Review

Association between particulate matter air pollution and risk of depression and suicide: systematic review and meta-analysis – RETRACTED

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Background

Some recent studies examined the effect of ambient particulate matter (PM) pollution on depression and suicide. However, the results have been inconclusive.

Aims

To determine the overall relationship between PM exposure and depression/suicide in the general population.

Method

We conducted a systematic review and meta-analysis of case-crossover and cohort studies to assess the association between $PM_{2.5}$ (particles with an aerodynamic diameter of 2.5 μm or less) or PM_{10} (particles with an aerodynamic diameter between 2.5 and 10 μm) exposure and depression/suicide.

Results

A total of 14 articles (7 for depression and 7 for suicide) with data from 684 859 participants were included in the meta-analysis. With a 10 μg/m³ increase in $PM_{2.5}$ we found a 19% (odds ratio [95% CI] 1.19 [1.07, 1.33]) increased risk of depression and a marginally increased risk of suicide (odds ratio [95% CI] 1.05 [0.99, 1.11]) in the general population. We did not observe any significant associations between increasing exposure to PM_{10} and depression/suicide. Sensitivity and subgroup analyses were used to determine the robustness of results. The strongest estimated effect of depression associated with $PM_{2.5}$ appeared in a long-term lag pattern (odds ratio [95% CI] 1.25 [1.07, 1.45], $P < 0.01$) and cumulative lag pattern (odds ratio [95% CI] 1.26 [1.07, 1.48], $P < 0.01$).

Conclusions

The meta-analysis suggested that an increase in ambient $PM_{2.5}$ concentration was strongly associated with increased depression risk in the general population, and the association appeared stronger at long-term lag and cumulative lag patterns, suggesting a potential cumulative exposure effect over time.

Declaration of interest

None.

Keywords

Particulate matter; depression; suicide; meta-analysis.

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Burden of mental disorders and PM pollution

Mental disorders are highly prevalent in the population and have recently been identified as an essential contributor to global disease burden.[1] In 2016, depressive disorder accounted for about 44 million disability-adjusted life-years (DALYs) and 34.1 million years lived with disability.[2] Suicide, another mental health problem closely associated with depressive disorder, was the second leading cause of death among those aged 15−29 years and the 17th leading cause of death in the general population in 2015.[3]

Ambient particulate matter (PM) pollution – one of the most important environmental risk factors for human health – was responsible for 105.7 million DALYs globally in 2016, ranking sixth among behavioural, environmental and occupational, and metabolic risk factors.[4] It was also among the top ten risk factors for attributable deaths in 195 countries and territories, including India and China, where it ranked the third and fourth place in 2016, respectively.[4] Since the prevalence of depression and suicide has been increasing rapidly and effective treatments for depression are not easily accessible,[1−3] it is important to investigate relevant risk factors and public prevention methods for these mental health issues.

Relevance and lack of epidemiological studies

Previous epidemiological and experimental studies have linked air pollution to diseases of the central nervous system, behaviour deficits, neuroinflammation and neuropathology in humans and animals.[5−7] There has been an increasing number of studies investigating the association between mental health problems and air pollution[8−21] following the discovery of a possible mechanism of inflammation and oxidative stress.[22−25]

Therefore, we conducted the first meta-analysis for cohort and case-crossover studies on ambient PM and mental health (specifically depression and completed suicide) in the general population. We also investigated the potential pattern of association over different lag times and subgroups divided by study characteristics such as gender ratio, country/region, study design and study quality.

Methods

Search strategy

We identified relevant publications before 13 March 2018 by systematic searches in the following literature databases: PubMed, Medline, Embase, Ovid and Web of Science. We also searched the reference lists of all identified relevant publications and the following grey literature databases: SIGLE, Social Care Online, British National Bibliography for Report Literature and NTIS. We conducted a literature search for particulate matter, depression or suicide using 'AND' as the combining term for the two search themes (see details in Supplementary Table 1 available at https://doi.org/10.1192/bjp.2018.295).

Inclusion criteria

Two reviewers (S.W. and X.G.) collected articles eligible for further review by performing an initial screening of identified abstracts or titles, followed by a full-text review. Discrepancies were resolved by consensus. The broad inclusion criteria for articles were: (a) original studies and reporting on the association of PM and depression

or suicide in a cohort study (prospective cohort or historical cohort) or case-crossover design for the general population; (b) results were reported in a quantitative exposure–response relationship manner (relative risk/odds ratio and 95% CIs); (c) daily air PM data were ambient and obtained from multiple air monitoring stations; (d) studies had outcomes for incidence of depression, depressive symptoms or completed suicide; and (e) efforts had been taken to control for important confounding factors including demographic variables (such as age, gender, jobs and income) and meteorological variables (such as temperature, humidity and sunshine duration).

Exclusion criteria

The exclusion criteria for articles were: (a) not original and other animal studies, toxicological studies, case reports, case series and duplicates; (b) inadequate information after contacting the authors; (c) not full-length articles or did not provide calculable or reported relative risk/odds ratio and 95% CIs; (d) the definition of depression or suicide was uncertain or suicide events were uncompleted; (e) study participants were selected from special population subgroups with high risk of neurological and psychological disease; and (f) study designs were cross-sectional designs or time-series designs.

Data extraction

Two reviewers (S.W. and X.G.) extracted the following information about the studies independently using a form developed for this review: study characteristics (study name, authors, publication year, journal, study design, location, population, follow-up years and sample size), participants' characteristics (mean age and gender ratio), PM exposure variable ($PM_{2.5}$ or PM_{10}), exposure concentration (mean/median), outcome measure (depression or suicide definition), effect estimates (relative risk/odds ratio), lag time, analytic strategy (statistical models and confounders included in the models) and funding information. Discrepancies were resolved by consensus and a third author (Q.L.) was available to determine eligibility if consensus could not be reached. When extracted information remained unclear after inspection of the full text, we contacted the relevant authors to seek clarity and details on this issue. If several effect estimates with different lag times were reported in the same article, we extracted all estimates for statistical analyses; if several statistical models were provided in the same article, we extracted effect estimates from the model which adjusted for the largest number of covariates in the relevant multivariate analyses.

Quality assessment

Quality assessment was performed using the Newcastle–Ottawa Scale, considering the following three general aspects: the selection of the study groups, the comparability of the groups and the ascertainment of either the exposure or outcome of interest for case-crossover or cohort studies, respectively (see details in Supplementary Table 2).[26] A study could be awarded, for each variable within each assessment domain, a possible maximum total score of nine (four for selection, two for comparability and three for exposure/outcome ascertainment). A study with a final score of more than six was regarded as high quality.[27] The quality assessment was conducted independently by two reviewers (Q.L. and X.G.) and the results were reconciled until a consensus was reached.

