality and hospitalization Files according to ICD-10: I21	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: age, race, smoking status, total pack-years, body mass index, marital status, alcohol consumption, second-hand smoke exposure at home, dietary fat, dietary fiber, dietary calories, physical activity, menopausal status, hormone therapy use, family history of MI or stroke, blood pressure medication, and aspirin use, and for contextual variables (income, income inequality, education, population size, racial composition, and unemployment)	Good
Atkinson et al. (2013)	The United Kingdom (UK)	**Target Population**: General **Sample size**: 836,557 **Follow up**:2003-07 **Sex**: M&F **Age**: 40 to 89 years	**Source of data**: The national emission inventories (NAEI) **Exposure assessment**: air dispersion models **Type**: Annual averages of PM_{10}	**Number of cases**: 13,956 **Diagnose**: Reviewing medical records based on ICD-10: I21-23	**Index**: HR(95%CI) per 3 μg/m^3 increment of PM **Adjustment**: age and sex, smoking, BMI, Diabetes and hypertension, IMD	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Koton et al. (2013)	Israel	**Target Population**: Patients with MI **Sample size**: 1120 **Follow up**:1992–2005 **Sex**: M&F **Age**: ≤ 65 years	**Source of data**: Air-quality monitoring stations in central Israel **Exposure assessment**: Geocoded residential addresses and linear regression model to estimate $PM_{2.5}$ from PM_{10} **Type**: Annual averages of $PM_{2.5}$	**Number of cases**: 341 **Diagnose**: Medical records by a senior cardiologist	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: age and gender, smoking, diabetes, hypertension, dyslipidemia, leisure time physical activity, Killip class, thrombolysis, coronary artery bypass graft surgery within 45 days, percutaneous coronary angioplasty within 45 days, Charlson index and chronic CHD, education, income, employment, neighborhood SES. Employment.	Good
Nishiwaki et al. (2013)	Japan	**Target Population**: middle-aged Japanese **Sample size**: 62,142 **Follow up**:1990–2005 **Sex**: M&F **Age**: 40–69 years	**Source of data**: The Ministry of the Environment **Exposure assessment**: The nearest station to postal address **Type**: Annual averages of PM_{10}	**Number of cases**: NC. **Diagnose**: Questionnaire and reviewing medical records according to MTDCT criteria.	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: age, sex, body mass index, smoking status, environmental smoking status, and alcohol consumption.	Good
Cary et al. (2019)	UK	**Target Population**: General **Sample size**: 207 042 **Follow up**: 2005-11 **Sex**: M&F **Age**: 40–79 years	**Source of data**: London Atmospheric Emissions Inventory **Exposure assessment**: KCLurban dispersion model **Type**: Annual averages of $PM_{2.5}$	**Number of cases**: 2582 **Diagnose**: Medical records based on ICD-10: I21-23	**Index**: HR(95%CI) per 1 μg/m^3 increment of PM Adjustment: age, gender, smoking and BMI, IMD.	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Hartiala et al. (2016)	USA	**Target Population**: patients undergoing elective diagnostic coronary angiography. **Sample size**: 5854 **Follow up**: 3 years **Sex**: M&F **Mean Age (SD)**: 64 (11)	**Source of data**: The US Environmental Protection Agency's (EPA) Air Quality System (AQS) database **Exposure assessment**: Zip code by inverse distance-squared weighting. **Type**: Monthly average of $PM_{2.5}$	**Number of cases**: 288 **Diagnose**: Verified medical records	**Index**: HR(95%CI) per 1 $\mu g/m^3$ increment of PM **Adjustment**: age, sex, education level, and current smoking.	Good
Kim et al. (2017)	Korea	**Target Population**: General **Sample size**: 136 094 **Follow up**:2007-13 **Sex**: M&F **Age**: ≥ 18 years	**Source of data**: The Korean Ministry of Environment **Exposure assessment**: ZIP code **Type**: Monthly average of $PM_{2.5}$ and PM_{10}	**Number of cases**: 354 **Diagnose**: ICD-10: I2-123	**Index**: HR(95%CI) per 1 $\mu g/m^3$ increment of PM **Adjustment**: age, sex, socioeconomic status, hypertension, diabetes mellitus, dyslipidemia, chronic renal failure, end-stage renal diseases, ischemic heart disease, peripheral arterial disease, chronic obstructive pulmonary disease, and malignancy, body mass index, fasting blood glucose, total cholesterol, and hemoglobin. Composite cardiovascular events were a composite of cardiovascular death, acute myocardial infarction, congestive heart failure, and stroke.	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Downward et al. (2018)	Netherlands	**Target Population**: General **Sample size**: 33,831 **Follow up**:1993–2010 **Sex**: M&F **Age**: 20–70 years	**Source of data**: Measurements in 242 monitoring sites **Exposure assessment**: LUR models **Types**: Annual averages of $PM_{2.5}$, PM $_{2.5–10}$, and PM_{10}	**Number of cases**: 797 **Diagnose**: Medical records based on ICD-10: I21-23	**Index**: HR(95%CI) per 5 μg/m^3 increment of $PM_{2.5}$ and $PM_{2.5–10}$ and per 10 μg/m3 Increment of PM_{10} **Adjustment**: smoking status (including number of cigarettes and duration of smoking), diet (intake of fruit and vegetables), alcohol consumption, BMI, recruitment year, gender, marital status, education level, and area-level economic status.	Good
Gandini et al. (2018)	Italy	**Target Population**: General **Sample size**: 74,989 **Follow up**: 1999–2008 **Sex**: M&F **Age**: > 35 years	**Source of data**: National Integrated Modelling system for International Negotiation on atmospheric pollution **Exposure assessment**: atmospheric chemical transport model (CTM) **Type**: Annual average of $PM_{2.5}$	**Number of cases**: NC **Diagnose**: Italian National Institute of Statistics records based on ICD-9: 410	**Index**: HR(95%CI) per 10 μg/m^3 increment of PM **Adjustment**: age, gender, educational level, living with partner, occupational status, smoking habit, physical activity status, type of municipality (rural, urban, metropolitan areas) and BMI.	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Loop et al. (2018)	USA	**Target population**: General **Sample size**: 17,126 **Follow up**: 2003-12 **Sex**: M&F **Age**: ≥ 45 years	**Source of data**: EPA Air Quality System (AQS) and the National Aeronautics and Space Administration (NASA) Aqua satellite **Exposure assessment**: Regression models **Type**: Annual average of $PM_{2.5}$	**Number of cases**: 413 **Diagnose**: Medical record review and interview by Physicians	**Index**: HR(95%CI) per 2.7 μg/m^3 increment of PM **Adjustment**: 1-year mean temperature, season, race, region, urbanicity, income, education, age, gender, pack-years, BMI, alcohol use, physical activity, calendar year, statin use, antihypertensive medication use, and diabetes.	Good
Bai et al. (2019)	Canada	**Target Population**: General **Sample size**: 5,141,172 **Follow up**: 2001-15 **Sex**: M&F **Age**: 35 to 85 years	**Source of data**: the National Air Pollution Surveillance network and the Interagency Monitoring of Protected Visual Environments network (IMPROVE) **Exposure assessment**: global atmospheric chemistry transport model (GEOS-Chem CTM), combined with a geographically weighted regression model **Type**: Annual average of $PM_{2.5}$	**Number of cases**: 197,628 **Diagnose**: physician-diagnosed cases of MI recorded obtained from the Ontario Myocardial Infarction Database (ICD-10: I21)	**Index**: HR(95%CI) per 3.5 μg/m^3 increment of PM **Adjustment**: age and sex only, and stratified region, neighborhood -level recent immigrants (arrived in the 5 years prior to census), unemployment rate, education, and annual household income, urban residency and a north/south indicator	Good

