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Traffic-related air pollution and lung cancer: A meta-analysis

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Abstract

Background: We conducted a meta-analysis to evaluate the association between traffic-related air pollution and lung cancer in order to provide evidence for control of traffic-related air pollution.

Methods: Several databases were searched for relevant studies up to December 2013. The quality of articles obtained was evaluated by the Strengthening the Reporting of Observational Studies in Epidemiology checklist. Statistical analysis, including pooling effective sizes and confidential intervals, was performed.

Results: A total of 1106 records were obtained through the database and 36 studies were included in our analysis. Among the studies included, 14 evaluated the association between ambient exposure to traffic-related air pollution and lung cancer and 22 studies involved occupational exposure to air pollution among professional drivers. Twenty-two studies were marked A level regarding quality, 13 were B level, and one was C level. Exposure to nitrogen dioxide (meta-odds ratio [OR]: 1.06, 95% confidence interval [CI]: 0.99–1.13), nitrogen oxide (meta-OR: 1.04, 95% CI: 1.01–1.07), sulfur dioxide (meta-OR: 1.03, 95% CI: 1.02–1.05), and fine particulate matter (meta-OR: 1.11, 95% CI: 1.00–1.22) were positively associated with a risk of lung cancer. Occupational exposure to air pollution among professional drivers significantly increased the incidence (meta-OR: 1.27, 95% CI: 1.19–1.36) and mortality of lung cancer (meta-OR: 1.14, 95% CI: 1.04–1.26).

Conclusion: Exposure to traffic-related air pollution significantly increased the risk of lung cancer.

Introduction

It is estimated that there were 1.825 million lung cancer cases globally in 2012, accounting for 13.0% of all cancer cases, and 1.59 million deaths from lung cancer, responsible for 19.4% of deaths from all cancers.[1] Air pollution is currently the principal issue in the field of environmental health, among which outdoor air pollution causes 1.3 million deaths in urban areas worldwide and indoor air pollution is responsible for two million premature deaths in developing countries.[2] Vehicle emissions are a major source of outdoor air pollution, producing gaseous and particulate pollutants including carbon monoxide, ozone, particulate matter, nitrogen dioxide aldehydes, benzene, 1,3 – butadiene, polycyclic aromatic hydrocarbons, and metals.[3] Pollution from vehicles causes a broad range of acute and chronic diseases, including lung cancer. It was estimated that 11 395 deaths and 232 646 disability adjusted life years (DALYs) were attributed to motorized road transport globally in 2010.[4] In Western countries, the histological distribution of lung cancer has changed during the past decades, showing an increase in adenocarcinomas and a decrease in squamous-cell carcinomas; this transition is associated with tobacco blends[5] and ambient air pollution.[6,7] People inhale 10 000 liters of air per day and even though the concentration of harmful substances in the air seems trivial, the amount breathed in per day cannot be ignored. Too few data are available to draw meaningful inferences of non-occupational exposure to traffic-related air pollution and lung cancer. Most studies respecting traffic-related air pollution in occupational settings also have failed to adequately account for confounding in their analyses, despite the availability in many cases of a large amount of data on potential

confounders and effect modifiers.[8] Additionally, varied methods and measurements are employed in studies. Therefore, the objective of this meta-analysis is to clarify the potential association between pollutants of traffic-related air pollution with lung cancer, and also the risk of lung cancer among professional drivers occupationally exposed to vehicle emissions.

Materials and methods

Data sources and searches

We searched PubMed, Embase, and the Cochrane library for studies published in English, as well as the China National Knowledge Infrastructure, Wanfang, and SINOMED databases for studies published in Chinese, up to December 2013, evaluating the association between traffic-related air pollution and lung cancer incidence and mortality. Literature research was performed using keywords including: "traffic related;" "motor vehicles;" "lung cancer;" "air pollution;" "carbon monoxide;" "oxides;" "particulate matter;" "ozone;" "sulfur dioxide;" "relative risks;" "incidence;" "mortality;" and corresponding keywords in Chinese. Specific search strategies are presented in detail in Appendix S1. We also screened the reference lists and included additional relevant studies.

Study selection

Inclusion criteria

Observational epidemiological studies (case-control, cohort, nested case-control studies) were included in our analysis. Effect sizes with corresponding 95% confidence intervals (CIs) indicating association between traffic-related air pollution and lung cancer (odds ratio [OR], hazard ratio [HR], relative risk [RR], standardized mortality ratio [SMR], standardized incidence ratio [SIR]) are reported, as well as methods used to adjust confounders. Except for studies on occupational exposure to air pollution, the method and period of measurement of each pollutant was required. Traffic-related air pollutants included carbon monoxide (CO), nitrogen monoxide (NO), nitrogen dioxide (NO_2), nitrogen oxides (NO_X), sulfur dioxide (SO_2), ozone (O_3), particulate matter with an aerodynamic diameter of less than 10 μm (PM_{10}), and particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$). In terms of studies on occupational exposure to air pollution, the specific occupation and location of exposure was required. The criteria for selection of lung cancer cases was also required, and the number of lung cancer cases had to be larger than 30.

Exclusion criteria

Studies with poor quality (ranked C) and/or insufficient data, and duplicate publications were excluded from our analysis.

We included only one article for each study considering the time published, calculation methods, and participants. With respect to studies of ambient exposure reporting effective amounts of air pollution with both lung cancer incidence and mortality, we only included effective numbers of lung cancer incidence once pooled. If a study reported effective numbers of different categories of professional drivers with lung cancer, we included all of these.