Statistical analyses

The odds ratio was used as the common measure of association across studies. The relative risk was considered equivalent to odds ratio because the depression and suicide prevalence in the general population was less than 5%. The odds ratios were pooled using the random-effects model. Forest plots were produced to visually assess the odds ratios and corresponding 95% confidence intervals across studies. The heterogeneity of odds ratios across studies was evaluated by the Q statistic and the I^2 statistic. To evaluate the possibility of publication bias, we conducted funnel plot analysis and performed the Begg rank correlation test for funnel symmetry.

For studies that reported stratified risk estimates by lag patterns such as single-day lag (e.g. lag 0 means the present-day exposure of depression or suicide measurement, lag 1 means the day before, and so on) or cumulative lag (e.g. lag 0–1 means the moving average of the present day and the previous day, lag 0–2 means the moving average of the present day and the previous 2 days), each subgroup and lag time was included in our meta-analysis separately. If several lag estimates were reported in the same article, we chose the lag pattern with the largest estimate size used to assess overall risk estimates. In addition, we pooled the various estimates according to lag patterns (short-term exposure [<40 days] and long-term exposure [≥40 days]) and specific lag times separately and only pooled estimates where two or more estimates were available.

We also performed sensitivity analyses by omitting one study at a time and subgroup analyses stratified by participants' gender ratio, study location, study design, study quality and three categories of quality assessment (selection, comparability and exposure/outcome) to evaluate the impact of individual studies and study characteristics on the results.

We performed all analyses using R statistical software (R version 3.4.2 for Windows) with the package 'metafor'. Final estimated effects were expressed as odds ratios associated with a fixed increment of PM (10 µg/m^3 for $PM_{2.5}$ or PM_{10}), and a two-sided P-value of <0.05 was considered statistically significant.

Results

Literature search

The search strategy identified 1167 articles and 1 additional article was extracted from a reference list. After the first round of screening based on titles and abstracts using the inclusion/exclusion criteria, 26 articles remained for further evaluation as shown in Fig. 1. After screening the full text and contacting authors for more details, 14 articles met the inclusion criteria and were included in the meta-analysis,[8–21] with 7 articles for the depression outcome[8–14] and 7 articles for the suicide outcome.[15–21]

Study characteristics

Characteristics of the 14 included articles are shown in Table 1. There were six time-stratified case-crossover studies and one cohort study for suicide; for depression there were three time-stratified case-crossover studies and four cohort studies. Study locations included North America, Europe and Asia. The total number of participants investigated in these studies was 684 859, including 429 678 (ranging from 1148 to 265 749) for suicide and 255 181 (ranging from 1367 to 118 602) for depression. The proportion of male participants ranged from 0 to 78.3% (excluding three studies which did not provide this information) and mean age ranged from 41.3 to 72.4 years (excluding two studies which lacked this information).

Mean concentrations of PM exposure ranged from 9.8 to 84.9 µg/m^3 for $PM_{2.5}$ and 24 to 106.8 µg/m^3 for PM_{10}. Four studies used an exposure measure of PM_{10}; five studies used $PM_{2.5}$; four studies used both $PM_{2.5}$ and PM_{10}; one study did not report on the exposure concentration. Compared with World Health Organization (WHO) air quality guidelines,[28] we found that $PM_{2.5}$ concentrations in four of the included studies were close to the guideline (10 µg/m^3), three studies were close to 20 µg/m^3 and only two were higher than 60 µg/m^3 (Fig. 2). In contrast, concentrations of PM_{10} were generally much higher than the guideline
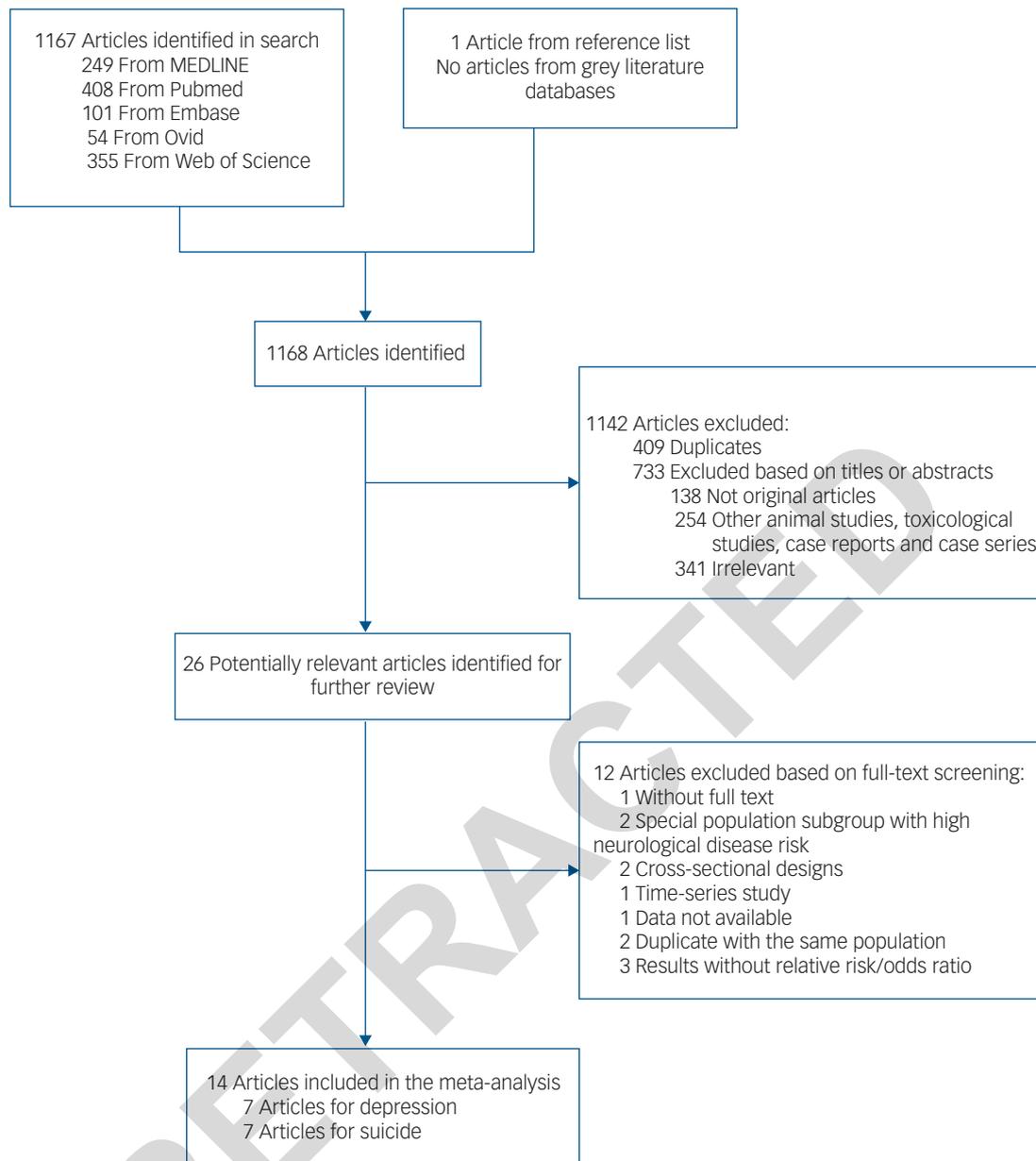
Fig. 1 Literature search for the meta-analysis.

