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Long-term exposure to air pollution and cognitive function in older adults: a systematic review and meta-analysis

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Background: Now more than ever before, air pollution and cognitive decline are global concerns. Credible links are now emerging between exposure to specific pollutants and cognitive decline. However, the role of specific pollutants on different cognitive domains in adults are inconclusive as the pathways to cognitive decline remain poorly understood.
Objective: To systematically review and meta-analyse the evidence for the association between long-term air pollution exposure and cognitive function in adults.
Data sources: Web of Science, PubMed, Embase searched up to February 2021 with no language restrictions. Individual studies were identified from similar review articles.
Eligibility criteria: Studies investigating the long-term (>3 years) associations between airborne pollutants and cognitive function in older adults (>50 years old).
Results: From 1996 records, 26 satisfied the inclusion criteria. The total sample size included over 2.4 million (53.8% female) subjects with ages ranging from 45 to 100 years (estimated mean age 70 years). Only 18/26 publications included both male and female subjects. Pollutants reported included particulate matter ≤2.5 μm ($PM_{2.5}$); particulate matter ≤10 μm (PM_{10}); nitrogen dioxide (NO_2); nitrogen oxide species (NO_x) and ozone (O_3). Papers showed great variance in their study characteristics, air pollution modelling methodology and assessment of cognitive domain. Long-term exposure to increased levels of $PM_{2.5}$ and NO_2 were most strongly associated with increased risk of dementia. Decline in cognitive function, executive function, memory and language were most strongly associated with greater exposure to $PM_{2.5}$, PM_{10} and NO_2 to varying degrees.

Abbreviation

95% CI, 95% confidence interval; AD, Alzheimer's disease; B, regression coefficient; BC, black carbon; CDR, clinical dementia rating; CERAD, consortium to establish a registry for Alzheimer's disease; CHD, coronary heart disease; CO, carbon monoxide; CVD, cardiovascular disease; CVLT, california verbal learning test; DM, diabetes mellitus; DSM-IV, diagnostic and statistical manual of mental disorders, fourth edition; HR, hazard ratio; HTN, hypertension; ICD-9-CM, international classification of disease, ninth edition, clinical modification; IHD, ischaemic heart disease; IQ, intelligence quotient; LM, logical memory; MCI, mild cognitive impairment; MMSE, mini mental state examination; MS, multiple sclerosis; NH_3, ammonia; NMVOC, non-methane volatile organic compounds; NO_x, nitrogen oxide species; NO_2, nitrogen dioxide; O_3, ozone (trioxygen); OR, odds ratio; PD, Parkinson's disease; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than 2.5 micrometres; PM10, particulate matter with an aerodynamic diameter less than 10 micrometres; PNam, accumulation mode particle number; ppb, parts per billion; SM, semantic memory; SOx, sulfur oxide species; SPMSQ, short portable mental state questionnaire; TRAP, traffic related air pollution; $\mu g/m^3$, micrograms per cubic metre; VEM, visual episodic memory; WAIS-IV, Wechsler Adult Intelligence Scale, fourth edition.

Conclusion: An increasing number of studies are supporting the hypothesis that greater exposure to air pollutants is associated with decline in cognitive functions.

KEYWORDS

air pollution, cognition, neurological, neurodegeneration, systematic review, dementia, particulate matter

Introduction

Normal ageing, mild cognitive impairment and dementia

The rate of age-related decline in mental ability shows significant heterogeneity among older adults, resulting in a large spectrum of what we would consider "*normal*" brain ageing (1). The latest review of dementia and cognitive decline published by Age UK divides brain function into 3 types: automatic functions [for example breathing, digestion and homeostasis]; motor function [encompassing movement, balance and speech]; and cognitive function [thoughts, emotions, learning, memory, comprehension and decision making] (2). Healthy decline of cognitive function in older people is a concept unconsciously but unanimously accepted and is well summarised by Harada et al. (3).

Defining MCI is more challenging due to a lack of standardised diagnostic criteria (4). It is generally accepted as the intermediate state between healthy ageing and dementia whereby a person experiences dementia-like symptoms such as memory loss, but these symptoms are not severe enough to significantly interfere with daily life. Estimating the prevalence, incidence and social burden of MCI is complex (5). However, it is believed 5%–20% of adults over 65 have MCI (6).

Statistics released by the WHO in 2020 approximate that 5%–8% of adults aged 60 and over have dementia, equating to around 50 million people worldwide, 60% of whom live in low- and middle-income countries (7). This number is projected to increase to 82 million by 2030 and 152 million by 2050. Whilst this is largely attributable to the globally ageing population, the fact that dementia is currently ranked at the seventh leading cause of death highlights the need for preventative action (8).

Air pollution

Air pollution is estimated to kill nearly 6.5 million people annually, being the largest environmental factor globally (9), and is a leading risk factor for mortality (10). In 2017, the global burden of disease of air pollution was measured at 147 million DALYs. Exposure to polluted air is a global crisis with over 90% of the world's population still living in areas where air quality levels exceed WHO limits (11). The highest concentrations of air pollution and indeed its burden of disease are recorded in low- and middle-income countries (10), and are also a key factor in terms of social inequalities outcomes in UK (12). Furthermore, older adults and children are thought to be more vulnerable to the effects of noxious pollutants (13).

Cognitive decline, dementia and air pollution

A number of conceivable biological mechanisms exist to explain how pollutants may damage cognitive health. More is known about the toxic effects air pollution can have on respiratory and cardiovascular health but recently studies suggest they both may facilitate cognitive impairment. Hüls et al. (14) describe how lung function partially mediated visuo-construction performance. Meanwhile, Saito et al. (15) highlight the interrelationship between AD and CVD risk factors and the potential role of β-amyloid. Alternatively, inhaled pollutants, particularly those of smaller aerodynamic diameters, may access the brain directly via the olfactory bulb (16). At a cellular level, Zhang et al. (17) reported $PM_{2.5}$ triggered oxidative stress and myelin sheath degradation in murine models. Additionally, Woodward et al. (18) suggested pollutants activate the transmembrane protein toll-like receptor 4, which is involved in inflammatory signalling. Like other cerebrovascular risk factors, the harmful effects of air pollution likely accumulate over a lifetime. Greater exposure to $PM_{2.5}$ has been linked to neuroinflammation, altered immune responses and accumulation of amyloid β-42 and α-synuclein in the brains of children and young adults in Mexico City (19), and the likely mechanisms of its neurological effects including neurodegeneration, are reviewed in Olasehinde and Olaniran (20).

A 2019 report released by the Alzheimer's Society outlined the possible link between air pollution and dementia (21). Similarly, a 2017 Lancet commission included air pollution as a potential risk factor for dementia (22). Nevertheless, a direct causal link has yet to be proven and neither air pollution nor pollution in general were mentioned in the most recent global action plan on dementia (23). The length of clinical trial needed to ascertain the effect of air pollution on cognitive function is unattainable; therefore, longitudinal observation studies are likely to provide the best evidence. Ambient polycyclic aromatic hydrocarbons negatively affect different cognitive functions throughout the lifespan, with general memory being mostly affected in older adults (24). Various reviews have summarised the increasing body of evidence that suggests long-term exposure to air pollution is associated with increased risk of dementia and cognitive decline (25–29). However, only one comprising evidence until 2018 conducted a systematic search (26), and did not meta-analyse the data. We conducted a systematic review of the sources published until 2021 and a meta-analysis on the differential impact of specific air pollutants [$PM_{2.5}$, PM_{10}, NO_2, NO_x and O_3] on cognitive functions specifically in the elderly. Pollutants have explicit sources (30). Comparing the severity by which each pollutant negatively affects cognitive functions will

allow public health bodies to prioritise the most harmful pollutants; and in turn, tackle their sources.

