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Review article

Exercise and air pollutants exposure: A systematic review and meta-analysis

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ABSTRACT

This review aims to systematically review and synthesize scientific evidence for the influence of air pollution exposure and outdoor exercise on health. We conducted a literature search in the PubMed, Cochrane, EMBASE, and Web of Science for articles that evaluated the combination effect of air pollution exposure and exercise on health. Questionnaires regarding exposure history, or studies examining indoor air pollution were excluded. Each included study needs to have clear exercise intervention plan. The pooled estimates of the combination effect of air pollution exposure and outdoor exercise on health were calculated in the meta-analysis. The quality of each included study was assessed and the quality of evidence for each outcome assessed in the meta-analysis was also measured. Twenty-five studies were identified. Six studies addressed ozone exposure, four diesel exhaust exposure, six traffic-related air pollution, ten particulate matter (PM) exposure. Only peak expiratory flow (effect size [ES] = −0.238, 95% confidence interval [CI] = −0.389, −0.088) was found to be significantly decreased after exercise intervention in a polluted environment in the meta-analysis. Seven studies reported exposure to air pollutant during exercise was associated with an increased risk of airway inflammation and decrements in pulmonary function. Six studies discovered that exposure of traffic pollution or high PM during exercise may contribute to changes in blood pressure, systemic conduit artery function and micro-vascular function. The combination effect of air pollution and exercise was found to be associated with the increased risk of potential health problems of cardiopulmonary function, immune function, and exercise performance.

1. Introduction

Air pollution endangers human health, which has aroused deep concern in most regions of the world. Many evidences indicate that nitrogen dioxide (NO_2), ozone (O_3), and particulate matter of less than 2.5 μm in aerodynamic diameter (PM2.5), as main pollutants, are associated with higher resting blood pressure [1], chronic obstructive pulmonary disease (COPD) [2], pulmonary infection [3], and even premature deaths [4].

The positive effect of exercise on health has gained a wide recognition, which drives the popularity of indoor and outdoor recreational physical activities. Several studies suggested that compared with indoor exercise, outdoor exercise can significantly reduce depression and perceived stress [5]. However, outdoor activities might increase the risk of air pollutants exposure, especially in the countries or regions with serious air pollution, such as China, India, and Mexico. In addition, dense population in these countries also leads to a relative lack of stadium and gymnasium, thus people have to choose parks, squares and streets as their main places for recreation or exercise. It promotes the development of some mass outdoor exercise, such as marathon, meanwhile also further increase the exposure to air pollution. According to the 2016 report of Chinese marathon, the national marathon events and the participants appeared a blowout type growth [6]. Comparing with 2015, the national marathon events raised 1.5 times in 2016, with nearly 2 million 800 thousand of participants in China [6]. Even a few marathon events have to be held on the days with heavy air pollution.

Outdoor physical activity requires a healthy air quality. However, regarding people living in countries or cities with heavy air pollution, outdoor physical activity is becoming more and more harmful to health. Regular outdoor exercise can improve health, meanwhile it might also increase the risk of pollution exposure, which would fall into a dilemma [7,8]. Some previous studies demonstrated that air pollutant exposure during exercise could cause inflammation [9], cognitive impairment

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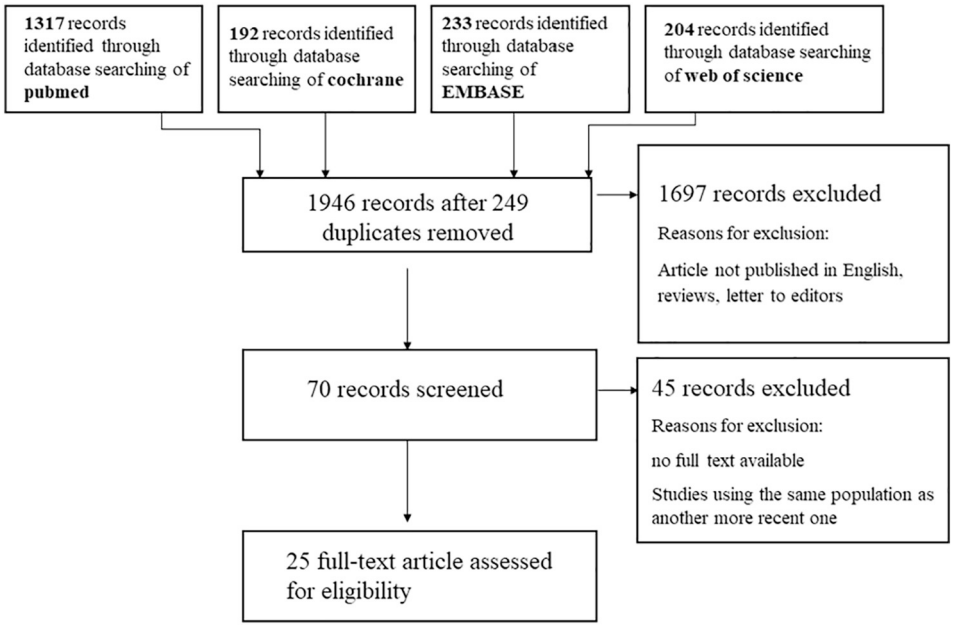

Fig. 1. Flow chart of literature search.

[10], and other health hazard [11]. Other studies, however, indicated that regular exercise might reverse the harmful of the air pollution [12–15]. Thus, it is very urgent to investigate the combined effect of exercise and air pollution on health. The purpose of this study was to systematically review and synthesize scientific evidence for the influence of air pollution exposure and outdoor exercise on health. We described the current literature to identify knowledge gaps and future research opportunities.

2. Methods

2.1. Search strategy

A keyword search was performed in four databases-PubMed, Cochrane, EMBASE, and Web of Science. Retrieval spanned the period 1990–2017. The search algorithm included all possible combinations of keywords from the following two groups: (1) "exercise", "physical training", "aerobic fitness", "physical activity", and "physical exercise"; and (2) "air pollution", "air quality", "nitrogen dioxide (NO_2)", "sulfur dioxide (SO_2)", "ozone (O_3)", "carbon monoxide (CO)", "particulate matter", "PM_{10}", and "$PM_{2.5}$". Titles, abstracts, and full-text articles of potentially relevant studies were independently screened by three researchers (FQ, YY, and YD). In addition, to identify additional relevant studies, we conducted a reference list research and a cited reference search on the full-text articles.