Study ID	Country	Study characteristics	Particulate measurement	MI assessment	Risk measurement	Risk of bias
Bai et al. (2019)	Canada	**Target Population** : General **Sample size**: 1,127,209 **Follow up**: 1996–2012 **Sex**: M&F **Age**: 30–100 years	**Source of data**: The National Air Pollution Surveillance network and the Interagency Monitoring of Protected Visual Environments network (IMPROVE) **Exposure assessment**: global atmospheric chemistry transport model (GEOS-Chem CTM), combined with a geographically weighted regression model **Type**: Annual average of $PM_{2.5}$	**Number of cases**: 43,745 **Diagnose**: physician-diagnosed cases of MI based on recorded obtained from the Ontario Myocardial Infarction Database according to ICD-10: I21	**Index**: HR(95%CI) per 2.2 μg/m^3 increment of PM **Adjustment**: age, sex, tract-level percentage of recent immigrants, percentage of the population aged ≥ 15 years without employment, percentage of the population aged ≥ 15 years with less than a high school education, and annual household income, hypertension, diabetes, CHF, chronic obstructive pulmonary disease, asthma, and cancer.	Good
Danesh Yazdi et al. (2019)	USA	**Target Population**: General **Sample size**: 11,084,660 **Follow up**: 2000-12 **Sex**: M&F **Age**: not reported	**Source of data**: the EPA Air Quality System (AQS), **Exposure assessment**: Satellite remote sensing, land use, and chemical transport models **Type**: Annual average of $PM_{2.5}$	**Number of cases**: 570,668 **Diagnose**: physician-diagnosed cases of MI based on recorded obtained from the Center for Medicare and Medicaid Services denominator file according to ICD-9: 410	**Index**: HR(95%CI) per 1 μg/m^3 increment of PM **Adjustment**: sex, race, state, Medicaid eligibility, ozone, year, median house value, percent owner occupied housing, percent living below poverty, population density, and median household income.	Good

8.2. Risk of bias in individual studies

We assessed the selected studies in terms of risk of bias. The Newcastle-Ottawa Scale (NOS) developed for investigating the quality of cohort studies was used [45]. The NOS is largely used due to recommendations from the Cochrane Collaboration [46]. This tool has three broad categories, including selection (four criteria), comparability of study groups (two criteria), and assessment of the outcome (three criteria). The scale ranged between 0 (the lowest study quality) and

9 (the highest study quality) points. The final quality score according to the NOS was provided in the Table 1 for each included study.

9.2. Summary measures

We included only prospective cohort studies. All studies were reported HR and 95% CI for developing of MI per specific unit increase in PM levels. For estimating the total effect of exposure to PM on the risk of MI, because some studies reported HR (95% CI) for PM_{10}, $PM_{2.5,}$ or/and $PM_{2.5-10}$ [30, 35, 39], we only included the estimated risk per PM_{10} due to overlapping. Moreover, we found two studies reported HR of MI for different PM diameters on the same population [40–41]. For total effect analysis, we only considered one of them reported HR of MI for PM_{10} [40] but for subgroup analyse according to PM diameters we included both studies [40–41]. Similarly, there were two studies on the same population and PM diameter [27–28]. We first used fixed effects meta-analysis model, then the estimated pooled HR (95% CI) was considered. In the present study, we assumed a linear relation between PM air pollution and MI. If applicable, we standardized the risk of MI per 1 μg/m^3 increment of PM air pollution by using the following formula:

$$\text{Standardized HR (95 \% CI) of MI} = e^{\left(\text{Ln (Original Estimated HR[95 \% CI])} * \frac{1}{\text{Original increment}}\right)}$$