Methods

Databases, sources and searches

The databases Web of Science, PubMed and Embase were searched from inception up to the 6th of February 2021. Each database was subject to three different search strategies:

1. (air pollution) AND inflamm* AND brain
2. (air pollution) AND brain AND cogn*
3. (air pollution) AND brain AND (dementia OR Alzheimer*)

The title and abstract for all records were screened and any duplicates were removed. Each paper was evaluated against the inclusion and exclusion criteria set out below. Additional appropriate papers were identified using the bibliographies of the included studies as well as relevant review articles.

Inclusion criteria

Primary studies with:

- Assessment of exposure to air pollution explained in the Methods section;
- Assessment of cognitive function reflected in outcome measures evaluated in relation to any air pollutant;
- Cohort mean age >50 (clinically considered a middle-age reference). Although no restrictions are imposed to the age range, it is worth noting that cognitive ageing begins in the 20s, and older age is often categorised as 60/65+ albeit variations depend on location, circumstances, etc., so a study including younger (i.e., close to or above 20 years old) individuals is included as long as the mean age of the whole sample is above 50 years old;
- Minimum exposure time of at least 3 years, being 36 months the upper limit for considering exposure to outdoor air pollutants as short-term.

Exclusion criteria

- Studies using non-human subjects;
- Studies reporting non-primary research i.e., review articles;
- Studies where full text was inaccessible (i.e., this considered for reproducibility purposes).

Data were extracted using standard extraction tables. Information collected included: sample size, study characteristics, gender ratio, mean age, age range, cardiovascular comorbidities, air pollutant component, pollutant modelling method, exposure time and cognitive-related outcome measure.

Risk of bias

Each individual study included was assessed for risk of bias across four parameters: generalisabilty, exposure measurement, outcome measurement, and adjustment for confounders.

Generalisability

Low risk of bias in terms of generalisability was defined as a source with a sample size greater than 1,000 that included both sexes and had an age range of over 10 years. Additionally, although inclusion criteria varied considerably amongst the primary sources, studies that used more than one cognitive function test at baseline were considered low risk.

Exposure assessment

Outlining the accuracy of pollutant exposure modelling is difficult as a diverse range of methods exist and often air quality data is estimated. A study was considered low risk of bias if authors used a minimum standard method to assess exposure. An example of a "*minimum standard*" method is land-use regression models described by the European Study of Cohorts for Air Pollution Effects (31). Atmospheric models using emissions data would be preferable.

Assessment of outcomes

The definition of cognitive function is not universal and therefore multiple techniques are used to investigate it. Studies that employed appropriate tools and criteria to assess dementia or distinct cognitive functions were considered having low risk of bias in assessing outcomes. An example of an appropriate tool is the neuropsychological test battery of CERAD Neuropsychological Assessment Battery (32), noting that the mini-mental state examination (MMSE) results alone may be considered insensitive for capturing normal-range differences in non-clinical samples.

Adjustment for confounders

When multiple models were reported, data were extracted from only the model that had adjusted for the most confounders (e.g., modifiable and non-modifiable vascular risk factors, socioeconomic status, ethnicity, family history of any neurodegenerative disease including dementia subtypes, etc.). Studies that identified and adjusted for five or more confounding factors were considered having low risk of bias in this regard.

Statistical analysis

Studies were firstly divided based on the air pollutant they reported on, and then scrutinised further depending on the cognitive domain they assessed. Cognitive domains/functions for this review were ascertained after analysing the reported data based on authors' own nomenclature. Any air pollutant or cognitive domain that was reported by fewer than five studies was governed insufficient to be included in the meta-analysis. HR, OR and β with 95% CI were used for the meta-analysis, which were

conducted using MedCalc (https://www.medcalc.org/). Data is presented in tables and forest plot graphs to visualise the difference in reported effect sizes between studies. In instances where data was reported with a standard error [SE] measurement as opposed to a CI; the formula $CI = mean \pm SE \times 1.96$ was used in line with Altman et al. (33). For articles reporting β, or which provided data to calculate it, fixed effects were determined using a Fisher Z transformation of the β coefficients. The random effects model (34) general estimate was given after analysing heterogeneity using the I^2 and Cochran's Q statistics (35). Results from each meta-analysis are provided in the **Supplementary Material**.

Results

Search results

A total of 1,996 records were identified using three separate search strategies (See **Supplementary data spreadsheet**). Removing duplicates left 866 unique studies. From these, 832 papers were excluded based on inclusion and exclusion criteria. The full-text screening of the remaining papers against the inclusion and exclusion criteria listed above yielded a total of 26 papers. A further paper was identified from individual records. **Figure 1** shows the flow chart for study inclusion.

Study characteristics

Study characteristics are shown in **Table 1**. In total, over 2.4 million subjects, 53.8% of which are female, were included in the 26 studies. However, the geographical area covered is limited given the overlap in the samples. The sample from two studies (42, 43) was from Northern Manhattan, four studies (44, 46, 50, 51) used data from a USA-wide study on women's health, two studies analysed data from London (56, 57), three studies (37, 39, 40) analysed data from Ruhr and adjacent areas in Germany, three studies used data from the Taiwanese National Registry (47, 52, 60), one study used data from a multicentre ageing Korean study (36), and three studies used data from a municipality in northern Sweden (59, 61, 62). Nineteen papers included both male and female participants in their cohort. The age of participants ranged from 45 to 100 years with an estimated mean age of 70 years. Cardiovascular comorbidity data was extracted due to the well-described association between air pollution and vascular conditions (63). Median exposure time estimated across the sample was 10 years, with only 4/26 studies with relatively small samples analysing exposure for 20 years or more. These were Schikowski et al. (37) (789 individuals, 22-years exposure to NO_2, NO_x, $PM_{2.5}$ and PM_{10}), Ranft et al. (39) (399 individuals, 20-years exposure to PM_{10}), Ailshire et al. (51) (779 individuals, approximately 23-years exposure to $PM_{2.5}$), and Russ et al. (54) [572 individuals exposed to CO, NH_3, NMVOC, NO_x, $PM_{2.5}$, and SO_x for most of their lifetime (~60 years)]. Only

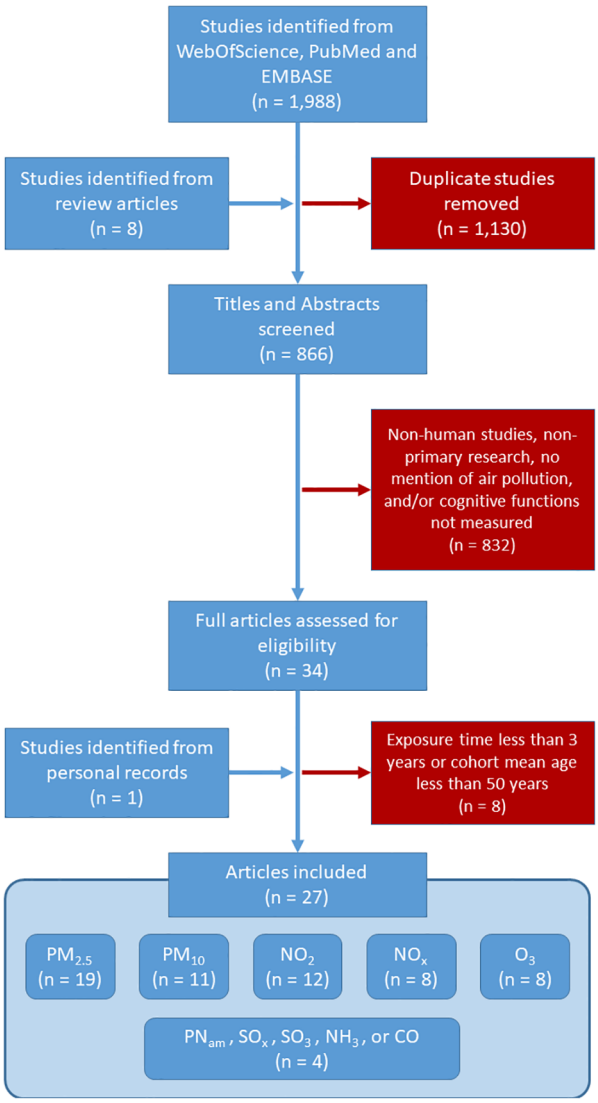

FIGURE 1
Literature search flow diagram. Duplicates made 56.8% of the titles from all three databases enquired. The final proportion of papers analysed were 76.5% of those which had the full text analysed, after excluding non-human studies and those who either did not mention the sources of air pollution or did not measure any cognitive function.