2.2. Study selection criteria

Eligibility criteria for studies based on participant, exposure/intervention, outcome, study design, and language, were used to identify studies. The inclusion criteria were following: (1) Participant: healthy person had no history of respiratory or cardiovascular disease, without geographical restriction. No restrictions for sex or age were made; (2) Exposure/intervention: exposure was defined as variety of biological and abiotic components from outdoor, including carbon monoxide (CO), nitrogen monoxide (NO), nitrogen dioxide (NO_2), nitrogen oxides (NOx), sulfur dioxide (SO_2), ozone (O_3), and particulate matter (PM). Questionnaires regarding exposure history, or studies examining indoor air pollution were excluded. Each included study needs to have clear exercise intervention plan, including exercise duration, intensity, frequency, and type; (3) Outcome: the three types of outcomes are cardiopulmonary function outcomes, immune function outcomes, and exercise performance outcomes. Cardiopulmonary function outcomes include forced expiratory volume in one second (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), forced expiratory flow at 25–75% of forced vital capacity ($FEF_{25–75\%}$), blood pressure, vascular function, and heart rate variability (HRV). Immune function outcomes include differential cell counts (lymphocytes/neutrophils), cytokines concentrations (IL-6/TNF-α/ICAM-1), inflammatory markers (CRP/NO), and cluster of differentiation (CD40/CD63/CD42). Exercise performance outcomes include aerobic fitness (12-min running test/VO2max/VO2) and maximal work accumulation. (4) Study design: randomized clinical trials, before-and-after trials, crossover randomize study, and other experimental research designs; and (5) Language: article written in English.

2.3. Data extraction and preparation

Two of the authors (FQ and YY) independently extracted data from each included study using a data collection form including the following variables: first author and year of publication, study design, sample size, proportion of males, age range, sample characteristics, exposure, intervention, outcome measures, and study finding. Whenever possible, we contacted corresponding authors to obtain additional information and numerical results which were not reported in articles.

2.4. Meta-analysis

Meta-analysis was performed to estimate the pooled effect size of exercise intervention on cardiopulmonary function and inflammation in a polluted environment. Cardiopulmonary function included pulmonary function such as FVC, FEV1, PEF, and $FEF_{25–75\%}$ and inflammation included indicators such as exhaled NO, blood leukocyte counts, and blood neutrophil counts. The pooled effect size is the mean difference when indicators of cardiopulmonary function and inflammation were measured pre/post exercise intervention. Several studies were excluded from the meta-analysis due the following reasons: effect size was not reported [16–21]; standard deviation or standard error of effect size was not reported [22]; outcomes of

Table 1
Basic characteristics of the studies included in the review.

Study ID	First author (year)	Study design	Sample size (male %)	Age range/mean (SD)	Sample characteristics	Exposure
1	Aris R, D Christian, D Sheppard, et al. [37]	Before-after study	10 (60%)	21–31	Healthy, athletic subjects	0.20 ppm ozone
2	Barath S, NL Mills, M Lundback, et al. [29]	Crossover study	18 (100%)	21–30	Healthy, non-smoking males with normal pulmonary function	Diesel exhaust (approximately 250 μg/m^3)
3	Bos I, P De Boever, J Vanparijs, et al. [42]	Before-after study	24 (37.5%)	18–60	Untrained healthy participants	Ultrafine PM (UFPM) 0.02–1 μm
4	Castillejos M, DR Gold, AI Damokosh, et al. [30]	Before-after study	40 (55%)	7.5–11	School children	Ozone (49 ppb–365 ppb)
5	Cutrufello PT, KW Rundell, JM Smoliga, et al. [23]	Crossover study	16 (100%)	18–23	Healthy, nonsmoking male collegiate athletes	Particulate matter (PM1)
6	Giles LV, C Carlsten and MS Koehle [16]	Crossover study	8 (100%)	29 (6)	Healthy, endurance-trained males and nonsmoker	Diesel exhaust (DE) containing 300 μg/m^3 of PM2.5.
7	Giles LV, JP Brandenburg, C Carlsten, et al. [17]	Crossover study	18 (100%)	24.5 (6.2)	Healthy, Recreationally active males	Diesel exhaust (DE) containing 300 μg/m^3 of PM2.5
8	Girardot SP, PB Ryan, SM Smith, et al. [38]	Before-after study	354 (43.5%)	≥18	Healthy, volunteers embarking on day hikes	Ozone and PM2.5 exposure
9	Gomes EC, V Stone and G Florida-James [39]	Crossover study	10 (100%)	24 (6)	Male, endurance runners	0.1 ppm ozone
10	Gomes EC, V Stone and G Florida-James [24]	Crossover study	10 (100%)	24 (6)	Male, endurance runners	0.1 ppm ozone
11	Jacobs L, TS Nawrot, B de Geus, et al. [40]	Before-after study	38 (74%)	28–58	Adults, cycling to work at least twice a week	Traffic-related air pollution (TRAP)
12	Jarjour S, M Jerrett, D Westerdahl, et al. [22]	Before-after study	15 (73.3%)	23–48	Healthy, nonsmoking and regular cyclists	Traffic-related air pollution (TRAP)
13	Kubesch N, A De Nazelle, S Guerra, et al. [41]	Crossover study	28 (46.4%)	21–53	Non-smoking healthy adults	Traffic-related air pollution (TRAP)
14	Kubesch NJ, A de Nazelle, D Westerdahl, et al. [28]	Crossover study	28 (46.4%)	21–53	Non-smoking healthy adults	Traffic-related air pollution (TRAP)
15	Matt F, T Cole-Hunter, D Donaire-Gonzalez, et al. [34]	Crossover study	30 (50%)	19–57	Healthy adults	Traffic related air pollution (TRAP)
16	Rundell KW, BA Spiering, JM Baumann, et al. [18]	Before-after study	9 (100%)	19.3 (1.22)	College ice-hockey players	High PM1: 143,501 ± 58,565 particles/cm^3 Low PM1: 5309 ± 1942 particles/cm^3
17	Rundell KW, JR Hoffman, R Caviston, et al. [25]	Before-after study	16 (100%)	20.5 (2.37)	Intercollegiate athletes	High PM1: 348,600 ± 121,600 particles/cm^3 Low PM1: 2260 ± 500 particles/cm^3
18	Rundell KW, JB Slee, R Caviston, et al. [20]	Before-after study	12 (100%)	20.5 (2.42)	Physically fit, non-asthmatic, nonsmoking males	High PM1: 252,290 ± 77,529 particles/cm^3 Low PM1: 7382 ± 1727 particles/cm^3
19	Rundell KW and R Caviston [19]	Before-after study	15 (100%)	19.5 (1.13)	Healthy, non-asthmatic, nonsmoking ice hockey players	High PM1: 336,730 ± 149,206 particles/cm^3 396,200 ± 82,564 particles/cm^3 Low PM1: 2260 ± 500 particles/cm^3
20	Sawyer K, JS Brown, MJ Hazucha, et al. [26]	Before-after study	10 (20%)	18–35	Healthy, non-smoking adults	Ozone (0.2 ppm)
21	Shah AP, AP Pietropaoli, LM Frasier, et al. [31]	Crossover study	16 (50%)	26.9 (6.5)	Healthy, non-smoking adults	Carbon ultrafine particles (50 μg/m^3)
22	Strak M, H Boogaard, K Meliefste, et al. [32]	Before-after study	12 (33%)	23–57	Students and employees of Utrecht University	Traffic-related air pollution was characterized by measurements of PM10
23	Wauters A, F Esmaeilzadeh, S Bladt, et al. [27]	Crossover study	25 (100%)	23.0 (0.4)	Healthy, non-smoker subjects	Diesel exhaust (DE) containing 300 μg/m^3 of PM2.5.
24	Weichenthal S, M Hatzopoulou and MS Goldberg [33]	Crossover study	53 (0%)	18–45	Healthy, non-smoking women in Montreal, Canada	Traffic related air pollution (TRAP)
25	Stieb DM, R Shutt, L Kauri, et al. [21]	Before-after study	77 (51.9%)	≥55	Healthy, non-smokers, without seasonal allergies	CO, NO_2, O_3, $PM_{2.5}$, SO_2

Table 2
Intervention, measures of outcome, and findings in the studies included in the review.