Data extraction and analysis

Two of the authors extracted data independently from each article based on study design, age, sampling of participants, measurement of pollutants, source of lung cancer cases, effect sizes, and corresponding confidential intervals, with covariates adjusted. Discrepancies were resolved through discussion and consultation with a third author where necessary. We performed meta-analysis to obtain the weighted average of effect measures using RevMan V.5.2 (The Cochrane Collaboration, Oxford, UK). A Cochran Q statistic test was employed to evaluate heterogeneity between study results. Statistic significance was defined as <0.10. The percentage of variation as a result of heterogeneity was tested with I^2 statistics. Effect sizes weighted by inverse variances were pooled with a fixed effect model when there was less than 50% variation because of heterogeneity and $P > 0.10$, otherwise a random effect model was employed.

Quality assessment of studies

The quality of reporting was evaluated using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist for cohort, case-control, and cross-sectional studies, version 4.[9] Two authors evaluated each article independently and counted the number of STROBE criteria fulfilled. Considering that STROBE criteria are normally used to evaluate the quality of observational epidemiological studies, with respect to studies of pooled analysis and re-analysis when extracting data from other studies, STROBE criteria were adjusted. Specifically, item No.10, item No.14, and item No. 12c-No. 13c were not used while evaluating the quality of studies related to arrival of study size, dealing with missing data, and characteristics of participants, which were reported in previous articles. The studies were classified as having: A, more than 80% of STROBE criteria fulfilled; B, 60–80% of STROBE criteria fulfilled; or C, less than 60% of STROBE criteria fulfilled.[10]

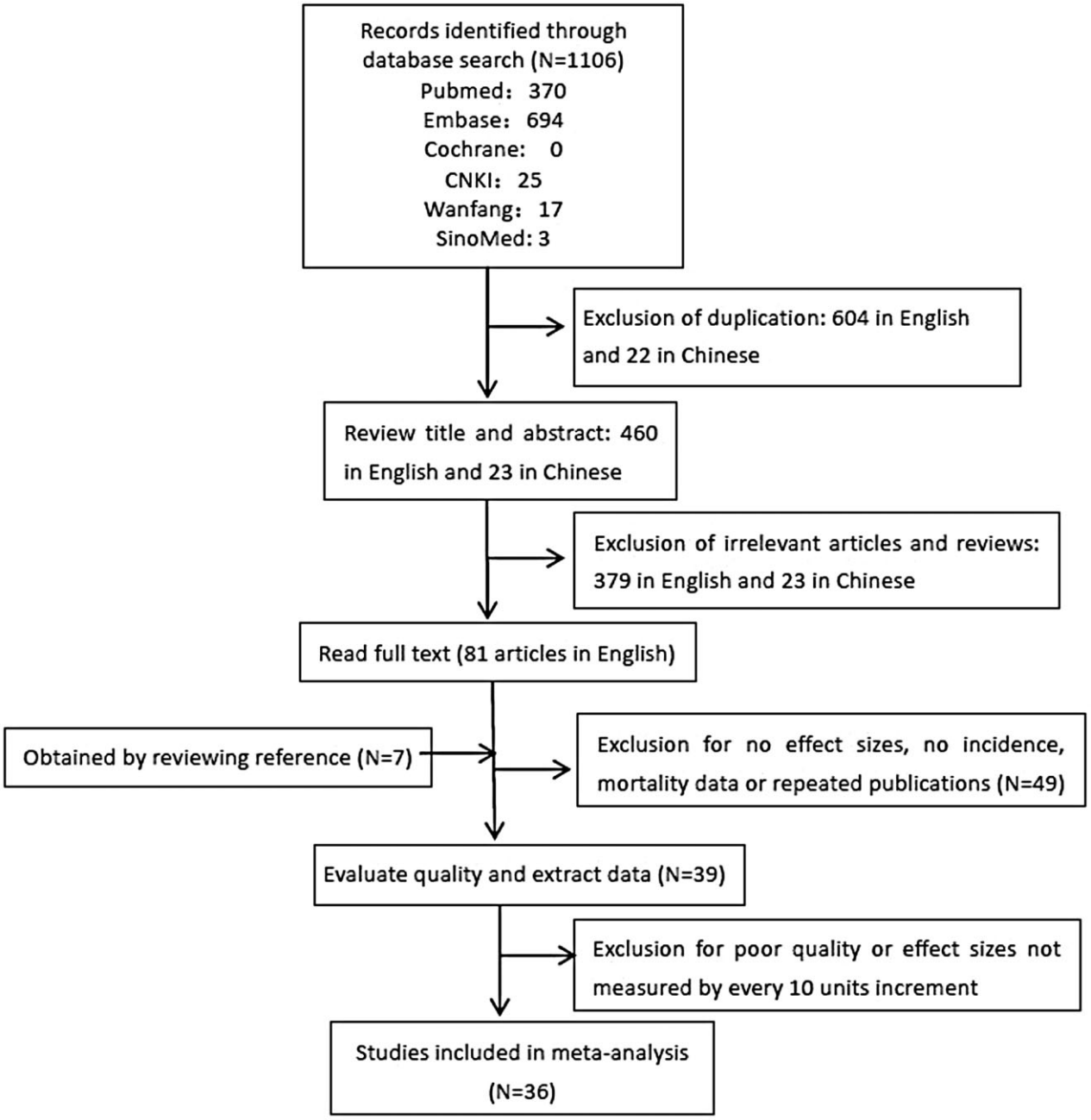

Figure 1 Flow diagram of study selection.