10.2. Synthesis of results

The Random-effects model through a generic inverse-variance method was used to calculate the pooled HR (95%CI) for incidence of MI [47]. Heterogeneity presented with calculated I^2 index and I^2 values of 0%, 25%, 50%,and 75% represent no, low, moderate, and high heterogeneity, respectively [48–49]. We used the Jackknife approach to investigate the impact of each study on the pooled effect size and the heterogeneity across studies [52]. Besides, Subgroup analyses according to gender (female or both male and female subjects, study population (subjects without MI history and those with MI/CHD history), and diameter of PM ($PM_{2.5}$, $PM_{2.5-10}$, and PM_{10}) were performed. P-value of less than 0.05 was chosen to test null hypotheses in all analysis. Stata software version 14 was used to data analysis.

11.2. Risk of bias across studies

The Egger’s and bagger's tests employed to investigate publication bias [50–51]. The p-value less than 0.05 chosen to test a significant publication bias across studies. In addition, Visual inspection of funnel plot was presented.

3. Results

1.3. Study selection

Flow diagram of systematic review process was presented in the Fig. 1. Totally, search in selected databases was derived to identify 3190 literature. After removing duplicate records, we screened 1795 records by title and abstract. Then, we retrieved the full text of 430 potentially relevant articles. After excluding 413 papers by reasons, eventually, the number of 17 prospective cohort studies entered in this systematic review and meta-analysis [26–42].

2.3. Study characteristics

As provided in Supplemental Table 1, we included the number of 17 prospective cohort studies with more than 18 million participants and 800,000 cases of MI. The large number of the included studies (10 out of 17) was performed in North America region (the eight studies in the United States of America and the two studies in Canada). Besides, there were four studies came from Europa region (two studies from the United Kingdom, another study from Netherlands, and the other study from Italy), two studies from East Asia (one study from Korea and another study from Japan), and one study from Middle East (Israel). All studies carried out on adult subjects (the youngest age was ≥ 18 years). Most of the studies included both female and male subjects but in the four studies participants had female gender. In the 14 studies only subjects without CVDs included but in the three studies participants had previous history of MI or CVDs. Most studies used the different models to determine the rate of exposure to PM for the subjects (12 studies). By considering the aerodynamic diameter of particulates, we observed in the nine studies only PM < 2.5 μm investigated and in the three studies only PM ≤ 10 μm considered. Furthermore, in the other three studies assessed both PM < 2.5 and PM ≤ 10 μm. Moreover, one study investigated PM < 2.5 and PM 2.5–10 (Coarse) and in the other in addition to PM < 2.5 and PM 2.5–10 μm included PM ≤ 10 μm. the majority of included studies diagnosed MI based on medical records registers by ICD-9 codes 140 (three studies) and/or ICD-10 codes I21(three studies) or I21-23(four studies). All studies provided the adjusted hazard ratio (HR) and 95 % confidence interval (CI) of per specific unit increment of PM.

3.3. Risk of bias within studies

The results of risk of according to the NOS tool indicates all included studies have good quality (all studies met 3/4 items of Selection part, 1/2 items of Comparability par, and 2/3 items of Outcome part).

4.3. Results of individual studies

The results of studies were differed according to type of PM. OF the 13 studies investigated the risk of MI per specific unit increment of PM ≤ 2.5 μm, seven studies reported a higher risk of MI that in the most of them (five studies) the risk was significant. Besides, in the other six studies did not show a higher risk of MI that even in a study the risk of MI decreased per specific unit increment of PM ≤ 2.5 μm. for particulates with aerodynamic range of 2.5 to 10 μm, of 3 six studies investigated association, the number of two studies found a significantly higher risk of MI and another study did not observe a higher risk of MI per increasing in the PM. In related to PM ≤ 10 μm, we found 6 studies examined the relationship. Of three studies reported a higher risk of MI, the risk of MI was significant in two studies. Moreover, in the other three studies did not find a higher risk of MI per increment of PM.

5.3. Synthesis of results

As showed in Fig. 2, the pooled HR (95%CI) of MI per 1 μg/m^3 increment of PM_{10} was estimated at 1.02(1.01, 1.03). Furthermore, we observed a significantly high heterogeneity across studies (I^2 = 96.8% [p-value < 0.001]). By considering the study population (subjects without MI history and those with MI/CHD history), As showed in Fig. 3, the pooled HR (95% CI) per 1 μg/m3 increase in PM for studies considered subjects without MI history and those with MI/CHD history were calculated 1.02(1.00, 1.03) and 1.05(1.01, 1.08). In addition, I^2 (P-value) were 94.7(< 0.001) and 16.1 % (0.303), respectively. We also performed subgroup analysis according to gender, including female and both genders. As plotted in Supplemental Fig. 2, there was no significant higher risk of MI in female subgroup, but we found a significantly higher risk of MI in the other subgroup. Apart from, we used the Jackknife approach to investigate the impact of each study on the pooled effect size and the heterogeneity across studies (see Fig. 4). After excluding Kim et al study as presented in Fig. 5, we again found a significantly higher risk of MI per 1 μg/m^3 increase in PM_{10} (HR = 1.01, 95% CI[1.00, 1.02]), but with a slightly lower heterogeneity (I^2 = 91.7 % [P-value < 0.001]). Furthermore, subgroup analyses according to the aerodynamic diameter of PM was carried out. Accordingly, we classified studies into three subgroups including $PM_{2.5}$, $PM_{2.5-10}$, and PM_{10}. As presented in Fig. 6, the pooled HR (95%CI) per 1 μg/m^3 increase in $PM_{2.5}$ was estimated 1.01 (1.00, 1.02) with I^2 = 91.1 % (P-value < 0.001). It remains significant after excluding subjects with MI/CHD history (See Supplemental Fig. 3). Per 1 μg/m^3 increase, the pooled HR (95% CI) and I2 (P-value) were calculated 1.40 (0.87, 1.94) and 99.3 (p < 0.001) for $PM_{2.5-10}$ and 1.01 (0.99, 1.02) and 67.3 (p = 0.009). It should be noted we observed the same results for PM_{10} after subgroup analysis based on type of population (Supplemental Fig. 4).