Study ID	Author (year)	Intervention	Outcome measures	Study finding
1	Aris R, D Christian, D Sheppard, et al. [37]	Exercised for 2 h in atmospheres containing HNO_3 fog (0.5 mg/mL), H_2O fog, or clean, filtered air. After a 1 h break, they exercised for an additional 3 h in an atmosphere containing 0.20 ppm O_3	FEV1, FEV1/FVC, $FEF_{25–75\%}$, FVC, sRaw, O_3-sensitive	Prior exposure to HNO_3 or H_2O fog does not potentiate, but may attenuate, O_3-lnduced decrements in pulmonary function. Increased methacholine responsiveness in O_3-sensitive subjects suggests that airway hyper responsiveness may be a risk factor for O_3 sensitivity even among healthy, asymptomatic athletes
2	Barath S, NL Mills, M Lundback, et al. [29]	Moderate exercise (average minute ventilation, 20 L/min/m^2 body surface) on a bicycle ergometer alternating with rest at 15-minute intervals	Forearm blood flow (FBF), IL-6, TNF-a, P-selectin, ICAM-1, CD40	Exposure to diesel exhaust generated under transient running conditions, as a relevant model of urban air pollution, impairs vasomotor function and endogenous fibrinolysis in a similar way as exposure to diesel exhaust generated at idling
3	Bos I, P De Boever, J Vanparijs, et al. [42]	Aerobic training at 75% of maximal heart rate, 3 sessions a week, 12 week	Aerobic fitness (12-min running test), exhaled nitric oxide levels, blood counts	Exercising in an urban environment with high traffic-related air pollution exposure increases markers of respiratory and systemic inflammation.
4	Castillejos M, DR Gold, AI Damokosh, et al. [30]	Two cycles of treadmill exercise (15 min) and rest (15 min) for a total of 1 h of intermittent exercise. Subjects exercised alternately during low ozone hours and during peak O_3 hours	FEV1, FEV1/FVC, $FEF_{25–75\%}$, FVC	A modest acute response to O_3 has been observed for children with higher levels of pulmonary function
5	Cutrufello PT, KW Rundell, JM Smoliga, et al. [23]	Submaximal exercise for 20 min followed by a 6 min maximal work accumulation exercise test in either high PM (HPM) or low PM (LPM) conditions on two consecutive days. After a 7-day washout period, subjects completed identical exercise trials in the alternate condition	Maximal effort 6-min cycle ergometer trials, pulmonary arterial pressure (PP), flow-mediated vasodilation (FMD) of the brachial artery	Exercise performance declined in high PM conditions in part due to impaired vasodilation in the peripheral vasculature
6	Giles LV, C Carlsten and MS Koehle [16]	Test days consisted of a 60-min exposure to either filtered air (FA) or DE, followed by a 20 km cycling time trial	FEV1, FEV1/FVC, $FEF_{25–75\%}$, FVC	A 60-min exposure to DE prior to exercise significantly attenuated exercise-induced bronchodilation and significantly increased heart rate during exercise. Pre-exercise exposure to diesel exhaust did not significantly impair 20 km cycling time trial performance
7	Giles LV, JP Brandenburg, C Carlsten, et al. [17]	Performed 30-min trials of low-intensity (30% of power at VO_{2peak}) and high intensity (60% of power at VO_{2peak}) cycling as well as rest.	Oxygen consumption (VO_2), CO_2 production (VCO_2), RER, maximal exercise trials	The greater responses during low-intensity exercise in DE could have implications for individuals with cardiopulmonary disease. During DE could impair performance in self-paced exercise
8	Girardot SP, PB Ryan, SM Smith, et al. [38]	Day hikers of the Charlies Bunion trail during 71 days of fall 2002 and summer 2003. The Charlies Bunion trail is an approximately 6.7 km (one-way)	FEV1, FEV1/FVC, $FEF_{25–75\%}$, FVC	No significant associations of acute changes in pulmonary function with either pollutant was found
9	Gomes EC, V Stone and G Florida-James [39]	8 km time trial run on a treadmill. The participants were required to complete as fast as they could.	FEV1, $FEF_{25–75\%}$, FVC, PEF	There were no significant changes between pre/post pulmonary function measures or between trials
10	Gomes EC, V Stone and G Florida-James [24]	8 km time trial run on a treadmill. The participants were required to complete as fast as they could.	IL-6, IL-8, CC16, neutrophil counts, albumin	Ozone-polluted elicits an early epithelial damage and antioxidant protection process in the upper respiratory airways of athletes immediately after performing 8 km time trial run.
11	Jacobs L, TS Nawrot, B de Geus, et al. [40]	Two exercise trials during two exposure scenarios. Cycled for about 20 min in real traffic near a major bypass road in Antwerp and in a laboratory with filtered air. The total trajectory is 5750 m long.	Exhaled nitric oxide (NO), plasma interleukin-6 (IL-6), platelet function, Clara cell protein in serum, blood cell counts	Traffic-related exposure to particles during exercise caused a small increase in the distribution of inflammatory blood cells in healthy subjects.
12	Jarjour S, M Jerrett, D Westerdahl, et al. [22]	Cycle on two routes – a low-traffic bicycle Boulevard route and a high-traffic route. Each participant cycled on the low-traffic route once and the high-traffic route once. The two routes were similar in length (8–9.5 km)	FEV1, FVC, FEV1/FVC ratio, $FEF_{25–75\%}$	The pulmonary function results indicate that elevated pollutant exposure may not have acute negative effects on healthy cyclists.
13	Kubesch N, A De Nazelle, S Guerra, et al. [41]	2 h exposure in high or low-TRAP environment, each at rest and combined with intermittent moderate PA, consisting of four 15 min intervals alternating rest and cycling on a stationary bicycle.	Systolic (SBP), diastolic blood pressure (DBP)	Intermittent PA attenuates the TRAP-related increases in SBP. We showed that in low-TRAP environments intermittent PA has stronger beneficial effects on SBP than in high-TRAP environments.
14	Kubesch NJ, A de Nazelle, D Westerdahl, et al. [28]	Four different exposure scenarios: 2 h exposure in a high and low TRAP environment, each at rest and in combination with intermittent moderate exercise, consisting of four 15 min rest and cycling intervals.	FEV1, FVC, FEV1/FVC ratio, $FEF_{25–75\%}$, FeNO, blood cell counts, IL-6, IL-8, IL-10, TNF-α, CRP, blood cell counts	In a healthy population, intermittent moderate PA has beneficial effects on pulmonary function even when performed in a highly polluted environment.