(20 μg/m^3). In all studies investigating the impact of both PM$_{2.5}$ and PM$_{10}$, an increase in PM$_{2.5}$ was associated with a higher risk of depression and suicide than a similar increase in PM$_{10}$.

Outcome assessment was consistent for completed suicide as the studies used either the ICD code (ICD-9 [1978]: E950.0–E958.9 and ICD-10 [1992]: X60-X84 or Y10-Y34) or suicide records. In contrast, outcome assessment for depression varied across different studies: two studies ascertained depression mood/symptoms using depression scales or interviews, whereas five studies ascertained a diagnosis of depression mainly using the ICD code. With regard to the statistical analyses, most studies used Cox proportional hazard models or logistic regression models adjusted for meteorological variables and demographic characteristics.

Overall analyses

The overall meta-analysis showed that an increase of 10 μg/m^3 in PM$_{2.5}$ or PM$_{10}$ was associated with increased risk of depression and suicide (Fig. 3).

Depression outcome

We pooled nine effect estimates examining the association of PM$_{2.5}$ with depression and found that an increase of 10 μg/m^3 in PM$_{2.5}$ was associated with a 19% higher risk of depression (odds ratio [95% CI] 1.19 [1.07, 1.33]), whereas the pooled effect estimate for PM$_{10}$ was insignificant (Fig. 3). No evidence of publication bias was observed for the depression outcome with PM$_{2.5}$ ($P = 0.761$) and PM$_{10}$ ($P = 0.233$) (see funnel plot details in Supplementary Fig. 1).

According to the lag patterns shown in Table 2, exposure to PM$_{2.5}$ was positively associated with depression risk for short-term, long-term, single-day and cumulative lag patterns, and the strongest pooled odds ratio appeared at the long-term lag pattern (odds ratio [95% CI] 1.25 [1.07, 1.45], $P < 0.01$) and cumulative lag pattern (odds ratio [95% CI] 1.26 [1.07, 1.48], $P < 0.01$). In contrast, pooled effect estimates for PM$_{10}$ and depression were insignificant for all lag patterns. The association between PM$_{2.5}$ and depression was positive at all specific lag times and significant at a

Table 1 Characteristics of studies included in the meta-analysis

ID	Study	Study design	Location	Population	Period	Sample size	Age (mean)	Gender (% male)	Exposure	Exposure concentration (mean/median, μg/m³)	Outcome (definition)	Statistical model	Confounders	Funding
1	Cho et al (2014)[13]	Time-stratified case-crossover	Korea	General	2005–2009	4985	43.9	25.2	PM10	54.15	Emergency department visits for depressive episodes (ICD-10: F32)	Cox proportional hazard model	Meteorological variables and demographic characteristics	Yonsei University College of Medicine, Seoul, Korea
2	Kim et al (2016)[14]	Cohort	Korea	General	2007–2010	27 270	≤65	54.2	PM2.5	26.7	Major depressive disorder (ICD-10: F32 with antidepressant prescription)	Cox proportional hazards model	Demographic characteristics	Ministry of Science, ICT, etc.
3	Szyszkowicz et al (2016)[15]	Time-stratified case-crossover	Canada	General	2004–2011	118 602	≤65	Unknown	PM2.5	9.8[a]	Emergency department visits for depression (ICD-10: F32, F33)	Conditional logistic regression	Meteorological variables and demographic characteristics	None
4	Zijlema et al (2016)[16]	Cohort	Europe	General	LifeLines 2007–2013	32 145	43.8	43.1	PM2.5; PM10	PM2.5 25[a]; PM10 24[a]	Depressed mood (MINI diagnostic interview, ≥5)	Logistic regression	Demographic characteristics	European Union Seventh Framework Programme
					KORA 2004–2005 and 2006–2008	5314	55.3	48.5			Depressed mood (PHQ-9 interview version, ≥5)			
					FINRISK 2007	1367	51.9	43.6			Depressed mood (CES-D-11 questionnaire, ≥21)			
5	Kioumourtzoglou et al (2017)[17]	Cohort	US	Middle-aged and older women	1996–2008	41 844	66.6	0	PM2.5	12.6	Depression (a physician diagnosis or use of antidepressant medication)	Cox proportional hazards model	Demographic characteristics	National Institutes of Health and National Institute of Environmental Health Sciences
6	Pun et al (2017)[18]	Cohort	US	General	2005–2006, 2010–2011	4008	Wave 1 69.3; wave 2 72.4	Wave 1 49.9; wave 2 45.6	PM2.5	11.1[a]	Depressive symptoms (CESD-11, ≥9)	Generalised linear mixed model	Demographic characteristics	National Institute of Environmental Health Sciences, etc.
7	Wang et al (2018)[19]	Time-stratified case-crossover	China	General	2014–2015	19 646	46	33.1	PM2.5 PM10	PM2.5 63.5; PM10 106.8	Depression admissions (ICD-10: F32, F33, F34.1 and F41.2)	Conditional logistic regression	Meteorological variables and demographic characteristics	Unknown
8	Kim et al (2010)[20]	Time-stratified case-crossover (random-effect estimate)	Korea	General	2004	4341	≤65	69.1	PM2.5 PM10	Unknown	Completed suicide (unknown)	Conditional logistic regression	Meteorological variables and demographic characteristics	Center for Environmentally Friendly Vehicle of the Eco-STAR project of the Ministry of Environment, Korea
9	Bakian et al (2015)[21]	Time-stratified case-crossover	US	General	2000–2010	1546	41.3	78.3	PM2.5 PM10	PM2.5 11.38[a]; PM10 33.21[a]	Completed suicide (unknown)	Conditional logistic regression	Meteorological variables and demographic characteristics	Veterans Integrated Service Network 19, etc.
10	Lin et al (2016)[22]	Time-stratified case-crossover	China	General	2003–2012	1550	≤65	56.8	PM10	81.2[a]	Completed suicide (ICD-10: X60–X84)	Conditional logistic regression	Meteorological variables and demographic characteristics	National Natural Science Foundation of China, etc.