6.3. Risk of bias across studies

We did not show a significant publication bias across studies according to both Begg's Test (P-value = 0.102) Egger's test (P-value = 0.729). The funnel plot also was provided in supplemental Fig. 1.

4. Discussion

According to the best of our knowledge, this systematic review and meta-analysis study was the first attempt to investigate the effect of long-term exposure to PM air pollution on the incidence of MI. Overall, The number of 17 prospective cohort studies with more than 18 million participants and 800,000 cases of MI was included. Obtained results indicated per 1 $\mu g/m^3$ increment of PM_{10}, the risk of MI raised significantly by 2% averagely. This finding was in line with some studies found a significantly greater risk of CVDs results from long-term exposure to PM [8,12,53]. Besides, in comparison to previous meta-analysis investigated the short-term effect of exposure to PM_{10} on the risk of MI, we observed stronger association between PM and MI [22–25]. Furthermore, subgroup analysis based on types of study population reveals subjects with MI/CHD history in comparison to who without MI history had a significantly 3 % greater risk of MI per 1 $\mu g/m^3$ increase in the levels of PM averagely. Apart from this, by considering aerodynamic diameter of PM, We found only a significant stronger risk of MI per 1 $\mu g/m^3$ increase in PM with aerodynamic diameter less than 2.5 µm, but not for $PM_{2.5–10}$ and PM_{10}. This finding was in line of several previous studies reported a significantly association between $PM_{2.5}$ and CVD influence and mortality [12,13,54]. This finding also confirms the greater effect of the smaller size fractions of PM on the cardiovascular system [2, 55]. In sum, this study indicates a significant association between long-term exposure to PM $\leq$ 10 $\mu g/m^3$ and the developing of MI. Although biological mechanisms underlining the association not fully understood, the possible biological pathways were discussed with details in several invaluable studies [2, 56–59]. Briefly, PM air pollution can result in impairments in the cardiovascular system, including heart, vascular, and blood through several pathways, including lung inflammation, neuroendocrine activation, particle translocation, and undefined bloodborne mediator. It is supposed that in long-term exposure to PM, these impairments can raise the developing of cardiovascular morbidity and mortality [2].

This study accompanied with several advantages. This study was the first attempt to quantify the long-term effect of exposure to PM on the incidence of MI. We included the prospective cohort studies with appropriate sample size (more than 18 million participants), cases of MI (more than 800,000 cases). However, there are some shortcomings in the both study and outcome levels that should be taken into account when interpreting the results of this review. First of all, for measuring exposure to PM, the included studies applied various methods having different precision. Moreover, most studies did not determine exposure to PM in other situations such as indoor and occupational sources. Apart from, PM health effects can be vary depending on its nature. Studies did not account this and only considered the diameter of PM. The studies provided adjusted HR (95% CI) of MI per different increases in PM levels. Thus, we assumed a linear relation between PM and MI and standardized the risk of MI per 1 µg/m3 increase in PM levels. This also can be associated with error in measuring the effects size of association between. Second, the definition of MI across studies is problematic. Some studies used ICD codes but the others did not. Among studies provided ICD codes, some studies defined MI as ICD-9: 410 or ICD-10:I21 (primary MI) but the others considered both primary and secondary types of MI and applied ICD-10: I21-23. Last but not the least, we found a high heterogeneity across studies. What is more, in the large number of included studies, MI incidence data obtained from registry information. This can potentially increase the risk of non-differential bias because of coding errors. Third, confounding effect is another important limitation across studies. Recent meta-analysis study has indicated that exposure to environmental noise can be associated with higher risk of MI [60]. The most selected studies did not adjust this effect. None of the included studies did not adjust exposure to occupational risk factor such as noise, shift work and life style risk factors such as sleep status, diets patterns, and physical activity that according to previous studies can be associated with the higher odds of MI. Forth, combining HR (95% CI) adjusted for different covariates may have reduced the consistency across studies and reduced the precision of our summary estimates. Finally, although subgroup analyses based on type of population and sensitivity analyses according to Jackknife approach were performed, we found a high heterogeneity, especially in studies conducted among subjects without history of MI. More studies are needed to explore the sources of heterogeneity.

5. Conclusion

This study was the first attempt, according to the best of our knowledge, to investigate the effect of long-term exposure to PM air pollution on the risk of MI. Obtained results indicated a significantly higher risk of MI per 1 µg/m3 increase in the level of PM_{10}. Moreover, Subgroup analysis based on types of study population reveals subjects with MI/CHD history in comparison to who without MI history had a significantly greater risk of MI per 1 µg/m3 increase in the levels of PM_{10}. Considering aerodynamic diameter of PM shows only a significant stronger risk of MI per 1 µg/m3 increase in $PM_{2.5}$. More studies are warranted to overcome the above-mentioned limitations and confirm our findings.