(*continued on next page*)

Table 2 (*continued*)

Study ID	Author (year)	Intervention	Outcome measures	Study finding
15	Matt F, T Cole-Hunter, D Donaire-Gonzalez, et al. [34]	Four 2-h exposure scenarios that included either rest or intermittent exercise in high- and low-traffic environments. Intermittent moderate exercise (50–70% maximum HR), consisting of four 15 min rest and cycling intervals.	FEV1, FEV1/FVC, $FEF_{25–75\%}$, FVC, PEF	PA could decrease the immediate and delayed negative impact of high PM concentrations upon respiratory airways.
16	Rundell KW, BA Spiering, JM Baumann, et al. [18]	6-min cycle ergometer trials in low and high PM1. Subjects were encouraged to exercise at the highest intensity sustainable for the test duration and to accumulate the maximal amount of work.	FEV1, $FEF_{25–75\%}$, FVC, PEF	PM1 inhalation during exercise promotes a predominately leukotriene-mediated response.
17	Rundell KW, JR Hoffman, R Caviston, et al. [25]	Exercise trials involved 30 min of running at between 85 and 90% of maximal heart rate while inhaling low or high PM1.	Flow-mediated brachial, artery dilation (FMD), reoxygenation slope-to-baseline	Acute inhalation of high PM1 typical of urban environments with exercise impairs both systemic conduit artery function and microcirculation.
18	Rundell KW, JB Slee, R Caviston, et al. [20]	Exercise trials involved 30 min of running at between 85 and 90% of maximal heart rate, inhaling low or high PM1	NO_3, eNO, MDA, FEV1, $FEF_{25–75\%}$, FVC, PEF	High PM1 inhalation during exercise caused a reduced alveolar contribution to eNO. NO_3 and eNO variables were decreased and were related to impaired pulmonary function.
19	Rundell KW and R Caviston [19]	Maximal effort 6-min cycle ergometer trials while breathing low or high PM1.	Maximal effort 6-min cycle ergometer trials	Acute inhalation of high (PM1) typical of many urban environments could impair exercise performance.
20	Sawyer K, JS Brown, MJ Hazucha, et al. [26]	15 min of moderate bicycle exercise, three graded and increasing 5-min submaximal exercise workloads (ranging from 25 to125 W)	nitric oxide (NO)	Physiological changes induced by moderate exercise did not have a dramatic effect on NO concentration.
21	Shah AP, AP Pietropaoli, LM Frasier, et al. [31]	2-h mouthpiece exposure to either filtered air or carbon UFP, with four 15-min exercise periods on a bicycle ergometer (target minute ventilation 20 L/min/m^2 body surface area).	HR × BP, Forearm blood flow, pre-exposure baseline in peak flow, NO	Inhalation of 50 μg/m^3 carbon UFP during intermittent exercise impairs peak forearm blood flow during reactive hyperemia in healthy human subjects.
22	Strak M, H Boogaard, K Meliefste, et al. [32]	cycled a low- and a high-traffic intensity route during morning rush hour in Utrecht, The Netherlands The low-traffic route (7.7 km) The high-traffic route (8 km)	FEV1, FVC, PEF, exhaled NO (FENO)	Exposure to ultrafine particles and soot during cycling was weakly associated with increased exhaled NO, indicative of airway inflammation, and decrements in pulmonary function 6 h after exposure.
23	Wauters A, F Esmaeilzadeh, S Bladt, et al. [27]	Exercise during exposure sessions. Two groups of exercise, 20 min/group, a 20 min rest between two exercise groups.	CD62P, CD63, CD42, PAC-1, Platelet function, complete blood counts	Diesel exhaust exposure induces platelet activation as illustrated by a dose-response increase in the release of CD62P and CD63.
24	Weichenthal S, M Hatzopoulou and MS Goldberg [33]	Exposed to traffic pollutants for 2 h on three separate occasions during cycling on high and low-traffic routes as well as indoors.	Micro-vascular function, Blood pressure, HRV	Exposure to traffic pollution may contribute to acute changes in blood pressure, autonomic and micro-vascular function in women.
25	Stieb DM, R Shutt, L Kauri, et al. [21]	30 min of prescribed outdoor activity, such as walking, at the same time and in the same location every day and to expend a similar level of effort each day.	Blood pressure, peak expiratory flow rate (PEFR), oximetry, heart rate variability (HRV), endothelial function, spirometry, fraction of exhaled nitric oxide (FeNO)	Significant associations between air pollution and subclinical adverse changes in cardio-respiratory physiological measures among older adults in a rural area characterized by moderate concentrations of regional pollutants—ozone and PM2.5—and low concentrations of traffic and industrial air pollutants.

Table 3
Results from meta-analysis and publication bias tests.

Health-related outcomes	Indicators	First author (year)	I^2 index	Pooled effect size (95% CI)	Model	Publication bias test	
						p-Value for Egger's test	p-Value for Begg's test
Cardiopulmonary function under O3 pollution	FVC (L)	Girardot (2006); Gomes (2010)	2.6%	0.004 (−0.044, 0.052)	Fixed-effect	NA	0.317
	FEV1 (L)	Girardot (2006); Gomes (2010)	68.0%	−0.077 (−0.254, 0.101)	Random-effect	NA	0.317
	PEF (L/s)	Girardot (2006); Gomes (2010)	0.0%	−0.238 (−0.389, −0.088)	Fixed-effect	NA	0.317
	FEF_{25-75}	Girardot (2006); Gomes (2010)	92.7%	−0.075 (−0.310, 0.160)	Random-effect	NA	0.317
Respiratory inflammation under PM pollution	eNO (ppb)	Bos (2013); Jacobs (2010)	97.4%	1.644 (−4.115, 7.402)	Random-effect	NA	0.317
	LEU (per μL)	Bos (2013); Jacobs (2010)	97.6%	419.075 (−273.246, 1111.396)	Random-effect	NA	0.317
	NEU (per μL)	Bos (2013); Jacobs (2010)	93.4%	354.939 (−88.703, 798.582)	Random-effect	NA	0.317

Note: LEU: Blood leukocyte counts; NEU: Blood neutrophil counts.

cardiopulmonary function and inflammation were inconsistent with others [23–28]; no effect size was reported pre-exercise or post-exercise [29–33]; and standardized effect size (i.e. mean difference with standard error) was unable to be captured due to limited information reported [28,34]. Heterogeneity of each study was assessed using the I^2 index. The level of heterogeneity represented by I^2 was interpreted as modest to moderate ($I^2 \leq 50\%$) and substantial to considerable ($I^2 > 50\%$). A fixed-effect model was evaluated when modest to moderate heterogeneity was present, and a random-effect model was evaluated when substantial to considerable heterogeneity was present. Publication bias was assessed by Begg's and Egger's tests and visual inspection of the funnel plot. All statistical analyses were conducted using the Stata 13 SE version (StataCorp, College Station, TX). All analyses used two-sided tests, and p-values less than 0.05 were considered statistically significant.