Results

A total of 1106 articles were identified, including 370 from Pubmed, 694 from Embase, and 45 from Chinese databases, with no Cochrane library articles (Fig 1). After reading full texts, 39 studies were left; however, the effect sizes of two articles were not measured by every 10 unit increments,[11,12] and one article ranked "C" in terms of the quality of the study.[13] Therefore, 36 studies were finally included in our pooled analysis, among which 14 evaluated the association of ambient exposure to traffic-related air pollution,[14–27] and 22 reported professional drivers' risk of lung cancer.[28–49] Two articles included data from the European Prospective Investigation into Cancer and Nutrition;[15,21] to avoid duplication we included data of SO_2 exposure from one[21] and NO_2 exposure from the other.[15]

Table 1 Characteristics and evaluation of quality of 14 studies on ambient exposure to traffic-related air pollution

Study ID (Reporting quality)	Location and study design	Age (years)	Total participants	Lung cancer cases	Exposure† (μg/m^3)	Exposure assessment	Outcome	Outcome assessment	Covariates adjusted for
Yorifuji et al. 2013[14] (A)	Shizuoka, Japan, Cohort	65–84	14001	116	NO2: 35.11	LUR modeling	Lung cancer and hemorrhagic stroke	Obtained from the database of the Ministry of Health,Labor and Welfare of Japan	Age, sex, smoking, BMI, hypertension, diabetes, financial capability and area mean taxable income
Raaschou-Nielsen et al. 2013[15] (A)††	European, 17 cohorts	42.8–73.1 (mean age)	2380–108018	18–678	PM10: 13.5–48.1, PMcoarse:4.0–20.8PM2.5: 6.6–31.0, PM2·5absorbance: 0.5-3.2 NO2: 5.2–59.8 NOX: 8.7–107.3	LUR model	Lung cancer	Histology	Age, sex, calendar time, smoking related variables, occupation, fruit intake, marital status, educational level, employment status and area-level socioeconomic status
Jerrett et al. 2013[16] (B)	California, U.S. Cohort	≥30	73711	1481	PM2.5: 14.09 NO2: 12.27‡ O3: 50.35‡	Monthly average monitoring data and LUR models	All cause of death including lung cancer	Ascertained by volunteers and using the National Death Index	Lifestyle, dietary, demographic, occupational and educational factors
Hystad et al. 2013[17] (A)	8 provinces, Canada, Case-control	63.5 and 59.0(mean age for cases and controls)	5897	2390	PM2.5: 11.9 NO2: 15.4‡ O3: 20.3	Fixed site monitoring data and proximity measures	Lung cancer	Histology	Age, sex, educational attainment, smoking related variables, alcohol and meat consumption, occupational exposure and geographic covariates.
Cesaroni et al. 2013[18] (B)	Roma, Italy, Cohort	≥30	1265058	12208	NO2: 44 PM2.5: 23	LUR modeling and PM2.5 dispersion model	All cause of death including lung cancer	Obtained from Lazio regional health information system	Sex, marital status, place of birth, education, occupation, and area-based socioeconomic position
Cao et al. 2010[19] (B)	17 provinces, China, Cohort	55.8 (mean age)	70947	624	TSP: 289 SO2: 73 NOX: 50	Fixed-site monitoring data	All cause of death including lung cancer	Hospital records and death certificates	Age, sex, BMI, physical activity, education, smoking status, age at starting to smoke, cigarettes per day, alcohol intake, and hypertension
Beelen et al. 2008[20] (A)	Netherlands, Case-Cohort	55–69	120852	2183	BS: 11.6, NO2: 36.9 SO2: 13.7 PM2.5: 28.2	Regulatory monitoring data and LUR models	Lung cancer	Histopathology and cytopathology	Full cohort: age, sex, smoking status and area level indicators of socioeconomics
Vineis et al. 2006[21] (A)	9 countries, Europe, Nested case-control	60.4 and 60.0 (mean ages for cases and controls)	1008	271	NO2: 12.0–64.7§ PM10: 19.9–73.4§ SO2: 1.1–30.6§	Home addresses and data from monitoring stations	Lung cancer	Histological conformation	Age, sex, country, smoking status, time since recruitment, education, BMI, physical activity, cotinine, occupational index and intake of fruit, vegetables, meat, and alcohol)
Laden et al. 2006[22] (B)	6 cities, U.S. Cohort	25–74	8096	226	PM2.5: nearly 10–40§	Fixed air-monitoring station	All cause of death including lung cancer	Data obtained from National Death Index	Current or former smoking, number of pack-years of smoking for former and current smokers separately, education, and body mass index
Jerrett et al. 2005[23] (A)††	Los Angeles, U.S. Cohort	NA	22905	434	PM2.5: 9.0–27.1§	Data from state and local district monitoring stations	All cause of death including lung cancer	NA	Age, sex, age, O3(average of 4 highest 8 h maxima) and 44 other covariates including lifestyle, dietary, demographic, occupational and educational factors
Filleul et al. 2005[24] (A)	7 towns, France, Cohort	25–29	14284	178	SO2: 17–85 TSP: NA BS: 18–152 NO2: 12–61 NO: NA	Data from centrally located pollution monitoring station	All cause of death including lung cancer	Data from specialized department of the National Institute of Health and Medical Research (INSERM)	Age, smoking habits, body mass index, educational level, occupational exposure, and stratified by sex
Nafstad et al. 2003[25] (A)	Oslo, Norway, Cohort	40–49	16209	422	NOX: 10.7¶ SO2: 9.4¶	Model calculations using data for observed concentrations and emission from point sources	Lung cancer	Obtained from Norwegian cancer register	Age, smoking habits, physical activity, occupation, height and weight
Pope et al. 2002[26] (A)	50 states. U.S. Cohort	≥30	Approximately 500000	NA	PM2.5: 17.7	Inhalable particle monitoring network and National Aerometric Database	All cause of death including lung cancer	Death certificates	Age, sex, race, smoking, education, marital status, body mass, alcohol consumption, occupational exposure and the diet
Nyberg et al. 2000[27] (A)	Stockholm, Sweden, Case-control	40–75	3406	1042	NO2: 19.85¶ SO2: 52.75¶	Source-specific emission data and dispersion modeling	Lung cancer	Histology and cytology	Age, selection year, smoking, radon, socioeconomic grouping, occupational exposure to diesel exhaust, other combustion products and asbestos, and employment in risk occupation.