Declarations

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Author contributions: All authors contributed to the study conception and design. Design of the work raised by [M.Kh]. Material preparation, data collection and analysis were performed by [R.S], [F.O] and [F.R]. The first draft of the manuscript was written by [M.Kh] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

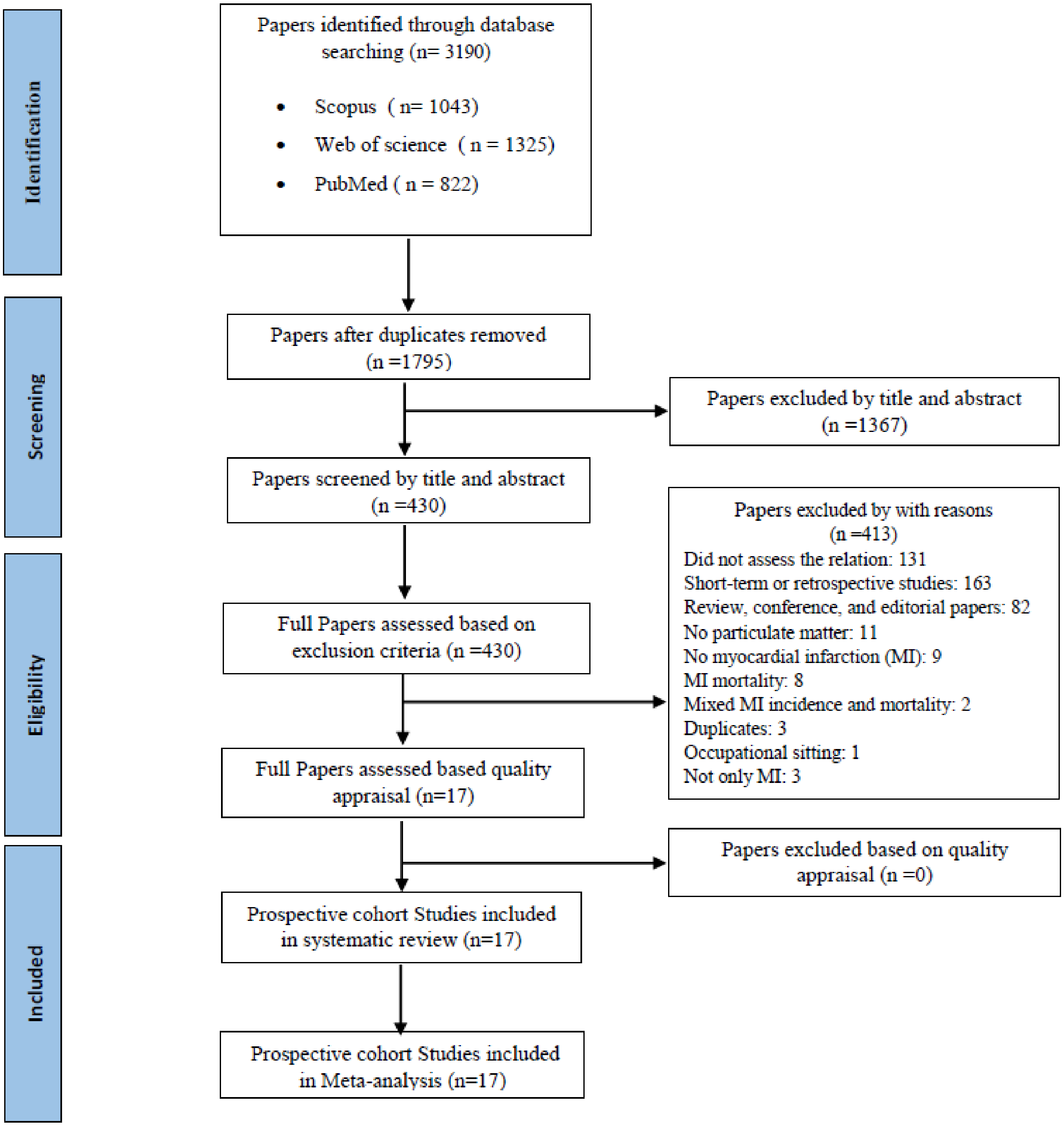

Figure 1

Flow diagram of systematic review process.