2.5. Study quality assessment

In this study, we used the National Institutes of Health's Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group to assess the quality of each included study [35]. This tool was only employed to measure strength of scientific evidence rather than determine the inclusion of studies. Each study was rated using this assessment tool based on 12 criteria. For each criterion, a score of one was assigned if the response was “yes”, otherwise a score of zero was assigned when the response was either “no”, “cannot determine”, “not applicable”, or “not reported”. A total score ranging from zero to 12 was calculated by summing up all criterion's scores. To rate the quality of evidence for each outcome assessed in the meta-analysis, we applied Grading of Recommendations, Assessment, Development and Evaluations (GRADE). A summary of findings table was developed by using GRADE Pro online software [36].

3. Results

Fig. 1 shows a flow chart of the search screening process. The search resulted in 1317 publications derived from PubMed, 192 studies from Cochrane, 233 studies from EMBASE, and 204 studies from Web of Science. 249 duplicate papers were excluded. In the title/abstract screening process, 1697 articles were excluded due to reasons such as review articles, case reports, epidemiological studies, animal study, no study outcome regarding exercise intervention, and indoor pollution exposure rather than outdoor pollution exposure. The remaining 70 articles were reviewed in full text against the eligibility criteria. 45 studies were excluded due to unavailable full-text (n = 5), published in non-English (n = 3), against other study selection criteria (n = 37). Finally, 25 studies were included in the review.

Among the 25 studies included in the review, thirteen studies adopted a before-after study design and the rest (n = 12) adopted a crossover study design (Table 1). The majority of studies (n = 23) recruited adults aged 18–55 years, one study [21] recruited individuals over 65 years old, and one study [30] recruited school children (7.5–11 years). Seventeen studies focused on healthy general population and eight studies focused on professional athletes. In addition, the eligible studies comprised four distinct exposure pollutants: ozone exposure [24,26,30,37–39], diesel exhaust (DE) exposure [16,17,27,29], traffic-related air pollution (TRAP) [22,28,33,34,40,41], and particulate matter (PM) [18–20,23,25,28,31,32,34,42].

Table 2 summarizes the intervention, measures of outcomes, and findings of the studies included in the review. Three of 25 studies [21,38,42] adopted a long-term (10–12 WK) exercise intervention, and the rest focused on the effect of short-term exercise on health. The majority of studies (n = 12) adopted an exercise intervention with a bout aerobic exercise, duration of exercise 20 min to 3 h, types of exercise such as cycling, hiking, and running. Seven studies adopted one or two moderate intensity intermittent exercises [27–31,34,41], and

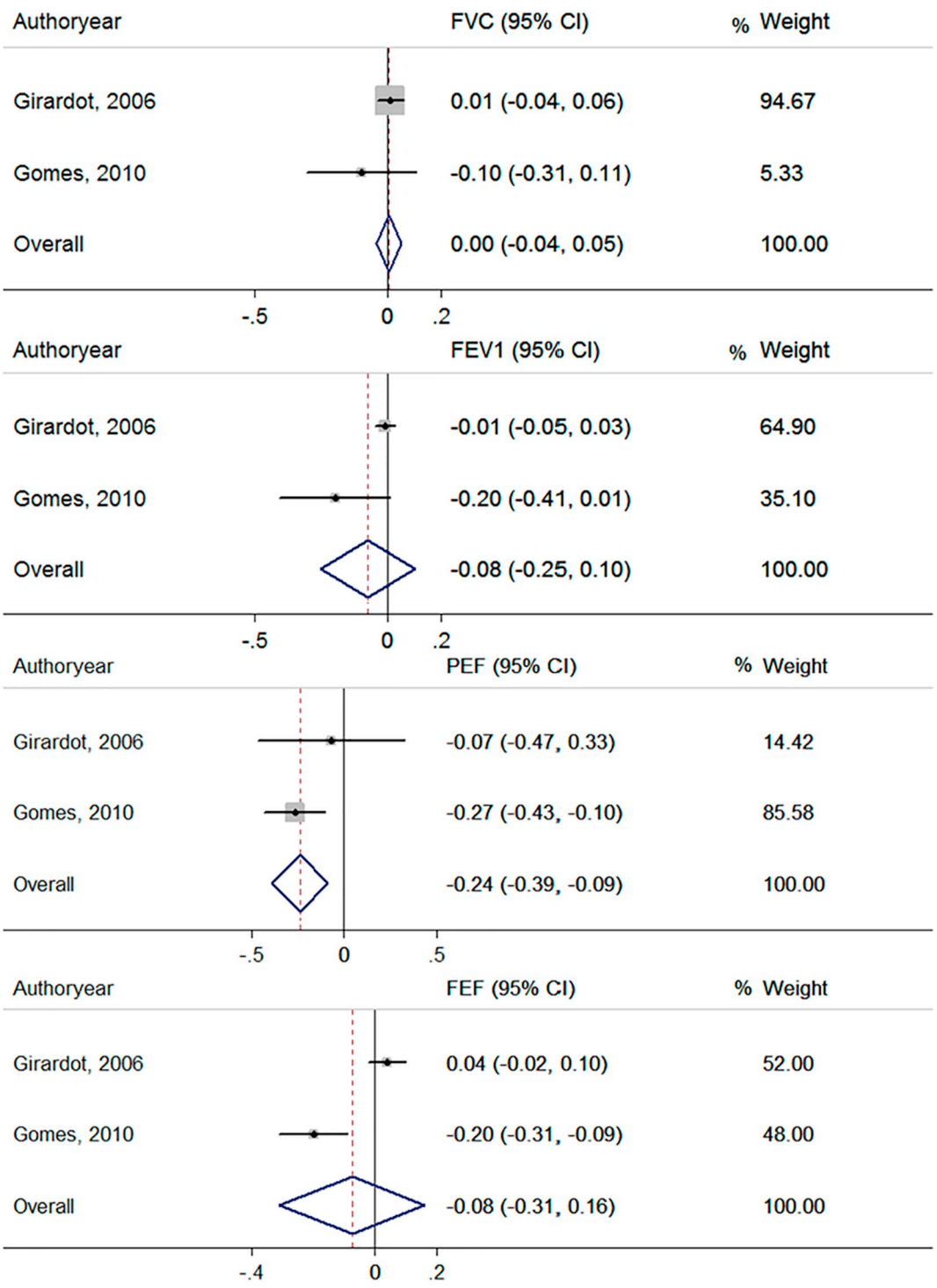

Fig. 2. Forest plots for cardiopulmonary function.

three studies adopted a 6 min maximal work accumulation exercise test [18,19,23].