the studies from USA included ethnicity as covariate in the analyses or restricted the analysis to a certain ethnic group. For example, Paul et al. (45) only included latino (mainly Mexican-Americans) individuals, and Ailshire et al. (51) only included pure black and white individuals and not those with mixed race/ethnicity.

Quality of the studies included

Risk of bias for the studies included can be seen in **Table 2**. In general the quality of the studies included was good and the risk of bias, as per the categories defined above, was low with only five studies been considered of moderate risk, mainly owed to the relatively small sample sizes and the use of not widely used tools

TABLE 1 Sample characteristics in the included studies.

Publications	Inclusion criteria	Male/ female	Mean age (SD)	Age range	Cardiovascular comorbidities
Shin et al. (36)	Dementia-free community residents aged 70–84 enrolled in the Korean Frailty and Aging Cohort study who had not moved address within a year	1,377/1,519	76 (3.9)	70–84	Not analysed
Schikowski et al. (37)	Age >55	0/789	73.4 (3.1)		CVD (66.4%)
Power et al. (38)	Reside within range of black carbon model, no history of stroke	680/0	71 (7)	51–97	Not analysed
Ranft et al. (39)	Resided at same address for 20 years	0/399	74.1 (2.6)	68–79	HTN (66%)
Nussbaum et al. (40)	No history of overt CVD, no history of severe psychiatric disorders	344/271	61.5 (6.7)	55–85	CHD (1.6%), DM (14.6%)
Crous-Bou et al. (41)	MMSE > 26, CDR = 0, no cognitively disabling disorders, no potential autosomal dominant AD family history	346/612	57 (7.0)	45–74	HTN (18.9%), DM (4.6%), HChol (31.3%)
Kulick et al. (42)	Excluded if substantial cognitive problems or diagnosis of dementia at baseline	1,751/3,579	75.2 (6.46)		HTN (77%), DM (27.2%)
Kulick et al. (43)	Excluded if substantial cognitive problems or diagnosis of dementia at baseline	1,555/3,266	76.3 (6.6)		HTN (80%), DM (29%)
Petkus et al. (44)	Cognitively normal at baseline	0/2,202		66–83	HTN (37%), DM (5.6%), CVD (16%)
Paul et al. (45)	Cognitively normal at baseline	656/938	70.2 (6.8)	60–101	DM (32%)
Younan et al. (46)	Age >65, free from dementia at baseline	0/998		73–87	HTN (35.5%), DM (3%), CVD (14%)
Lo et al. (47)	Age >65, SPMSQ score >3, no history of stroke	1,289/952	73.6 (4.9)		HTN (26.6%), DM (10.2%), CVD (15.7%)
Cerza et al. (48)	First-time hospitalisation due to dementia	8,416/13,132	77	65–100	CVD (31%)
Chen et al. (49)	Resided in Ontario >5 years, age 55–85, free from dementia, PD and MS at baseline	966,246/ 1,100,393	66.8 (8.2)	55–85	HTN (48%), DM (15%), CHD (10%)
Cacciottolo et al. (50)	Free from dementia at baseline, excluded individuals with epsilon 2/2, 2/3, 2/4 alleles	0/3,647		65–79	Not analysed
Ailshire et al. (51)	Age >55, resided near air monitoring station	304/475	67.9 (9.8)	55–98	Not analysed
Jung et al. (52)	Free from AD at baseline, Age >65	43,988/ 61,764		>65	HTN (63%), DM (33%)
Gatto et al. (53)	Cognitively normal as baseline, free from comorbidities	308/1,188	60.5 (8.1)		Not analysed
Russ et al. (54)	Sat Moray House test in 1947, air pollution data was available for lifetime residence	304/268	10.9 (0.3) [1947], ~70 [2017]	~70, 59 yrs expo-sure	Not analysed
Chen et al. (55)	Free from dementia at baseline	0/7,479	71 (3.8)	65–80	HTN (?%)
Tonne et al. (56)	Postcode could be linked to modeled air pollution	~1,865/996	66 (6)		DM (16%), Stroke/TIA (5%)
Carey et al. (57)	Age 50–79, registered to 1 of 75 GP practices within M25, free from dementia, not living in care home	65,130/ 65,848		50–79	DM (7.8%), IHD (7.6%), Stroke (2.8%)
Cleary et al. (58)	Age >60, MMSE > 0, diagnosis of cognitive impairment in at least one follow-up visit	2,401/2,715	76.8 (7.7)	60–101	Not analysed
Oudin et al. (59)	Age >55, Free from dementia at baseline	773/1,033	~70		HTN (34%), DM (7%), Stroke (7%)
Chang et al. (60)	Age >50, air pollution data available, no history of head injury, stroke or dementia	13,606/ 15,941	61.4 (8.5)		HTN (39%), DM (12%), IHD (18%)
Oudin et al. (61)	Age >60			60–85	Not analysed
Oudin et al. (62)	Age >55, free from dementia at baseline	773/1,033	~70		HTN (34%), DM (7%), Stroke (7%)

for assessing the outcome, limiting the reproducibility of their findings.

Air pollutants

Table 3 shows the pollutant modelling method, pollution component, sources, geographical areas covered, and exposure time from the 27 included studies. $PM_{2.5}$ was included in 19 studies, PM_{10} in 11, NO_2 in 12, NO_x in eight, and O_3 in eight. Four of the studies included reported effects of other pollutants, but each of these (i.e., individually) were reported in less than three studies and ruled insufficient in data to be further meta-analysed. The included studies used a range of pollutant modelling methods, with refined land-use regression model being the prevalent (in 9/26 studies). Interpolation of data from local monitoring stations was used by four studies. Four other studies reported exposure assessment by constructing spatiotemporal models using Bayesian Maximum Entropy method. The remaining publications used less popular methods of exposure assessment. Exposure time ranged 3–60 years.

Regarding pollution sources, only one study (51) analysed neighbourhood-stress-related pollution sources [i.e., neighbourhood upkeep, presence (or not) of trash, and deteriorating buildings vs. not], and another (38) focused on exposure to black carbon. Traffic as pollution source was

TABLE 2 Assessment of bias for the studies included.