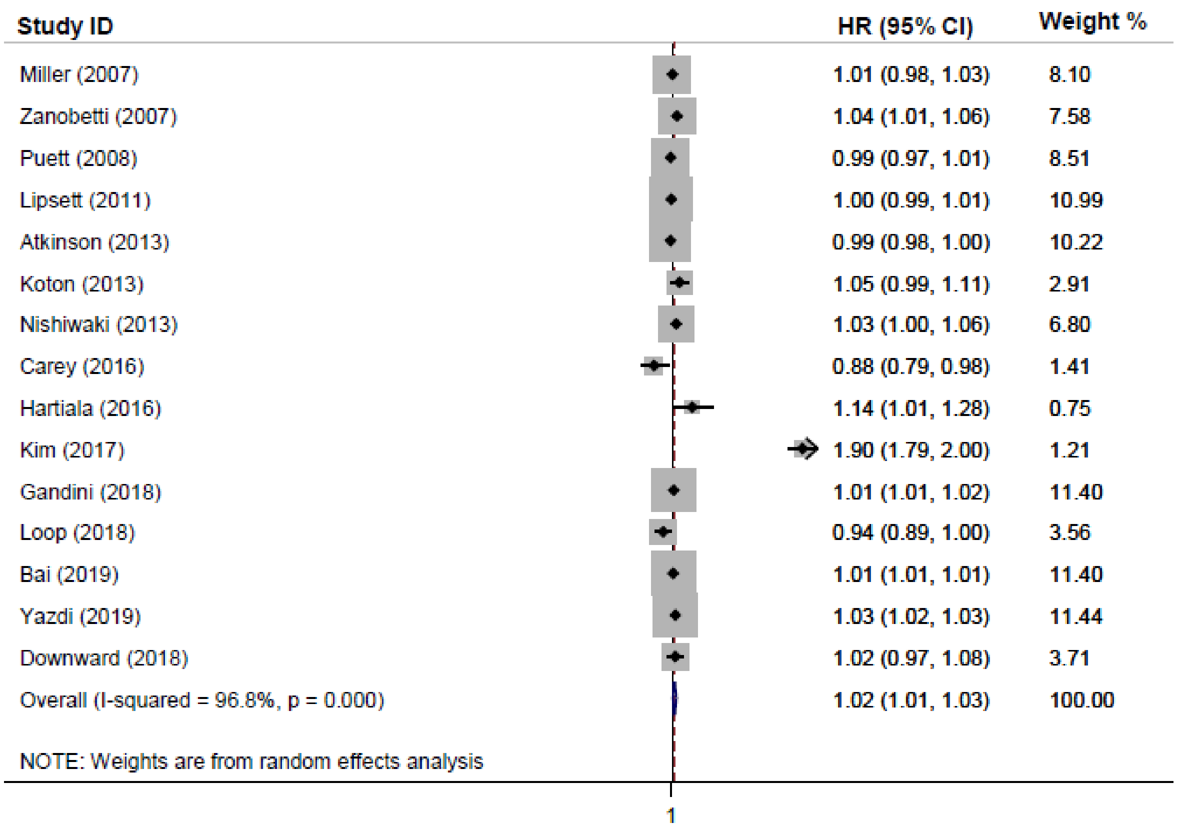

Figure 2

Forest plot for the association between Particulate matter (PM) air pollution with aerodynamic ≤ 10 μm and the risk of myocardial infarction (MI). HR, hazard ratio; CI, confidence interval.

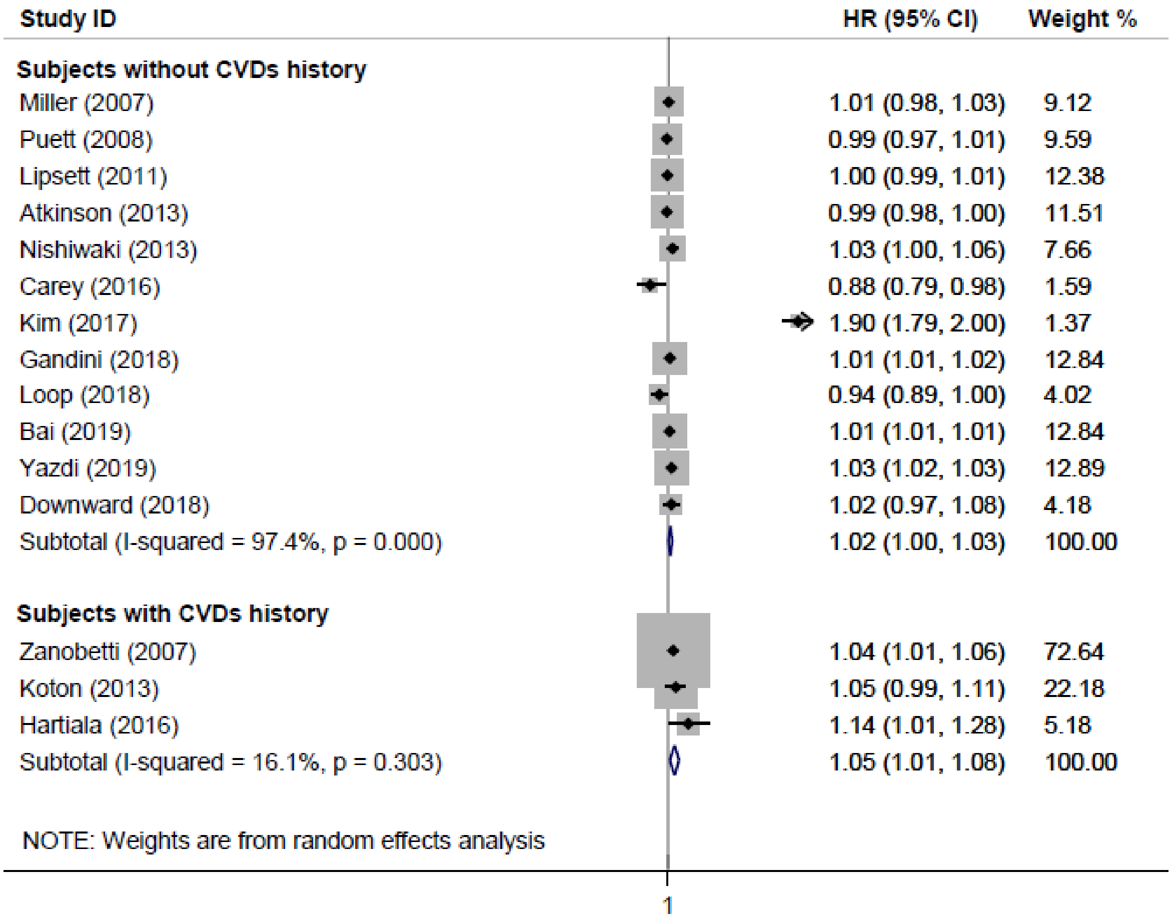

Figure 3

Forest plot for the association between Particulate matter (PM) air pollution with aerodynamic ≤ 10 μm and the risk of myocardial infarction (MI) according to the study population (with or without CVDs). CVDs, cardiovascular diseases; HR, hazard ratio; CI, confidence interval.