Most studies reported outcome variables including pulmonary function, cardiovascular function, and immunologic function. Twelve studies reported the effects of exercise and pollutants on pulmonary function [16–18,20,22,28,30,32,34,37–39], in which FEV1, FVC, FEV1/FEC, and $FEF_{25–75\%}$ were mainly selected outcomes. Blood pressure, endothelial function, and micro-vascular function were used to assess the effects of exercise and pollutants on cardiovascular function in seven studies [21,23,25,29,31,33,41]. To estimate the changes of immune function influenced by air pollution and exercise, eleven studies [20,21,24,26–29,31,32,40,42] mainly focused on blood counts, cytokines (IL-6, IL-8, IL-10, and TNF-α), and inflammation-relate protein (CRP, FeNO, CC16, CD62P, CD63, and CD40). In addition, four studies assessed athletic performance [17,19,23,42].

Table 2 also presents the mainly findings of these studies, in which merely three studies reported physical activity could delay the negative impact of pollutant on health [28,34,41]. Kubesch and Matt reported a positive effect of performing an intermittent moderate physical activity in a highly traffic-related polluted environment on healthy participants' pulmonary functions [28,34]. Moreover, Kubesch et al. [41] discovered intermittent physical activity attenuates the TRAP-related increases in

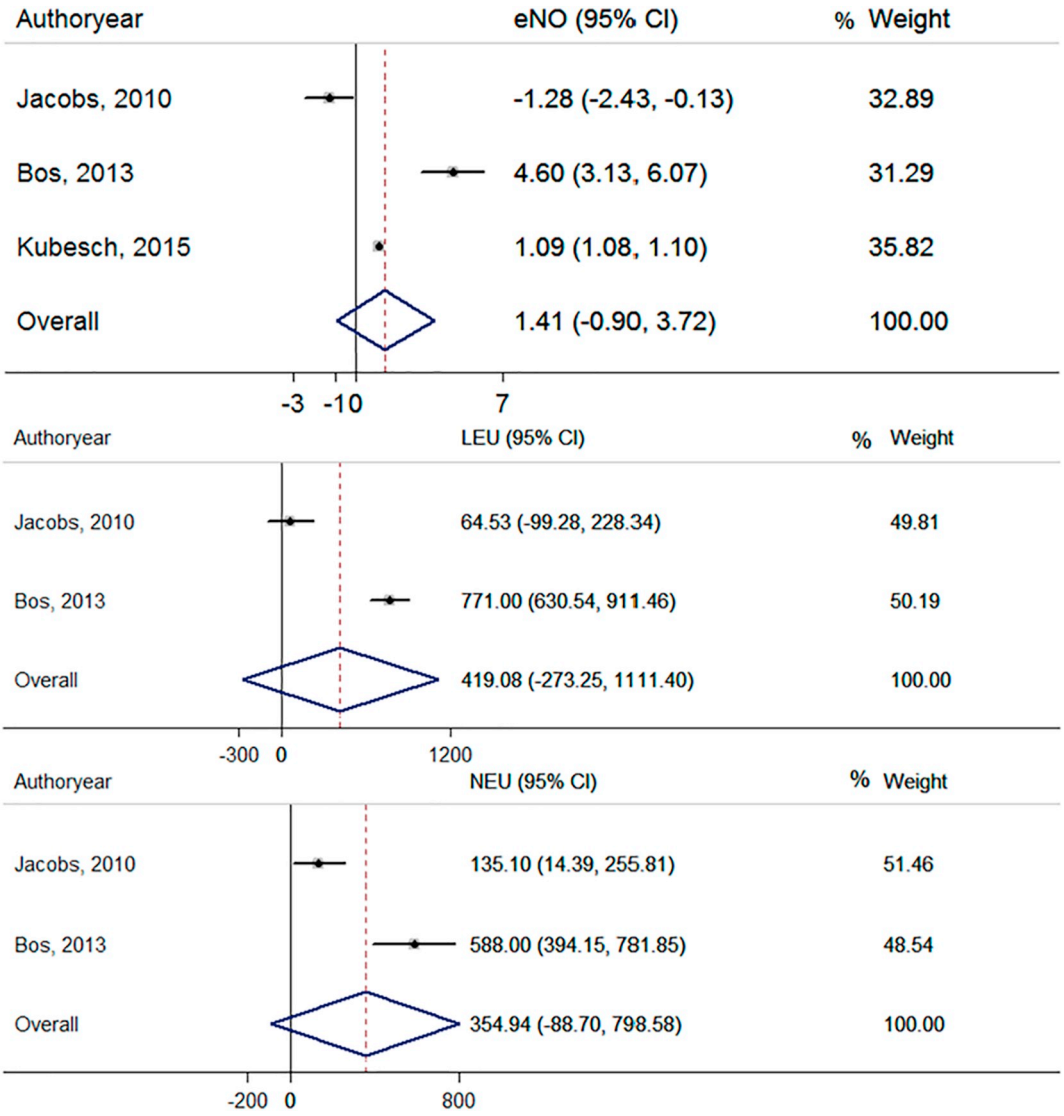

Fig. 3. Forest plots for respiratory inflammation.

systolic blood pressure (SBP), and exercising in low-TRAP environments has stronger beneficial effects on SBP than in high-TRAP environments. In addition, only five studies indicated no dramatic effect of exercise on health function in polluted atmospheric environment [17,22,26,38,39].

The remaining seventeen studies revealed that regular exercises in environment with high concentration of air pollutant could impair health function (Table 2). Seven studies reported exposure to air pollutant (ozone, PM, or diesel exhaust exposure) during exercise was associated with an increased risk of airway inflammation, and decrements in pulmonary function [16,18,20,21,30,32,37]. Six studies discovered that exposure of traffic pollution or high PM during exercise may contribute to changes in blood pressure, systemic conduit artery function and micro-vascular function [21,23,25,29,31,33]. Several studies also found the up-regulated of inflammatory factor (IL-6, IL-8, TNF-a, ICAM-1) and immunomodulatory protein (CC16, CD62P, CD63, CD40) after exercise with air pollutant exposure, which related to inflammation and metabolic syndrome [24,27,29,40]. In addition, three studies showed exercise performance declined in HPM conditions [19,30,42].

Table 3 summarizes modeling results from the meta-analysis. Regarding cardiopulmonary function indicators, only PEF (effect size [ES] = −0.238, 95% confidence interval [CI] = −0.389, −0.088) was found to be significantly decreased after exercise intervention in a polluted environment, whereas none of FVC (ES = 0.004, 95% CI = −0.044, 0.052), FEV1 (ES = −0.077, 95% CI = −0.254, 0.101), $FEF_{25–75\%}$ (ES = −0.075, 95% CI = −0.310, 0.160) were found any significant changes after exercise intervention in a polluted environment. Similarly, all indicators of inflammation were not found significantly variations before and after exercise intervention (Figs. 2 and 3). No publication bias was identified as neither of the Egger's tests and Begg's tests was statistically significant (Fig. 4). However, visual inspection of the funnel plots indicates the possibility of publication bias regarding the pooled effect estimates of $FEF_{25–75\%}$, eNO, LEU, and NEU in response to an exercise intervention in a polluted environment.