Publications	Risk level assessment results				Overall Risk of Bias
	Generalisability	Exposure measurement	Outcome measurement	Adjustment for confounders	
Shin et al. (36)	Low	Low	Low	Low	Low
Schikowski et al. (37)	Moderate (sample size <1,000, female)	Low	Low	Low	Moderate
Power et al. (38)	Moderate (sample size <1,000, male)	Low	Low	Low	Low
Ranft et al. (39)	Moderate (sample size <1,000, female)	Low	Low	Low	Low
Nussbaum et al. (40)	Moderate (sample size <1,000)	Low	Low	Low	Low
Crous-Bou et al. (41)	Moderate (sample size <1,000)	Low	Low	Moderate (3 confounders)	Moderate
Kulick et al. (42)	Low	Low	Low	Low	Low
Kulick et al. (43)	Low	Low	Low	Low	Low
Petkus et al. (44)	Moderate (female)	Low	Low	Low	Low
Paul et al. (45)	Moderate (only Mexican-Americans in a small region)	Low	Low	Low	Low
Younan et al. (46)	Moderate (sample size <1,000, female)	Low	Low	Low	Low
Lo et al. (47)	Low	Low	Moderate (SPMSQ)	Low	Low
Cerza et al. (48)	Low	Low	Low	Low	Low
Chen et al. (49)	Low	Low	Low	Low	Low
Cacciottolo et al. (50)	Moderate (female)	Low	Low	Low	Low
Ailshire et al. (51)	Moderate (sample size <1,000, mixed ethnicity excluded)	Low	Moderate (SPMSQ)	Low	Moderate
Jung et al. (52)	Low	Low	Low	Low	Low
Gatto et al. (53)	Low	Low	Low	Low	Low
Russ et al. (54)	Moderate (sample size <1,000)	Moderate (EMEP4UK model)	Moderate (IQ)	Moderate (3 confounders)	Moderate
Chen et al. (55)	Moderate (female)	Low	Low	Low	Low
Tonne et al. (56)	Low	Low	Low	Low	Low
Carey et al. (57)	Low	Low	Low	Low	Low
Cleary et al. (58)	Low	Low	Low	Low	Low
Oudin et al. (59)	Low	Low	Low	Low	Low
Chang et al. (60)	Low	Low	Low	Low	Low
Oudin et al. (61)	High (data unavailable)	Low	Low	Low	Moderate
Oudin et al. (62)	Low	Low	Low	Low	Low

considered in all studies, either directly or indirectly (i.e., considered within geocoded data).

Cognitive-related outcome measures

Table 4 displays the cognitive-related outcome measurements each paper used to assess dementia, executive function, cognitive function, memory and language. Seven articles reported incident dementia cases; one focused solely on incident AD; one used dementia hospitalisations and another combined both incident dementia and dementia hospitalisations. Seven of the papers used an internationally recognised definition of dementia: five referring to an edition (ninth or tenth) of the ICD and two implementing the DSM-IV. Cognitive functions were assessed using a variety of methods. For general cognition, three papers included the CERAD neuropsychological battery; four incorporated MMSE and three used results of assessment of other domains to form a cognition composite. Less consistency was seen in the assessment of the other three cognitive domains (i.e., executive function, memory and language).

Association between pollutants and dementia

$PM_{2.5}$

For $PM_{2.5}$, as Figure 2 shows, four out of seven studies comprising 2,307,016 individuals, among whom the most relevant vascular comorbidity was hypertension (i.e., 45.88% were hypertensive), reported a significant association between increased exposure and an increased risk of dementia (49, 50, 52, 57).

Other pollutants

Fewer studies described the association between the other pollutants and dementia (Table 5). Three papers found a statistically significant increased risk of dementia with increasing exposure to NO_2 (49, 57, 60). Paul et al. (45) reported rising levels of NO_x to be associated with a significant increased risk of dementia. Four other papers discussed the impact of O_3 on dementia risk; with two finding a positive association (48, 52).

TABLE 3 Air pollutants analysed in the studies included.

Publications	Pollutant modelling method	Air pollution component	Exposure time (SD)	Geographical region/source
Shin et al. (36)	Average concentrations as measured hourly by the Korean Air Pollutants Emission Service in 2013–2017	PM_{10}, NO_2, CO, SO_2, and O_3	4 years	South Korea (nationwide)
Schikowski et al. (37)	Land-use regression model	$PM_{2.5}$, PM_{10}, NO_2, NO_x	22 years	Ruhr (urban) area, Germany, and two rural areas in the Southern Muensterland/traffic, steel and coal industries
Power et al. (38)	Land-use regression model	BC ($PM_{2.5}$)	3–11 years	USA-wide, but living within-range of exposure to black carbon
Ranft et al. (39)	Monitoring stations—total suspended particles	PM_{10}	5 years	Ruhr (urban) area, Germany, and rural counties north of Ruhr/traffic, steel and coal industries
Nussbaum et al. (40)	Land-use regression model	$PM_{2.5}$, PM_{10}, NO_2, NO_x, PN_{am}	10 years	Three adjacent cities (Bochum, Essen, and Mülheim/Ruhr) in the urban and industrialized German Ruhr Area
Crous-Bou et al. (41)	Land-use regression model	$PM_{2.5}$, PM_{10}, NO_2, NO_x	>3 years	City of Barcelona, Spain/geocoded data
Kulick et al. (42)	Universal kriging regression framework	$PM_{2.5}$, PM_{10}, NO_2	Unclear (~6 years average)	Northern Manhattan, New York, USA
Kulick et al. (43)	Universal kriging regression framework	$PM_{2.5}$, PM_{10}, NO_2	~6 years	Northern Manhattan, New York, USA
Petkus et al. (44)	Bayesian Maximum Entropy method to construct spatiotemporal models	$PM_{2.5}$	3 year average	USA-wide (48 states), source lacks geographical data/geocoded residential data and chemical transport models
Paul et al. (45)	CALINE4—Gaussian dispersion model	TRAP-NO_x	10 years	Sacramento Valley, California, USA/traffic
Younan et al. (46)	Bayesian Maximum Entropy method to construct spatiotemporal models	$PM_{2.5}$	3 year average	USA-wide (48 states), source lacks geographical data/geocoded residential data and chemical transport models
Lo et al. (47)	Monitoring stations—ultraviolet absorption and beta-gauge	PM_{10}, O_3	3 years	Taiwan/air monitoring stations in cities and counties
Cerza et al. (48)	Land-use regression model	$PM_{2.5}$, PM_{10}, NO_2, NO_x, O_3	10.6 years	Rome, Italy/traffic, land, air stations
Chen et al. (49)	Land-use regression model	$PM_{2.5}$, NO_2, O_3	~11 years	Ontario, Canada (urban and rural)
Cacciottolo et al. (50)	Bayesian Maximum Entropy method to construct spatiotemporal models	$PM_{2.5}$	8–10years	USA-wide (48 states), source lacks geographical data/geocoded residential data and chemical transport models
Ailshire et al. (51)	Monitoring stations	$PM_{2.5}$	~23 years	USA-wide/neighbourhood stress [upkeep, presence (or not) of trash and deteriorating buildings vs. not]
Jung et al. (52)	Monitoring stations—ultraviolet absorption, beta-gauge, nondispersive infrared absorption, chemiluminescence and ultraviolet fluorescence	$PM_{2.5}$, O_3	~10 years	Taiwan/air monitoring stations in cities and counties
Gatto et al. (53)	Geographical information system	$PM_{2.5}$, NO_2, O_3	~7 years	Los Angeles Basin, California, USA
Russ et al. (54)	EMPE4UK model	$PM_{2.5}$, NO_x, CO, NH_3, NMVOC, SO_x	~60 years	City of Edinburgh and Lothian areas, Scotland, UK
Chen et al. (55)	Bayesian Maximum Entropy method to construct spatiotemporal models	$PM_{2.5}$, diesel PM	7.7 years	USA-wide (48 states), source lacks geographical data/geocoded residential data and chemical transport models
Tonne et al. (56)	Dispersion modelling system	$PM_{2.5}$, PM_{10}	~5 years	Greater (rural) and City of London, England, UK/traffic and geocoded residential and working-place data
Carey et al. (57)	Dispersion modelling system	$PM_{2.5}$, NO_2, O_3	6.9 years	Greater (rural) and City of London, England, UK/traffic and geocoded residential data
Cleary et al. (58)	Combination of ground-level air monitoring data and simulated O_3 data	O_3	~4.4 years (0.6)	USA-wide
Oudin et al. (59)	Land-use regression model	NO_x	~15 years	Municipality of Umeå (urban and rural), northern Sweden/traffic and geocoded residential data
Chang et al. (60)	Air quality monitoring stations	NO_2, CO	Unclear (data collected over ~13 years)	Taiwan
Oudin et al. (61)	Land-use regression model	NO_x	8.6 years (4.4)	Municipality of Umeå (urban and rural), northern Sweden/traffic and geocoded residential data
Oudin et al. (62)	Land-use regression model	$PM_{2.5}$	11.4 years	Municipality of Umeå (urban and rural), northern Sweden/geocoded residential data, wood stoves or wood boilers

TABLE 4 Cognitive-related outcome measures of the studies included.