(Continued)

Table 1 (Continued)

ID	Study	Study design	Population	Location	Period	Sample size	Age (mean)	Gender (% male)	Exposure	Exposure concentration (mean/median, µg/m³)	Outcome (definition)	Statistical model	Confounders	Funding
11	Casas et al (2017)[23]	Time-stratified case-crossover	General	Belgium	2002–2011	20 533	≤65	71.6	PM10	29.0	Completed suicide (ICD-10: X60–X84 or Y10–Y34)	Conditional logistic regression	Meteorological variables and demographic characteristics	Belgian Science Policy Office
12	Min et al (2018)[24]	Cohort	General	Korea	2002–2013	265 749	≤65	54.6	PM10	55.11	Completed suicide (ICD-10: X60–X84)	Cox proportional hazard model	Meteorological variables and demographic characteristics	Ministry of Education, Science and Technology
13	Li et al (2018)[25]	Time-stratified case-crossover	General	China	2009–2012	1148	Unknown	Unknown	PM2.5	84.9	Completed suicide (ICD-10: X60–X84)	Poisson regression	Meteorological variables and demographic characteristics	National Natural Science Foundation of China, etc.
14	Kim et al (2018)[26]	Time-stratified case-crossover	General	Korea; Japan; Taiwan	Korea 2001–012; Japan 1979–2009; Taiwan 1994–2007	134 811	Unknown	Unknown	PM2.5; PM10	PM2.5 26.0[a]; PM10 80.6[a]	Completed suicide (ICD-9: E950.0–E958.9 and ICD-10: X60–X84)	Conditional Poisson regression	Meteorological variables and demographic characteristics	Global Research Laboratory and Senior Research grant of the National Research Foundation, etc.

MINI, Mini-International Neuropsychiatric Interview; PHQ-9, Patient Health Questionnaire 9; CESD-11, Center for Epidemiological Studies Depression Scale 11.
a. If there were more than one mean value of pollutants stratified by case or control group, region, lag day, etc., the highest value was extracted.

lag of 3, 4 and 5 days as well as at the 1-year moving average, with the strongest association at the 1-year moving average (odds ratio [95% CI] 1.14 [1.04, 1.25]) (Fig. 4). Pooled effect estimates for risk of depression associated with exposure to PM_{10} were insignificant at all specific lag times (data not shown).

Suicide outcome

We found that the overall result of four effect estimates examining the risk of suicide associated with $PM_{2.5}$ was positive and marginally significant (odds ratio [95% CI] 1.05 [0.99, 1.11], $P < 0.10$), whereas the overall result of six effect estimates for PM_{10} was insignificant (Fig. 3). No evidence of publication bias was observed for the suicide outcome with $PM_{2.5}$ ($P = 1.000$) and PM_{10} ($P = 0.272$) (see funnel plot details in Supplementary Fig. 1).

Exposure to $PM_{2.5}$ was positively associated with suicide risk at a single-day lag pattern and marginally significant ($P < 0.10$) at short-term and cumulative lag patterns (Table 2). However, no lag pattern result was significant for PM_{10} (Table 2). For different lag times, the positive association between $PM_{2.5}$ and suicide risk was found to be significant at all specific lag times including at a lag of 0, 1, 2 and 3 days and a lag of 0–1, 0–2 and 0–3 days, with the strongest association shown at a lag of 2 days (odds ratio [95% CI] 1.08 [1.08,1.09]) (Fig. 4). Pooled effect estimates for risk of suicide associated with exposure to PM_{10} were insignificant at all common lag times (data not shown).

Sensitivity and subgroup analyses

Depression outcome

Sensitivity analyses indicated that the significance of depression risk associated with $PM_{2.5}$ and PM_{10} was robust. The study by Pun *et al* (2017)[13] had the largest influence on the depression risk associated with $PM_{2.5}$: the pooled odds ratio without this study decreased from 1.19 (95% CI 1.07–1.33) to 1.03 (95% CI 1.01–1.05) (Supplementary Table 3).

The pooled depression risk associated with $PM_{2.5}$ stratified by gender ratio was significant (odds ratio [95% CI] 1.22 [1.01, 1.48]) in the subgroup with male proportion ≤50% but not in the subgroup with male proportion >50% (odds ratio [95% CI] 1.20 [0.85, 1.70]) (Table 3). Regarding study location, the depression risk associated with $PM_{2.5}$ was significant in studies conducted in Europe (odds ratio [95% CI] 1.57 [1.04, 2.35]) and Asia (odds ratio [95% CI] 1.42 [1.11, 1.80]), but only marginally significant in North America (odds ratio [95% CI] 1.11 [0.99, 1.26]). The pooled depression risk was significant in both cohort studies and case-crossover studies, and was stronger in cohort studies (odds ratio [95% CI] 1.34 [1.14, 1.56]). In study quality assessment, five studies scored more than six and were classified as high-quality studies and two studies scored five were classified as medium-quality studies (Supplementary Table 2). The pooled odds ratio of depression associated with $PM_{2.5}$ in high-quality studies was 1.03 (95% CI 1.01–1.04), which was lower than that for medium-quality studies (odds ratio [95% CI] 1.45 [1.14, 1.85]). In addition, subgroup results of the quality assessment categories demonstrated that the differences between high-quality and medium-quality studies were mainly due to variation in comparability and exposure/outcome scores, even though all combined odds ratios were significant. Specifically, medium-quality studies used statistical models only adjusted for demographic confounders but not meteorological confounders and the follow-up time was inadequate (Supplementary Table 2). The pooled risk for studies using depression mood or symptoms as the outcome definition (odds ratio [95% CI] 1.45 [1.14, 1.85]) was higher than that for studies using depression diagnoses as the outcome definition (odds ratio