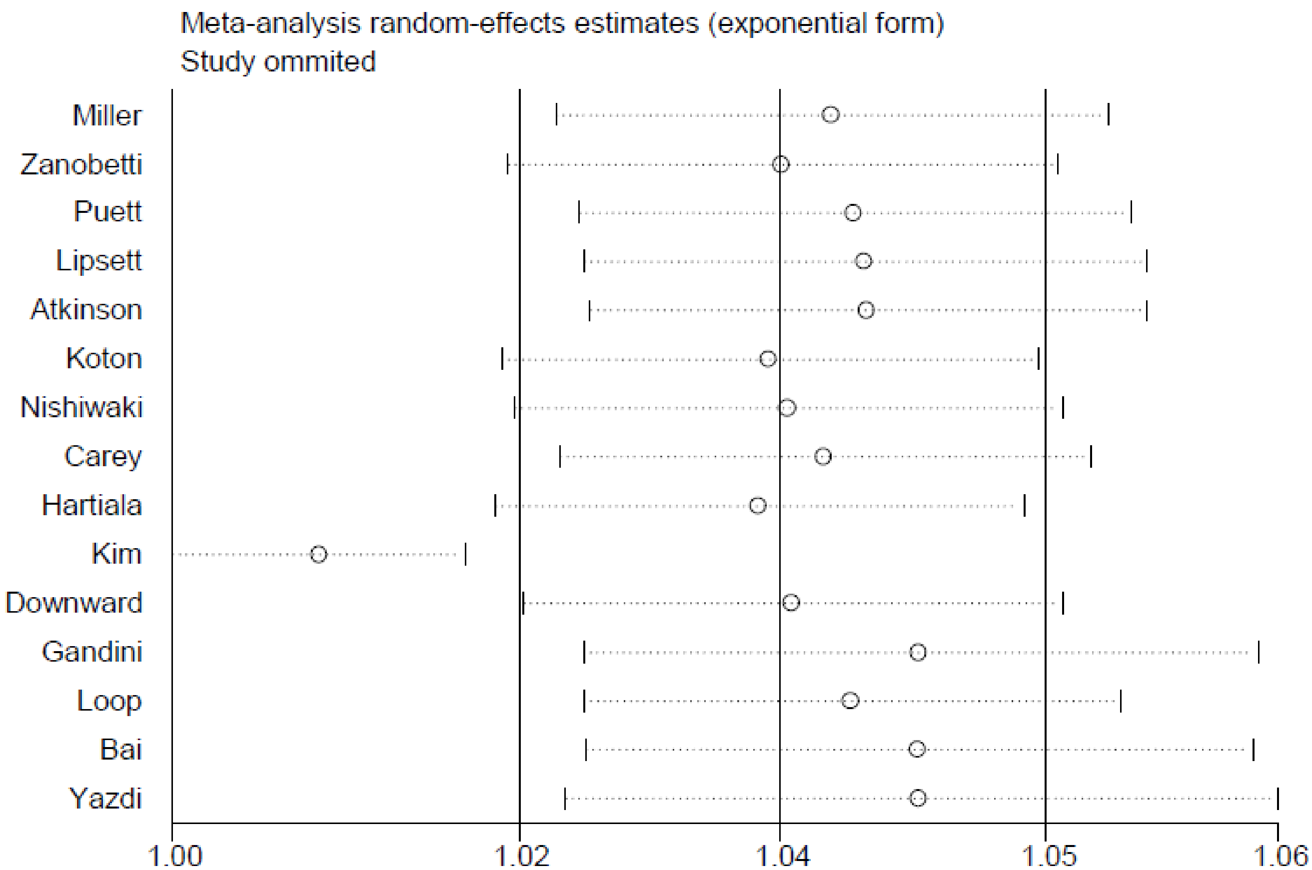

Figure 4

Sensitivity analysis using the jackknife approach.