	Author	Cognitive-related outcome measurement
Dementia	Cerza et al. (48)	Dementia hospitalisations using ICD-9-CM
	Chen et al. (49)	Incident dementia or dementia hospitalisation using ICD-9-CM
	Cacciottolo et al. (50)	Incident dementia by "central adjudication"
	Jung et al. (52)	Incident Alzheimer's disease using ICD-9-CM
	Carey et al. (57)	Incident dementia using ICD-10-CM
	Chen et al. (55)	Incident dementia
	Paul et al. (45)	Incident dementia using standard diagnostic criteria from American Psychiatric Association
	Chang et al. (60)	Incident dementia using ICD-9-CM
	Oudin et al. (62)	Incident dementia using DSM-IV
	Oudin et al. (59)	Incident dementia using DSM-IV
Executive function	Shin et al. (36)	Frontal assessment battery score
	Schikowski et al. (37)	Trail making test A, B and B/A
	Nussbaum et al. (40)	Problem solving, figural fluency, concept shifting and susceptibility to interference
	Crous-Bou et al. (41)	Psychomotor speed, visual processing, executive function, and non-verbal and verbal reasoning—WAIS-IV
	Kulick et al. (42)	Controlled oral word association test, identities and oddities
	Kulick et al. (43)	Controlled oral word association test, odd man out, digit reordering
	Gatto et al. (53)	Symbol digit modalities test, trail making test, letter-number sequencing, Shipley Institute of Living Scale (abstraction subtest)
Cognitive function	Shin et al. (36)	MMSE-KC (Korean version of the MMSE) and digit span test
	Schikowski et al. (37)	CERAD, MMSE
	Crous-Bou et al. (41)	Modified-Preclinical Alzheimer Cognitive Composite
	Kulick et al. (42)	Mean of all tests: selective reminding test, controlled oral word association test, identities and oddities, BNT, animal naming, comprehension subtest, colour trails
	Kulick et al. (43)	Mean of all tests: controlled oral word association test, odd man out, digit reordering, modified CVLT, grooved pegboard, letter-number sequencing, symbol digit modalities test
	Cacciottolo et al. (50)	CERAD neuropsychological battery, MMSE
	Ailshire et al. (51)	SPMSQ
	Russ et al. (54)	IQ
	Gatto et al. (53)	Mean of all tests: symbol digit modalities test, trail making test, letter-number sequencing, Shipley Institute of living scale (abstraction subtest), CVLT (immediate + delayed recall), paragraph recall (immediate recall + delayed recall), judgement of line orientation, block design, faces (immediate + delayed recall), category fluency, Boston naming test
	Power et al. (38)	MMSE, the digit span backward test, a verbal fluency task, constructional praxis, immediate + delayed recall of a 10-word list, pattern comparison task.
	Ranft et al. (39)	CERAD neuropsychological battery
	Lo et al. (47)	SPMSQ
	Clearly et al. (58)	Clinical Dementia Rating Scale
Memory	Shin et al. (36)	Word list learning (memory, recall and recognition) tests scores
	Schikowski et al. (37)	Word list recall, and learning (overall) tests scores
	Nussbaum et al. (40)	Figural memory and verbal learning tests scores
	Crous-Bou et al. (41)	Memory binding test
	Kulick et al. (42)	Selective reminding test
	Kulick et al. (43)	Modified CVLT
	Pektus et al. (44)	Learning/IR memory
	Younan et al. (46)	Immediate recall, new learning and delayed recall (CVLT Composite score)
	Gatto et al. (53)	Paragraph recall (immediate + delayed recall), faces (immediate + delayed recall), category fluency, Boston naming test
	Tonne et al. (56)	20-word free recall test
	Oudin et al. (61)	Immediate free recall, delayed cued recall
Language	Nussbaum et al. (40)	Semantic and phonemic verbal fluency, vocabulary
	Kulick et al. (42)	BNT, animal naming, comprehension subtest, colour trails
	Kulick et al. (43)	Grooved pegboard, letter-number sequencing, symbol digit modalities test

Association between pollutants and executive function

$PM_{2.5}$

As Figure 3A illustrates, two of six papers reported a statistically significant decrease in executive function associated with increased levels of $PM_{2.5}$ exposure (42, 43), but the samples of both publications had considerable overlap, as the Washington Heights Inwood Community Aging Project (WHICAP) provides data for both publications. Hence, these results are obtained from data from 5,330 residents in the northern Manhattan area of New York City. The total effect was small and not statistically significant ($\beta = 0.0171$, 95% CI [−0.745 to 0.108]).

PM_{10}

For PM_{10}, only one paper of six described a significant negative association between executive function and long term

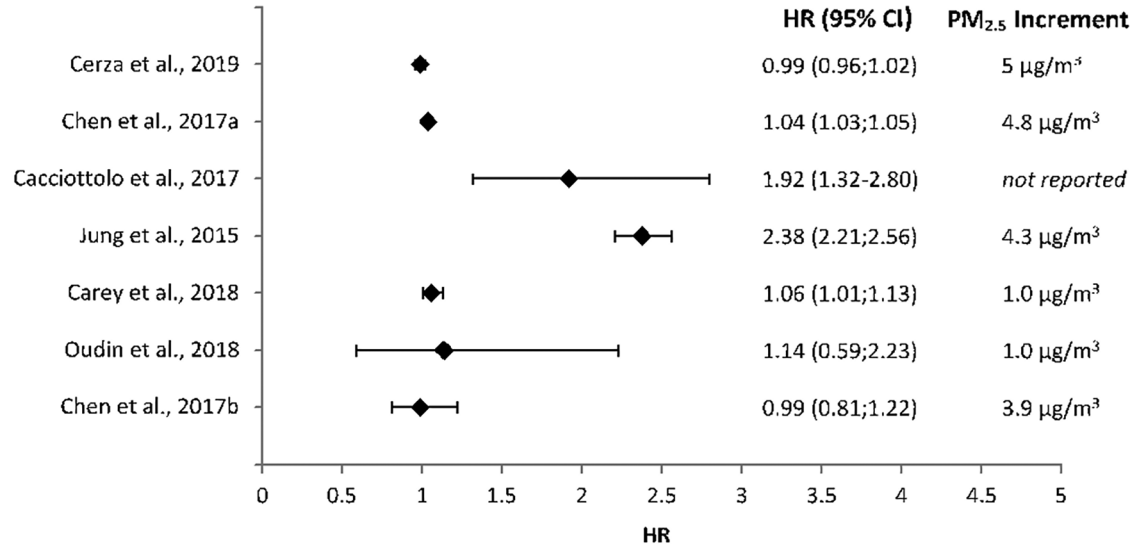

FIGURE 2
Forest plot of the effect of $PM_{2.5}$ in dementia risk across all studies that evaluated their putative association, in terms of hazard ratios and their 95% confidence intervals.

exposure (43) (Figure 3B). The total effect was small- to-moderate and not statistically significant ($\beta = 0.0787$, 95% CI [−0.0451 to 0.200]).