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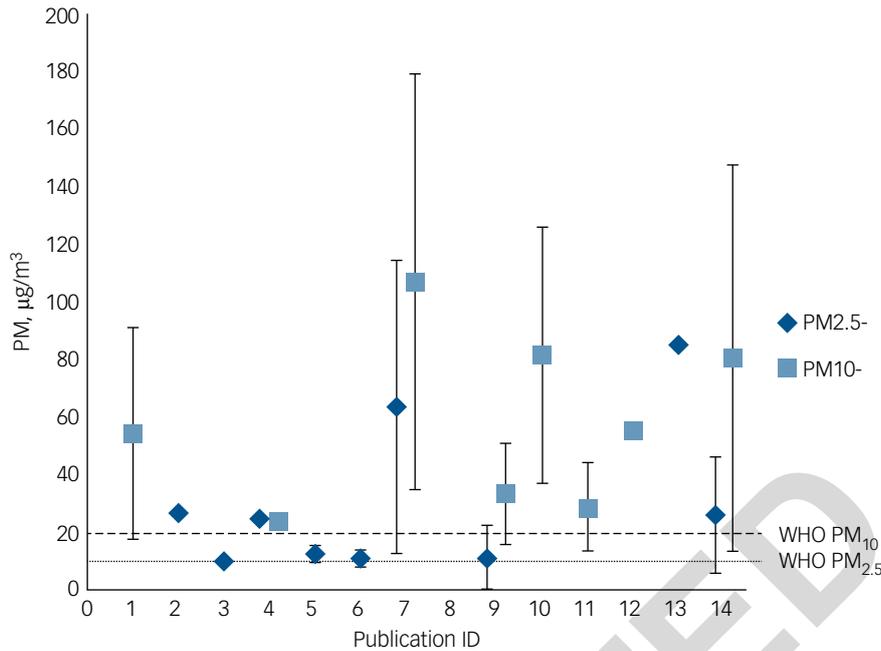
Fig. 2 Particulate matter exposure levels (mean ± SD or median, µg/m³) in studies included in the meta-analysis. PM, particulate matter; WHO, World Health Organization.

[95% CI] 1.03 [1.01, 1.04]). These subgroup results based on outcome assessment were consistent to the subgroup results based on study quality assessment. The depression risk associated with exposure to PM_{10} was insignificant in all subgroups (Table 3).

Suicide outcome

Sensitivity analyses appreciably changed the significance of suicide risk associated with $PM_{2.5}$ but not PM_{10}. The study by Li *et al* (2018)[20] had the largest influence on the suicide risk associated with $PM_{2.5}$: the pooled odds ratio without this study was significant at 1.08 (95% CI 1.08–1.09), whereas the overall pooled odds ratio with this study was only 1.05 (95% CI 0.99–1.11) (Supplementary Table 3).

Studies for the suicide outcome were all determined to be of high quality by quality assessment (Supplementary Table 2). Because gender ratio, study quality and categories of quality assessment were consistent in studies for the suicide outcome, we did not perform subgroup analyses based on these variables. The pooled suicide risk associated with $PM_{2.5}$ was 1.02 (95% CI 1.00, 1.04) for studies conducted in Asia whereas all subgroups were insignificant for PM_{10} based on study location (Table 3).

Discussion

After conducting our meta-analysis, we confirmed that exposure to $PM_{2.5}$ had a significant positive association with risk of depression and a marginally significant positive association with risk of suicide. For an increase of 10 µg/m³ in $PM_{2.5}$, we found a 19% increased risk of depression and a 5% increased risk of suicide in the meta-analysis. The pooled association between $PM_{2.5}$ and depression risk was robust in subgroup and sensitivity analyses, and there was no substantial publication bias. We did not observe any significant association between exposure to PM_{10} and risk of depression or suicide.

To investigate the time course of pollutant exposure–response relationships, we performed meta-analyses for different lag patterns and specific lag times. Pooled effect estimates were all positive over these different lag patterns and specific lag times for depression and suicide risk associated with $PM_{2.5}$. For the association between $PM_{2.5}$ and suicide, we found significant effect estimates at single-day lag pattern (Table 2) and different lag times, and the strongest effect estimates appeared at a lag of 2 days and a lag of 0–3 days (Fig. 4), suggesting that risk of suicide was mainly associated with short-term exposure to $PM_{2.5}$. In contrast, there was a 26% increased risk of depression at the cumulative lag pattern and a 25% increased risk of depression at the long-term lag pattern associated with exposure to $PM_{2.5}$, suggesting that the potential exposure effect was stronger after accumulative exposure over a long time period. Results for common lag times confirmed that the association was much stronger at a 1-year moving average than at short-term lag times (Fig. 4).

However, exposure to PM_{10} was not found to be statistically significantly associated with risk of depression and suicide overall as well as at different lag patterns and common lag times.

Epidemiological and experimental evidence

Depression disorder is a major mental health condition which could cause suicide[3] and is a common comorbidity for other illnesses such as cardiovascular disease,[29,30] stroke,[29–31] diabetes,[32] chronic obstructive pulmonary disease[33,34] and so on.

There is increasing epidemiological evidences for the association between air pollution exposure and mental health, not only depression and suicide, but also psychological stress[35–37] and anxiety.[13,38] Moreover, recent studies have investigated the potential associations between air pollution and central nervous system outcomes including autism spectrum disorders,[39] neurodevelopment in children,[40–42] neurodegenerative diseases[43–45] and stroke.[46] In support of the epidemiological studies, exposure to air pollutants has also been linked to cognitive function decline in animal models.[41]