Table 4 shows the criterion-specific and overall rating about the study quality assessment. The included studies on average scored 8.5 out of 12, with a range from 7 to 10. The 25 studies all clearly stated the study question/objective and study population, included representative participants who would be eligible for the intervention, consistently delivered the intervention, and conducted statistical tests to provide p values for the pre-to-post changes. Most studies (n = 25) included eligible participants meeting the prespecified entry criteria, clearly defined and consistently assessed outcome measures, and had follow-up loss rate less than 20%. Eight studies assessed outcome measures repeatedly before and after intervention. Seven studies had blinded

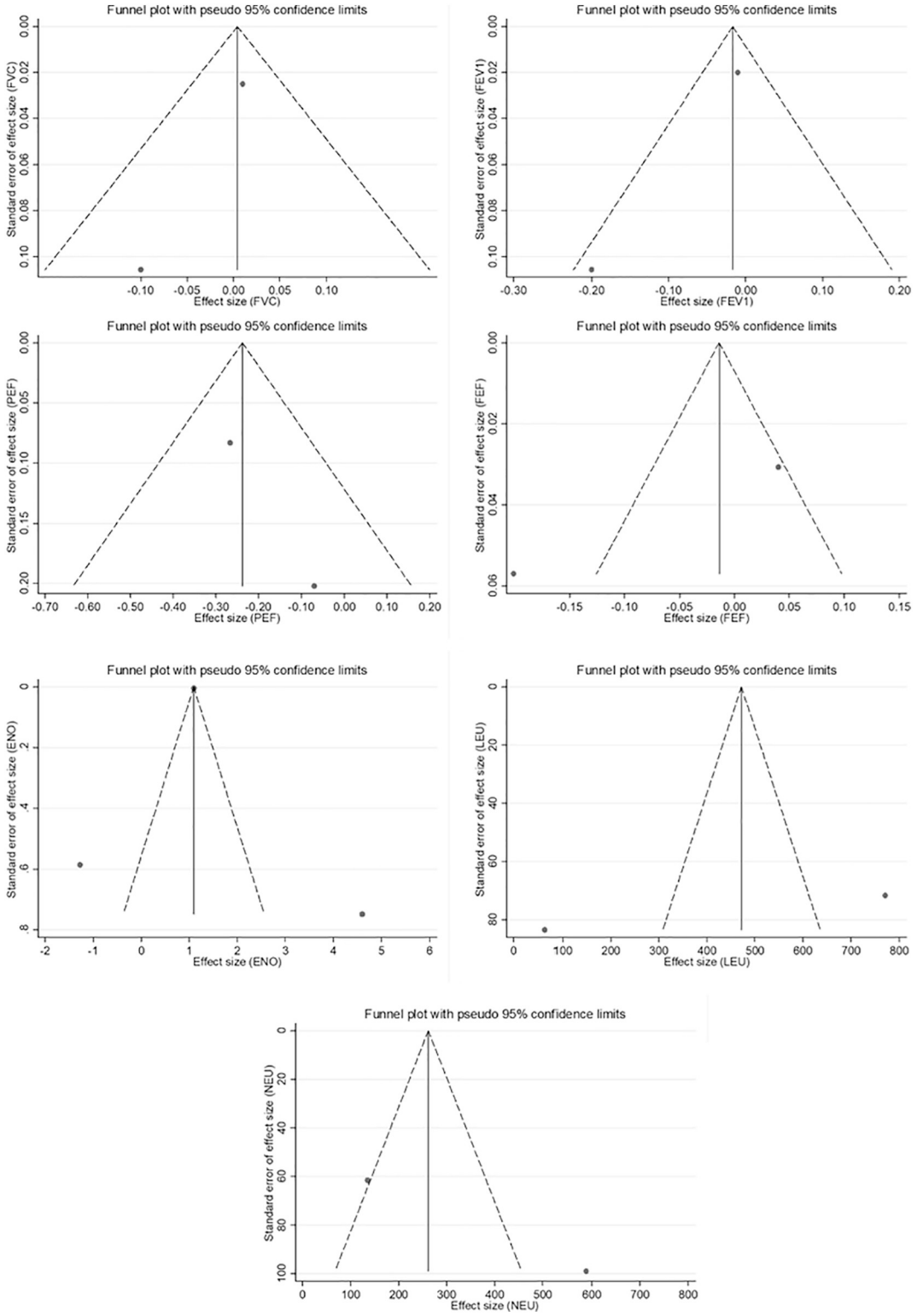

Fig. 4. Funnel plots for publication bias.

assessment to the participants' exposure/interventions. Only one study provided statistical power on sample size estimation. None of studies conducted intervention across different groups.

Table 5 reports the quality of evidence for all seven health outcomes assessed in the meta-analysis. The FVC and PEF outcomes were found "low" quality of evidence due to the lack of control group study design and the included studies adopted either before-after or crossover study design which was regarded as an observational study design in GRADE. Other health outcomes, such as FEV1, $FEF_{25–75\%}$, eNO, LEU, and NEU, were observed "very low" quality of evidence due to downgrades owing to the large heterogeneity and strongly suspected publication bias.

4. Discussion

This study reviewed and synthesized scientific evidence regarding the combination effect of physical activity and air pollutants exposure

Table 4
Quality assessment table.

Criteria	Study ID																									
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1. Was the study question or objective clearly stated?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2. Were the study population prespecified and clearly described?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3. Were the participants in the study representative of those who would be eligible for the intervention in the general or clinical population of interest?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4. Were all eligible participants that met the prespecified entry criteria enrolled?	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5. Was the sample size sufficiently large to provide confidence in the findings?	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Was the intervention clearly described and delivered consistently across the study population?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0	0	0	1	0	1	0	0
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10. Were statistical tests done that provided p values for the pre-to-post changes?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention?	0	0	0	0	0	1	0	0	0	0	0	0	1	1	1	1	0	0	0	1	1	1	0	0	0
12. If the intervention was conducted at a group level did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sum score	8	9	7	8	8	10	9	9	8	8	8	8	9	9	9	10	8	8	7	9	10	9	9	8	8

Table 5
GRADE summary of findings table showing the quality of evidence of an effect of pollution and exercise on health outcomes.