†Mean concentration of exposure. ‡Exposure concentration is measured by ppb. §Range of exposure concentration. ¶Median concentration of exposure. ††Studies evaluated with modified STROBE items. BS, black smoke; LUR, land-use regression; TSP, total suspended particles.

Table 2 Characteristics and evaluation of quality of 22 studies on occupational exposure to traffic-related air pollution

Study	Location and study design	Age (years)	Total participants	Lung cancer cases of drivers	Type of drivers	Duration of employment	Covariance	outcome assessment
Petersen et al. 2010[28] (A)	3 cities, Denmark cohort	22–67	2037	100	Bus drivers	0–44 years	Age, calendar time, city of employment, bus route and smoking habits	Data obtained from the Danish Cancer Registry
Merlo et al. 2010[29] (A)	Genoa, Italy cohort	NA	9267	235	Bus drivers	>6 months	length of employment, time since first employment and job title	death certificates
Consonni et al. 2010[30] (A)	Lombardy, Italy case-control	35–79	4220	149	Bus and truck drivers	>6 months	Residence, age, smoking, number of jobs held, and education	Pathology, cytology and clinical records
Birdsey et al. 2010[31] (B)	U.S. cohort	25–74	156241	557	truck drivers	6 years	age, racial group, sex and calendar period	Obtained from Social security Administration and the National Death Index
Garshick et al. 2008[32] (B)	U.S. cohort	>40	31135	323	Long-haul drivers	nearly 15 years	age, calendar, decade of hire, race, region, company and smoking	Obtained from National Death Index
Richiardi et al. 2006[33] (A)	Turin, Italy case-control	<76	1440	70	Professional drivers and transport conductors	>20 years	Age, cigarette consumption, exposure to occupations, education	Radiology, histology and cytology
Jarvholm and Silverman 2003[34] (B)	Sweden cohort	33–40 (mean)	140712	61 incident cases and 57 deaths	Truck drivers	not clear	Age, time period and smoking	Obtained from National Cancer registry and National death Registry
Soll-Johanning et al. 2003[35] (A)	Copenhagen, Denmark nested case-control	20–68	843	153	Bus drivers or tramway employees	13 years	Smoking	Obtained from Danish Cancer Registry
Elci et al. 2003[36] (B)	Turkey case-control	NA	2873	88	Unspecified	NA	age and smoking	Histology
Bruske-Hohlfeld et al. 1999[37] (A)†	Germany pooled case-control	60.5 for cases and 60.4 for controls	7039	3498	Professional drivers	nearly 16.0 for cases and 14.2 for controls	Smoking and asbestos exposure	Histology and cytology
Pezzotto and Poletto 1999[38] (A)	Rosario, Argentina case-control	60.1 and 60.1 for cases and controls	943	367	Unspecified	>33 years	age, smoking habit and lifelong cigarette consumption	histology and pathology
Hansen *et al*. 1998[39] (A)	Denmark case-control	18–66	28744	2251	Lorry, bus, taxi and unspecified drivers		NA	Obtained from Danish Cancer Registry
Muscat et al. 1998[40] (B)	U.S. case-control	58.9 for male cases and 58.6 for female cases	936	550	Unspecified	NA	Age, education, cumulative smoking	Histology
Jakobsson *et al*. 1997[41] (B)	4 counties, Sweden cohort	20–64	96438	604	Taxi drivers, long distance lorry drivers and short distance lorry drivers	>13 years	smoking	Obtained from National Swedish Cancer registry
Borgia et al. 1994[42] (B)	Rome, Italy cohort	40 (median)	2311	76	Taxi drivers	>13 years	NA	Obtained from Registry Office
Alfredsson et al. 1993[43] (B)	4 counties, Sweden cohort	20–64	9446	334	Bus drivers	>15 years	age, county	Obtained from National Cause of Death Registry
Burns and Swanson 1991[44] (B)	Detroit, U.S. case-referent	>40	9891	238	Unspecified	NA	diagnosis, race and smoking	Obtained from MDCSS system
Steenland *et al*. 1990[45] (A)	U.S. case-control	NA	2081	730	Long haul drivers and short haul drivers	23.4 for long haul drivers and 24.2 for others	age, smoking and asbestos	Death certificates
Boffetta et al. 1990[46] (A)	6 cities, U.S. case-control	nearly 60	7683	114	Truck drivers	NA	smoking, education, race, age, year of interview	Histology
Paradis et al. 1989[47] (A)	Montreal, Canada cohort	NA	2134	78	Bus drivers	>5 years	age, sex, cause of death	obtained from death registries
Hayes et al. 1989[48] (B)f	3 states, U.S. pooled case-control	NA	4861	320	Truck, bus, and taxi drivers, and chauffeur	>10 years	birth cohort, daily cigarette use and state	not clear
Boffetta et al. 1988[49] (A)	U.S. cohort	40–79	461981	48	Truck drivers	>6 years	age and smoking	Obtained from State Health Departments

†Studies evaluated with modified STROBE items.

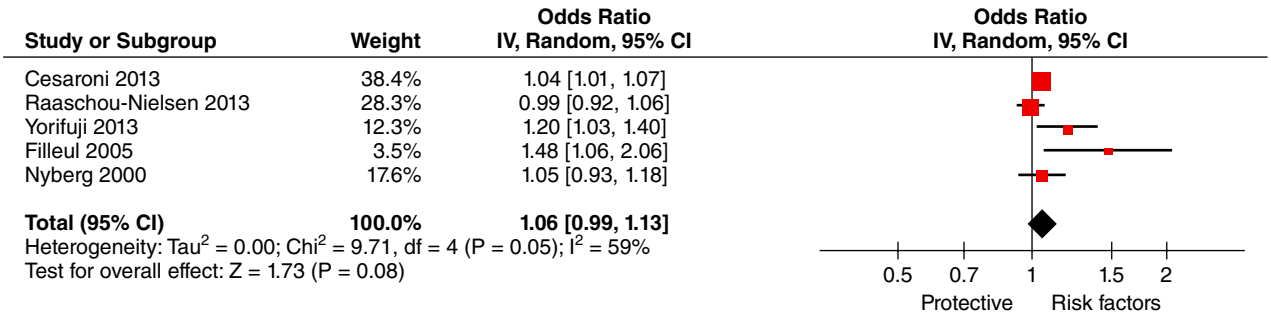

Figure 2 Lung Cancer and NO_2 (odds ratio per 10 μg/m³). CI, confidence interval.