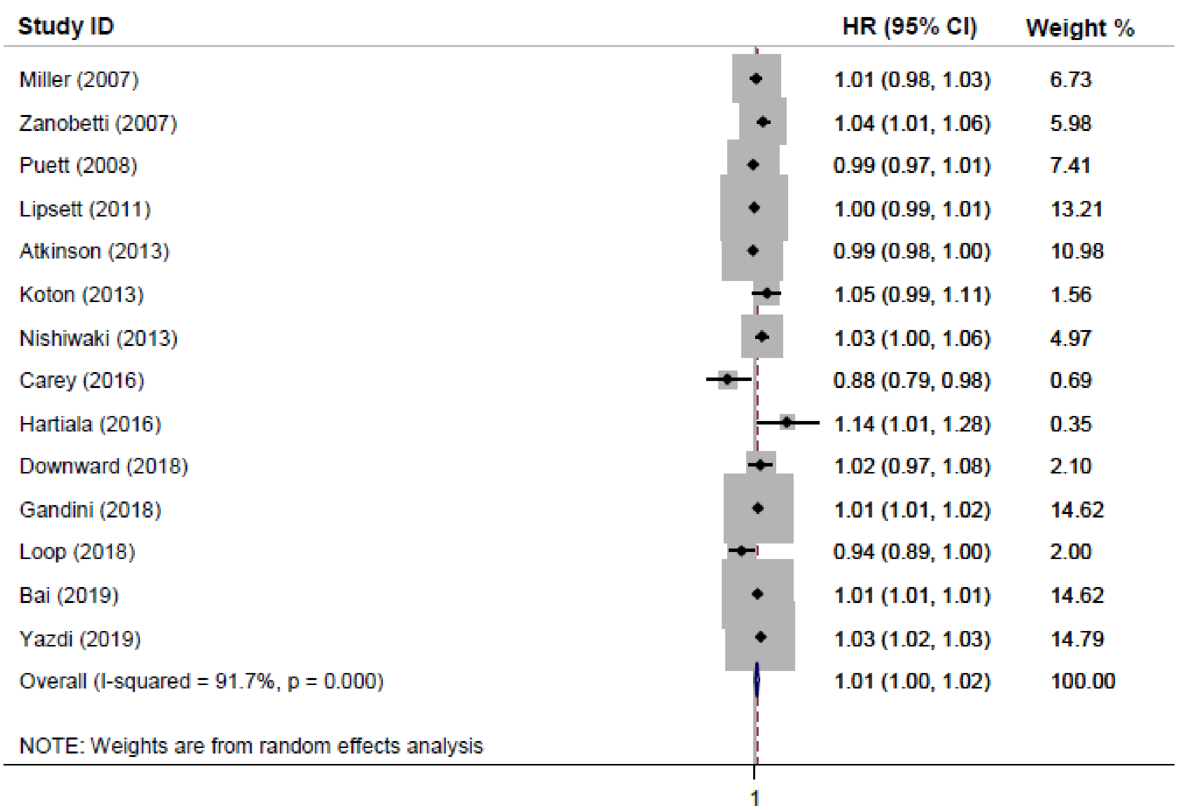

Figure 5

Forest plot for the association between Particulate matter (PM) air pollution with aerodynamic ≤ 10 μm and the risk of myocardial infarction (MI) after removing Kim study according to Jackknife approach. HR, hazard ratio; CI, confidence interval.

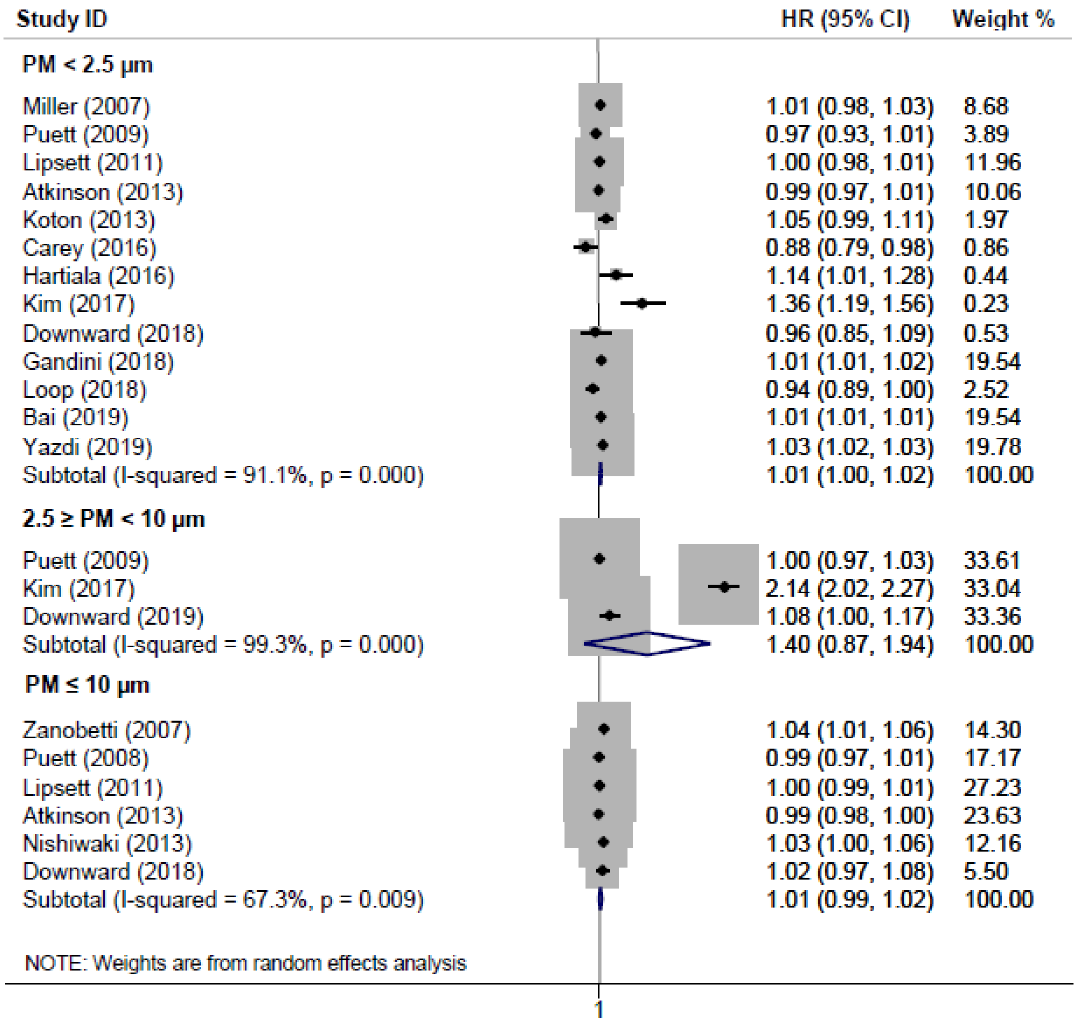

Figure 6

Forest plot for the association between Particulate matter (PM) air pollution and the risk of myocardial infarction (MI) according to PM diameters. HR, hazard ratio; CI, confidence interval.

Supplementary Files

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