Outcomes	Effects (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
FVC	The mean of FVC after exercise in a pullulated environment was 0.004 L higher (0.044 lower to 0.052 higher)	364 (2 studies)	⨁⨁◯◯ LOW	Data from before-after study and crossover studies begin with GRADE of low.
FEV1	The mean of FEV1 after exercise in a pullulated environment was −0.077 L higher (−0.254 lower to 0.101 higher)	364 (2 studies)	⨁◯◯◯ VERY LOW	Data from before-after study and crossover studies begin with GRADE of low; downgraded owing to the large heterogeneity.
PEF	The mean of PEF after exercise in a pullulated environment was −0.238 L/s higher (−0.389 lower to −0.088 higher)	364 (2 studies)	⨁⨁◯◯ LOW	Data from before-after study and crossover studies begin with GRADE of low.
$FEF_{25–75\%}$	The mean of $FEF_{25–75\%}$ after exercise in a pullulated environment was −0.075 higher (−0.310, lower to 0.160 higher)	62 (2 studies)	⨁◯◯◯ VERY LOW	Data from before-after study and crossover studies begin with GRADE of low; downgraded owing to the large heterogeneity and strongly suspected publication bias.
eNO	The mean of eNO after exercise in a pullulated environment was 1.644 ppb higher (−4.115, lower to 7.402 higher)	62 (2 studies)	⨁◯◯◯ VERY LOW	Data from before-after study and crossover studies begin with GRADE of low; downgraded owing to the large heterogeneity and strongly suspected publication bias.
LEU	The mean of LEU after exercise in a pullulated environment was 419.075 per μL higher (−273.246, lower to 1111.396 higher)	62 (2 studies)	⨁◯◯◯ VERY LOW	Data from before-after study and crossover studies begin with GRADE of low; downgraded owing to the large heterogeneity and strongly suspected publication bias.
NEU	The mean of NEU after exercise in a pullulated environment was 354.939 per μL higher (−88.703, lower to 798.582 higher)	62 (2 studies)	⨁◯◯◯ VERY LOW	Data from before-after study and crossover studies begin with GRADE of low; downgraded owing to the large heterogeneity and strongly suspected publication bias.

on people's health. Our primary research question was focused on the effect of all kinds of exercise on health, suffering from air pollution. Even though 25 studies were selected in this study, due to the difference in the types of air pollution exposure, types of exercise intervention, and health indicators in different studies, only 4 studies with 426 subjects were used in the meta-analysis to quantify the effect of the combined exercise and air pollution exposure on people's health. Meta-analysis found that physical activity in an ozone pollution environment can induce a positive effect on people's pulmonary function, especially for the PEF indicator. Other indicators of cardiopulmonary function and inflammation were not found significantly changes before and after exercise intervention under particulate matter exposure.

Nearly two thirds included studies show the combination of exercise and air pollutant could impair health function and athletic performance. For example, some literatures [18,19,23] reported that PM exposure would decline exercise performance and increase the incidence of cardiopulmonary impairment in exercising body. Among these studies, the peak concentration of ultrafine PM (115,000 to 134,000 particles·cm^{-3}) was as high as the levels of a busy street in Hong Kong (540,000 particles·cm^{-3}) [43] and a busy freeway in Los Angeles (800,000 particles·cm^{-3}) [44]. Therefore, it indicates that the air quality should be monitored before attending outdoor exercises, and avoiding high-pollution areas in rush hours is necessary to minimize the exposure to air pollution and limit the effects of air pollution. Additionally, some other changes of health indicators should deserve public attentions. A few of studies indicated that PM2.5 inhalation led to a synergetic release of CD62P (P-selectin) and CD63, and exercise could not reverse or weaken this impact [27,29]. P-selectin and CD63 could activate platelets and increase the risk of thrombotic, especially in patients with coronary heart disease, diabetes and atrial fibrillation [45,46].

Peak expiratory flow (PEF), as an important indicator for pulmonary function, represents the strength of respiratory muscle and the degree of airway obstruction. According to the results of previous studies, PEF appeared a significant improvement after aerobic exercise when participants (Untrained healthy subjects and/or athletes) were exposing O_3 during exercise [38,39]. In addition, two studies reported a positive effect of performing an intermittent moderate physical activity in a highly traffic-related polluted environment on healthy participants' pulmonary functions [34,41]. As for its mechanism, these articles explained that bronchodilatory effects induced by exercise were most likely due to an activation of β2-receptors by endogenous catecholamines [47]. Meanwhile, Kubesch discovered intermittent physical activity attenuates the TRAP-related increases in systolic blood pressure (SBP), and exercising in low-TRAP environments has stronger beneficial effects on SBP than in high-TRAP environments [28]. In addition, previous animal studies suggested that long-term moderate aerobic exercise training could offset the impact of air pollution and cigarette smoke on health [48], which may be involved the anti-inflammatory effects of aerobic exercise mediated antioxidant defense system [49–51]. A few literatures have suggested that air pollution can promote the production of free radicals and induce inflammation, while several research reported that exercise substantially inhibited the increase in reactive oxy gen species (ROS) in bronchoalveolar lavage fluid [13], gastrocnemius [52], and colon [53] exposed to air pollution, which indicate that the anti-inflammatory effect of exercise may be related to the scavenging of free radical.

In terms of the literatures have been retrieved, this review is the first study to devote to elucidating the synergistic effect of exercise and air pollution on health. However, several limitations pertaining to this review should be noted. Only a small number of studies examined the influence of air pollution exposure and outdoor exercise on health. Given the small number of studies, a dose-response meta-regression was indeterminate due to the lack of statistical power. Since only a few studies reported the change of pulmonary function, cardiovascular function, and immune function and exercise performance before and after exercise, pool effect estimates based on meta-analysis could not be obtained. Meanwhile, since the small number of studies included in the meta-analysis, publication bias tests were likely to be underpowered. All included studies were either before-after study design or crossover study design that involved no controlled experiment for exercise intervention, which were subjected to confounding bias. The heterogeneity pertaining to the exercise interventions and the study participants may have impacted the results. In addition, only few studies were included in the meta-analysis, which prevent us from conducting subgroup meta-analysis to assess the potential difference in the impact of alternative exercise interventions.

Overall, it is implying that pollutant concentration, pollutant species, and exposure duration, may impact the effect of exercise on health. Therefore, the single or fixed components of air pollutants exposure are necessary to assess their effect on health. Fixed components and concentrations of air pollutants exposure design will supply to more similar research in order to increase the number of included studies. Furthermore, serious health hazard related to exercising with air pollution exposure depends on exercise intensity, exercise duration, and exercise mode. A large number of studies were excluded due to lack of explicit exercise program, thus future studies should attach importance of the explicit exercise design of exercise types, intensity, duration, mode, and other complicated factors.

5. Conclusion

This study systematically reviewed and synthesized scientific evidence for the influence of air pollution and exercise on health. Exercise in a polluted air environment was found to be related with improved PEF but not other health indicators in the meta-analysis. The combination effect of air pollution and exercise was found to be associated with the increased risk of potential health problems of cardiopulmonary function, immune function, and exercise performance. However, the overall scientific evidence remains insufficient due to limited literatures, no randomized controlled trial for exercise intervention, and lack of population representativeness. Future studies should examine different exercise programs (exercise intensity, exercise duration, and exercise mode), different air pollution exposures (component and dose), and their combination effect on health.

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Conflict of interests

No conflict of interest, financial or otherwise, are declared by the authors.

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