Study characteristics

With respect to studies on ambient exposure to traffic-related air pollution, seven were conducted in Europe: four cohort studies,[18,20,24,25] two case-control studies,[21,27] and a pooled analysis.[15] Five studies were conducted in North America: four cohort studies,[16,22,23,26] and one case-control study.[17] Two cohort studies were conducted in Asia.[14,19] Table 1 provides details of these studies.

Respecting studies on professional drivers, 11 were conducted in Europe: five cohort studies,[28,29,34,41,42] five case-control studies,[30,33,35,39,43] and a pooled analysis.[37] Ten studies were conducted in America: four cohort studies,[30,32,47,49] five case-control studies,[38,40,44–46] and one pooled analysis.[48] One case-control study was conducted in Asia.[36] Table 2 provides details of these studies.

Exposure to nitrogen dioxide and lung cancer

The association between ambient exposure to nitrogen dioxide and lung cancer was estimated in five studies.[14,15,18,24,27] Considering significant heterogeneity (P = 0.05, I^2 = 59%), pooled effect size with a random effect model showed that ambient exposure to nitrogen dioxide increased the risk of lung cancer (meta-OR: 1.06, 95% CI: 0.99–1.13). (Fig 2)

Exposure to nitrogen oxides and lung cancer

The relationship between ambient exposure to nitrogen oxides (mainly NO and NO_2) was examined in two studies;[19,25] a fixed effect model was employed and the result showed an increased risk of lung cancer exposure to nitrogen oxides (meta-OR: 1.04, 95% CI: 1.01–1.07). (Fig 3)

Exposure to sulfur dioxide and lung cancer

The association of ambient exposure to sulfur dioxide and lung cancer was estimated in five studies.[19,21,24,25,27] Considering no heterogeneity (P = 0.48, I^2 = 0%), the effect size was pooled with a fixed effect model, which showed an increased risk of lung cancer exposure to sulfur dioxide (meta-OR: 1.03, 95% CI: 1.02–1.05). (Fig 4)

Exposure to fine particulate matter and lung cancer

The relationship between ambient exposure to fine particulate matter and lung cancer was examined in six studies.[17,18,20,22,23,26] As a result of heterogeneity (P = 0.02, I^2 = 64%), the pooled effect with a random effect model revealed an increased risk of lung cancer exposure to fine particulate matter (P = 0.02, I^2 = 64%). (Fig 5)

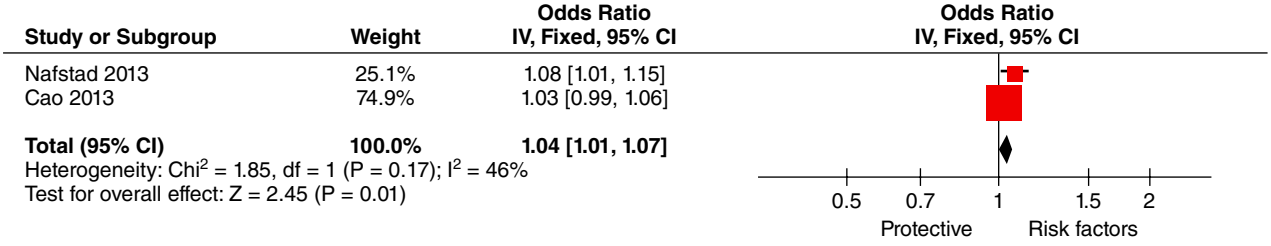

Figure 3 Lung Cancer and NO_X (odds ratio per 10 μg/m³). CI, confidence interval.

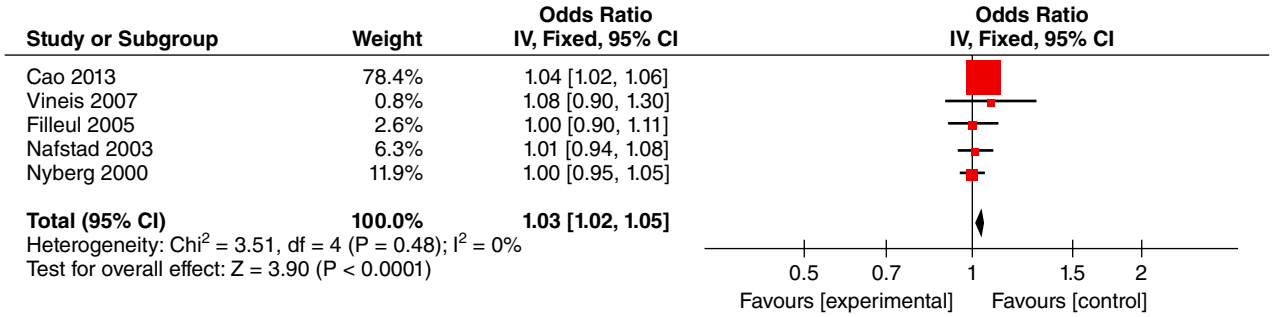

Figure 4 Lung Cancer and SO_2 (odds ratio per 10 μg/m³). CI, confidence interval.