NO_2

Seven papers discussed the impact of NO_2 on executive function with little agreement found (Figure 3C). A negative association was described by the two papers from Kulick et al. (42) featuring 5,330 residents from northern Manhattan, and by Shin et al. (36) on 2,896 Korean older adults, whilst (41) reported a positive association from an analysis involving 958 Catalans participants in the ALzheimer and Families (ALFA) study. Although the total effect yielded a strong correlation coefficient ($\beta = 0.225$), it was not statistically significant (95% CI [−0.177 to 0.562]).

Other pollutants

The only other significant result described was by Crous-Bou et al. (41), who found a positive association between NO_x and executive function (Table 5) in a study that uses data from 958 cognitively-normal individuals (MMSE > 26) from the City of Barcelona. The study concludes that urban environmental exposures, despite them being above the WHO annual guidelines, were not associated with cognitive performance, and suggests that the impact on executive function could be rather due to the environmental pollution effect on brain cortical thinning. The statistical analyses are adjusted for incidence of familial AD history, which is high in this cohort (84.7%), with 32.5% of the sample carrying the APOE ε4 allele.

Association between pollutants and general cognition

Statistically significant associations were mainly obtained from the two studies that used data from 5,330 residents in the northern area of Manhattan (42, 43), in measurements that combine a comprehensive battery of cognitive tests (Table 4), adjusted for individual (age, education, sex, race/ethnicity), neighbourhood sociodemographic variables (Census-based socioeconomic status z-score), and a cohort indicator to adjust for secular trends.

$PM_{2.5}$

Three of seven papers reported an increasing $PM_{2.5}$ level to have a significant negative impact on general cognition (38, 42, 43) (Figure 4A). But two (42, 43) use data from the same geographical area (i.e., northern Manhattan) and the other utilises a sample within-range of exposure to black carbon (38), which is a major contributor to $PM_{2.5}$. The total effect was moderate, but statistically significant ($\beta = -0.0899$, 95% CI [−0.157 to −0.0224], $P = 0.009$).

PM_{10}

Three of six papers described a statistically significant negative association between PM_{10} and general cognition (36, 42, 43) (Figure 4B), while Lo et al. (47) obtained a relevant effect (OR = 1.09, 95% CI [1.02–1.17], Table 5). But overall, the total effect, although small-to-moderate, was not statistically significant ($\beta = -0.0509$, 95% CI [−0.185 to 0.0848]).

NO_2

Similarly to PM_{10}, the same authors also reported an increasing exposure to NO_2 to have a significant negative association with

TABLE 5 Associations between long-term exposure to the different pollutants and cognitive functions or specific tests, reported by fewer than five studies, given either as hazard ratios or standardised beta coefficients, with 95% confidence intervals.

	Publications		
Dementia			
Pollutants		HR (95% CI)	PM_{10} increment
PM_{10}	Cerza et al. (48)	1.00 (0.98, 1.03)	10 μg/m^3
		HR (95% CI)	NO_2 increment
NO_2	Cerza et al. (48)	0.97 (0.96, 0.99)	10.0 μg/m^3
	Chen et al. (49)	1.10 (1.08, 1.12)	14.2 ppb
	Carey et al. (57)	1.15 (1.04, 1.28)	7.5 μg/m^3
	Chang et al. (60)	1.54 (1.34, 1.77)	3,173.2 ppb
		HR (95% CI)	NO_x increment
NO_x	Paul et al. (45)	1.25 (1.03, 1.52)	2.31 ppb
	Cerza et al. (48)	1.01 (1.00–1.02)	20 μg/m^3
	Oudin et al. (59)	1.05 (0.98, 1.12)	10 μg/m^3
		HR (95% CI)	O_3 increment
O_3	Cerza et al. (48)	1.06 (1.03, 1.08)	10 μg/m^3
	Chen et al. (49)	0.98 (0.96, 1.00)	6.3 ppb
	Jung et al. (52)	3.12 (2.92, 3.33)	10.9 ppb
	Carey et al. (57)	0.85 (0.76, 0.96)	5.6 μg/m^3
Executive function			
Pollutants		*β* (95% CI)	NO_x increment
NO_x	Schikowski et al. (37)	−0.02 (−0.15, 0.10)	4.7 μg/m^3
	Nussbaum et al. (40)	0.01 (−0.03, 0.05)	14.2 μg/m^3
	Crous-Bou et al. (41)	4.33 (0.43, 8.23)	31.6 μg/m^3 (SD)
		β (95% CI)	O_3 increment
O_3	Gatto et al. (53)	−0.66 (−1.35, 0.03)	15 ppb
	Shin et al. (36)	0.011 (0.002, 0.019)	4.3 ppb
Cognitive decline			
Pollutants		HR (95% CI)	$PM_{2.5}$ increment
$PM_{2.5}$	Cacciottolo et al. (50)	1.92 (1.32, 2.80)	12 μg/m^3 (threshold)
	Ailshire et al. (51)	1.03 (0.99, 1.07)	1 μg/m^3
		OR (95% CI)	PM_{10} increment
PM_{10}	Lo et al. (47)	1.09 (1.02, 1.17)	10 μg/m^3
		β (95% CI)	PM_{10} increment
	Shin et al. (36) (MMSE-KC)	−0.035 (−0.050, −0.020)	4.6 μg/m^3
	Shin et al. (36) (digit forward span)	−0.029 (−0.057, −0.001)	4.6 μg/m^3
	Shin et al. (36) (digit backward span)	0.022 (−0.008,0.053)	4.6 μg/m^3
		β (95% CI)	NO_2 increment
NO_2	Shin et al. (36) (MMSE-KC)	0.012 (0.001, 0.025)	7.7 ppb
	Shin et al. (36) (digit forward span)	−0.026 (−0.050, −0.003)	7.7 ppb
	Shin et al. (36) (digit backward span)	0.015 (−0.009, 0.040)	7.7 ppb
		β (95% CI)	NO_x increment
NO_x	Schikowski et al. (37)	−1.35 (−2.59, −0.10)	4.7 μg/m^3
	Crous-Bou et al. (41)	0.56 (−2.58, 3.70)	31.6 μg/m^3(SD)
		β (95% CI)	O_3 increment
O_3	Cleary et al. (58)	−0.27 (−0.40, −0.10)	−3.3 ppb
	Gatto et al. (53)	−0.08 (−0.45, 0.28)	15 ppb
	Shin et al. (36) (MMSE-KC)	0.045 (0.027, 0.062)	4.3 ppb
	Shin et al. (36) (digit forward span)	0.062 (0.029, 0.094)	4.3 ppb
	Shin et al. (36) (digit backward span)	−0.029 (−0.064, 0.006)	4.3 ppb
Memory			
Pollutants		*β* (95% CI)	PM_{10} increment
PM_{10}	Shin et al. (36) (word list memory)	0.049 (0.015, 0.083)	4.6 μg/m^3
	Shin et al. (36) (word list recall)	−0.011 (−0.033, 0.011)	4.6 μg/m^3
	Shin et al. (36) (word list recognition)	0.001 (−0.015, 0.016)	4.6 μg/m^3
		β (95% CI)	NO_2 increment
NO_2	Shin et al. (36) (word list memory)	0.034 (0.006, 0.063)	7.7 ppb
	Shin et al. (36) (word list recall)	−0.019 (−0.035, −0.003)	7.7 ppb
	Shin et al. (36) (word list recognition)	−0.003 (−0.015, 0.008)	7.7 ppb
		β (95% CI)	NO_x increment
NO_x	Schikowski et al. (37)	−0.01 (−0.16, 0.13)	4.7 μg/m^3
	Nussbaum et al. (40)	0.02 (−0.02, 0.06)	14.2 μg/m^3
	Crous-Bou et al. (41)	−1.30 (−3.71, 1.11)	31.6 μg/m^3(SD)
	Oudin et al. (61)	0.01 (−0.01, 0.02)	1 μg/m^3
		β (95% CI)	O_3 increment
O_3	Gatto et al. (53) (LM)	0.24 (−0.21, 0.68)	15 ppb
	Gatto et al. (53) (VEM)	0.01 (−0.42, 0.44)	15 ppb
	Gatto et al. (53) (SM)	−0.12 (−0.50, 0.26)	15 ppb
	Shin et al. (36) (word list memory)	0.009 (−0.031, 0.048)	4.3 ppb
	Shin et al. (36) (word list recall)	0.034 (0.018, 0.049)	4.3 ppb
	Shin et al. (36) (word list recognition)	0.010 (−0.001, 0.021)	4.3 ppb
Language			
Pollutant		*β* (95% CI)	$PM_{2.5}$ increment
$PM_{2.5}$	Nussbaum et al. (40)	−0.02 (−0.07, 0.03)	1.4 μg/m^3
	Kulick et al. (42)	−0.11 (−0.20, −0.02)	4.8 μg/m^3
	Kulick et al. (43)	−0.06 (−0.10, −0.03)	4.4 μg/m^3
		β (95% CI)	PM_{10} increment
PM_{10}	Nussbaum et al. (40)	0.00 (−0.04, 0.04)	2.0 μg/m^3
	Kulick et al. (42)	−0.11 (−0.16, −0.06)	9.9 μg/m^3
	Kulick et al. (43)	−0.03 (−0.04, −0.01)	8.8 μg/m^3
		β (95% CI)	NO_2 increment
NO_2	Nussbaum et al. (40)	0.00 (−0.04, 0.03)	5.3 μg/m^3
	Kulick et al. (42)	−0.24 (−0.33, −0.15)	12.3 ppb
	Kulick et al. (43)	−0.06 (−0.08, −0.03)	11.2 ppb
		β (95% CI)	NO_x increment
NO_x	Nussbaum et al. (40)	−0.01 (−0.05, 0.03)	14.2 μg/m^3