Although the exact mechanism has yet to be clarified, one hypothesis is that mental disorders occur because of oxidative stress and neuroinflammation pathways being induced by air pollutants. PM is a major air pollutant causing health damage and disease (such as cardiovascular disease,[47,48]) mainly by the inflammatory
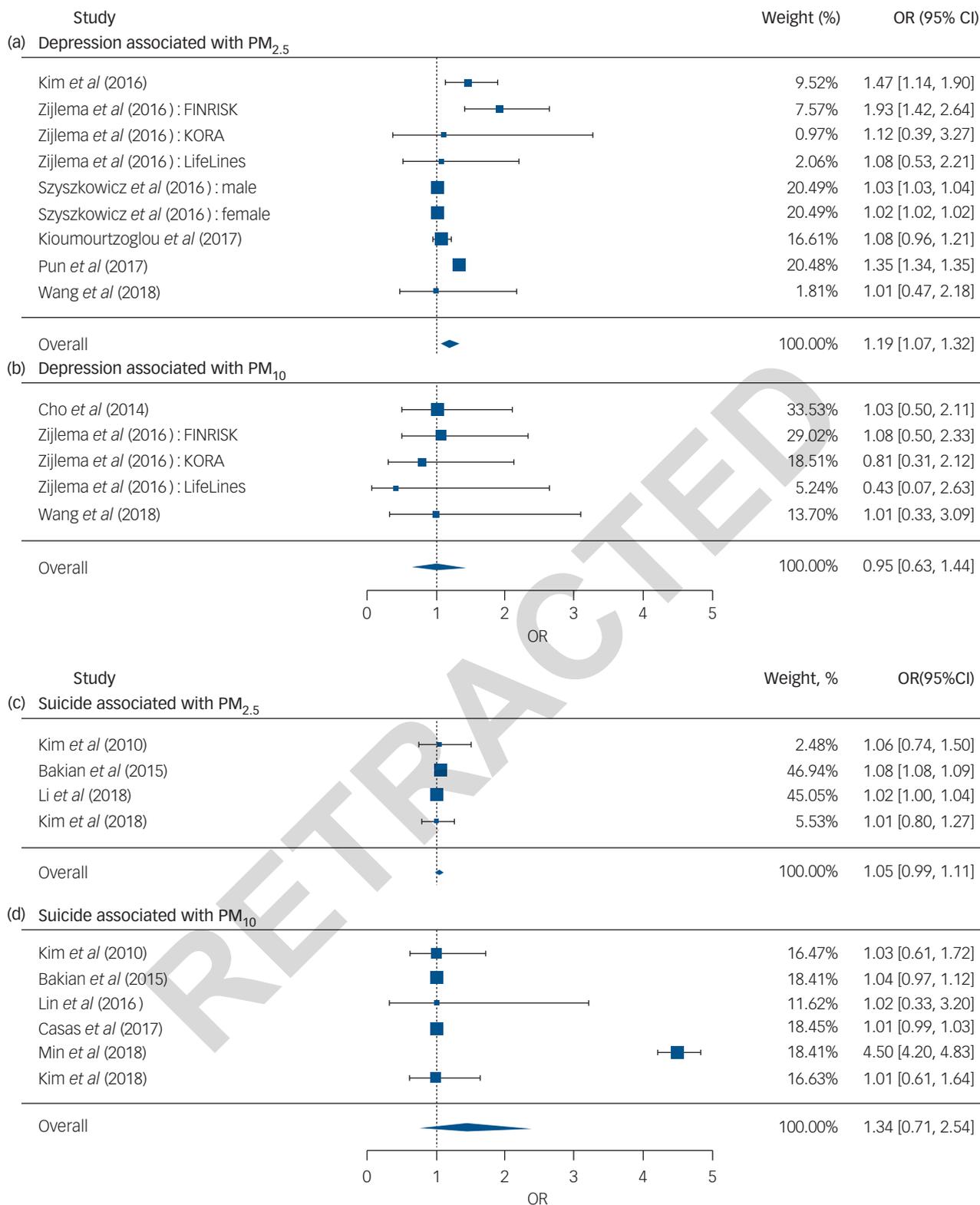
Fig. 3 Forest plots for overall analyses of (a–b) depression and (c–d) suicide risk associated with an increase of 10 μg/m³ in PM₂.₅ or PM₁₀, respectively. OR, odds ratio; PM, particulate matter.

and oxidative stress pathways.[49–51] Evidence from experimental investigation found that, as an essential stressor, PM is associated with increased depression-like responses in mice.[52] Mechanistic studies also showed that inflammation and oxidative stress are the two primary pathways for the neural system damage upon PM exposure.[22–25,49] The neural system is vulnerable to PM for its

high-energy use, low endogenous scavenger levels and high metabolic demands. PM, as an inflammatory stimulus, activates common processes in which cytokines and inflammatory signalling molecules provoke the dysregulation of the development of depressive disorders and their comorbidities, such as heart disease, diabetes and autoimmune conditions.[49]

Table 2 Overall combined effect estimates and analyses based on different lag patterns

Lag pattern	Overall	Short term	Long term	Single day	Cumulative
Depression associated with $PM_{2.5}$					
Number of estimates	9	7	3	6	4
Odds ratio (95% CI)	1.19 (1.07, 1.33)**	1.18 (1.04, 1.34)**	1.25 (1.07, 1.45)**	1.03 (1.01, 1.04)**	1.26 (1.07, 1.48)**
Heterogeneity, I^2	99.91%	99.98%	83.85%	89.39%	80.01%
P-value for heterogeneity	<0.001	<0.001	<0.01	<0.001	<0.01
Publication bias (Begg's test, P)	0.761	0.562	1.000	1.000	0.750
Depression associated with PM_{10}					
Number of estimates	5	5	0	5	2
Odds ratio (95% CI)	0.95 (0.63, 1.44)	0.95 (0.63, 1.44)	–	0.95 (0.64, 1.41)	1.02 (0.56, 1.87)
Heterogeneity, I^2	0	0	–	0	0
P-value for heterogeneity	0.908	0.908	–	0.909	0.972
Publication bias (Begg's test, P)	0.233	0.233	–	0.233	1.000
Suicide associated with $PM_{2.5}$					
Number of estimates	4	4	0	3	4
Odds ratio (95% CI)	1.05 (0.99, 1.11)[a]	1.05 (0.99, 1.11)[a]	–	1.08 (1.08, 1.09)**	1.05 (0.99, 1.10)[a]
Heterogeneity, I^2	93.63%	93.63%	–	0	92.73%
P-value for heterogeneity	<0.001	<0.001	–	0.820	<0.001
Publication bias (Begg's test, P)	1.000	1.000	–	1.000	1.000
Suicide associated with PM_{10}					
Number of estimates	6	5	1	5	6
Odds ratio (95% CI)	1.34 (0.71, 2.54)	1.01 (1.00, 1.03)	4.50 (4.20, 4.83)	1.00 (0.99, 1.01)	1.34 (0.71, 2.54)
Heterogeneity, I^2	99.69%	0	–	0	99.69%
P-value for heterogeneity	<0.001	0.965	–	0.972	<0.001
Publication bias (Begg's test, P)	0.272	0.817	–	0.817	0.272

Odds ratios were shown per 10 µg/m^3 increase in $PM_{2.5}$ or PM_{10}. Effect estimates in Zijlema *et al* (2016)[16] were reported in three cohort groups: LifeLines, KORA and FINRISK.
a. $0.05 < P < 0.10$.
** $P < 0.01$.

On the other hand, PM inhalation can also provoke increased expression of redox/glucocorticoid-sensitive genes in rats, suggesting the involvement of the hormonal pathway in the mental health disorders associated with PM.[53] Chronic activation and inappropriate regulation of the hypothalamic–pituitary–adrenal axis have been associated with adverse neurobehavioural effects, including depression and anxiety disorders.[53] Given the close relationship between air pollution exposure and mental health disorders, exposure to air pollutants could increase the risk of completed suicide.