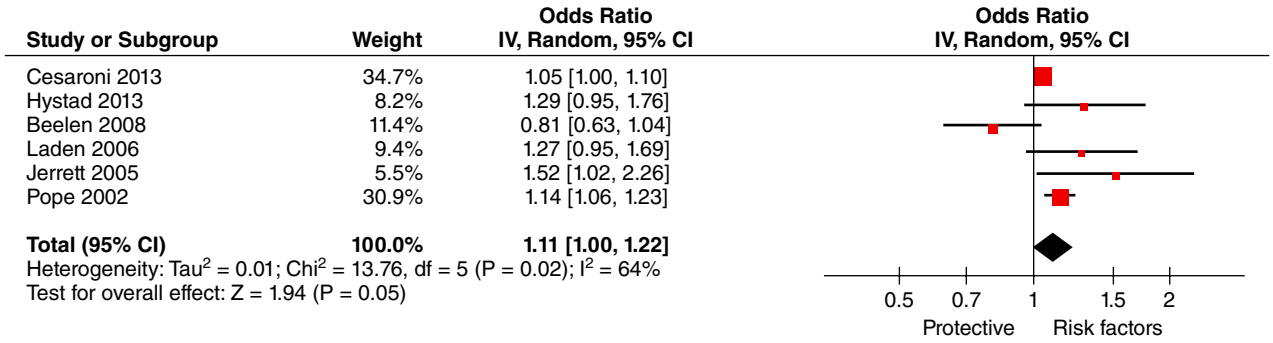

Figure 5 Lung Cancer and $PM_{2.5}$ (odds ratio per 10 μg/m³). CI, confidence interval.

Exposure to other pollutants and lung cancer

Some studies reported the association between exposure to coarse particulate matter and ozone with lung cancer,[11,12,15–17] but effect sizes calculated with varied measurements could not be pooled in our meta-analysis; therefore, we collected all pollutant-specific effect sizes calculated with different measurements. These are listed in Table 3.

Risk of lung cancer among professional drivers

The risk of lung cancer incidence among professional drivers was examined by 14 studies.[28,30,33–41,44,46,48] Considering heterogeneity ($P = 0.02$, $I^2 = 44\%$), the pooled effect size with a random effect model showed an increased risk (meta-OR: 1.27, 95% CI: 1.19–1.36). (Fig 6)

The risk of lung cancer mortality was evaluated by 10 studies.[13,29,31,32,34,42,43,45,47,49] The pooled effect size with a random model revealed an increased risk (meta-OR: 1.14, 95% CI: 1.04–1.26). (Fig 6)

Our results illustrated that no significant difference existed between risks of professional drivers developing and dying of lung cancer (confidence intervals overlap). We pooled the effect sizes respecting incidence and mortality, which showed

Table 3 Association between air pollution and lung cancer with varied measurements of effect sizes

Increase	Number of studies	OR 95%CI
NO_2		
4.1167 ppb	1	1.11 (1.02, 1.21)
8 ppb	1	1.06 (0.97, 1.15)
10 ppb	1	1.11 (1.00, 1.24)
10 μg/m³	6	1.04 (1.01, 1.07)
16 μg/m³	1	1.46 (0.92, 2.32)
30 μg/m³	2	0.88 (0.75, 1.04)
NO_X		
10 μg/m³	2	1.04 (1.01, 1.07)
20 μg/m³	1	1.01 (0.95, 1.07)
SO_2		
4 ppb	1	1.09 (0.98, 1.21)
10 μg/m³	5	1.03 (1.02, 1.05)
20 μg/m³	2	0.88 (0.75, 1.04)
PM 2.5		
5.3037 ppb	1	1.06 (0.95, 1.18)
10 μg/m³	6	1.08 (1.04, 1.12)
O_3		
10 ppb	1	1.09 (0.85, 1.39)
24.1782ppb	1	0.86 (0.75, 0.99)
PM10		
6 μg/m³	1	1.00 (0.92,1.08)
7 μg/m³	1	1.84 (1.23,2.74)
10 μg/m³	1	1.22 (1.03, 1.45)