cognitive function: Kulick et al. (42, 43), and Shin et al. (36), although in the latter this was only evident in one out of the three assessments of general cognition (i.e., the digit forward span test) (Figure 4C). The overall effect was strong and statistically significant (β = −0.308, 95% CI [−0.544 to −0.0274], P = 0.032).

Other pollutants and assessments of general cognitive function

Lo et al. (47) and Cacciottolo et al. (50) both reported an increased risk of cognitive decline with increasing levels of $PM_{2.5}$ and PM_{10} respectively. Similarly, Schikowski et al. (37) and Cleary et al. (58) both revealed a negative association

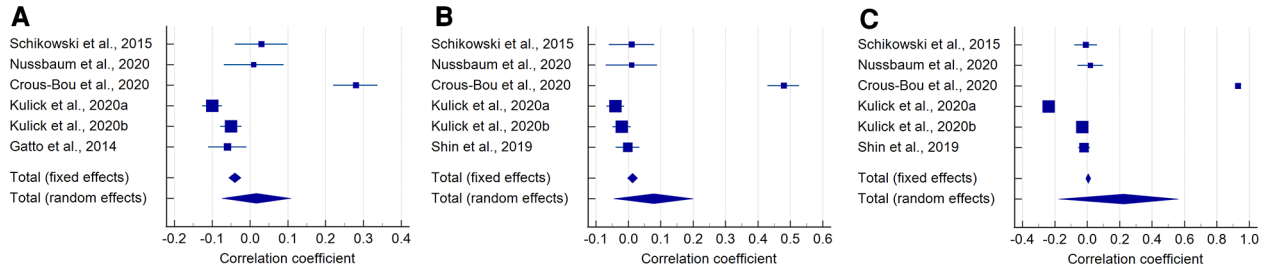

FIGURE 3
Forest plot of the effect of $PM_{2.5}$ (A), PM_{10} (B), and NO_2 (C) in executive function across all studies that evaluated their putative association.

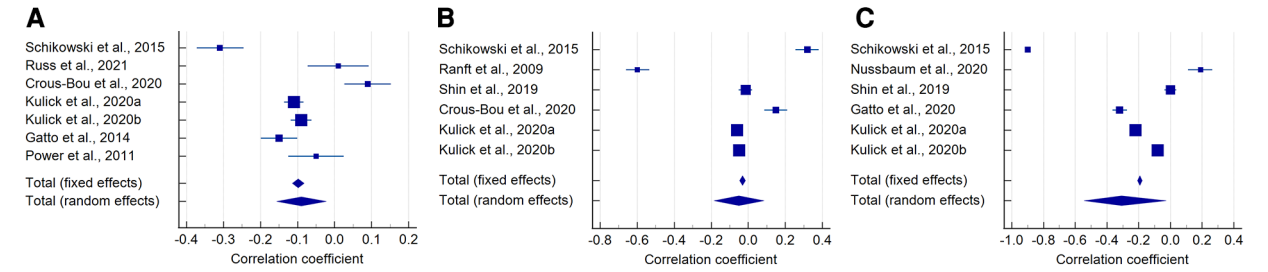

FIGURE 4
Forest plot of the effect of $PM_{2.5}$ (A), PM_{10} (B), and NO_2 (C) in general cognition across all studies that evaluated their putative association.

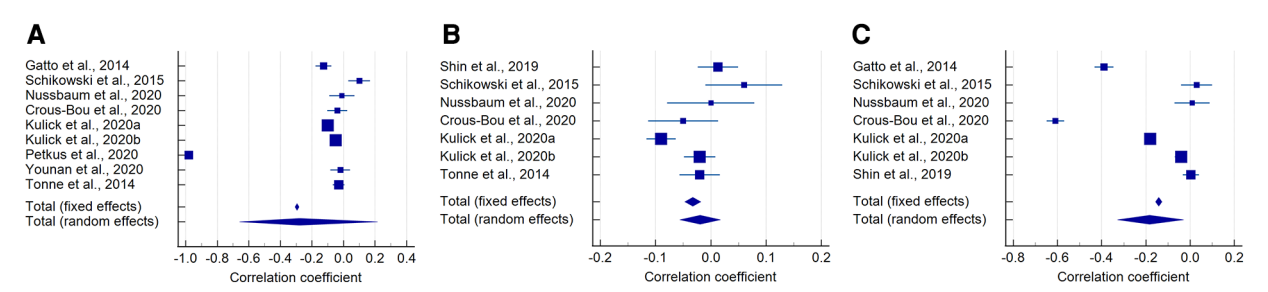

FIGURE 5
Forest plot of the effect of $PM_{2.5}$ (A), PM_{10} (B), and NO_2 (C) in memory across all studies that evaluated their putative association.

between cognitive function and NO_x and O_3 respectively (Table 5). The latter study also highlights the statistically significant association with traffic load in carriers of one or two APOE risk alleles (i.e., ε3, ε4). Shin et al. (36) found a positive association between O_3 and the results from two (out of three) of the tests that assessed cognitive function (i.e., MMSE-KC and digit forward span), and a negative association of O_3 and SO_2, with the results from the digit backward span test (Table 5). Although the strengths of the associations in this relatively large study ($n = 2{,}896$) were small, it is worth nothing that they accounted for a large number of covariates, including age, sex, body mass index, smoking, alcohol intake, physical activity, education, household income, marital status, Carlson's comorbidity index, length of time at the same residence, meteorological data, and residence area, in addition to the average concentrations of each of the pollutants.