We also found that $PM_{2.5}$ may play a more important role than PM_{10} in all studies investigating the influence of both $PM_{2.5}$ and PM_{10}. Although PM_{10} has also been identified as a strong inflammatory stimulus, $PM_{2.5}$ is thought to exert greater toxicity because of smaller physical sizes and higher concentrations of adsorbed or condensed toxicants on the surface. Compared with larger particles, $PM_{2.5}$ could be inhaled into the lungs more easily, where it then enters the circulatory system and – by activating pro-inflammatory cytokines – subsequently causes systemic and neuronal inflammation and oxidative damage,[54] possibly leading to mental disorders and other nervous system diseases.[43,55]

Subgroup analyses

We did subgroup analyses with a major focus on depression risk associated with PM, and found appreciable differences in effect estimates over subgroups for $PM_{2.5}$ but not PM_{10}. The pooled risk of depression associated with $PM_{2.5}$ was significant in both cohort studies and case-crossover studies. The magnitude of the effect estimate was smaller for case-crossover studies than for cohort studies. This may be explained by the fact that cohort studies mainly investigated depression risk at a long-term lag pattern whereas case-crossover studies investigated depression risk at a short-term lag pattern, and long-term exposure to PM may increase the health risk more substantially than short-term exposure.

Moreover, the pooled association for $PM_{2.5}$ and depression was still significant after excluding medium-quality and low-score studies in three quality categories, suggesting that the result was robust and reliable. Contributing factors for the relatively low scores in quality assessment were mainly due to a failure to adjust for all possible confounders, including demographic characteristics (such as age, gender, jobs and income), meteorological variables (such as temperature, humidity and sunshine duration) and physical conditions (such as underlying diseases), as well as insufficient follow-up time in cohort studies. Ideally, one would adjust for these contributing factors in the statistical models to guarantee the comparability of the groups. However, all included cohort studies did not control for meteorological variables. Additionally, we could not identify whether the differences between outcome assessments were due to the severity of assessed outcomes or quality differences because the included studies which ascertained depression mood or symptoms were all medium-quality studies. Therefore, we need more high-quality evidence from long-term investigations that adjust for meteorological variables, demographic characteristics and underlying diseases to confirm the association.

The depression risk associated with $PM_{2.5}$ was significant in studies conducted in Europe and Asia but only marginally significant in North America, possibly because the $PM_{2.5}$ pollution in studies conducted in the North America subgroup[10,12,13] were all at low levels close to WHO air quality guidelines. These results suggest that high $PM_{2.5}$ levels may be associated with a greater risk of depression.

We also did subgroup analyses according to study characteristics. Because of the lack of individual data, we only divided studies into subgroups based on the proportion of males in the study population and did not find any obvious differences in risk of depression associated with $PM_{2.5}$ in populations with male proportion ≤50% and those with >50% males.

Strengths and limitations

This study provides a comprehensive evaluation for the association between ambient PM and completed suicide and depression, two major disorders of mental health, in the general population and thus has fair representativeness. Meanwhile, all these included studies were published in the past decade, suggesting an increasing
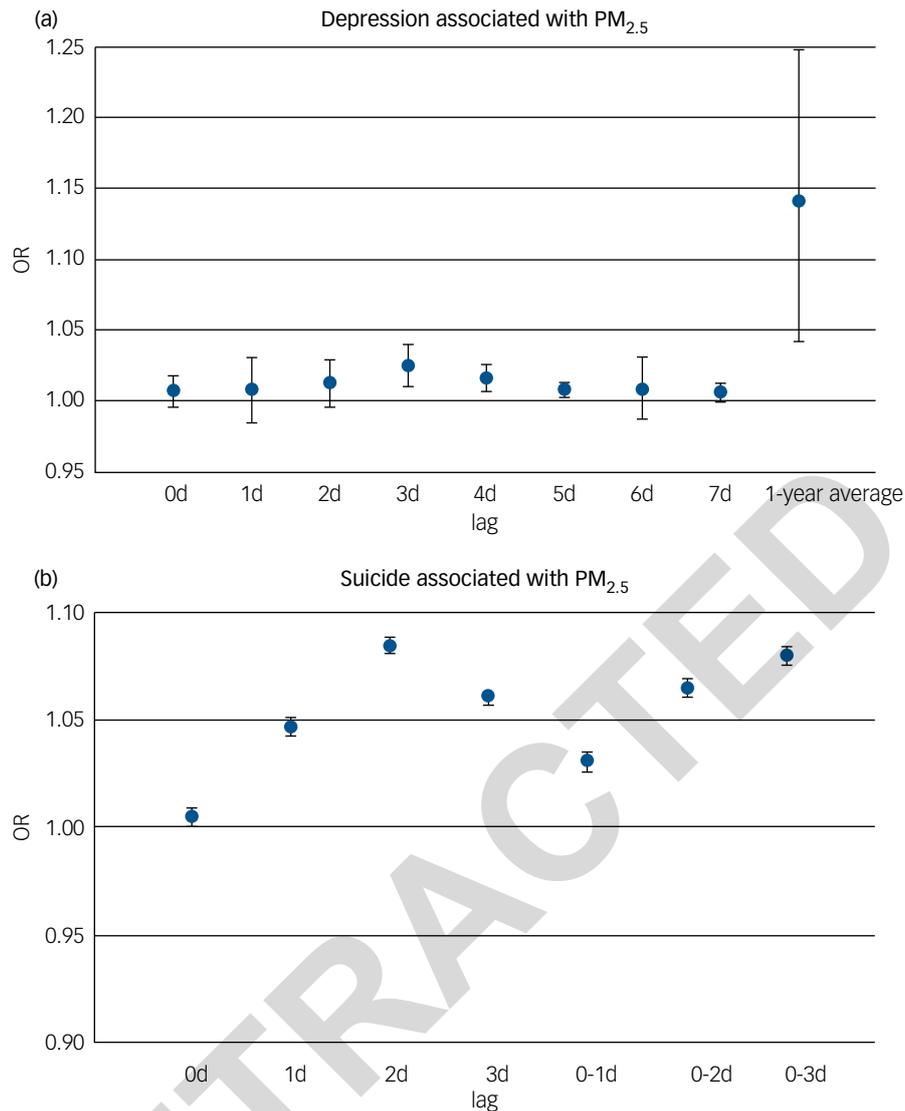
Fig. 4 Meta-analysis according to common lag times for (a) depression and (b) suicide risk associated with an increase of 10 μg/m³ in PM_{2.5}. OR, odds ratio; PM, particulate matter.

concern for the mental health disorders associated with air pollution. Our meta-analysis has several limitations. First, there is the issue of heterogeneity in the definition of depression among studies. The included studies for depression used two major tools for evaluation of depression: two studies ascertained depression mood/symptoms using different scales whereas five studies ascertained depression diagnosis mainly using the ICD codes. We were not able to perform a more detailed subgroup analysis due to the limited number of relevant articles in the literature. Moreover, we could not analyse the influence of depression severity on results because of the lack of relevant information in included studies. However, we used random-effect model to control for the heterogeneous effects of the depression criteria and disease severity and confirmed the association between PM and depression.[56] Second, PM_{2.5} concentrations in most included studies of depression were relatively low and close to WHO air quality guidelines. Therefore, further studies in areas with high PM_{2.5} levels are needed to investigate the depression risk associated with higher PM_{2.5} exposure. Moreover, the elemental composition of PM_{2.5} in different countries would also contribute to the heterogeneity of associations.