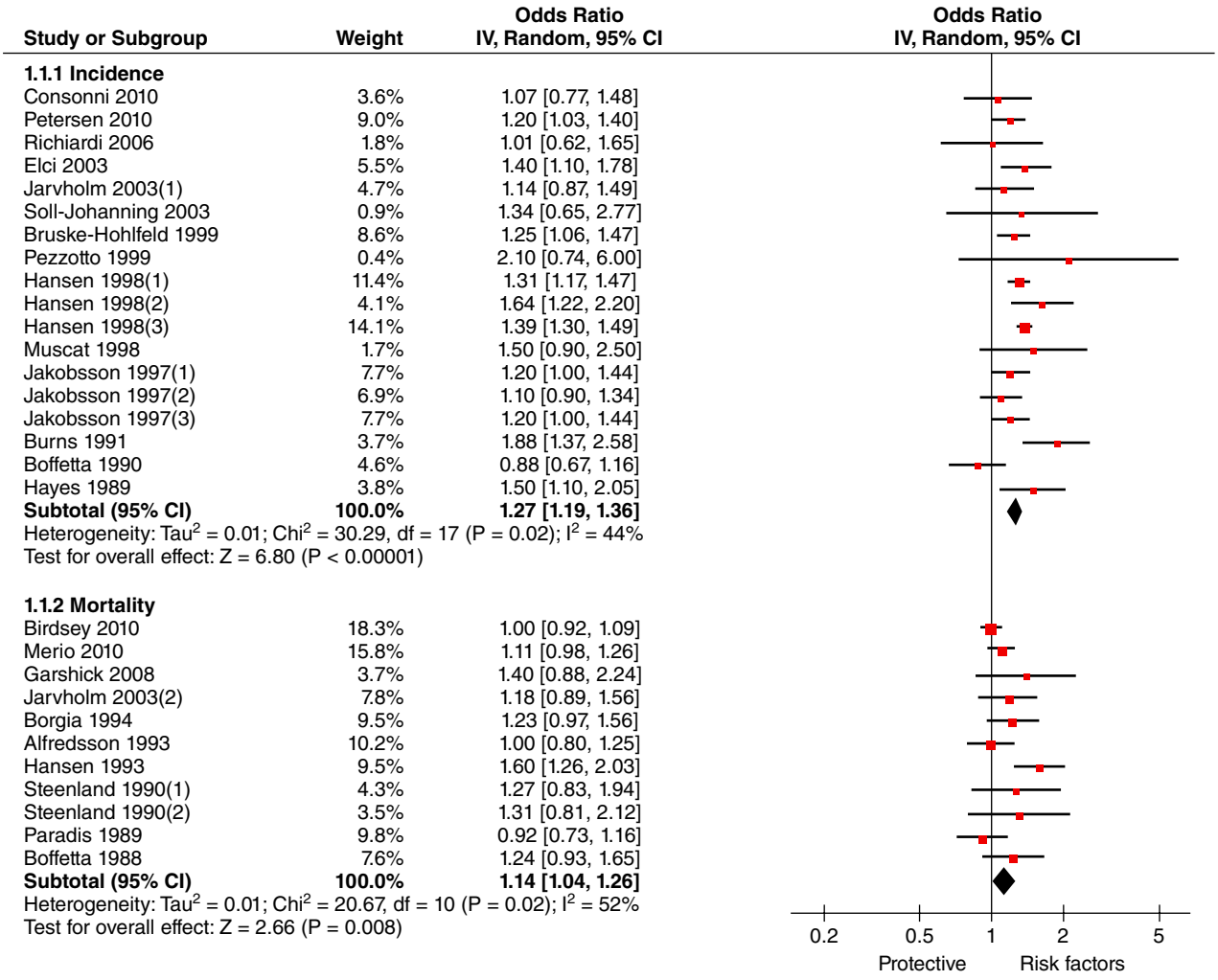

Figure 6 Forest plot of the association of occupational exposure of drivers and lung cancer incidence and mortality. CI, confidence interval.Note:1. Jakobsson *et al*.[41] evaluated the risk of lung cancer among three kinds of professional drivers, taxi drivers, long distance lorry drivers and short distance lorry drivers, and we included three effect sizes, which were noted as Jakobsson *et al*.[41] (1), Jakobsson *et al*.[41] (2) and Jakobsson *et al*.[41] (3). Similar treatment was applied to Hansen *et al*.[39] and Steenland *et al*.[45]2: As all effect sizes were represented with two decimal places, because of the difference in calculation precision, several odds ratios were slightly different from those reported originally, such as Pezzotto and Poletto.[38]

a significantly higher risk (meta-OR: 1.22, 95% CI: 1.14–1.31). (Fig 7) Studies on occupations other than professional drivers were also identified in our literature search, such as truck industry workers,[50] railway workers,[51] and filling station attendants.[52] However this data was not included in our meta-analysis, because there were limited articles after duplicate exclusion or the effect size could not be extracted, particularly for professional drivers.

Discussion

Outdoor air pollution is derived from resources other than vehicle emissions, including industry, energy, and household heating. However, vehicle emissions account for 25–40% of air pollution.[3] The International Agency for Research on Cancer recently reviewed toxicological and epidemiologic evidence and classified diesel engine exhaust as carcinogenic to humans (Group 1).[53]

The results of our meta-analysis indicate that ambient exposure to nitrogen oxides, sulfur dioxide, and fine particulate matters significantly increase the risk of lung cancer. Most ambient nitrogen dioxide is derived from oxidation of nitrogen monoxide, which is mainly produced by vehicle emissions. Nitrogen dioxide involves a series of photochemical reactions induced by sunlight. During the process, nitrate, sulphate, and organic aerosol are produced which further promote the formation of particulate matter and harmful secondary pollutants.[54] Animal studies indicate that the inha-