Association between pollutants and memory

$PM_{2.5}$

A significant negative association between long-term exposure to $PM_{2.5}$ and memory was described by only two of seven studies (43, 44) (Figure 5A). Therefore, the overall effect was not statistically significant ($\beta = -0.279$, 95% CI [−0.659 to 0.214]).

PM_{10}

Just one of seven papers reported a significant negative association between memory and increasing PM_{10} exposure (43) (Figure 5B). The total effect was, as expected, also not statistically significant ($\beta = -0.0194$, 95% CI [−0.0562 to 0.0173]).

NO_2

Four of seven studies found increasing NO_2 exposure levels to be significantly negatively associated with memory (41–43, 53) (**Figure 5C**), from geographically distant samples in northern Manhattan, Los Angeles basin (both in opposite USA coasts), and the city of Barcelona in Spain. Shin et al. (36) obtained conflicting results all with small effects among the three tests that evaluated memory: word list memory, recall and recognition. Schikowski et al. (37) and Nussbaum et al. (40), both with the smallest samples within the group ($n = 615$ and $n = 789$ respectively), also obtained small and not statistically significant effects. Overall, the total effect between memory and NO_2 exposure was moderate-to-strong and statistically significant ($\beta = -0.183$, 95% CI [−0.328 to −0.029], $P = 0.019$).

Other pollutants

No significant associations were found between memory and exposure to NO_x or O_3 (**Table 5**).

Association between pollutants and language

The two articles that used a sample from northern Manhattan also reported significant negative associations between the language domain and all three of $PM_{2.5}$, PM_{10} and NO_2 (42, 43) (**Table 5**).

Discussion

The present review meta-analyses data on long-term effect of environmental air pollutants in cognition in older adults, to inform environmental and developmental policies in an era of urbanisation and growth of the adult population. Evidence presented by the included studies suggested a link between long-term exposure to air pollutants, especially $PM_{2.5}$ and NO_2, and increased risk of dementia. Although tabulated and meta-analysed here for the first time, this is largely in congruence with existing literature. In a previous review (26), suggested increasing exposure to $PM_{2.5}$, NO_2 and NO_x increased the risk of dementia. The adverse effect of $PM_{2.5}$ in dementia, and, specifically in Alzhéimer's disease (AD) was also highlighted by Tsai et al. (64) in their meta-analysis, which also included sources that analysed short-term effects. Inflammation, oxidative stress, and microglial activation are implicated as key factors driving progressive neuron damage in AD. Although how the pathological neuroimmune process occurs remains a point of debate, the lung-brain axis hypothesis has shown encouraging results to answer this question. It holds that pulmonary response from inhaled pollutants causes circulating signals in serum, independent of traditional cytokines that elevate the neuroimmune response to augment central nervous system deterioration, process that is further augmented by age (65). For example, experimental animal studies have documented microglial activation due to diesel exhaustion (66) and O_3 (65, 67) inhalation.

Although there is evidence to suggest exposure to all the pollutants analysed can have an adverse effect on cognitive functions independently, our results suggest the strongest link is seen with $PM_{2.5}$ and NO_2. For general cognition and memory, our results suggest a possible association between greater long-term exposure to these two pollutants and a decrease in both cognitive domains. Peters et al. (26) reported more ambiguous results from fewer sources, published until September 2018, covering effects from 1 to 15 years, and did not meta-analyse the data. Another relevant systematic review and meta-analysis (24) also obtained similar results, but it assesses the effect of ambient polycyclic aromatic hydrocarbons on cognitive functions in different lifetime periods of exposure combining different exposure times (i.e., not distinguishing between short and long-term exposure).

Our analyses could not confirm a correlation between the air pollutants analysed by the studies included and language or executive function. Although only three studies examined the effect of air pollution on language, the current evidence base suggests that again, long-term exposure to not only $PM_{2.5}$ and NO_2, but also to PM_{10}, is negatively associated with language. But the studies that found this association are from the same geographical area, reported comparatively higher concentration of the air pollutants, and had a wider inclusion criteria, only excluding those with substantial cognitive problems or dementia diagnosis at baseline (42, 43). Whilst studies exploring O_3 tended to point towards an increasing exposure causing a decrease in all cognitive domains, evidence was lacking and most results were not significant. Overall, pooled effects of the three main pollutants meta-analysed did not show statistically significant associations between them and executive function either.

Strengths and limitations

All similar reviews tend to have broader inclusion criteria, possibly as a result of the small body of evidence currently available, or focus on the effect of different confounds, for example, the income level in the affected areas (29). Only one, with differing methodology and inclusion/exclusion criteria, conducted a systematic search (26). This is the first systematic review and meta-analysis to look specifically at long-term air pollution exposure and cognition in older adults. Additionally, strict inclusion criteria combined with a thorough risk of bias analysis ensured only the most relevant and robust studies were included. Also, all outcome measures were standardised for meta-analysing the data, facilitating comparison and an objective assessment of the effects of the pollutants analysed in cognition in the elderly.

Aside from the publications that analyse dementia risk, which does indicate cognitive decline from an unknown baseline, most of the cognitive function measures are a conflation of differences in an unknown initial level and an unknown amount of age-related cognitive decline, the admixture of which is age moderated

within a population. As age was adjusted for in all models from the publications analysed, it will be difficult to ascertain whether or not older adults are more susceptible to a larger effect/difference in cognitive ability due to exposure to the different pollutants. Despite the strengths of the present work mentioned above, the search strategy itself was somewhat limited due to time constraints and so although three popular databases were systematically searched, it is possible that other relevant publications not indexed in these databases were missed. Furthermore, assessing precise air pollution exposure, even when geocoded, is not an exact science and gives rise to limitations. For example, most pollutants (except ozone) will be highly spatially correlated and often implausible to separate effects. Therefore, our results must be interpreted with caution. Moreover, the sheer complexity in defining cognitive function and its domains combined with the plethora of tests that were used to examine them exposed incomparable data. Standardising increments of pollutant level as well as exploring the relationship between length of exposure and cognitive domains would make for more easily interpretable data.

The publications included are not representative of the most polluted countries and areas on the planet. Most publications were from the USA, followed by specific regions in Germany, Sweden, Spain, UK, and the isle of Taiwan. Highly populated countries and areas like mainland China, India, Mexico City with an increasing ageing population are not represented in the analysis. Entire continents like South America, Africa and Australia, are not represented, and neither are areas affected by ecological catastrophes that cause environmental pollution (e.g., wild fires). Global policies that foster research in these areas are, therefore, needed.

Conclusion and future work

Our results support a potential role for long-term exposure to air pollution and an increased risk of both dementia and cognitive function in the elderly. Further works are needed to improve exposure assessment—better specified pollution models and more geographically specific estimates that capture people's "activity spaces" (i.e., home/work/recreation/travel). Also, this review highlights the need for further understanding the interaction effects of environmental pollution and socioeconomic status and ethnicity in order to inform policies to improve the life of underserved population groups that may have greater susceptibility to environmental pollution. While this review suggests the most problematic pollutants are $PM_{2.5}$ and NO_2, the current evidence base requires strengthening before these associations are universally accepted. The global health burden of dementia and cognitive decline may be decreased if public health policies target to decrease air pollution levels, but further research will allow more specific recommendations to be made.

Author contributions

JMcL and MCVH equally participated in study conception, data extraction, data generation, data analysis, writing, revising and approving the manuscript SC and JP participated in data analysis, revising, editing and approving the manuscript.

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Conflict of interest

The author (MCVH) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fenvh.2023.1205443/full#supplementary-material.

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