Third, the number of studies included in this meta-analysis is relatively small and may have led to the marginal significance of

suicide risk associated with PM_{2.5}. More epidemiological evidence is needed to confirm the association of PM with suicide. Additionally, due to lack of individual characteristic data, we could not investigate the potential difference in exposure–response relationships in different population subgroups divided by individual characteristics. In particular, some evidence suggests that depressive symptoms are highly prevalent in the elderly.[57]

Clinical implications

Our findings suggest that individuals exposed to PM_{2.5} may be at a higher risk of depression or suicide. Because of the ubiquitous existence of PM pollution and the prevalence of depression and suicide, the associated disease burden of mental health would be substantial at the population level. Therefore, it is important to develop relevant public prevention methods for depression and suicide. Targeted strategies such as more stringent air pollution standards, air quality control measures and individual protection behaviours may be helpful to prevent the onset and exacerbation of depression or to decrease suicide cases due to air pollution, especially in heavily polluted regions and high-risk groups. In addition, several researchers[58–61] implied that melatonin might play a role in

Table 3 Subgroup analyses based on study characteristics

	Number of estimates	Odds ratio (95% CI)	I^2 value	P-value for heterogeneity
Gender ratio[a]				
Depression associated with $PM_{2.5}$				
Male proportion ≤50%	7	1.22 (1.01, 1.48)*	99.93%	<0.001
Male proportion >50%	2	1.20 (0.85, 1.70)	86.39%	0.007
Depression associated with PM_{10}				
Male proportion ≤50%	5	0.95 (0.63, 1.44)	0	0.908
Male proportion >50%	0	–	–	–
Study location				
Depression associated with $PM_{2.5}$				
North America	4	1.11 (0.99, 1.26)[b]	99.96%	<0.001
Europe	3	1.57 (1.04, 2.35)**	27.94%	0.250
Asia	2	1.42 (1.11, 1.80)**	0	0.365
Depression associated with PM_{10}				
Europe	3	0.89 (0.50, 1.58)	0	0.638
Asia	2	1.02 (0.56, 1.87)	0	0.972
Suicide associated with $PM_{2.5}$				
North America	1	1.08 (1.08, 1.09)	–	–
Asia	3	1.02 (1.00, 1.04)*	0	0.978
Suicide associated with PM_{10}				
North America	1	1.04 (0.97, 1.12)	–	–
Europe	1	1.01 (0.99, 1.03)	–	–
Asia	4	1.53 (0.54, 4.39)	95.75%	<0.001
Study design				
Depression associated with $PM_{2.5}$				
Cohort design	6	1.34 (1.14, 1.56)**	75.20%	0.001
Case-crossover design	3	1.03 (1.01, 1.04)**	93.57%	<0.001
Depression associated with PM_{10}				
Cohort design	3	0.89 (0.50, 1.58)	0	0.638
Case-crossover design	2	1.02 (0.56, 1.87)	0	0.972
Study quality				
Depression associated with $PM_{2.5}$				
High quality	5	1.03 (1.01, 1.04)**	88.90%	<0.001
Medium quality	4	1.45 (1.14, 1.85)**	47.08%	0.129
Depression associated with PM_{10}				
High quality	2	1.02 (0.56, 1.87)	0	0.972
Medium quality	3	0.89 (0.50, 1.58)	0	0.638
Study quality-selection category score (4)[c]				
Depression associated with $PM_{2.5}$				
4	1	1.47 (1.14, 1.90)	–	–
3	8	1.16 (1.04, 1.30)**	99.92%	<0.001
Depression associated with PM_{10}				
3	5	0.95 (0.63, 1.44)	0	0.908
Study quality-comparability category score (2)				
Depression associated with $PM_{2.5}$				
2	3	1.03 (1.01, 1.04)**	93.57%	<0.001
1	6	1.34 (1.14, 1.56) **	75.20%	0.001
Depression associated with PM_{10}				
2	2	1.02 (0.56, 1.87)	0	0.972
1	3	0.89 (0.50, 1.58)	0	0.638
Study quality-exposure/outcome category score (3)				
Depression associated with $PM_{2.5}$				
3	4	1.03 (1.01, 1.04)**	90.60%	<0.001
2	2	1.35 (1.34, 1.35)**	0	0.498
1	3	1.57 (1.04, 2.35)*	27.94%	0.250
Depression associated with PM_{10}				
3	2	1.02 (0.56, 1.87)	0	0.972
1	3	0.89 (0.50, 1.58)	0	0.638
Outcome assessment				
Depression associated with $PM_{2.5}$				
Depression mood or symptoms	4	1.45 (1.14, 1.85)**	47.08%	0.129
Depression diagnoses	5	1.03 (1.01, 1.04)**	88.90%	<0.001
Depression associated with PM_{10}				
Depression mood or symptoms	3	0.89 (0.50, 1.58)	0	0.638
Depression diagnoses	2	1.02 (0.56, 1.87)	0	0.972

Odds ratios were shown per 10 μg/m³ increase in $PM_{2.5}$ or PM_{10}. Effect estimates in Zijlema et al (2016)[16] were reported in three cohort groups: LifeLines, KORA and FINRISK. PM, particulate matter.
a. Two studies did not report gender ratio.
b. $0.05 < P < 0.10$.
c. The number included in the title of the subgroups indicate one category score number of the study quality assessment scale. For example, "Study quality-selection category score (4)" indicates that in the selection category of study quality assessment scale, the possible maximum total score is 4. Thus, these single-standing numbers in the left-hand column are referring to subgroups with different scores in relevant categories.
*$P < 0.05$, **$P < 0.01$.

the prevention or treatment of depression associated with $PM_{2.5}$. However, because the mechanism by which $PM_{2.5}$ increases the risk of depression is unclear, the efficacy of the first melatonergic antidepressant agomelatine[62] is yet to be explored in the treatment of $PM_{2.5}$-related depression. Thus, the positive association between PM pollution and depression/suicide offers a new insight and consideration for the treatment of depression and other mental disorders through reducing individual exposure to PM pollution and alleviating oxidative stress in the nervous system.

Future epidemiological studies are needed to confirm the association for PM and suicide and explore the association patterns of PM with depression and suicide in different population subgroups, and experimental studies are also encouraged to investigate the underlying mechanism for the reported associations.

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Supplementary material

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