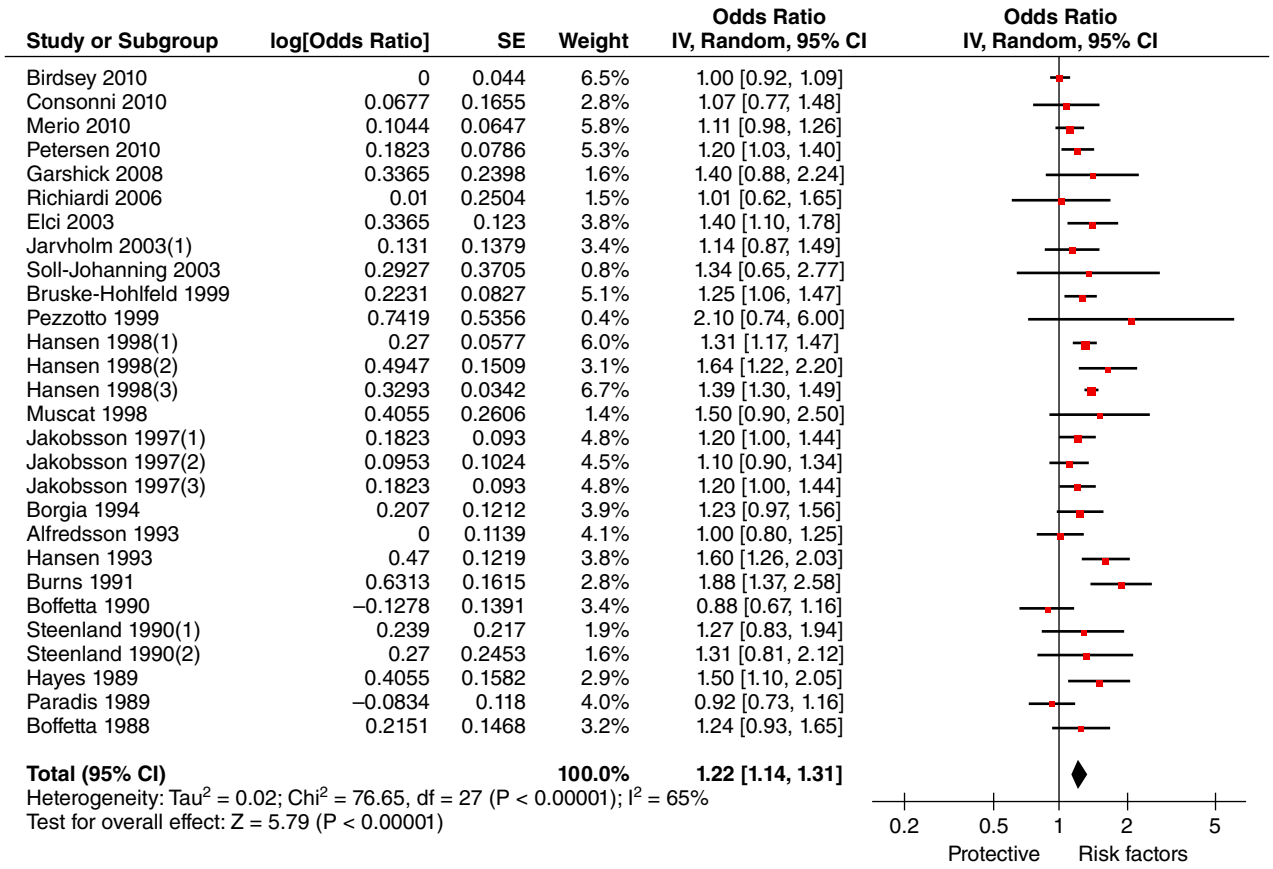

Figure 7 Forest plot of the risk of lung cancer among professional drivers (pooled effect sizes of incidence and mortality).Note: Jarvholm and Silverman[34] reported effect sizes of both lung cancer incidence and mortality, but we only included incidence data in this figure, noted as Jarvholm and Silverman[34] (1). CI, confidence interval.

lation of sulfur dioxide causes multi-organ DNA lesions, including in the lung, which can develop into mutation, cancers, and relevant diseases.[55] The surfaces of fine particles can absorb various chemicals. Compared with coarse particles, fine particles are more likely to pervade indoors and be inhaled deeply in the lung; therefore ambient exposure to fine particles is more prevalent.[56] According to the latest cancer registry data, in China the incidence and mortality rates of lung cancer both ranked first among cancers.[57] In 2010, air pollution was the fourth leading risk factor for the disease in China.[58] Thus, the association between air pollution and lung cancer should be viewed as a major public health threat. Despite this data, of the studies we obtained through our literature search, only one cohort study was conducted in China.[15] However, Zhang *et al.* examined the correlation of ambient SO_4^{2-} level and lung cancer in Beijing, and according to Zhou *et al.*, a higher exposure to particulate air pollution increased the risk of cardiopulmonary mortality among Chinese men.[59,60] Considering various components, distributions of air pollution geologically, and different effects of air pollution on people in varied age groups,[61] the results of studies conducted in Western populations cannot be directly extrapolated to China. Surveillance data indicates that the exposure level of air pollution in China is much higher than in Western countries. For instance, during the first half of 2013, the average concentration of PM2.5 and PM10 in 74 Chinese cities were 76 μg/m^3 and 123 μg/m^3 respectively,[62] but PM2.5 and PM10 in nine European regions reported by Raaschou-Nielsen[15] ranged from 6.6–31.0 μg/m^3 and 13.5–48.1 μg/m^3, respectively. In light of our results that the risk of lung cancer increases with a higher exposure level, the association between air pollution and lung cancer may be much stronger in heavily polluted areas.[63] In order to provide basic data for scientific research and policymaking aimed to prevent air pollution, more environmental monitoring stations need to be established in China, especially in rural areas.[19] More studies need to be conducted to illustrate the distribution of varied pollutants and their relationships with diseases. China will soon implement the fifth set of light vehicle emission limits and measurement methods; however, these do not provide limits for sulfur dioxide emissions.[64] Considering the significant asso-

ciation between exposure to sulfur dioxide and lung cancer, the government and relevant associations should limit vehicle emissions of sulfur dioxide and strengthen the management of vehicle emissions.

Through our literature review, the evaluations of the risk of lung cancer among professional drivers are relatively consistent, which might be attributed to a higher exposure to relevant pollutants and longer duration compared with controls. In some studies, the association between professional exposure to air pollution and lung cancer was found to be insignificant. However, as hazardous pollutants including carbon monoxide, nitrogen oxides, particulate matter, and polycyclic aromatic hydrocarbons are produced in the process of gasoline and diesel combustions,[3] the government should cooperate with the automobile industry, energy department, and transportation companies to promote the consumption of cleaner fuels, such as natural gas and electricity. As professional drivers must pass regular examinations to get their driver's licenses, they must maintain a certain level of health to perform their jobs, known as the healthy worker effect.[65] However, the general population includes individuals unemployed as a result of poor health and related conditions. The duration of employment might not be an accurate predictor of cumulative exposure to traffic-related air pollution, which potentially leads to an underestimation of the risk of lung cancer because of exposure misclassification.[28]

Because of the limited studies obtained, we were not able to employ subgroup analysis by regions, gender, and smoking status. We could not use controls for these variables with multi-regression models, which potentially leads to bias to some extent. As some studies did not provide effect sizes measured by every 10 $\mu g/m^3$ increment of exposure, the exclusion of such studies might also cause a selection bias. Considering the existence of interactions between pollutants, individual analysis of one particular pollutant might overestimate its effect on lung cancer.[66]

Conclusion

Exposure to nitrogen dioxide, nitrogen oxide, sulfur dioxide, and fine particulate matter were positively associated with a risk of lung cancer. Occupational exposure to air pollution among professional drivers significantly increased the incidence and mortality of lung cancer.

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Disclosure

No authors report any conflict of interest.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 Strategy of literature search.

